Volume 120 Supplement 1 October 2016 ISSN 0168-8227
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International Diabetes Federation

DIABETES RESEARCH AND CLINICAL PRACTICE

Official Journal of the International Diabetes Federation

Abstracts of the 11th IDF-WPR Congress 2016 & 8th AASD Scientific Meeting
27th-30th October, 2016, Taipei, Taiwan

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Diabetes Research and Clinical Practice

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Volume 120/S1 (2016)

International Diabetes Federation

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Diabetes Research and Clinical Practice is an international journal for healthcare providers and clinically oriented researchers that publishes high-quality original research articles and expert reviews in diabetes and related areas. The role of the journal is to provide a venue for dissemination of knowledge and discussion of topics related to diabetes clinical research and patient care. Topics of focus include translational science, genetics, immunology, nutrition, psychosocial research, epidemiology, prevention, socio-economic research, complications, new treatments, technologies and therapy. *Diabetes Research and Clinical Practice* is the official journal of the International Diabetes Federation.

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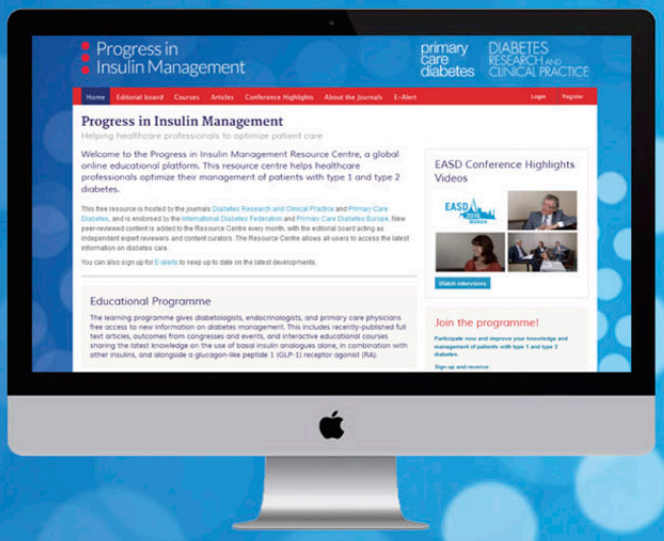

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& 8th AASD Scientific Meeting
27th-30th October, 2016, Taipei, Taiwan

About

The 11th International Diabetes Federation Western Pacific Region Congress (11th IDF-WPR Congress) and the 8th Scientific Meeting of the Asian Association for the Study of Diabetes (8th AASD Scientific Meeting) is held on October 27 to 30, 2016 in Taipei, Taiwan.

The main theme of the 11th IDF-WPR Congress and 8th AASD Scientific Meeting is set as "Create a new dimension in diabetes: Prevention, Protection and Care". This congress includes Plenary Lectures to highlight the major developments in diabetes in recent years and over 40 symposia to cover major fields for diabetes care. We have recruited more than 3000 participants from 46 countries, invited more than 160 speakers to deliver 250+ speeches. In addition, there are 77 oral presentations and 484 posters will be displayed during the congress. With 22 member associations of WPR, we believe this congress can serve as a platform for every participant and provide an exchange between individuals and institutions to discuss the current status of diabetes research in challenging areas.

The congress is also in conjunction with Asia-Pacific Diabetes and Obesity Study Group (APDO) Symposium 2016, the Study Group of Molecular Diabetology in Asia (MDIA) Symposium 2016, the 7th Asian Diabetic Surgery Summit (ADSS) 2016 and the annual meeting of local organizers: "37th Annual Meeting of the Chinese Taipei Diabetes Association", "Bi-Annual Meeting of the Taiwanese Association of Diabetes Educators 2016", "Annual Meeting of Taiwan Society for Metabolic and Bariatric Surgery (TSMBS) 2016". Moreover, the "IDF-WPR Asia-Pacific Diabetes Epidemiology and Education Training Course 2016", "IDF-WPR Education Program: Train the Trainers program 2016" and 2016 Young Leaders in Diabetes (YLD) program will also be held concurrently.

With the above-mentioned activities and experiences to be shared in this grand Congress, it is believed the care quality of diabetes health in the world could be enhanced.

Program at a glance of the 11th IDF-WPR Congress 2016 & 8th AASD Scientific Meeting

Plenary, Keynote, Presidential Lecture	Diabetes Performance Measures (IDF-WPR)	Bariatric Surgery-An Update (AASD)	Early Screening and Intervention of Prediabetes and Diabetes (IDF-WPR/AASD)	Delay Diabetes Complication (IDF-WPR/AASD)	Beta Cell Replacement Therapy and Imaging (AASD)	Optimizing Diabetes Therapy (AASD)	Diabetes Education (IDF-WPR)	Psychosocial Status of Diabetes (IDF-WPR)	Special Seminar	Meet the Expert	APDEC 2016 & Train the Trainers program 2016	Joint Meeting: MDIA, ADSS, TSMBS, APDO, TADE	Oral Presentation	Lunch/Evening Seminar

<table>
<tr><td>Date</td><td>Wednesday, Oct. 26</td><td colspan="3">Thursday, Oct. 27</td></tr>
<tr><td>Venue</td><td>Taipei Teacher's Hostel</td><td>Taipei Teacher's Hostel</td><td colspan="2">Taipei International Convention Center (TICC)</td></tr>
<tr><td>Location</td><td>Room 120</td><td>Room 120</td><td>1F Lobby</td><td>401</td></tr>
<tr><td>08:00-10:00</td><td rowspan="4">APDEC 2016</td><td rowspan="4">APDEC2016</td><td rowspan="3"></td><td>WPR
Executive Board Meeting</td></tr>
<tr><td>10:00-12:00</td><td>AASD
Executive Board Meeting</td></tr>
<tr><td>12:00-13:30</td><td></td></tr>
<tr><td>13:30-17:00</td><td>Registration (13:30-17:00)</td><td>WPR Council Meeting</td></tr>
<tr><td>17:00-18:15</td><td></td><td></td><td colspan="2">EV01
Updates on GLP-1 receptor agonists and cardiovascular diseases (Location: 101AB)</td></tr>
</table>

Program at a glance of the 11th IDF-WPR Congress 2016 & 8th AASD Scientific Meeting

Plenary, Keynote, Presidential Lecture	Diabetes Performance Measures (IDF-WPR)	Bariatric Surgery- An Update (AASD)	Early Screening and Intervention of Prediabetes and Diabetes (IDF-WPR/AASD)	Delay Diabetes Complication (IDF-WPR/AASD)	Beta Cell Replacement Therapy and Imaging (AASD)	Optimizing Diabetes Therapy (AASD)	Diabetes Education (IDF-WPR)	Psychosocial Status of Diabetes (IDF-WPR)	Special Seminar	Meet the Expert	APDEC 2016 & Train the Trainers program 2016	Joint Meeting: MDIA, ADSS, TSMBS, APDO, TADE	Oral Presentation	Lunch/Evening Seminar

Date	DAY 1 Friday, Oct. 28										
Venue	Taipei International Convention Center (TICC)										Taipei World Trade Center (TWTC)
Location	1F Lobby	3F Plenary Hall	201ABC	201DEF	101AB	101CD	102	103	3F South Lounge	4F Joy Lounge	
09:00-10:00	Registration (07:30-17:00)	**Opening Ceremony**							APDEC 2016 & Train the Trainers program 2016	Diabetes Hacking Medicine	
10:00-10:30		**IDF-WPR Presidential Lecture** *Prof. Wayne H -H Sheu*									Poster Presentation, Exhibition & IDF-WPR Village Exhibition (10:00-17:00)
10:30-11:00		**Coffee Break @ TWTC**									
11:00-12:00		**Keynote Lecture** *Prof. Takashi Kadowaki*									
12:10-13:30			**LN01** Tonghua Dongbao	**MP01** Meet the Expert			**LN02** LG Life Science				
13:30-15:15		**SP01** AASD DM Guideline Symposium	**S01** Current Diabetes Burden and Performance in WPR (I)	**S02** Update of Bariatric/Metabolic Surgery	**S03** Screening of Diabetes: How and Why?	**SP02** Taiwanese Diabetes Care 3.0 – Improving Efficiency through Automation	**S04** [MDIA] Genetic Architecture of T2DM	**OL01** Epidemiology and Prevention of Diabetes			
15:15-15:30											
15:30-15:45		**Coffee Break & Poster Session (A-C) @ TWTC**									
15:45-17:30			**S05** Current Diabetes Burden and Performance in WPR (II)	**[7th ADSS & TSMBS]**	**S06** Childhood Obesity and Diabetes: Environmental Risk Factors, Screening, and Intervention	**SP03** Using Big Data for Research and Care in Diabetes	**S07** [MDIA] Mitochondria in Diabetes	**OL02** Pathogenesis of Obesity, Diabetes, and Diabetic Complications			
18:00-20:00		**Welcome Reception (TICC – 3F Banquet Hall)**									

Program at a glance of the 11th IDF-WPR Congress 2016 & 8th AASD Scientific Meeting

Plenary, Keynote, Presidential Lecture	Diabetes Performance Measures (IDF-WPR)	Bariatric Surgery- An Update (AASD)	Early Screening and Intervention of Prediabetes and Diabetes (IDF-WPR/AASD)	Delay Diabetes Complication (IDF-WPR/AASD)	Beta Cell Replacement Therapy and Imaging (AASD)	Optimizing Diabetes Therapy (AASD)	Diabetes Education (IDF-WPR)	Psychosocial Status of Diabetes (IDF-WPR)	Special Seminar	Meet the Expert	APDEC 2016 & Train the Trainers program 2016	Joint Meeting: MDIA, ADSS, TSMBS, APDO, TADE	Oral Presentation	Lunch/Evening Seminar

Date	DAY 2 Saturday, Oct. 29											
Venue	Taipei International Convention Center (TICC)											Taipei World Trade Center (TWTC)
Location	1F Lobby	3F Plenary Hall	201ABC	201DEF	101AB	101CD	102	103	3F Banquet Hall	3F North Lounge	3F South Lounge	
08:00-09:00	Registration (07:30-18:00)	**AASD Award Ceremony & Lecture - The Yutaka Seino Distinguished Leadership Award**									APDEC 2016 & Train the Trainers program 2016	Poster Presentation, Exhibition & IDF-WPR Village Exhibition (10:00-17:00)
09:00-10:45		**S08 Cardiovascular Disease and Diabetes – Clinical and Translational**	**S09 Pancreas Transplanta-tion**	**S10 [MDIA] The Role of Epigenetics in Diabetes and Its Complications**	**S11 Orally Administrated Antidiabetic Agents**	**S12 Who Does What in the Health Care for Diabetes in Taiwan**	**S13 [APDO] Obesity and Diabetes**		**S14 Strategies to Reduce Barriers in Diabetes Care in WPR, What Need to Be Done**	**[7th ADSS & TSMBS]**		
10:45-11:05		**Coffee Break & Poster Session (D) @ TWTC**										
11:05-11:25		**AASD Presidential Lecture** *Prof. Lee-Ming Chuang*										
11:25-12:10		**Plenary Lecture (I)** *Prof. Paul Zimmet*										
12:10-13:30			**LN03 Novartis**	**LN04 Servier**	**LN05 Novo Nordisk**	**LN06 Lilly**	**LN07 MSD**	**LN08 Pfizer**	**LN09 BI**	**LN10 Takeda**		
13:30-14:15		**Plenary Lecture (II)** *Prof. Mark McCarthy*										
14:15-16:00		**S15 DM Nephropathy: Risk, Mechanism, Management and Outcome**	**S16 Islet Transplanta-tion**	**S17 [MDIA] Environmental Pollutants and Diabetes**	**S18 Injectable Antidiabetic Agents (I): GLP-1 Receptor Agonists**	**S19 Nutrition, Exercise and Self Management of Diabetes (I)**	**S20 [APDO] Adipocyte Biology and Insulin Resistance**	**OL03 Diabetes Complications: Epidmeiology and Biomarkers**		**[TSMBS] (Chinese Session)**		
16:00-16:20		**Coffee Break & Poster Session (E-F) @ TWTC**										
16:20-18:05		**S21 Diabetic Neuropathy: Clinical update**	**S22 Stem Cell Therapy**	**OL04 Genetics and Epidemiology**	**OL05 Treatment of Diabetes**	**S23 Nutrition, Exercise and Self Management of Diabetes (II)**	**S24 [APDO] Hot Topics in Diabetes and Obesity (I)**	**OL06 The Pancreatic Islet and Bariatric Surgery**		**[TSMBS] (Chinese Session)**		
18:30-20:30		**Culture Night (TICC - 3F Banquet Hall)**										

Program at a glance of the 11th IDF-WPR Congress 2016 & 8th AASD Scientific Meeting

Plenary, Keynote, Presidential Lecture	Diabetes Performance Measures (IDF-WPR)	Bariatric Surgery- An Update (AASD)	Early Screening and Intervention of Prediabetes and Diabetes (IDF-WPR/AASD)	Delay Diabetes Complication (IDF-WPR/AASD)	Beta Cell Replacement Therapy and Imaging (AASD)	Optimizing Diabetes Therapy (AASD)	Diabetes Education (IDF-WPR)	Psychosocial Status of Diabetes (IDF-WPR)	Special Seminar	Meet the Expert	APDEC 2016 & Train the Trainers program 2016	Joint Meeting: MDIA, ADSS, TSMBS, APDO, TADE	Oral Presentation	Lunch/Evening Seminar

Date	**DAY 3 Sunday, Oct. 30**									
Venue	Taipei International Convention Center (TICC)									Taipei World Trade Center (TWTC)
Location	1F Lobby	3F Plenary Hall	201ABC	201DEF	101AB	101CD	102	103	3F Banquet Hall	3F South Lounge	
08:00-09:45	**Registration (07:30-15:30)**	**S25 Diabetic Eye Disease: Early Detection, and Treatment**	**S26 Islet Imaging**	**S27 Associations of Life Events/Life Stress with Diabetes Control**	**S28 Injectable Antidiabetic Agents (II): Insulin**	**S29 Diabetes Education: Patient Centered Approach**	**S30 [APDO] Incretin/Islet Biology and Insulin Secretion**		**S39 [TADE] Integration of Diabetes Management in Taiwan**	**APDEC 2016 & Train the Trainers program 2016**	**Poster Presentation, Exhibition & IDF-WPR Village Exhibition (09:30-16:00)**
09:45-10:15		**Coffee Break & Poster Session (G-I) @ TWTC**									
10:15-11:00		**Plenary Lecture (III)** *Prof. Victor J. Dzau*									
11:15-12:00		**Plenary Lecture (IV)** *Prof. Rury Holman*									
12:10-13:30			**LN11 Ascensia**	**LN12 Sanofi**	**LN13 Novo Nordisk**	**LN14 AstraZeneca**	**LN15 Zespri**	**LN16 Pfizer**	**LN17 BI**		
13:30-15:15		**S31 Diabetes Foot : Learning from Diabetes Foot Care Program**	**OL07 Laboratory Medicine for Diabetes**	**S32 Association of Daily Problem Solving/Coping/Social Supports with Diabetes Control**	**S33 Closed-Loop System and CGM**	**S34 Peer Leaders in Diabetes Management**	**S35 [APDO] Hot Topics in Diabetes and Obesity (II)**	**OL08 Nutrition, Diabetes Education and Management Systems**	**S40 [TADE] Self-management of Diabetes Education**		
15:15-15:35		**Coffee Break & Poster Session (J-K) @ TWTC**									
15:35-17:20		**SP04 WPR Disaster Program**	**OL09 Novel Treatment for Diabetes and Diabetic Complications**	**S36 Association of Psychosocial Factors with Diabetes Control**		**S37 Using Health Information Technology for Diabetes Care**	**S38 [APDO] Hot Topics in Diabetes and Obesity (III)**	**OL10 Novel Biomarkers for Diabetes**	**S41 [TADE] Nutrition in Diabetes Life Care**		
17:20-18:00		**Closing Ceremony**									

Volume 120/S1
October 2016

Diabetes Research and Clinical Practice

Contents

Oral Presentations

Poster Presentations

* Joint program of the AASD, APDO, MDIA or TADE etc.

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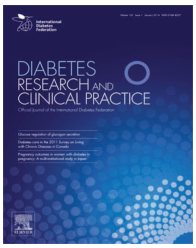

Speech Abstracts

Keynote Lecture

KN-01

Adiponectin and its receptors: A major role in type 2 diabetes and obesity-linked diseases

Takashi KADOWAKI[1]. [1]*Department of Diabetes and Metabolic Diseases, Graduate School of Medicine, The University of Tokyo*

Adiponectin is an adipocyte hormone that is most abundantly expressed in white adipose tissue, whose function was entirely unknown. We and others discovered that adiponectin enhances insulin sensitivity and possesses anti-diabetic actions. We subsequently identified and cloned the receptors of adiponectin (AdipoR1 and AdipoR2), which represent a new receptor superfamily containing seven-transmembrane domains. AdipoR1 and AdipoR2 regulate the burning of glucose and fatty acids and enhance insulin sensitivity. In obese subjects, the expression of not only adiponectin but also AdipoR1 and AdipoR2 is reduced, which is the main cause of various diseases associated with obesity such as type 2 diabetes, metabolic syndrome, cardiovascular disease and short life. We developed a small-molecule adiponectin receptor agonist (AdipoR Agonist: AdipoRon) and showed that orally administered AdipoRon activates the same signaling pathway as caloric restriction and physical exercise, thereby improving obesity-related diseases as a whole, including type 2 diabetes, and actually working as a health- and longevity-promoting drug. Most recently, we succeeded in elucidating the three-dimensional structure of adiponectin receptors, and is conducting research toward identifying the mechanism of adiponectin actions at the atomic level, and optimizing adiponectin receptor agonists, based on the three-dimensional structure data.

Plenary Lecture

PL-01

Diabetes: Is this the greatest epidemic in the history of mankind

Paul ZIMMET[1]. [1]*Monash University, Melbourne, Australia*

Diabetes has been seriously underrated as a global public health issue. The last three decades have witnessed an epidemic rise in the number of persons with diabetes, especially type 2 diabetes. The main burden lies in developing nations where more than 80% of the people with diabetes live. While aging, urbanization and associated lifestyle changes are the major determinants for the rapid increase, adverse intrauterine environmental and the resulting epigenetic changes may be major factors contributing to the epidemic in many developing countries. Diabetes risk through epigenetic changes can be transmitted inter-generationally thus creating a vicious cycle that will continue to feed the diabetes epidemic. History provides important lessons such as those from major catastrophic events such as the Dutch Winter Hunger and Chinese famines. The Chinese famine may have been the trigger for what may be viewed as a diabetes "avalanche" many decades later in China. More than 60% of the people with diabetes live in Asia with almost one third in China. The spectacular rise in diabetes poses huge social and economic problems to most nations in Asia and could impede national and regional development. More action is required to understand the drivers of the epidemic to provide the rationale for prevention strategies. Unless drastic steps are taken through national prevention programmes to curb the escalating trends in all the countries, the social, economic and health care challenges are likely to be insurmountable. More reliable estimates of the future burden of diabetes are urgently needed. It is apparent that the IDF have consistently underestimated the global burden. In 2011, their estimate was already 371 million people with diabetes yet this had earlier been predicted as the forecast 20 years hence for 2030. Type 2 diabetes will remain one of the greatest challenges to human health for many years to come. To meet the challenge we must also direct attention to see which countries may bear the brunt of diabetes in the future and to plan the resources need to address it.

PL-02

From p-values to proteins: Using genetic and genomic data to deliver biological insights and clinical opportunities for type 2 diabetes

Marc McCARTHY[1,2]. [1]*Wellcome Trust Centre for Human Genetics, University of Oxford,* [2]*Oxford Centre for Diabetes, Endocrinology and Metabolism, University of Oxford, Oxford, UK*

The growing prevalence of type 2 diabetes highlights the limitations of available preventative options, and high rates of diabetes complications attest to the inadequacies of current treatments. Novel therapeutic strategies need to be informed by a more complete understanding of the molecular and physiological basis of disease, delivering validated interventional targets and biomarkers to define disease risk, progression, and subtype.

My group, working within large global consortia, uses human genetics to deliver this understanding. Growing availability of exome sequence and array data now delivers coding variant associations that can plug directly into functional studies. However, the main repository of variant association for T2D remains ~100 common variant signals uncovered by GWAS, most of which map outside coding sequence. We are implementing a multifaceted approach that combines genome-scale and focused functional studies to unlock the biology within these loci.

We use fine-mapping to improve localisation of causal variants, and map these onto regulatory annotations from key tissues, most notably the human islet. This provides a platform for identifying downstream transcripts through

tissue-specific cis-eQTL analyses and conformational capture. We combine these "regulatory variant" data with transcript level information to define the best-supported transcripts in each GWAS region. Finally, we connect loci through analyses of protein-protein interaction, co-expression and pathway data. These efforts are starting to bear fruit, with around one-third of GWAS signals now featuring a well-supported priority transcript. We follow up these priority candidates through cellular, molecular, rodent and human studies to consolidate mechanistic evidence. To build engagement, we are co-developing, via the Accelerating Medicines Partnership, a dedicated T2D knowledge portal that facilitates access to these data for the wider research community.

PL-03

Precision medicine 2016: Opportunities & challenges

Victor J. DZAU[1]. [1]*National Academy of Medicine, Washington, DC, USA*

Since the turn of the century, the global research community has made significant progress in genomics and other omics-based fields, biostatistics, bioinformatics, and computational biology, including the application of these fields to medicine. These efforts have resulted in new diagnostic and therapeutic advances based on an improved understanding of the molecular basis of disease in individual patients, heralding a new era of precision medicine. Precision medicine has the potential to guide health care decisions toward the most effective prevention of disease or treatment for a given patient, and thus, improve care quality, while reducing the need for unnecessary diagnostic testing and therapies. Moreover, when applied at the population level, precision medicine holds immense promise for public health, particularly in disease prevention and risk assessment. Despite recent breakthroughs, there are notable challenges and barriers to broad precision medicine implementation and integration in clinical and preventive practice. For example, there are concerns that technologies may drive up costs in the short run and also may further advance disparities in health care delivery. A lack of sufficient IT infrastructure, as well as effective training for the medical workforce may impede integration into clinical practice. Furthermore, concerns about data ownership, privacy, and sharing must be addressed before precision medicine can be broadly implemented.
Dr. Dzau will discuss the potential of precision medicine to revolutionize medicine and improve health, barriers and challenges to its introduction and use at scale in disease prevention and treatment, and future policy directions to help overcome these challenges.

Presidential Lecture

PR-01

The unrelenting challenge of diabetes in our world: Small step and big changes

Wayne H-H. SHEU[1]. [1]*Taichung Veterans General Hospital, Taichung, Taiwan*

On behalf of Chairman, 11th IDF-WPR Congress and Chair of IDF WPR, 206-2017, I would like to take this opportunity to welcome all the delegates to attend this exciting meeting.
The number of people with diabetes, including those in Western Pacific Region, has continuously rising during the past decades. Despite that well established known traditional risk factors for diabetes (eg, genetic, lifestyle, and behavioral risk factors), recent researches have focused on identifying the contributions of genetic and epigenetic mechanisms. Given the unrelenting increases in global health expenditure attributable to diabetes, an integrated and comprehensive approach is needed to prevent diabetes as well as provide good care in people with diabetes and related complications.
What is the next step in addressing the epidemic of diabetes in our region? It is clear that the development of new drugs and regimens are not sufficient. In consideration of wide diversity of populations, cultures, medical systems and economic developments in this region, I believe that all stake holders should be linked together to solve these complex barriers. The emphasis has to be on prevention at level before disease occurrence but also prevention of diabetes related complications, for example the community-based prevention programs and education campaigns run by local governments and professional societies.
Perhaps new incentives, in particularly targeting educations, are needed to encourage the all professionals work with patients themselves, families and the medical community to provide performances-based plus values-added diabetes care. It is time for an entirely different approach. All of us have to reach out, and together, we can have a small step and get big changes.

PR-02

Biological role of ALDH2 in metabolic diseases – Asian perspectives

Lee-Ming CHUANG[1]. [1]*Department of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan*

The *ALDH2* gene encodes mitochondrial aldehyde dehydrogenase 2 (ALDH2), which catalyzes the metabolism of acetaldehyde and other bioreactive aldehydes, including propionaldehyde, butyraldehyde, and 4-hydroxynonenal (4-HNE). Increased 4-HNE level in adipose tissue contributes to insulin resistance and diabetes. An E487K mutation, denoted as ALDH2*2, encoded by the rs671 A allele of the *ALDH2* gene, results in a reduction of enzymatic activity by ~90%. The rs671 variant is present in a substantial proportion of the East Asian population (560 million) but not in Western populations. The Asian flush syndrome is thus named as a result of marked elevation of circulating acetaldehyde after alcohol drinking in carriers of mutant alleles. Recently, a large-scale meta-analysis in East Asian population identified strong associations of genetic variations of the *ALDH2* gene with many parameters of the metabolic syndrome and the risk of cardiovascular diseases. We also documented that genetic variations of the *ALDH2* gene were associated with development of hypertension through gene and alcohol interaction. In normal population, subjects carrying *ALDH2* mutation have lower estimated glomerular filtration rate (eGFR). In patients with type 2 diabetic, genetic variations of the *ALDH2* gene are also associated with urinary albumin-creatinine ratio. In the *aldh2**2-knockin mice model, we also observed reductions in eGFR, glucose tolerance and insulin sensitivity, and presence of hepatic steatosis due to increased body weight on high-fat high-sucrose diet. With the introduction of small-molecule chaperone for mutant ALDH2 such as alda-1, our findings provide a therapeutic opportunity for the huge population carrying this mutation and herald the era of precision medicine by considering high prevalence of the *ALDH2* genetic variations in East Asian populations.

Current Diabetes Burden and Performance in WPR

S01-1

DiabCare Malaysia: Journey to improving diabetes care in Malaysia

Mafauzy MOHAMED[1]. [1]*Health Campus, Universiti Sains Malaysia, Malaysia*

Type 2 DM is a growing epidemic in Malaysia. The prevalence of T2DM had risen from 11.6% in 2006 to 15.2% in 2011 in adults aged ≥18 years and is expected to rise to about 22% in the year 2020. DiabCare is a project started in Europe to provide large scale, standardized information about status of diabetes management and diabetes related complications. The data could facilitate healthcare policy and improve the status of diabetes care. DiabCare Asia started in 1997 and involved many countries. The methodology involves collecting data on demographics, treatment, diabetes control and complications on a standardized case record form. Questionnaires on patient health, treatment adherence and hypoglycemia were also administered. In Malaysia, as a result of previous DiabCare studies, the Ministry of Health had set up Diabetes Resource Centres, trained more diabetes nurse educators, made HbA1c test widely available and implemented standardized follow-up protocols.

In DiabCare 2013, 19 hospitals with a total of 1,668 patients were involved in the study. Mean age of the patients was 57.8 years; BMI 29.0 kg/m^2; 48.7% led a sedentary lifestyle; mean HbA1c 8.5%; 23.7% had HbA1c <7.0%; mean LDL 2.62 mmol/L with 90% on treatment; mean BP 139.8/78.7 mmHg with 86% on treatment; 10.9% had history of myocardial infarction; 7.0% had history of stroke/TIA; 27.8% had microalbuminuria and 23.4% had macroalbuminuria; 23.6% had non-proliferative and 12.0% had proliferative retinopathy; 41.0% had peripheral neuropathy. The most common OAD used was metformin (78.6%) followed by SUs (35.4%); 65.4% were on insulin and the most common insulin used was premix insulin (44.6%). Only 26.0% adhered completely to diet advice; 19.1% to exercise recommendation; 72.5% to oral medications and 54.0% to insulin injections treatment.

In summary, DiabCare studies had provided valuable input in determining diabetes care in Malaysia. DiabCare 2013 had shown improvement in the care of diabetic patients but more efforts need to be done to achieve better control and reduce complications.

S01-2

Diabetes care in Australia

Margaret McGILL[1]. [1]*Diabetes Centre, Royal Prince Alfred Hospital, University of Sydney, Sydney, Australia*

Australia is not exempt from the burden of diabetes. Fortunately however, universal health insurance (Medicare) provides free or subsidized diabetes treatment in primary care and public hospitals. People with diabetes can choose to have health insurance and access private specialist/hospital diabetes care. Common diabetes medications are subsided by the government Pharmaceutical Benefits Scheme. Australia has a National Diabetes Strategy which contains 7 goals but the challenge is its implementation which needs both top down and bottom up strategies to reduce the diabetes burden. Unique to Australia is the National Association of Diabetes Centres (NADC). The NADC supports organizations rather than individuals. Membership (n = 109 Centres) is via a stringent accreditation process and sets standards for 4 types of membership (i) Centres of Excellence, (ii) Tertiary Centres (iii) Care Centres and (iv) Affiliate Centres. A major function of the NADC is the biannual, cross-sectional Australian National Diabetes Audit (ANDA) which provides, through the standardized collection of a minimum dataset, an overview of the clinical status of people who attend specialist services. ANDA results provide a mechanism for establishing benchmarks so that participating organisations can evaluate their individual site against peers. A fundamental role of the NADC is also to provide an annual forum for organisations to showcase their successful and innovative clinical strategies, thus promoting sharing and learning. This meeting is in addition to the annual scientific congress. The NADC developed and promotes the "Diabetes Management in General Care Settings" course which is a national program focusing on the educational needs of nurses and allied health professionals working in primary care. In recent years there has been an increasing focus on the role of primary care in providing diabetes services. This change in the model of care has highlighted the importance of integration of services underpinned by data collection between primary and tertiary care. An example of this is the research findings from the Royal Prince Alfred Hospital Diabetes Centre. Through interrogation of our extensive Diabetes Centre database we have shown the poor prognosis of youth onset type 2 diabetes with outcomes much worse than for type 1. A minimum data set from local primary care network demonstrated equally poor indicators. These outcomes have ramification for clinical practice and demonstrated the need for innovative translational programs for the betterment of care to the community we serve. The burden is high and requires strategies to focus urgently on prevention, early detection and improved care.

S01-4

Meeting the needs of diabetes care in old people

Nigishi HOTTA[1]. [1]*Japan Organization of Occupational Health and Safety, Chubu Rosai Hospital, Nagoya, Japan*

As the patients with diabetes become older, they face physiologic, cognitive, financial, and personal changes which they may have little control. It is known that at least 20% of peoples over the age of 65 years have diabetes. In Japan, there are about 25% over the age of 65 years among the total population. This number can be expected to increase rapidly in the coming decade. Thus, it becomes the serious matter in Japan.

Older persons with diabetes are at an increased risk for functional limitation with diabetic complications and/or comitant of other diseases. Therefore, it is important for all older persons with diabetes primarily responsible individual goals and priorities in collaborations with the health care team. Functional ability is the degree of independence with which a person is able to perform common activities of daily living. Each patient's total functioning is divided into four major areas such as physical, cognitive, emotional, and psychosocial.

In my presentation, cognitive dysfunction in older patients with diabetes is talked from the viewpoint of prevention and treatment.

S01-5

Current diabetes care status in Korea

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Diabetes mellitus is an increasing global health problem. Mortality from diabetes was 1.3 million people in 2010, twice as many as in 1990. Furthermore, diabetes increases the risk of disabling and life-threatening complications such as retinopathy, neuropathy, nephropathy, cardiovascular, and cerebrovascular diseases, peripheral artery occlusive diseases.

The prevalence of diabetes has increased significantly in recent decades. And the International Diabetes Federation states that 382 million people worldwide were suffering from diabetes in 2013, expected to rise to 592 million people by 2035. In a nationally representative sample of Korea aged 30 years or older, the prevalence of diabetes increased from 8.6% to 11.0% from 2001–2013. This number is expected to rise to 5.5 million by 2030, about 10.9% of the adult population aged 20 years or older.

The prevalence has especially increased in aged 70 years or older; the rate of diabetes was 27.6% in 2013, approximately twice as high as in 2001. In addition, obesity, which is the major causal factor detected in prediabetes and diabetes, increased from 29.2% to 31.8% during the same period. Also, there is an inverse linear relationship between body mass index (BMI) and age at the diagnosis of diabetes among those who are newly diagnosed. Average BMI decreased from

30.4 kg/m^2 in the youngest age group to 24.4 kg/m^2 in the oldest age group.
Several studies suggested that lowering blood pressure and cholesterol levels and avoiding tobacco diminish the incidence of cardiovascular diseases. Therefore, guidelines for diabetes care recommend risk-factor control and regular screening for complications in order to treat conditions related to diabetes in their early stages. In Korea, according to National Health Insurance Service (NHIS), medication adherence rate, which estimated using the medication possession ratio, was increased from 12.8 to 44.9 from 2002–2013. And, the proportion of people with diabetes who treated with antihypertensive medications increased from 56.0% to 62.5% from 2006–2013. And, 49.5% of people with diabetes were being treated with lipid-lowering medication in 2013, which is 1.8-fold higher than in 2006. According the Korea National Health and Nutrition Examination Survey (KNHANES) studies in 2014, 45.6% of people with diabetes achieved hemoglobin A1c (HbA1c) <7.0%, 72.8% of them achieved blood pressure (BP) <140/85 mmHg and 58.0% of them achieved LDL cholesterol <100 mg/dL. Only 19.7% of people with diabetes were revealed to be good control of all three targets (unpublished data). Control rates in 2014 were slightly improved compared with the reports in the 2005 health insurance data, where 40.3% achieved HbA1c <7.0%, 58.6% achieved blood pressure (BP) <140/90 mmHg, 38.3% achieved LDL cholesterol <100 mg/dL.
Nevertheless, subjects with type 2 diabetes had microvascular complications (end stage renal disease, 1.2%; diabetic retinopathy, 15.9%). And, the presence of macrovascular complications was higher in subjects with type 2 diabetes than those without diabetes (295 ischemic stroke, 248 ischemic heart disease, 41 cerebral hemorrhage per 10,000 persons in diabetic subjects; 62 ischemic stroke, 59 ischemic heart disease, 17 cerebral hemorrhage per 10,000 persons in non-diabetic subjects). Current smoking in people with diabetes was still higher in men (men, 43.2%; women, 6.4%).
Diabetes and cancer have been closely linked to each other epidemiologically and biologically. Convincing evidence indicates that diabetes is associated with increased risk for several cancers. In Korea, the presence of cancer-related hospitalization was higher in subjects with type 2 diabetes than those without diabetes. Specifically, in subjects with type 2 diabetes, hospitalization events of stomach cancer, colorectal cancer, liver cancer, pancreatic cancer, lung cancer were 37.9, 43, 48, 17.6, and 36 per 10,000 persons, respectively.
As the Korean population ages and diabetes prevalence increases, it becomes increasingly crucial to find ways to overcome problems to good diabetes management. Diabetes self-management education is an important element of care for all people with diabetes and those at risk for developing the disease. However, only 39.4% received education for diabetes management at least once in Korea. Therefore, systematic approach to management diabetes including self-management education is needed in order to prevent or delay the complications of diabetes. And, the government need to establish a long-term policy to address the growing burden posed by diabetes.

S05-1
Social-economic impact of diabetes in New Zealand
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As in many other developed countries, diabetes is one of New Zealand's fastest-growing long-term conditions. Rising occurrence replicates a blend of influences, including rising prevalence, better uncovering of cases through increased screening, slower development from uncomplicated to late-stage disease and demographic change.
An estimated 257,000 people in New Zealand have diabetes as at December 2014 or 6% of the population.
The prevalence of diabetes has been rising at an average of 7% per year for the last eight years.
The prevalence of diabetes is increasing across all ethnic groups and age groups; the largest increases in diabetes are among adults aged 25–44 years, and at least one in six adults aged 65 years and over has diabetes.
The increase in diabetes is consistent with trends in obesity.
The increasing occurrence of diabetes in New Zealand is having a foremost bearing on our health system.
Diabetes, because it is a long-term condition with the potential for severe complications, has high health costs. For example, the total direct health care costs for a person with diabetes in New Zealand are approximately three times those for people without diabetes.
More generally, the long-term effects of diabetes will have an inclusive bearing on society. This is because an increasing number of people may not be able to continue working as they did before the onset of their diabetes. The cost of this loss of productivity has been estimated as being more than direct health care costs.

S05-2
Socio-economic impact and initiatives of diabetes in Indonesia
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Indonesia is a growing diabetic epidemic country despite strong economic fundamentals, and improving standard of living. Existences of many barriers to appropriate diabetes care prevent many people from living a healthy and productive life. This abstract mainly focus on the burden of diabetes, barriers for improved diabetic care and steps that help Indonesia to overcome the barriers. It is reported that two-third of diabetes population is found in low to middle income countries. With the average of 6%, urban cities in Indonesia are populated with people living with diabetes. There are 7.6 million people living with diabetes and 12.6 million others have pre diabetes (National Health Survey in 2007). Fewer than half of those with diabetes are aware of their condition. Less than one percent of those who are aware and received diabetes treatment achieve their goal of treatment. As results from the under diagnosed and under treated, disability, loss of life and productivity due to diabetes complications burden may negatively affect the Indonesian economic progress. Today, with its low population growth rate (1% annual growth rate since 2006), coupled with solid productivity gains (5.6% of annual GDP rate) together with stable inflation rate Indonesia has strong, long term economic growth potential. The improving standard of living in Indonesia is bringing with its lifestyle changes that increase diabetes risk and prevalence, thereby hampering sustainable economic growth. Demand for healthcare, however, may outstrip the country's ability to provide it. Four key barriers of diabetes care in Indonesia include lack of awareness about diabetes in the general public and among some healthcare professionals and policy makers, inequity of healthcare supply and demand resulting from an expanding patient population and too few diabetes specialists, lack of resources in the public healthcare system and among Indonesian population, and that too few people receiving appropriate treatment. Analytical study was done to estimate long-term clinical and economic impact of a 1% HbA1c reduction in patients with type 2 diabetes in Indonesia. The analysis was performed using the published and validated CORE Diabetes Model over a time horizon of 35 years, with future costs and clinical benefits discounted at a rate of 3% per annum. The analysis compared patients outcomes in two groups. In the poorly controlled patient arm, HbA1c remained at 9.8%, in comparison with reducing mean HbA1c to 8.8% in the active arm. Mean HbA1c was assumed to remain unchanged throughout the analysis. All other physiological characteristics were equal in the two treatment arms. Results of the study showed that 1% reduction

in HbA1c from baseline led to improvements in both clinical and economic outcomes. Reducing HbA1c from 9.8% to 8.8% was predicted to improve life expectancy from 10.07 years to 10.69 years (a difference of 0.61 years) and quality-adjusted life expectancy from 6.56 quality-adjusted life years (QALYs) to 7.04 QALYs (a difference of 0.48 QALYs). In the reduced HbA1c arm, incidence of macular edema and background diabetic retinopathy were reduced by 20%, falling from 23.5% to 18.6% and from 29.0% to 23.7%, respectively. Incidence of micro albuminuria fell from 42.1% to 33.5%, incidence of gross proteinuria fell from 22.9% to 15.1% and incidence of end-stage renal disease fell from 13.7% to 8.3%. Also there is a significant reduction in diabetic foot complications, besides modest reduction in incidence of cardiovascular disease which was clinically more significant. Direct medical costs were lower by EUR 541 per patient in the reduced HbA1c group over the 35-year time horizon of the analysis. Cost savings were driven by the reduced expenditure as a result of renal complications (EUR 2,838 in the control arm versus EUR 2,040 in the active arm). Treatment costs as a result of cardiovascular disease, neuropathy/diabetic foot and eye disease were also lower in the reduced HbA1c group. This study concludes that 1% reduction in HbA1c from baseline was associated with improved life expectancy and quality of life, as well as being cost-saving over a 35-year time horizon.

Another study was done to estimate current direct costs associated with managing diabetes-related complications from a healthcare payer perspective in Indonesia. A structured literature search of EMBASE, Medline and the Cochrane Library databases was carried out to identify published studies containing the costs of diabetes-related complications and management in Indonesia. Results showed that Myocardial infarction was the most costly complication in the year of onset, associated with a cost of USD 22,673. Renal complications were also associated with significant costs. Transplantation was estimated to cost approximately USD 21,532 in the first year and USD 5,033 in each subsequent year, hemodialysis cost over USD 9,994 annually and peritoneal dialysis cost over USD 6,391 each year. Ketoacidosis and lactic acidosis were associated with costs of USD 1,007, whilst minor hypoglycemia was the least costly at USD 36. Neuropathy/diabetic foot complications especially gangrene treatment was the most costly, at a cost of USD 3,356 in the year of onset. Amputation was also associated with significant costs. Study concludes that estimates of complication costs suggest that the seven million patients with diabetes represent a substantial economic burden in Indonesia. Also, this study highlights that cardiovascular and renal complications pose major economic burden, both in the year of onset and subsequent years for diabetic patients in Indonesia. Key initiatives to overcome the barriers and their outcomes: Mapping out key barriers to diabetes care and control, national action plan 2015–2019 to control the rapid rise of non-communicable disease (NCD) in Indonesia including diabetes consists include the following initiatives; advocacy and Public Private Partnership (PPP), health promotion and reduce risk factors, strengthening healthcare service system within the scope of integrating NCD care at primary care, improving quality of human resources, improving access to medicines and infrastructure as well as synchronizing policy. Moreover, surveillance, monitoring and evaluation (monev) and research. Today, ranked as top seventh country with highest diabetes, the number has increased to 10 million people in Indonesia living with diabetes. Key stakeholders including government, national health insurance, HCP's, patient support groups, media and private sector are working in partnership to establish a functional health system in Indonesia that recognizes the importance of diabetes awareness, diagnosis and treatment. Awareness is low, and most people do not know what they do not know about diabetes, its care and its consequences. There is a great need to make care more accessible by improving HCP skills and by encouraging teamwork among healthcare disciplines. Currently, the ability to afford insulin in Indonesia is dependent on income and health insurance coverage, more people should be able to afford care. Through the National Healthcare Insurance, government will expand its 250 million citizens to health care by end of 2019. Lack of availability, this is where multi stakeholder partnership to make healthcare available and affordable in rural areas is a factor in suboptimal quality of care. The issues stemming from these barriers are interconnected and resolving them will require a patient-centric, holistic approach.

S05-3

Landscape of diabetes in the Philippines

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The Philippines is an archipelago composed of more than 7,500 islands and is considered the seventh most populated country in Asia, with a populace of over 100 million.

In the past decade, a decline has been seen in communicable diseases, such as tuberculosis and malaria, however non-communicable diseases have been on the rise. Diabetes now follows diseases of the heart, vascular system and malignant neoplasms as leading causes of death.

In the latest national survey, the prevalence of chronic energy deficient adults is lower compared to the prevalence of those who are overweight and obese. Almost half of the population is insufficient in physical activity. These are contributors to the rising epidemic of diabetes in the Philippines, where individuals affected are in the working age group and mostly living in urban areas. The increase in prevalence of diabetes and its implications is alarming for this emerging market economy and requires a more focused and unified intervention from all sectors.

Who Does What in the Health Care for Diabetes in Taiwan

S12-3

Health governance and strategy and the challenge of non-communicable diseases: Viewpoints from lifestyle intervention in diabetes prevention

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The issues of noncommunicable diseases (NCDs) prevention and control are a growing global public health concern, and a target of a 25% relative reduction in NCD mortality by 2025, known as the 25 × 25 strategy, has been proposed from WHO's Global NCD Action Plan. Control and Management of type 2 diabetes, a major NCD, through lifestyle intervention for primary prevention and secondary prevention is a high priority of health policy. In Taiwan, through the programs of Diabetes Shared Care Network and The Improvement Program of National Health Insurance Payment for Diabetes Medical Treatment by emphasizing integrated team work, the universal healthcare system has provided an affordable service for diabetes care. However, the primary prevention of diabetes, including screening and identifying high risk individuals as well as lifestyle intervention, is still a challenge in clinical practice. Prediction models for type 2 diabetes from cross-sectional and cohort data provided a useful tool for screening. In addition, the Diabetes Prevention Programs from various countries provided many feasible strategies to prevent diabetes occurrence. Moreover, secondary prevention of diabetes complications, through health promotion activities such as modest alcohol intake, smoking, dietary habits,

exercise, and leisure time physical activity among diabetic patients are still a difficult task, especially for optimal blood pressure, glucose and lipid level control. Evidence from clinical trial data, such as Steno-2 and Diabetes Complication Study, showed behavioral intervention as important tools for further cardiovascular risk prevention. Novel modalities, such as information technology and behavioral economics approaches, provide a new way for diabetes care through behavioral and lifestyle intervention. In addition, the approach through dietary modification of gut microbiota as a key organ involved in metabolism is considered a new way to control diabetes. In summary, Primary and secondary prevention of diabetes is still a big challenge; however, innovative modalities through evidence-based lifestyle and behavioral intervention programs will provide insightful strategy for diabetes control.

Update of Bariatric/Metabolic Surgery

S02-1
Current status of bariatric/metabolic surgery: ADSS data

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Obesity and associated type 2 diabetes mellitus (T2DM) is becoming a serious medical issue worldwide. Bariatric surgery has been shown to be the most effective and durable therapy for the treatment of morbid obese patients. The advent of bariatric surgery to treat T2DM morbidly obese patients offers a new paradigm in T2DM therapy. Bariatric surgery has been shown to confer long-term weight loss and glycemic control in obese diabetics. "Metabolic surgery" has been proposed as a treatment for T2DM in view of the relatively high remission rates with bariatric surgery (range 36–93%) compared to medical therapy alone. Increasing data indicates bariatric surgery, played as metabolic surgery, is an effective and novel therapy for not well controlled obese T2DM patients. Because Asian people had a higher incidence of T2DM and tend to have an earlier onset T2DM than Caucasian, Asian surgeons had more experience in using metabolic surgery to treat T2DM in low BMI patients. Subjects are recruited as part of a multi-institutional ADSS group consisting of 11 centers in 6 countries, including Hong Kong, India, Japan, Korea, Singapore and Taiwan. There were a total of 4,380 subjects registered in this study between September 1997 and December 2015. This report was performed to examine the recent advancement of metabolic surgery in Asia can be classified into 4 major fields. (1) ***Improvement of safety:*** Recent advancement in laparoscopic surgery has made this minimal invasive surgery more than ten times safe than a decade ago. The safety profile of laparoscopic bariatric/metabolic surgery is compatible with laparoscopic cholecystectomy now. (2) ***New metabolic surgery:*** Laparoscopic sleeve gastrectomy (LSG) is becoming the leading bariatric surgery because of its simplexes and efficacy. Other new procedures, such as single anastomosis (mini) gastric bypass and Duodeno-jejunal bypass with sleeve gastrectomy have all been accepted as treatment modalities for the bariatric/metabolic surgery. (3) ***Mechanism of metabolic surgery:*** Restriction is the most important mechanism for bariatric surgery. Weight regain after bariatric surgery is usually associated with loss of restriction. Recent studies demonstrated that gut hormone, microbiota and bile acid change after bariatric surgery may play an important role in durable weight loss as well as in T2DM remission. However, weight loss is still the cornerstone of T2DM remission after metabolic surgery. (4) ***Patients selection:*** Patients who may benefit most from bariatric surgery was found to be patients with insulin resistance. For T2DM treatment, the indication has been set to not well controlled (HbA1c >7.5%) with their BMI >27.5 Kg/m^2 in Asian. A novel diabetes surgical score, ABCD score, is a simple system for predicting the success of surgical therapy for T2DM.

S02-4
Management of residual diabetes and micronutrient deficiencies after bariatric surgery

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Bariatric surgery is regarded as "metabolic surgery" and "diabetic surgery" because of its noticeable effects on metabolic syndrome and type 2 diabetes. Although many studies show the effectiveness of bariatric surgery to treat diabetes, recent studies document that a growing number of patients with type 2 diabetes do not achieve "remission" of diabetes or are unable to sustain this effect long-term despite initial success with weight loss after bariatric surgery.

Some possible factors associated with diabetes non-remission or re-emergence were noted, such as older age, lower preoperative BMI, longer diabetes duration, insulin use, inadequate weight loss and weight regain, surgery type and severity of preoperative beta-cell dysfunction.

Currently, no clinical practice guideline is established for the patients with "residual" diabetes after bariatric surgery. According to the recommendation of ADA, metformin remains the first line agent for T2DM in that it improved insulin sensitivity. Thus the use of metformin for glycemic control after bariatric surgery is reasonable due to low risk of hypoglycemia and neutral/loss for weight gain. A report demonstrated accelerated absorption and bioavailability of metformin following gastric bypass and indicated that a reduce dose of metformin may be required for achieving glycemic control. In contrast, use of thiazolidinediones may hamper weight loss efforts despite increasing insulin sensitization and low risk of hypoglycemia.

Sulfonylurea drugs should generally be avoided in the immediate postoperative period when insulin secretion may enhance and increase the risk of hypoglycemia. However, in patients with residual diabetes after bariatric surgery, who cannot achieve the treatment goal by use of metformin, the addition of sulfonylurea to metformin may restore glycemia control by targeting pancreatic beta-cell failure.

Incretin analogue (i.e. DPP4 inhibitors and GLP-1 analogues) enhance glucose dependent insulin secretion and offer advantages for weight loss in obese type 2 diabetic patients but evidence for their use in bariatric surgery is lacking. For the favorable effects of SGLT2 inhibitors on glycemic control, weight loss and blood pressure, SGLT2 inhibitors maybe an attractive anti-diabetic agent to treat residual diabetes. However, the use of these drugs increases the risk of genital mycotic infection and dehydration.

For those patients with residual diabetes, who cannot achieve the treatment goal by oral anti-diabetic agents and/or GLP-1 analogues, insulin therapy is indicated. Besides, all diabetic patients underwent bariatric surgery should keep a lifelong lifestyle modification.

Deficiencies in micronutrients, which include trace elements, essential minerals, and water-soluble and fat-soluble vitamins, are common before bariatric surgery and often persist postoperatively, despite universal recommendations on multivitamin and mineral supplements. Recognition of the clinical presentations of micronutrient deficiencies is important, both to enable early intervention and to minimize long-term adverse effects.

Anemia without evidence of blood loss warrants evaluation of nutritional deficiencies as well as age appropriate causes during the late postoperative period. Iron status should be monitored in all bariatric surgery patients. Treatment regimens include oral ferrous sulfate, fumarate, or gluconate to

provide up to 150–200 mg of elemental iron daily. Intravenous iron infusion (preferably with ferric gluconate or sucrose) may be needed for patients with severe intolerance to oral iron or refractory deficiency due to severe iron malabsorption.
Baseline and postoperative evaluation for vitamin B12 deficiency is recommended in all bariatric surgery and annually in those with procedures that exclude the lower part of the stomach (e.g., LSG, RYGB). Oral supplementation with crystalline vitamin B12 at a dosage of 1,000 μg daily or more may be used to maintain normal vitamin B12 levels. Parenteral (intramuscular or subcutaneous) B12 supplementation, 1,000 μg/mo to 1,000–3,000 μg every 6 to 12 months, is indicated if B12 sufficiency cannot be maintained using oral or intranasal routes.
In patients who have undergone RYGB, BPD, or BPD/DS, treatment with oral calcium citrate and vitamin D (ergocalciferol [vitamin D2] or cholecalciferol [vitamin D3]), is indicated to prevent or minimize secondary hyperparathyroidism without inducing frank hypercalciuria. 1,200–1,500 mg of elemental calcium (in diet and as citrated supplement in divided doses), at least 3,000 international units of vitamin D (titrated to therapeutic 25-hydroxyvitamin D levels >30 ng/mL). In cases of severe vitamin D malabsorption, oral doses of vitamin D2 or D3 may need to be as high as 50,000 units 1 to 3 times weekly to daily, and more recalcitrant cases may require concurrent oral administration of calcitriol (1,25-dihydroxyvitamin D). A major clinical concern is the relationship between vitamin D deficiency and the development of metabolic bone diseases, such as osteoporosis or osteomalacia; metabolic bone diseases may explain the increased risk of hip fracture in patients after RYGB.

Screening of Diabetes: How and Why?

S03-1
Screening and diagnosis of diabetes mellitus in Taiwan
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In 2015, the Diabetes Association in Taiwan published its clinical practice guidelines for diabetes care. There are 3 different screening methods for diabetes in asymptomatic subjects suggested by the guideline. The first one is based on the service by the National Health Insurance in Taiwan. In adults aged 40–64 years, screening for diabetes every 3 years should be considered. For adults aged 65 or over, annual screening for diabetes is recommended. The second one is based on Taiwan Diabetes Risk Scores, which is a risk assessment calculator, to estimate the risk for undiagnosed diabetes. For subjects with very high risk for undiagnosed diabetes, annual screening is recommended. For subjects with high or moderate risk for diabetes, screening every 3 years is recommended. The third one is based on risk factors of diabetes. Subjects who have impaired fasting glucose, impaired glucose tolerance, or HbA1c 5.7–6.4% are suggested to be tested annually. For subjects with two or more risk factors, screening is recommended every 3 years. The guideline also suggests a screening algorithm to confirm the diagnosis of diabetes and to determine the need of oral glucose tolerance test, based on data of fasting plasma glucose and hemoglobin A1c. The diagnostic criteria for diabetes and for the category of increased risk for diabetes (pre-diabetes) remain the same as in the previous version. For the diagnosis of gestational diabetes mellitus (GDM), both one-step strategy and two-step strategy are recommended. The one-step strategy increases prevalence of GDM, but results in an improvement in maternal and fetal outcome and is cost-effective in Taiwan. Besides, the DAROC has also created an interactive website for the users to learn and get familiar with the screening of diabetes, the diagnosis of diabetes, and the treatment algorithm of the guideline.

S03-3
National survey on diabetes in China
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Non-communicable chronic diseases have become the leading causes of mortality and disease burden worldwide. As the most populous country, the rapid increase in morbidity and mortality from non-communicable diseases in China contributed to the pandemic, including diabetes. The prevalence of diabetes has increased significantly in recent decades and is now reaching epidemic proportions in China. The prevalence of diabetes was less than 1% in the Chinese population in 1980. In subsequent national surveys conducted in 1994 and 2000–2001, the prevalence of diabetes was 2.5% and 5.5%, respectively, and 9.7% in 2007. Although different sampling methods, screening procedures and diagnostic criteria were used, these data document a rapid increase in diabetes in the Chinese population. In 2010, we measured HbA1c, FPG, and 2-h PG in a large and nationally representative sample of 98,658 adults aged 18 years or older to estimate the prevalence and control of diabetes based on the 2010 ADA criteria in the general Chinese population. The estimated prevalence of diabetes and pre-diabetes in a representative sample of Chinese adults was 11.6% and 50.1%, respectively. Projections based on sample weighting suggest this may represent up to 113.9 million and 493.4 million adults, respectively. These findings indicate the importance of diabetes as a public health problem in China. The estimated percentage of ideal cardiovascular health was 0.2% in the general adult population in China (0.1% in men and 0.4% in women). We also reported for the first time, compared with the general population in China, most cardiometabolic risk factors were less prevalent in migrant workers. However, overweight, obesity and central obesity were more prevalent in male migrant workers than among men in the general population. Cardiometabolic risk profiles for migrant workers are not optimal and effective national interventions that can reach this special population are needed.

Childhood Obesity and Diabetes: Environmental Risk Factors, Screening, and Intervention

S06-1
Environmental factors associated with obesity and diabetes in Taiwanese children
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Background: The prevalence of childhood obesity has increased from 13% in 1986, 26.8% in 2001 and now 32.3% in 2010. The prevalence of impaired fasting glucose in Taiwanese adolescents is 22%. The rate of newly identified diabetes was 9.0 per 100,000 for boys and 15.3 per 100,000 for girls. Of 253 children with newly diagnosed diabetes, 24 (9.5%) had type 1 DM, 137 (54.2%) had type 2 DM, and 22 (8.7%) had secondary diabetes. Childhood obesity is the most contributing risk factor leading to type 2 diabetes, and also metabolic syndrome. We aim to explore the relationship amongst socio-demographic,

behavioural, household environmental and perinatal, factors and risks of childhood overweight and obesity in Taiwan.
Methods: Through literature review, and also one nationwide, representative study, named "Taiwan Children Health Study (TCHS)", a total of 7,930 nine to fourteen year-old children were recruited from 14 randomly selected Taiwanese communities in 2007 and 2010.
Results: By reviewing the literature, we summarized that family environment such as high maternal body mass index, and poor family affective responsiveness were associated with childhood obesity. Besides, school food environment, such as cheaper school meals, higher consumption of sugar-sweetened beverages, and more nearby fast food stores, convenience stores increased risk of obesity and central obesity. In TCHS cohort, 32.3% of the children were overweight and 17.5% were obese. Male gender, high birthweight, exposure to *in-utero* maternal smoking and current exposure to household environmental tobacco smoke (stronger effect of maternal than paternal smoking) were positively associated with childhood overweight/obesity. In contrast, higher parental education level, number of siblings, active exercise habits and taking vitamins were associated with reduced risks of childhood obesity. Birthweight revealed a J-shape relationship with the probability of childhood overweight/obesity.
Conclusions: This study uncovers several modifiable risk factors for childhood overweight and obesity, and parents are encouraged to provide an anti-obesity environment such as quitting smoking, controlling birthweight of child during pregnancy, and building up exercise habits.

S06-2
Screening of childhood type 2 diabetes in Japan

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In the 21st century, childhood type 2 diabetes (T2D) is increasing in prevalence all over the world, particularly among Asian populations. In Japan, a large number of children with T2D have been detected by a urine glucose screening program at schools since 1974. They are identified with mild symptoms of hyperglycemia without ketosis at the early stage of the disease. In Tokyo, together with the screening for hematuria and proteinuria to detect chronic renal disease, urine glucose testing was started in 1974. The school health law was revised to mandate urine screening of all primary and junior high school students for glucosuria in 1994. In regard to the method of testing, the participants are requested to collect first morning urine samples at home. If first urine sample is positive for glucose, a repeat urine test is requested on another morning. If the second test is also positive, measurement of FPG, HbA1c and an OGTT are performed to confirm the diagnosis of diabetes.
The Tokyo study have reported the incidence and clinical features in childhood T2D detected by the urine glucose screening program at schools in detail. During 1974–2015, a total of 11,652,205 school children, including 7,955,857 primary school children (PSC) and 3,606,348 junior high school children (JHSC), underwent the urine glucose testing. Of these, a total of 301 children, including 64 PSC and 237 JHSC, were diagnosed to have T2D. The overall incidence of childhood T2D was estimated to be 2.58/100,000/year, which is higher than that in childhood type 1 diabetes in Japan. JHSC had a significantly higher incidence of T2D than PSC (0.80 vs. 6.41/100,000/year, $P < 0.0001$). These findings are almost similar to those reported in other cities in Japan. In regard to changes in the annual incidence of T2D for 5-year period, those in 1981–2000 and 2006–2010 were significantly higher than that before 1980, whereas there was no significant difference between those in 2001–2005 and 2011–2015 and that before 1980. As for clinical features of T2D, 85% were obese (% overweight >20%) and 45% were severe obese (% overweight >50%). On the other hand, 58% children had family history of T2D in the first- and second-degree relatives.
In conclusion, a urine glucose screening program at schools may be useful to detect childhood T2D at the early stage, and it is crucial to create a strategy for prevention and treatment of the disease during childhood worldwide.

S06-3
The optimal exercise modality for childhood obesity prevention and treatment

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Obesity has been recognized as a major public health concern worldwide since it is strongly associated with co-morbid conditions such as metabolic syndrome, insulin resistance, type 2 diabetes (T2D), and cardiovascular disease (CVD) across age, gender, and ethnicity. It is well described that childhood obesity tends to track well into adulthood and also increases the risks of developing cardio-metabolic abnormalities as well as premature mortality in adulthood. Although the mechanisms or exact causes of the dramatic increase in childhood obesity have not been fully understood, the increased sedentary behaviors and reduced physical activity have been known as the major factors to the current obesity epidemic.
In adults, a number of well-controlled studies have reported significant reductions in obesity, in particular of abdominal obesity, and risk factors for T2D and CVD after regular exercise training (>150 min/week) even without calorie restriction or weight loss. Similar observations are also reported in youth; however, very little attention has been directed toward the effects of different exercise modalities on adiposity and risk factors associated obesity-related co-morbid conditions in youth.

Genetic Architecture of T2DM

S04-1
Genetic and genomic approaches to dissecting the pathogenesis of diabetes

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Novel therapies for type 2 diabetes (T2D) are needed. Large scale genetic association studies have identified multiple loci associated with T2D and offer an opportunity to identify and validate novel therapeutic targets for T2D. However, other approaches are required to help us identify actionable targets that underlie these associations. In particular, human genetics has yielded limited information as to the pathogenesis of insulin resistance. Additional genomic approaches are required to better understand this aspect of T2D pathogenesis.

S04-2
Recent progress in genetic research on type 2 diabetes and obesity in East Asian populations

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Type 2 diabetes (T2DM) and obesity are common metabolic diseases resulting from the complex interactions between genetic and environmental factors. Researchers have devoted enormous efforts for better understanding of the genetic architecture of these diseases. Since past decade, advances in genetic association studies, in particular the genome-wide association studies (GWAS), has facilitated the discovery of several dozen independent genetic loci for T2DM and obesity.

However, early GWAS of many complex diseases, including T2DM and obesity, interrogated mainly the common variants which tend to exhibit modest effect sizes. Furthermore, these common variants mostly located at intergenic or intronic region, where it is difficult to provide a clear explanation for their functional consequences. In recent years, the advancement in exome array genotyping and next-generation sequencing technologies has opened up a novel means for the discovery of low-frequency or rare variants that are enriched in the coding regions. These new approaches have facilitated the identification of variants that are more likely to have strong effects and even the population-specific variants. Ongoing large-scale genotyping and sequencing studies will continue to discover the low-frequency/rare and functional variants for T2DM and obesity. In this talk, a summary of our work on the genetics of T2DM and obesity; and the recent progress in the genetic studies of these diseases among other East Asian populations will be discussed.

Mitochondria in Diabetes

S07-1
ERK-c-Myc pathway as a novel pathway linking mitochondrial dysfunction and skeletal muscle insulin resistance

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Mitochondrial dysfunction plays an important role in pathogenesis of diabetes mellitus. It can affect both insulin resistance and impaired insulin secretion. There are various genetic and environmental factors contributing to mitochondrial dysfunction. We previously showed that mitochondrial dysfunction is related to reduced retinoid X receptor α (RXRα) levels which played an important role in transcriptional regulation of oxidative phosphorylation(OXPHOS) genes in cybrid cells carrying mitochondrial DNA 3243 A>G mutation.
In order to identify a novel pathway linking mitochondrial function and insulin resistance in common form of type 2 diabetes, we performed transcriptional profiling of skeletal muscles from subjects with or without type 2 diabetes mellitus. Through an integrative analysis of our dataset with four previous datasets, we identified 46 core gene sets associated with insulin resistance and focused on c-Myc with the highest regulatory power in the network of the core gene sets. c-Myc expression decreased in skeletal muscle from obese rodent model. In C2C12 myotubes, c-Myc transcriptional activity was decreased by palmitate or TNFα treatment inducing insulin resistance. Knockdown of c-Myc decreased expression of OXPHOS genes and PGC-1-related coactivator with no change in PGC1α. ERK regulated c-Myc induction by insulin, and palmitate abrogated insulin-induced c-Myc expression by modulating ERK activation. The unbiased integrative approach of transcriptional profiles revealed ERK-c-Myc pathway as a novel pathway for linking mitochondrial function and skeletal muscle insulin resistance, independent of PGC1α.

S07-2
Mitochondrial dysfunction and dysregulation of Ca^{2+} homeostasis in insulin insensitivity and diabetes

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Type 2 diabetes (T2D) and insulin resistance have attracted great attention of biomedical researchers because of astonishing increase in its prevalence. Decreased capacity of oxidative metabolism and mitochondrial dysfunction caused by aging, gene mutation or gene knockout are a major contributor to the development of T2D. Recent studies indicate that alteration of Ca^{2+} level and downstream Ca^{2+}-dependent signaling pathways appear to modulate the insulin signaling cascade, resulting in insulin resistance of adipocytes. Mitochondria and ER play an important role in the maintenance of intracellular Ca^{2+} homeostasis and their defects may be an etiology factor of insulin resistance and T2D. We demonstrated that mitochondria-associated ER membranes (MAMs) are essential for efficient communication between the ER and mitochondria. The abnormalities in the structure and function of MAMs in affected tissue cells in T2D and other metabolic disorders have been an important subject of study. Moreover, we demonstrated that dysregulation of intracellular Ca^{2+} homeostasis resulted from mitochondrial dysfunction or defects in the function of MAMs are involved in the impairment of adipocyte differentiation, leading to glucose intolerance and insulin insensitivity of mice. Based on these observations we suggest that the role of mitochondrial dysfunction and disturbance in Ca^{2+} homeostasis warrant further study in the development of effective therapeutics in the prevention and medication of insulin resistance and T2D.

S07-3
Study of insulin resistance and chronic inflammation in cybrid cells harboring diabetes-susceptible mitochondrial haplogroups

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There is evidence that mitochondria are involved in the development of diabetes. Quite a number of case studies such as MIDD (maternally inherited diabetes and deafness) and MELAS (mitochondrial encephalopathy, lactic acidosis and stroke-like episodes) have confirmed the link between mitochondrial genetic variations with diabetes. However, the role of mitochondria in the common type 2 diabetes, which has becoming a world-wide disease, deserves more investigation.
The advantage of using a cytoplasmic hybrid (cybrid) model to study the genetic effects of mitochondria is that the cells have the same nuclear genomic background. Cybrids derived from 143B osteosarcoma cell line and different mitochondrial haplogroups, including B4 (the major diabetes-susceptible haplogroup in Chinese population), D4 (the major diabetes-resistant haplogroup in Chinese population) and N9 (the diabetes-resistant haplogroup in Japanese population) were developed in vitro. Cybrid cells were cultured in a medium containing 25 mM glucose and stimulated with 0, 0.1, and 1.0 M insulin to elucidate the role of mitochondria in the pathogenesis of insulin resistance (IR).
Upon insulin treatment, the translocation of cytoplasmic GLUT1/GLUT4 to the cell membrane in cybrid D4 and N9 cells increased significantly, whereas the changes in B4 cells were not or less significant. On the contrary, the ratio of insulin-induced JNK and P38 to Akt phosphorylation was significantly greater in cybrid B4 cells than in cybrid D4 and N9 cells. The levels of DCF and MitoSOX Red, which are indicative of the oxidative stress, were significantly higher in the B4 cells in basal conditions and after insulin treatment. Following treatment with the antioxidant NAC, cybrid B4 cells showed significantly reduced insulin-induced phosphorylation of P38 and increased GLUT1/GLUT4 translocation to the cell membrane, suggesting NAC may divert insulin signaling from pro-inflammation to glucose uptake.
Comparison of mitochondrial dynamics, biogenesis, bioenergetics, autophagy and apoptosis revealed significant difference between cybrid B4 and D4, before and after insulin stimulation. Cybrid B4 showed a more fragmented mitochondrial network, impaired mitochondrial biogenesis and bioenergetics, increased apoptosis and ineffective autophagy and a low expression of fusion-related molecules. Upon insulin stimulation, increases in network formation,

mitochondrial DNA (mtDNA) content, and ATP production were observed only in cybrid D4. In cybrid B4, the imbalance of mitochondrial dynamics and impaired biogenesis and bioenergetics, and increased apoptosis were significantly improved in response to antioxidant treatment.
We concluded that the diabetes-susceptible mtDNA variants are themselves resistant to insulin. Mitochondria play an independent role in the pathogenesis of IR, possibly through altered production of intracellular ROS.

S07-4
Metabolism-secretion coupling in diabetic islets
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One of the characteristics of type 2 diabetes (T2DM) is that the insulin secretory response of β-cells is selectively impaired to glucose. In the GK rat, a genetic model of non-obese T2DM, glucose-induced insulin secretion (GIIS) is selectively impaired. The intracellular ATP elevation induced by high glucose is impaired in GK rats as well as in patients with T2DM. The impaired insulinotropic action of glucose in diabetic β-cells may be attributable to deficient ATP production derived from impaired glucose metabolism. Although there is evidence that islets in GK rat and human T2DM are oxidatively stressed, the association between oxidative stress and impaired intracellular ATP elevation in islets is yet unclear.
We propose that endogenous generation of reactive oxygen species (ROS) by activation of Src, a non-receptor protein-tyrosine kinase, plays an important role in GIIS in GK islets. Src was activated, which causes ROS production and mitochondrial dysfunction, in GK islets. Src inhibition decreased ROS production and restored the impairment of GIIS and ATP elevation in GK islets. In addition, GLP-1 signaling decreased Src activation and ROS production, and ameliorated impaired ATP elevation by high glucose dependently on Epac in GK islets.
12-h suppression of ROS by exposure to tempol, a superoxide dismutase mimic, plus ebselen, a glutathione peroxidase mimic (TE-treatment) improved GIIS and ATP elevation in GK islets. ATP production from mitochondrial fraction of GK islets in the presence of pyruvate and malate was not altered by TE-treatment. Lactate production was markedly increased in GK islets, which can reduce supply of pyruvate to mitochondria, together with reduced NADH-FADH2 supply to mitochondria due to reduced glycerol phosphate shuttle activity, leading to reduced ATP production. TE-treatment reduced lactate production and protein expression of lactate dehydrogenase (LDH) and hypoxia-inducible factor 1α (HIF1α) which regulates LDH expression. These results indicate that the Warburg-like effect, the characteristic aerobic metabolism in cancer cells by which lactate is overproduced with reduced linking to mitochondria metabolism, plays an important role in impaired metabolism-secretion coupling in diabetic β-cells and suggest that ROS reduction can improve mitochondrial metabolism by suppressing lactate overproduction through inhibition of HIF1α stabilization.

The Role of Epigenetics in Diabetes and its Complications

S10-3
Co-localization of NFIA and PPARγ controls the brown fat gene program
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Brown fat dissipates energy as heat and protects against obesity. Here, we identified nuclear factor I-A (NFIA) as a novel transcriptional regulator of brown fat by a genome-wide open chromatin analysis of murine brown and white fat followed by motif analysis of brown-fat-specific open chromatin regions. NFIA and the adipogenic master regulator, PPARγ, co-localize at the brown-fat-specific enhancers. Moreover, the binding of NFIA precedes and facilitates the binding of PPARγ, leading to increased chromatin accessibility and active transcription. Introduction of NFIA into myoblasts results in brown adipocyte differentiation. Conversely, the brown fat of NFIA knockout mice displays impaired expression of the brown-fat-specific genes and reciprocal elevation of muscle genes. Finally, expression of NFIA and the brown-fat-specific genes is positively correlated in human brown fat. These results indicate that NFIA is a key transcriptional regulator of brown fat and exerts its effects by co-localizing with PPARγ at cell-type-specific enhancers.

Environmental Pollutants and Diabetes

S17-1
Obesity and diabetes: roles of circulating environmental pollutants and its mitochondria inhibiting activity in pathogenesis
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Environmental chemicals have emerged as an important causal factor of obesity and diabetes, but their target has not been well understood. Based on the recognized role of abnormal mitochondrial function in diabetic pathogenesis, environmental pollutants were suspected to disrupt mitochondrial activities. Previously, we showed that in a case-control study, serum of diabetic or insulin resistant patients contained 30–50% higher in levels of environmental pollutants and 20% lower in mitochondria stimulating activities than the normal subjects. Total serum environmental pollutant levels were indirectly analyzed by assessing aryl hydrocarbon receptor (AhR) ligand-dependent transcription activities (AhRT) in sample sera. Mitochondria inhibiting activities of the subject sera were monitored by ATP contents and reactive oxygen species (ROS) amount in the serum-treated cells. Prospective study confirmed that AhRT was a strong predictive parameter for developing diabetes as cut-off point of AhRT was 1.96 (OR = 30.44, $p < 0.001$, n = 1,537, 95% C.I.). Similarly, ATP (<83.6%; OR = 8.83) and ROS (>122.4%; OR = 24.43) were found to be independent risk factors of diabetes ($p < 0.001$, 95% C.I.). Circulating environmental pollutants in diabetic patients disrupted mitochondria via AhR-mediated mechanism and AhR antagonists reversed the mitochondrial damages. We suggest that serum AhRT, ATP, and ROS parameters would be critical biomarkers to predict diabetes development and

provide novel therapeutic targets to manage metabolic syndrome in the future.

S17-2

Environmental pollutants and cardiovascular diseases

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There is now compelling evidences both from epidemiological and experimental studies that a large number of environmental contaminants with endocrine disrupting properties could be involved in the development of several of the classical risk factors for cardiovascular disease, such as diabetes, hypertension, obesity, hyperlipidemia and the metabolic syndrome. Furthermore, both epidemiological and experimental studies have shown that environmental contaminants from different chemical classes, such as PCBs, dioxins, phthalates and some toxic metals could be involved in atherosclerosis development, and the progression of atherosclerosis to lipid-rich, rupture-prone vulnerable atherosclerotic plaque.

It is therefore not surprising that several lines of evidences in humans point to the fact that environmental contaminants also could be involved in cardiovascular diseases. Data will be presented from accidents with massive contamination of a population, ecological data on human samples living close to contaminated places, occupational data for workers exposed to high levels of certain environmental contaminants being produced and classical epidemiological data on the associations between circulating levels of environmental contaminants and prevalent and incident cardiovascular disease in cross-sectional and prospective studies.

In conclusion, there is today so many studies pointing towards associations between background exposure to environmental contaminants and cardiovascular risk factors as well as atherosclerosis and overt cardiovascular disease that these evidences must be taken seriously, and as a consequence actions to reduce the human burden of environmental contaminants have to be taken.

S17-3

Are persistent organic pollutants a common soil of type 2 diabetes and type 3 diabetes (dementia)?

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Chronic exposure to low doses of persistent organic pollutants (POPs) has emerged as a new risk factor for type 2 diabetes. They are stored in the adipose tissue as typical strong lipophilic chemicals and move through the body with the serum lipids. POPs are mechanistically involved in the well-known association between obesity and type 2 diabetes.

Meanwhile, it is known that people with type 2 diabetes and its related conditions have a higher risk of developing dementia with aging. Alzheimer's disease, the most common form of dementia, is sometimes called as "type 3 diabetes". Currently, possible mechanisms linking type 2 diabetes and type 3 diabetes are insulin resistance and deficiency which can interact with amyloid-β protein and tau protein phosphorylation, each of which leads to the onset and development of Alzheimer's disease. However, chronic exposure to low doses of POPs can be a common risk factor for type 2 diabetes and dementia.

In several recent epidemiological studies, it was found that background exposure to POPs, especially organochlorine pesticides, was strongly related to the risk of cognitive impairment and dementia. In addition, the risk of aging or hypertension-related cognitive impairment was found to be higher when the elderly had high serum concentrations of organochlorine pesticides. As organochlorine pesticides are well-known neurotoxins at high doses, these findings may be biologically plausible. Even though exposure levels in the current general population are very low, current elders represent the first generation exposed to these chemicals during most of their life-time.

Even though insulin-related mechanisms are commonly investigated to associate these 2 very important diseases, here, we suggest a "common soil hypothesis" postulating that type 2 diabetes and dementia share common environmental antecedents such as exposure to POPs. Of importance, POPs can explain puzzling findings in obesity, weight loss, and dementia.

S17-4

Endocrine disrupting chemicals and risk of type 2 diabetes and cardiovascular disease: Focused on phthalates and perfluorinated chemicals

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A growing number of reports show that endocrine disrupting chemicals (EDCs) are associated with cardiovascular disease (CVD) risk factors. Information regarding the association between EDCs and CVDs are limited. Furthermore, there is no clear mechanism linking the atherogenic risk after phthalates or perfluorinated chemicals (PFCs) exposure.

From 2006 to 2008, we recruited 886 subjects in adolescents and young adults (12–30 years) in Taipei from a population-based sample to participate in this cardiovascular disease prevention examination. Each participant was subjected to interviews and biological sample collection to determine the relationship between cardiovascular and endocrine/metabolic biomarkers and concentrations of environmental pollutants, including phthalates, PFCs, and bisphenol A.

The YOung TAiwanese Cardiovascular Cohort (YOTA) study have demonstrated serum levels of perfluorononanoic acid (PFNA) positively associated with serum adiponectin and free thyroxin. Another result found that serum levels of perfluorooctane sulfate (PFOS) and PFNA associated with carotid intima-media thickness (CIMT). Recently, we started to investigate the health effects of Di-(2-ethylhexyl) phthalate (DEHP) exposure by measuring urinary phthalate metabolites and we found a significantly positive association between urinary mono(2-ethylhexyl) phthalate (MEHP) and endothelial microparticles (EMPs) and platelet microparticles (PMPs). Furthermore, we found a positive association between PFOS and CIMT that was more evident when serum levels of EMPs (CD31+/CD42a–) and PMPs (CD31+/CD42a+) were elevated. Another study in middle-aged Taiwanese adults, we also demonstrated serum PFOS may disturb glucose homeostasis and increase the risk of diabetes.

In conclusion, we have demonstrated phthalates and PFCs play the role of EDCs that significantly influenced the risk of type 2 diabetes and subclinical CVD. The positive relationship between emergent biomarkers of endothelial dysfunction and EDCs provides a possible mechanistic link between EDCs and cardiovascular health. A more clear and rigid regulation for the use of DEHP and PFOS should be highly recommended.

Cardiovascular Disease and Diabetes—Clinical and Translational

S08-1

Basic science of diabetic cardiomyopathy – a mechanism and role of mitochondria dysfunction

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Metabolic dysregulation plays a critical role during the development of diabetic cardiomyopathy and diabetes aggravates heart failure. Mitochondria are the major source of ATP production in the heart, via glycolysis and β-oxidation. Glycolytic Oxidative phosphorylation is significantly reduced in the diabetic myocardium, thereby creating a metabolic switch to selectively relying on β-oxidation, which is associated with lipotoxicity and inefficient energy conversion. We have shown that insulin stimulated Akt1 translocation to mitochondria and modulated mitochondria function in cardiac muscle, and translocation of Akt1 to mitochondria was significantly reduced in diabetic myocardium. Activation of Akt1 signaling in mitochondria increased glucose uptake, enhanced respiration efficiency, reduced superoxide generation, and increased ATP production. To elucidate the causal relationship between impaired Akt1 translocation to mitochondria in diabetic myocardium and the development of diabetic cardiomyopathy, we have generated a transgenic mouse line by knocking in a tamoxifen-inducible mitochondria-targeting dominant negative Akt (mdnAkt) into the Rosa26 locus (CAMDAKT mice). Cardiac specificity was achieved with the Cre-Lox strategy. After Tamoxifen induction, CAMDAKT mice developed heart failure within 7 days. Analysis showed altered mitochondria ultrastructure and loss of mitochondria cristae. These findings were followed by reduction of muscle mass, inflammation, cardiac fibrosis, and biventricular heart failure. Proteomic analysis indicated pyruvate dehydrogenase complex (PDC) as a signaling target of Akt1 in mitochondria. Akt1 interacted with the E3 subunit of PDC, activation of mitochondrial Akt1 increased pyruvate dehydrogenase (PDH) activity. We have computationally analyzed protein–protein domains interfacing Akt1/E3 interaction. Screening compounds library yielded two small molecules that structurally disrupted Akt1-E3 interaction. Further analysis with recombinant proteins confirmed interaction of Akt1-E3 and the small molecule compound suppressed Akt1 activation of PDC activity in cardiac mitochondria. These findings suggest that impaired Akt1 translocation to mitochondria played a critical role in the development of diabetic cardiomyopathy.

S08-2
Inspiration from the historical evolution of large-scale clinical studies in diabetes – the cardiovascular safety of hypoglycemic therapy

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The prevalence of diabetes increases with increasing age. Several diabetic guidelines indicate that T2DM patients have cardiovascular risk. Studies exploring the hypoglycemic strategies and the risk of CVD never stop. Cardiovascular safety has become one of the important factors to evaluate antidiabetic agents. A meta-analysis in 2007 showed that rosiglitazone increased cardiovascular death, causing the attention on the cardiovascular safety of hypoglycemic agents. FDA requires that cardiovascular safety must be evaluated in premarketing and postmarketing clinical trials for hypoglycemic agents. Many large-scale clinical studies for hypoglycemic agents, such as SAVOR, TECOS, EMPA-REG OUTCOME studies, all set cardiovascular death, nonfatal myocardial infarction and nonfatal stroke as the primary endpoints, and were all designed as multi-center, randomized, double-blind, placebo-controlled trials. The non-inferiority or superiority of the hypoglycemic agents compared to placebo was assessed independently. These large-scale clinical studies provide guiding benefits for appropriate selection and personal application of hypoglycemic agents in clinical practices.

DM Nephropathy: Risk, Mechanism, Management and Outcome

S15-2
Individualized blood pressure targets in Asian diabetic patients with or without nephropathy

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Diabetes is a leading cause of end stage renal disease which can be prevented by optimal control of cardiometabolic risk factors including blood pressure (BP), blood lipids, blood glucose as well as appropriate use of renin-angiotensin system inhibitors. Although there is broad consensus on the benefits of multi-factorial management on organ protection, the target values of BP control remains controversial. Several large scale studies including the ACCORD Trial failed to demonstrate reduction of BP to less than 120/80 mmHg conferred cardiovascular benefits and might increase adverse effects in high risk patients. Some of the controversies on intensity of BP management relate to the heterogeneous nature of risk factors and complications which interact with interventions to give rise to different consequences. Here, BP control remains a major modifying factor which can interact with blood glucose to reduce microvascular complications such as albuminuria and renal function as well as with lipids to reduce macrovascular diseases such as coronary heart disease and stroke. However, in high risk patients such as elderly or patients with generalised atherosclerosis or poor autoregulation, excessive reduction in BP may compromise blood flow to cause impaired organ functions such as kidney and heart. On the other hand, since young patients face long disease duration, early control of all risk factors including blood pressure, blood glucose and blood lipid is important to reduce lifetime risk for complications, such as diabetic kidney disease. In the ORIENT study which included Chinese and Japanese patients with type 2 diabetes, chronic kidney disease and macroalbuminuria, a post-hoc analysis showed linear association between follow up systolic BP and renal outcomes, where BP level of 120 mmHg was associated with the slowest rate of decline of renal function. In a recent meta-analysis, intensive BP control reduced albuminuria but not cardiovascular disease. Taken together, given the heterogeneous nature of diabetes with different combinations of age, sex, disease duration, risk factors, complications and co-morbidities, individualization of BP goal is as important as that for glycemic control.

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S15-3
Choice of antidiabetic agents and glycemic goals in patients with diabetic kidney disease

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Approximately 30% of diabetic subjects have chronic kidney disease (CKD). The choice of anti-diabetic agents in patients with CKD faces special challenges because CKD alters insulin sensitivity and clearance, glucose transport, and metabolism of anti-diabetic agents. CKD is also associated with increased CV and other complications. Inappropriate selection and dosage often aggravate renal dysfunction, cause hypoglycemia, morbidity and mortality, particularly CV diseases. The glycemic goal in CKD still is not defined. The KDOQI 2012 guidelines suggest a goal HbA1C of 7% to delay the progression of CKD. The Dialysis Outcomes and Practice Patterns Study (DOPPS) indicated that mortality increased when HbA1C moved from 7–7.9%. Apparently, the glycemic goal in diabetes with CKD is in this range. To reach this target, it is crucial to evaluate potential side effects of all anti-diabetic agents according to their safety, efficacy, renal metabolism and pharmacokinetics. Based on numerous trials, the dose of these anti-diabetic agents needs to be adjusted in patients with varying stages of CKD. Suggested dose adjustments are:

1. Metformin: Discontinued if eGFR < 30 mL/min, <1,000 mg/day if eGFR 30–45 mL/min/1.73 m^2.
2. Glimepiride, Glyburide (Glibenclamide): avoid use if eGFR <60 mL/min/1.73 m^2.
   Gliclazide: Reduce dose if eGFR <30 mL/min, avoid use if eGFR <15 mL/min/1.73 m^2.
   Glipizide: No dose adjustment required.
3. Repaglinide: Reduce dose if eGFR <30 mL/min; Nateglinide: Caution if eGFR <30 mL/min.
4. Acarbose: Avoid use if eGFR <30 mL/min; Miglitol: Avoid use if eGFR <30 mL/min.
5. Pioglitazone: No dose adjustment required, but caution if CKD, CHF and hypervolemia.
6. Exenatide: Avoid use if eGFR <30 mL/min, reduce dose if eGFR 30–50 mL/min/1.73 m^2.
   Liraglutide: No dose adjustment required if eGFR >30 mL/min/1.73 m^2.
   Lixisenatide: Caution if eGFR <50 mL/min/1.73 m^2.
7. Sitagliptin: 100 mg/day if eGFR >50 mL/min, 50 mg if eGFR 30–50, 25 mg if eGFR <30.
   Saxagliptin: 2.5–5 mg/day if eGFR >50 mL/min, 2.5 mg/day if eGFR <50 mL/min/1.73 m^2.
   Aloglitiptin: 25 mg/day if eGFR >50 mL/min, 12.5 mg if eGFR 30–50 mL/min, and 6.25 mg if eGFR <30 mL/min or ESRD. Linagliptin: No dose adjustment required.
8. Canagliflozin: Reduce dose if eGFR 45–59/min; Empagliflozin: Caution if eGFR <45 mL/min;
   Dapagliflozin: Avoid use if eGFR <60 mL/min/1.73 m^2.
9. Insulin: No dose adjustment if eGFR >50 mL/min, 25% or 50% reduction of total daily dose if eGFR 10–50 mL/min or <10 mL/min/1.73 m^2.

Diabetic Neuropathy: Clinical Update

S21-1
How to approach the patient with diabetic neuropathy – Screening and diagnosis

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Diabetic neuropathy is one of the most frequent neuropathy in clinical practice. The manifestations of diabetic neuropathy are very diverse ranging from focal involvement of carpal tunnel syndrome to systemic sensorimotor polyneuropathy and autonomic neuropathy. Major symptoms of diabetic neuropathy include reduced sensation which may lead to painless injury of the body, neuropathic pain of different characters such as burning or tingling, and veracious autonomic symptoms of gastroparesis, orthostatic hypotension, chronic diarrhea, and sexual dysfunctions etc. Efficient screening and accurate diagnosis of diabetic neuropathy are challenging tasks for clinical practice. Screening instruments include questionnaires and thermal thresholds on quantitative sensory testing which provide the first-line assessments of potential neuropathy. Further confirmation of neuropathy, in particular, degeneration of nerve fibers can be diagnosed with conventional nerve conduction studies for large-diameter nerves. Over the past decade, our group has developed a technique of skin biopsy to examine small-diameter sensory nerves which are responsible for thermal and nociceptive sensations. With a 3 mm punch and special staining on skin biopsy sections, nociceptive nerve fibers could be demonstrated and quantified, i.e. intraepidermal nerve fiber density (Eur J Neurol 17:903–912, 2010). This approach has become the standard for diagnosing small fiber neuropathy. Patients with diabetic neuropathy frequently had different types of neuropathic pain for example burning over the limbs or even the trunk. We tackled this issue by establishing contact heat evoked potential (Diabetes Care 33:2654–2659, 2010) and heat-activated functional magnetic resonance imaging (fMRI) (Hum Brain Mapp 34:2733–2746, 2013). These examinations demonstrated enhanced brain activations due to peripheral nerve degeneration. These assessments provide foundations for prescribing central-acting drugs for neuropathic pain, such as antidepressants and anticonvulsants as documented in various guidelines for neuropathic pain. This talk will focus on the recent advancements in screening and diagnosis of diabetic neuropathy.

S21-2
Current and future strategies for treatment of diabetic neuropathy

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Diabetic neuropathy is the most common complication in diabetic patients. The symptom of diabetic neuropathy may cause various problems in daily life and affect the prognosis of diabetic patients. Therefore, it is important to prevent the development and progression of diabetic neuropathy at an early stage.

It is obvious that the primary cause of diabetic neuropathy is hyperglycemia itself, and previous clinical trials such as DCCT, Kumamoto Study and EDIC Study demonstrated that strict glycemic control could prevent the development and progression of diabetic neuropathy. However, it is difficult to keep normal glucose levels for 24 hours in diabetic patients, especially in type 1 diabetic patients. Short-term hyperglycemia can switch on the pathogenic mechanisms. In addition, therefore, interventions to the pathogenic mechanisms beyond glucose are required.

Various factors such as the metabolic factors, vascular factors, and neurotrophic factors have been proposed to explain the pathogenesis of diabetic neuropathy. Among these factors, the role of metabolic factors has been most extensively investigated. Metabolic factors include polyol pathway hyperactivity, altered protein kinase C activity, increased oxidative stress, and enhanced non-enzymatic glycation. Each metabolic deficit was originally derived from an independent background. However, recent studies have reported close relationships between these abnormalities, and it is now clear that polyol pathway hyperactivity leads to other three metabolic deficits. Based on previous studies, furthermore, polyol pathway hyperactivity plays the major role in the development of diabetic neuropathy. Therefore, from the viewpoint of preventing diabetic neuropathy or treatment of mild diabetic neuropathy, aldose reductase inhibition would be the best therapeutic strategy. However, advanced

neuropathy with established nerve degeneration and capillary occlusion cannot be ameliorated only by aldose reductase inhibition, and further interventions with regenerative medicine would be required.
Previous studies reported that introduction of NGF, HGF or VEGF genes is a useful regenerative therapy of diabetic neuropathy. We reported the usefulness of local injection of basic FGF protein with cross-linked gelatin gel and transplantation of various kinds of progenitor cells such as endothelial progenitor cells (EPCs), mononuclear cells (MNCs), bone marrow-derived mesenchymal stem cells (MSCs), and iPS cell-derived neural crest cells (NCCs) on diabetic neuropathy with diabetic animal models. In addition, we have investigated the possibilities of incretin-related agents to regenerate nerve fibers.
In this session, an overview of current and future strategies for treatment of diabetic neuropathy will be presented.

S21-3
Recent management of diabetic distal symmetric polyneuropathy
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Diabetic peripheral neuropathy is a very common complication of diabetes often associated with considerable morbidity and mortality. It appears relatively early in the disease process. The most common manifestation is a distal symmetric polyneuropathy, but many patterns of nerve impairment can occur. Diabetic neuropathy is not a single entity, but includes several neuropathic syndrome. Autonomic neuropathy may effect almost every system of our body, and once it is well established in the patients with diabetes, it is very difficult to treat for us.
The treatment of diabetic neuropathy is classified to symptomatic- and causal-therapy. Current strategies for the treatment of distal symmetric polyneuropathy are based on the following: ①reduction of risk factors including poor glycemic control, ②treatment based on pathogenetic mechanisms, ③symptomatic treatment for such being neuropathic pain, and ④treatment of diabetic foot, autonomic and other complications. The previous three topics are talked over in my presentation.
There are some differences of risk factors between type1 and type2 diabetes but mostly similar. Major factors are poor glycemic control with age and duration of diabetes but the development of diabetic neuropathy is also partly associated with hypertension, hyperlipidemia, obesity and cigarette smoking. Recently, there are the new appearance of useful drugs for diabetic painful neuropathy such as pregabalin and duloxetine. As the treatment based on pathogenetic mechanisms, many drugs have developed till today. However, unfortunately, most of their clinical trials have failed to show its efficacy. Only epalrestat, an aldose reductase inhibitor and α-lipoic acid, an anti-oxidant are available in clinical use at limited countries.
We need for further experimental and clinical researches to find more effective, novel compounds being able to slow, prevent and/or reverse diabetic neuropathy.

Diabetic Eye Disease: Early Detection, and Treatment

S25-1
Epidemiology of diabetic retinopathy, diabetic macular edema and vision loss due to diabetes
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Diabetes is a major public health problem affecting 415 million people worldwide in 2015 and the number is expected to rise to 642 million by 2040. In 2010, approximately a third of those with diabetes were found to have signs of DR and of these, a further one third were found to have vision-threatening DR, including diabetic macular edema (DME). With the rising prevalence of diabetes (in particular type 2), ageing of the population and increased life expectancy, number of persons with diabetic retinopathy (DR) is also expected to increase substantially. In view of the increasing burden of diabetes and DR, there has been significant global public attention and research in recent years on understanding the epidemiology of diabetes and DR, in an effort to develop long-term strategies to manage this major public health problem. This talk will highlight the recent trends in the epidemiology of DR with a particular focus on the burden, awareness, population differences, risk factors, and screening of DR/DME.

S25-2
The pathogenesis and risk factors of diabetic retinopathy and macular edema
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The understanding of the pathogenesis of diabetic retinopathy is constantly evolving with new research. The major risk factors for diabetic retinopathy include duration of diabetes, hyperglycemia, and hypertension, but these account for only a small amount of the variation in the risk of diabetic retinopathy. Studies have shown that factors such as dyslipidemia, ethnicity, genetics, nephropathy myopia and ocular surgery contribute to the risk. Chronic exposure to hyperglycemia and other known risk factors results in a cascade of biochemical and physiologic changes that ultimately lead to microvascular damage and retinal dysfunction. Implicated pathways include the accumulation of sorbitol and advanced glycation end-products, oxidative stress, protein kinase C activation, inflammation, and upregulation of the renin-angiotensin system and vascular endothelial growth factor.

S25-3
Diabetic eye diseases
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The eye is one of the major organs affected by diabetic mellitus. Structural and functional changes can be seen from the cornea through the crystalline lens to the vitreo-retinal tissues. Diabetic vitreoretinopathy is the most important category related to diabetic eye diseases. The basic pathogenesis of diabetic vitreoretinopathy involves retinal vascular permeability changes and vascular occlusion, which cause macular edema and the development of retinal fibrovascular proliferation through the excessive production of various angiogenic factors. The progression of fibrovascular proliferation may induce vitreous hemorrhage, traction macular elevation and traction retinal detachment, leading to severe bilateral visual loss. In this presentation, clinical manifestations, update treatment strategies and outcome will be briefly reviewed.

Diabetes Foot: Learning from Diabetes Foot Care Program

S31-1
Diabetic foot problems and education programme on the diabetic foot in Western Pacific Region
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The number of diabetic foot lesions and consequently amputations is increasing in the Western Pacific region (WPR). However, there are quite a few foot care specialists such as podiatrists or chiropodists in WPR and there is much ignorance amongst medical staff as to how to identify and educate those at risk and treat those who develop problems. Furthermore, the regional characteristics of diabetic foot, especially the risk factors for amputation and the methods of cost-effective interventions, remain unknown.
In order to combat against this devastating problem, we launched International Diabetes Federation (IDF)-Western Pacific Region (WPR) Diabetic Foot Care Project (IDF-WPR DFC) meeting in 2011 which was succeeded to AASD Diabetic Foot Care Project in 2016. We have invited the doctors and nurses every year from Mongolia, China, the Philippines, Taiwan, Vietnam, Cambodia, Thailand, Malaysia, Singapore, Indonesia, Australia, and Fiji to share the knowledge and expertise in the management of diabetic foot problems. Besides the meetings, we held the practical training course of diabetic foot care for doctors and nurses in Kyoto and Osaka, Japan.
Through IDF-WPR DFC project, we have collected the clinical data of diabetic foot from those countries in order to develop regional clinical guidelines directly applicable to the regional lifestyle.
In my presentation, I would like to introduce the regional problems based on these data.

S31-2

Foot care in diabetes in Australia

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There is evidence that major amputations due to diabetes are reducing in some diabetes high-risk foot care services in Australia, yet diabetes remains the main cause of non-traumatic lower limb amputations domestically and it appears to be relatively underfunded compared with other diabetes complications. Well-established contemporary evidence-based clinical care guidelines in foot care in diabetes exist in national and state-based formats including from leading medical and scientific bodies such as the Australian Diabetes Society and NHMRC Australia. Educational programs in diabetes foot care for patients and for health care professionals have been developed including on-line and these complement the IDF-WPR educational initiatives. Ongoing challenges remain in broadly geographically mapping high risk foot care services in diabetes in Australia, in defining optimal local health care pathways for patients with foot problems who have varying risk and needs and are managed in mixed public and private health care systems, in accreditation and credentialing diabetes high risk foot care services, and in developing a national database plus collaborative sites for multicentre studies. This presentation will address some current key data, progress being made, and challenges to come, in this country, which has a well-developed health care system yet where demands in delivery of care by geographical size including the need for rural and regional care, add complexity. Some of the vehicles to aid realizing systematised delivery of foot health care in diabetes will be highlighted, including bodies such as the National Association of Diabetes Centres, Diabetes Australia, stratified care and online health pathways, multi-disciplinary organisational input, and telemedicine. Finally, some novel multicentre studies in diabetes high risk foot care will also be addressed. It is planned that this presentation will support a blueprint for equity of access to quality care in all aspects of diabetes foot care, including in aiding leadership across the region.

S31-3

From multidisciplinary care for limb-threatening diabetic foot ulcers in a university hospital to the ongoing diabetic foot working group in Taiwan

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Diabetic foot ulcers are the leading cause of non-traumatic amputation. According to a nationwide cohort study in Taiwan, approximately 4,500 diabetic patients undergo lower-extremity amputations annually. The aim of this study was to share 30 years of experience of multidisciplinary care for patients with diabetic foot ulcers in Chang Gung Memorial Hospital, and discuss difficulties in cooperation between departments in real-world practice. We also summarize the characteristics, classification, treatment strategies and outcomes of our patients with diabetic foot ulcers, and review studies of factors associated with lower-extremity amputations, in-hospital complications, and long-term survival. We use data on diabetic foot ulcers from the national health insurance claims database to examine trends in foot ulcers in Taiwan. In addition, we present data from the ongoing diabetic foot working group of the Diabetes Association in Taiwan with regards to improvements in limb preservation, not only in treatment but also prevention.

Pancreas Transplantation

S09-1

Pancreas transplantation in Korea

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Background: Diabetes mellitus has been treated with oral diabetic drug and/or insulin. However the increased morbidity and mortality even under insulin treatment is largely attributable to the diabetic complications that occur over time. Pancreas transplantation (PT) is an ultimate treatment of insulin requiring diabetes. Currently much improvement in patient and graft survival, and decrease of post-operative morbidity have been brought by technical refinement, better immunosuppressants, and better post-operative management. We hereby report the outcomes of PT performed in Korea.
Methods: All the recipients who underwent deceased donor or living donor PT from July 1992 to December 2015 in Korea were enrolled in this study. We reviewed retrospectively. We analyzed graft and patient survival with Kaplan-Meier method.
Results: Totally 475 cases of pancreas transplantation have been performed from July 1992 to December 2015 at 14 transplant centers in Korea. Indication for pancreas transplantation was type I diabetes in 399 (84%) patients and type II diabetes in 76 (16%) patients. Pancreas donor was deceased donor in 453 cases (95.6%) and living donor in 22 cases (4.6%). Type of transplantation was simultaneous pancreas kidney transplantation in 294 recipients (61.9%), pancreas transplantation alone in 126 (26.5%), and pancreas after kidney transplantation in 55 (11.6%). Median follow-up duration was 108.0 months post-transplantation (range 0–281 months). Overall patient survival rates at 1, 5 and 10 years were 95.3%, 91.3%, and 87.8%. Overall graft survival rates at 1, 5, and 10 years were 87.4%, 77.3%, and 67.6% respectively. Since 2000, Overall graft survival rates at 1, 5 and 10 years were 93.8%, 87.7%, and 85.9% respectively.
Conclusion: Recently graft outcomes have been improved and post-operative morbidity decreased. Considering the quality of life and long-term patient survival, PT can be an effective

treatment strategy in non-obese diabetic patients requiring insulin regardless of type of diabetes.

S09-3

Pancreas transplant – Taipei Veterans General Hospital experience

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Type 1 diabetes eventually leads to nephropathy, neuropathy, retinopathy and angiopathy after 10–30 years. Currently, pancreas transplant is the treatment of choice in tight control of blood sugar for IDDM patients, and further to stabilize, prevent or even to reverse the diabetic complications.

We will present our experience in pancreas transplant which was initiated on September 19, 2003. From September 2003 to June 2016, there were 126 pancreas transplants performed for 120 patients at Taipei Veterans General Hospital, with 36 SPK, 15 PAK, 57 PTA and 18 PBK. Most (78.5%) of our pancreas transplants were for IDDM patients. The blood sugar usually returned to normal level within 5 hours (median) after revascularization of the pancreas grafts. The fasting blood sugar maintained within normal range thereafter throughout the whole clinical course in most cases. There were 2 surgical mortality. The technical success rate was 96%. Excluding the 4 cases with technique failure, overall 1-year pancreas graft survival is 98.5% and 5-year is 94.1%, with 100% 1-year for SPK, 97.1% 1-year for PTA, 100% 1-year for PAK and 100% 1-year for PBK.

In conclusion, pancreas transplant provided an ideal insulin-free solution for IDDM and selected NIDDM. Pancreas transplant could be performed with similar successful rate irrespective of the type of pancreas transplant at our hospital.

Islet Transplantation

S16-1

Current status of clinical islet transplantation

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Islet transplantation is a promising therapy for patients with type 1 diabetes and severe hypoglycemia. Several studies have shown that high levels of insulin independence and good control of hypoglycemia can be achieved in the short term. However, long term results are not as good and five year insulin independence rates although improving show progressive loss of function over time. In two recent multicenter trials – one in North America and one in Australia- similar results were achieved. Approximately 85% of patient achieved the primary end point of HbA1c <7.0% and absence of hypoglycemia in presence of detectable c-peptide. With multiple transplants approximately 60% were insulin independent. Over time there was a progressive deterioration in function. In the North American study graft function had dropped from 87% to 72% by 24 months. Whereas, in the Australian study, graft survival was 64% at 5 years after transplantation. Patients with acceptable graft function have a remarkable improvement in their diabetic control and complete resolution of difficult to control hypoglycemia. As a result there is a profound improvement in quality of life and many recipients are able to return to work. Islet transplantation does come with its own problems particularly regarding complications and tolerability of immunosuppression. In a study where continuous insulin infusion (CSII) was compared with islet transplantation for severe repeated hypoglycemia the data suggested that in subjects with severe hypoglycemia, CSII was an appropriate therapy, which substantially reduced the frequency and severity of hypoglycemia but did not remove the need for islet transplantation in the majority of individuals. CSII reduced duration of time with blood glucose <4 mmol/L and significantly improved glycemic variation as compared with MDI, the latter potentially accounting for reduced frequency of severe hypoglycemia. However, islet transplantation eliminated hypoglycemia regardless of whether insulin independence was achieved. Frequency, severity and risk of hypoglycemia as measured by, respectively, CGM percentage of time in hypoglycemia, HYPOscore, and glycemic variability at 12 months post islet transplantation all returned to levels as good as, or better than, those reported in type 1 diabetes without problems with hypoglycemia. Transplantation reduced HbA1c and mean glucose at 12 months, benefits that were not seen with changing to CSII. The study provided further evidence that in appropriately selected patients with severe hypoglycemia with large glycemic variability, islet transplantation provides superior glycemic control and reduction in hypoglycemia over and above that achieved with CSII.

S16-2

Clinical islet transplantation from allogeneic toward xenogeneic

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In 2014, opinion leaders of beta cell replacement therapy discussed the current status and future of the therapy at the Oxford University. At the meeting, it was revealed that approximately one-eighth of type 1 diabetic patients with prolonged diabetic history (>20 years) suffered unaware hypoglycemia and 7–10% of cause of death of type 1 diabetes was hypoglycemia. Beta-cell replacement therapy including pancreas and islet transplantation is the best treatment for preventing severe hypoglycemia, however due to donor shortage, only at most only 0.1% of type 1 diabetic patients can receive beta-cell replacement therapy. Donor shortage is the most serious issue.

To alleviate donor shortage, we have conducted islet transplantation using non-heart beating donor, living donor islet transplantation and improving the efficacy of islet transplantation. However, none of them can solve the issue of donor shortage.

Establishment of islet transplantation using non-human pancreas donor (bio-artificial islet transplantation) can solve the donor shortage issue. Three major resources of islets for bio-artificial islets are porcine islet, ES cell derived islet and iPS cell derived islets. Among them porcine islets have several advantages including previous clinical experiences, clean and healthy islets from healthy designated pathogen free donor, possible gene modification to improve clinical outcomes.

Encapsulated neonatal porcine islet transplantation has been conducted under comprehensive New Zealand regulation. The study had four different dose groups: 5,000 IE/kg (n = 4), 10,000 IE/kg (n = 4), 15,000 IE/kg (n = 4), and 20,000 IE/kg (n = 2). There were four serious adverse events related to the procedure, which were resolved without residual effects. Tests for PERV DNA and RNA were negative in the blood of all patients. In terms of efficacy, the number of episodes of unaware hypoglycemia was reduced 1 year after transplantation in all dose groups.

To improve the clinical outcome, the Ricordi isolation method and injection of ETK solution into pancreata were introduced, which resulted in a high islet yield (approximately 180,000 IE/piglet). Next clinical trial was performed in Argentina. Subanalysis of the efficacy dataset demonstrated that when a dose of 10,000 IE/kg was transplanted twice, HbA1c levels <7% for more than 2 years, with a significant reduction of in the number of episodes of unaware hypoglycemia.

Xenogeneic islet transplantation can be a viable option for unstable type 1 diabetes, and the next research target should be curing type 1 diabetes with xenogeneic islet transplantation.

S16-3
Clinical islet autotransplantation: Beyond simple replacement of islet cell mass
Kwang-Won KIM[1]. [1]*Gachon University Gil Medical Center, Incheon, Korea*

Islet autotransplantation (IAT) is performed when the pancreas is removed for treatment of benign pancreatic diseases. In chronic pancreatitis with intractable abdominal pain, IAT after total pancreatectomy has been proven to reduce abdominal pain by total pancreatectomy while avoiding brittle diabetes. In contrast to the islet allotransplantation, IAT is not vulnerable to immune rejection, recurrent autoimmunity, or beta-cell toxicity of immunosuppressants. For this reason, IAT represents the maximum functional potential of transplanted islets, with some reported cases of unexpected insulin independence in low-dose autologous islet transplants.
Besides the proven efficacy of IAT in intractable chronic pancreatitis, we have examined the efficacy of IAT after partial pancreatectomy for treatment of benign tumor. We reported the outcome of the 20 patients who underwent IAT after 50% to 60% partial pancreatectomy in this clinical setting. Although the 7-year diabetes-free survival rate was not different between control and IAT groups, prolonged diabetes-free survival was observed in patients who underwent IAT when a high islet yield (>5,154 islet equivalents per gram of pancreas) during the islet isolation was achieved. The islet yield and islet function in this clinical setting was superior to those of allogeneic islet transplantation. In addition, we have shown that transplanted islets can promote the regeneration of endogenous beta-cells and differentiation of adult stem cells into beta-cells in experimental models of IAT after partial pancreatectomy.
In conclusion, IAT after partial pancreatectomy for benign tumors could be a promising indication of IAT. IAT in this setting may improve the metabolic milieu after the pancreatic resection, and is a unique opportunity for understanding the biologic effect of intraportal islet transplantation beyond the simple replacement of islet cell mass.

Stem Cell Therapy

S22-1
Expandable human pancreatic progenitor cells – a novel inroad toward the production of β cells
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Type 1 diabetes (T1D) results from the autoimmune destruction of pancreatic β cells that secrete insulin. One potential cell-based therapy for this chronic disease is the production of functional β cells from the directed differentiation of human pluripotent stem cells. Such *in vitro* derived β cells would then be transplanted into T1D patients to liberate them from lifelong insulin dependency. To this end, several reports emerged over the last year that detail more efficient differentiation protocols that yield ~35% insulin-containing β cells after at least four weeks of *in vitro* differentiation. Importantly, these β-like cells were able to restore normoglycemia in rodent models of T1D. Although an improvement over previous methods, undesirable polyhormonal cells (~15%) and hormone-negative cells (~50%) were consistently produced alongside β-like cells. Furthermore, differentiation output varied considerably depending on the human embryonic stem cell (hESC) or human induced pluripotent stem cell (hiPSC) line used. We reason that one way to address both the limits of efficiency and reproducibility from line-to-line is to develop tools to capture and stably expand stage-specific, multipotent β-cell progenitors. Pure populations of these self-renewing progenitors would then allow for further, and we propose, more homogeneous differentiation toward the insulin-secreting β cell. This strategy eliminates the need (and significant cost) of sequentially differentiating hESC or hiPSC from pluripotent cell type, to mesendoderm, to definitive endoderm, to gut endoderm and finally to pancreatic endoderm. We have thus developed conditions for culturing hPSC-derived multipotent pancreatic progenitors, which are capable of long-term expansion and are much closer developmentally to β cells. These "ePP" cells express markers characteristic of endogenous human pancreatic progenitors, including the key transcription factors PDX1 and SOX9. Exposure to differentiation cues induces upregulation of markers of the exocrine, endocrine and ductal pancreatic lineages indicating multi lineage potency. Their ability to further differentiate into β cells is currently being evaluated *in vitro* and *in vivo* in immunodeficient mice.

S22-2
Generation of insulin-producing β-like cells from human iPS cells
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ES cells and iPS cells are considered to be potential alternative cell sources for the transplantation therapy as well as cell models for biological studies. Up to date, studies to generate the pancreatic beta cells from pluripotent stem cells have achieved remarkable progresses. However, it still remain elusive whether the derived pancreatic beta cells resemble the human beta cells and could be used in clinical settings.
We have been trying to establish culture systems to generate insulin-producing beta cells using mouse and human ES/iPS cells. In an attempt to search for novel molecules that promote differentiation and/or proliferation of pancreatic beta-cells, we established a screening system, and screened a chemical library consisting of low molecular bioactive chemical compounds of which the pharmaceutical actions are already known. Through studies on revealing the targets of the chemical compounds, we identified molecules that function in regulating pancreatic beta cell differentiation. We also extend the chemical screening using mouse mature islets, to identify molecules that regulate beta cell mass.
Besides chemical screening, we also analyzed the importance of amino acids in the media. We found that methionine metabolism is crucial for the maintenance of pluripotency in human pluripotent cells. Deprival of methionine rendered the cells at a poised state for differentiation, and thus increased the efficiency for differentiation. The details will be discussed at the meeting.

S22-3
Autologous hematopoietic stem cell transplantation in type 1 diabetes
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Type 1 diabetes (T1DM) is an autoimmune disease resulted from T cell-mediated destruction of insulin-producing pancreatic β-cells. Therapies aiming at block of T cell autoimmunity and preservation of the remaining β-cell function are of great significance in managing T1DM. Hematopoietic stem cells (HSCs) are multipotent stem cells residing in the bone marrow. Voltarelli JC et al. were the first in the world to apply

immunosuppression followed by autologous nonmyeloablative hematopoietic stem cell transplantation (AHST) in new-onset T1DM, which resulted in exogenous insulin independence for adequate glycemic control. However, patients with previous diabetic ketoacidosis (DKA), which is frequently occurred in Chinese T1DM patients, were excluded in this study. Besides, mechanisms underlying AHST-induced reconstitution of immune system was not clear. Thus, in 2006, we initiated the first trial in China to examine the therapeutic effect and mechanisms of AHST in Chinese T1DM.

From 2006 to 2008, 13 new-onset T1DM, 10 of them with DKA, were subjected to nonmyeloablative AHST. Eleven patients required significantly reduced doses of insulin, accompanied by decreased HbA1c and increased C-peptide concentrations. Three patients achieved insulin independence for 7–54 months, two of whom presented DKA at onset. The immune system was reconstituted after AHST as characterized by the decreased numbers of different subsets of lymphocytes within 3–6 months, and the gradually increased numbers thereafter. Moreover, pro-inflammatory cytokines were significantly reduced, while the levels of IL-4, IL-10 and TGF-β remained unchanged or increased, indicating a reconstituted anti-inflammatory environment. In parallel, β-cell antigen-specific humoral responses was attenuated after AHST, as proved by the decreased levels of serum islet autoantibodies. To further determine the effect of DKA on the efficacy of AHST in T1DM, 28 patients (11 presented DKA) who received AHST in our and the other Chinese center were analyzed, we finally proved that AHST achieved a greater efficacy in patients without DKA. In 2014, D'Addio et al. made a multi-center analysis by pooling data of 65 patients together from two Chinese centers and one Polish center. It showed that 59% achieved insulin independence within 6 months after AHST, 32% remained insulin independent till 48 months, but 52% of treated individuals experienced adverse effects.

Nonmyeloablative AHST represents an effective treatment for selected T1DM patients. Potential mechanisms include elimination of a pro-inflammatory immune system, generation of a new adaptive immune system, and stimulation of the regeneration of islet β-cells. However, the long-term effects and safety of AHST remains to be validated, and safer HSC-based therapeutic options are required.

S22-4

Amelioration of type 1 diabetes using direct hepatocyte reprogramming approaches

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Type 1 diabetes mellitus is characterized by complete loss of β-cells due to T-cell mediated autoimmune attack leading to a deficiency of insulin. Transplantation of islets isolated from the cadaveric donor pancreas has proved to be an effective treatment for patients with type 1 diabetes mellitus. However, this transplantation therapy is severely limited by the lack of islet donors. Moreover, patients received the allogeneic islet transplantation were still suffering from side effects of the immunosuppressive medications. Hence, the possibility of producing immune-tolerable β-cells would be a key challenge for developing cell-based therapeutics for type 1 diabetic patients. We and others had previously demonstrated hepatocytes can be transdifferentiated to insulin-producing β-cells after introducing Pdx1. Our recent findings further revealed PDGF facilitates direct lineage reprogramming of hepatocytes to functional β-like cells induced by Pdx1 and Ngn3. However, it is unclear whether these transdifferentiated β-cells are glucose responsive and immune-tolerable in autoimmune diabetic status.

The liver not only has remarkable capacities to regenerate after injury, but also an immune privileged organ. We therefore hypothesize β-cells derived from hepatocyte reprograming may possess characteristics for avoiding attack from autoreactive immune cells. In current work, we performed direct conversion approaches by introducing three transcriptional factors to primary hepatocytes isolated from Non-obese diabetic (NOD) mice which spontaneously develop autoimmune diabetes. We demonstrated that simultaneously expressing Pdx1, Ngn3, and PDGFRα could induce direct reprogramming of hepatocytes of NOD mice to insulin-producing cells display characteristics of pancreatic β-cells including expression of *mafa*, *nkx2.2*, *rfx6*, *kir6.2*, *glut2* and *proprotein convertase 1/3* and possessing the capability to secrete insulin responding to stimulatory levels of glucose. Autologous transplantation of hepatocyte-derived β-like cells to diabetic NOD mice significantly improved hyperglycemic status without needs of tolerogenic treatments. Further characterization demonstrated that β-like cells derived from hepatocyte reprogramming displayed reduced levels of MHC class I molecules and autoantigens such as *gad65* and *iapp* and also expressed PD-L1 and PD-L2. The results explain why hepatocyte-derived β-like cells were immune-tolerable. The findings from the present work raises the possibility of developing cell therapeutic strategy for patients with type 1 diabetes via autologous hepatocyte reprogramming.

Islet Imaging

S26-1

Non-invasive pancreatic beta-cell imaging using radiolabeled exendin probe

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Impaired insulin secretion due to beta-cell dysfunction or death as well as insulin resistance are main factors in the pathophysiology of diabetes. Measurement of beta-cell mass (BCM) is currently possible only by histological examination using pancreas tissue specimens and no non-invasive method is available for determining BCM *in vivo*. Accurate measurement of BCM could provide important information on the pathophysiology of the disease and lead to novel classifications and treatment. We have been trying to develop a non-invasive probe to enable evaluation of BCM using radiolabeled exendin targeting glucagon like peptide-1 receptors (GLP-1R) expressed on beta-cells.

In this study, we investigated whether the BCM can be quantified non-invasively by positron emission tomography (PET) or single-photon emission computed tomography (SPECT) targeting GLP-1R. We synthesized [^{18}F]-labeled, [^{123}I]-labeled, and [^{111}In]-labeled exendin for PET and SPECT imaging. These probes were evaluated by binding affinity assay, autoradiography, biodistribution, and PET or SPECT imaging. The probes were accumulated in murine islets and bound to GLP-1R specifically. PET or SPECT imaging of mice injected with these probes revealed remarkable accumulation of radioactivity in pancreas. We then used diabetic model mice such as streptozotosin-injected mice and NOD mice to

compare radiolabeled probe accumulation with other, conventional methods for quantification of BCM. In this symposium, I present our up-to-date data on this non-invasive method of evaluation of beta-cell mass.

S26-2

Magnetic resonance imaging of islet grafts

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The development of islet imaging techniques can improve the diagnosis and characterization of diabetes mellitus. Recently, noninvasive magnetic resonance imaging (MRI) has been used to monitor the mass, function, death, vascularity, innervation, autoimmune activation and infiltration of endogenous and grafted islets in animals and humans.

Although islet transplantation is a promising approach, substantial graft loss can occur owing to allorejection, autoimmune attack, glucotoxicity, mechanical stress and microenvironmental disruption of the islets during transplantation. The use of MRI to assess transplanted islets can help to optimize transplantation protocols, explore the anatomy and physiology of transplanted islets and study the immunology of islet engraftment. In the past years, MRI has been used to detect transplanted islets labeled with dextran-coated superparamagnetic iron oxide (SPIO), such as ferumoxide (Feridex®, Endorem™) and ferucarbotran (Resovist®) in mice, rats, baboons, nonhuman primates, and humans. In 2010, Saudek et al. first reported MR detection of ferucarbotran-labeled islets up to 24 weeks in the liver of 8 C-peptide negative diabetic recipients.

Recently, we developed an in situ coating method for preparing ferrofluids coated with γ-ray irradiated chitosan and proved that the chitosan-coated SPIO (CSPIO) nanoparticles have potential as an MR T2 contrast agent. In addition, we demonstrated that CSPIO nanoparticles were taken up by islets in vitro, did not affect insulin secretion and death rates of islets, and could be visualized by MR imaging for long-term tracking of mouse islet isografts and allografts.

In conclusion, MRI represents a valuable platform for a thorough investigation of transplanted islets. In the future, repeated systemic administration of β-cell specific agents to islet recipients and multimodality approaches, such as PET–MRI, would enable the method to be used in a wide variety of diagnostic and therapeutic applications in diabetes.

Orally Administered Antidiabetic Agents

S11-3

Multifunctional nanoparticles for oral protein drug delivery

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Calcium (Ca^{2+}) has a crucial role in maintaining the intestinal protease activity and in forming the apical junctional complex (AJC) that preserves epithelial barrier function. Ethylene glycol tetraacetic acid (EGTA) is a Ca^{2+}-specific chelating agent. To maintain the concentration of this chelator in areas where enzyme inhibition and paracellular permeation enhancement are needed, this study synthesized a poly(γ-glutamic acid)-EGTA conjugate (γPGA-EGTA) to form nanoparticles (NPs) with chitosan (CS) for oral insulin delivery. Results of our molecular dynamic (MD) simulations indicate that Ca^{2+} ions could be specifically chelated to the nitrogen atoms, ether oxygen atoms, and carboxylate oxygen atoms in $[Ca(EGTA)]^{2-}$ anions. By chelating Ca^{2+}, γPGA-EGTA conferred a significant insulin protection effect against proteases in intestinal tracts isolated from rats. Additionally, calcium depletion by γPGA-EGTA could stimulate the endocytosis of AJC components in Caco-2 cell monolayers, which led to a reversible opening of AJCs and thus increased their paracellular permeability. Single-photon emission computed tomography images performed in the biodistribution study clearly show the ^{123}I-insulin orally delivered by CS/γPGA-EGTA NPs in the heart, aorta, renal cortex, renal pelvis and liver, which ultimately produced a significant and prolonged hypoglycemic effect in diabetic rats. The above results confirm that this γPGA-EGTA conjugate is a promising candidate for oral insulin delivery.

Injectable Antidiabetic Agents (I): GLP-1 Receptor Agonists

S18-1

Pleiotropic actions of GLP-1 RA

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Glucagon-like peptide 1 (GLP-1) is an incretin hormone secreted primarily from the intestinal L-cells in response to meals which modulates nutrient homeostasis via actions exerted in mutliple tissues and cell types. GLP-1 and its analogs, as well as compounds that inhibit endogenous GLP-1 breakdown, have become an effective therapeutic strategy for many subjects with type 2 diabetes. Considering the wide distribution of the GLP-1 receptor, it is perhaps unsurprising the GLP-1 exerts pleiotropic effects beyond glucose lowering. These include appetite regulation, inhibition of gastric acid secretion and gastric emptying, regulation of hepatic glucose production, regulation of cardiac function and bone resorption, and cardiovascular effects. In this lecture, I will review pancreatic and extrapancreatic effects of GLP-1.

S18-2

Incretin-based therapy on diabetic nephropathy

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Incretin-based anti-hyperglycemic drugs, DPP-4 inhibitors and GLP-1 receptor agonists, are widely used for treatment of type 2 diabetes. Incretin was originally designated as a gut-derived insulinotropic factor. Because receptors of incretin are expressed not only in pancreatic β-cells but also in extra-pancreatic tissues(1), extra-pancreatic effects in addition to pancreatic effects are expected. Furthermore, DPP-4 can inactivate several peptide hormones in addition to incretin, “incretin” and “beyond incretin” effects are also expected.

We have shown that GLP-1 receptors are expressed in glomerular capillary and vascular walls, but not in tubuli, in the mouse kidney. C57BL/6-Akita mice are diabetic and nephropathy-resistant. We have generated C57BL/6 Akita GLP-1 receptor-deficient mice and revealed that these mice have higher urinary albumin levels and more advanced meangial expansion than C57BL/6-Akita mice, despite comparable levels of hyperglycemia. KKTa-Akita mice are diabetic and nephropathy-prone and treatment of these mice with

liraglutide, a GLP-1 receptor agonist, suppressed the progression of nephropathy. These results indicated that GLP-1 has a crucial role in protection against diabetic nephtropathy(2).
We have next examined the effects of linagliptin, a DPP-4 inhibitor, on KKTa-Akita mice. Linagliptin treatment increased urinary sodium excretion, in addition to suppression of albuminuria. Increased urinary sodium excretion was still observed in GLP-1 receptor-deficient KKTa-Akita mice but not observed in liraglutide-treated KKTa-Akita mice, indicating that increased urinary sodium excretion is GLP-1-independent. SDF-1 expression was increased in glomerular podocytes and distal nephrons in diabetic mice and linagliptin further augmented renal SDF-1 expression. As treatment with SDF-1 receptor antagonists with KKTa-Akita mice reduced urinary sodium excretion, DPP-4 inhibition, independent of GLP-1 receptor signaling, contributes to protection of the diabetic nephropathy through SDF-1-dependent amelioration of renal hemodynamics(3).

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S18-4
GLP-1 receptor agonists and cardiovascular safety
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Clinical treatment with glucagon-like peptide-1 receptor agonists has shown benefits in weight reduction, blood pressure lowering, improving dyslipidemia and cardiovascular surrogate biomarkers. Nevertheless, long-term cardiovascular outcome trials (CVOT) for three DPP4-inhibitors (the SAVOR-TIMI53, EXAMINE, and TECOS trials) all showed non-inferior results for major adverse cardiovascular events (MACE) compared to standard treatment. Moreover, a slight increase in the risk of heart failure was observed in the SAVOR-TIMI53 trial, raising concerns of cardiovascular safety in incretin-based therapy. More recently, two CVOTs of GLP-1 receptors have been reported. The ELIXA trial showed non-inferior results, while the LEADER trial demonstrated beneficial cardiovascular effects. Compared to the EMPA-REG trial in which reductions were found in cardiovascular mortality and heart failure, the LEADER trial reported that liraglutide treatment significantly reduced both cardiovascular mortality and the risk of MACEs. In this talk, we review the published trials in detail and examine the findings related to cardiovascular safety and treatment efficacy.

Injectable Antidiabetic Agents (II): Insulin

S28-2
New developments in basal insulin therapies
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Diabetes mellitus is a growing epidemic worldwide. Insulin therapy has been used for nearly a century now, saving the lives and improving the care of millions of patients. Insulin therapy has undergone significant evolution over the years attempting to mimic normal physiology and accommodate to the normal daily routine of our patients. The long-acting insulin analogs glargine and detemir showed lower variability and longer duration of action compared to the earlier NPH insulin and can be administered only once a day. Novel ultra-long acting basal insulins introduced to the market in recent years further enhanced these benefits due to their even longer half-life. Insulin degludec forms hexamers and di-hexamers in the subcutaneous tissue resulting in a depot from which the monomers are slowly released. Clinical studies in patients with type 1 and type 2 diabetes demonstrated similar reductions in HbA1c with degludec vs. glargine with lower rates of nocturnal hypoglycemia. Insulin glargine U-300 forms a subcutaneous depot with a smaller surface area compared to insulin glargine U-100 creating a prolonged release and a flatter PK/PD profile. Similar HbA1c reduction and lower rates of hypoglycemia were observed with the use of glargine U-300 compared to glargine U-100 in patients with type 1 and type 2 diabetes. PEGylation of insulin lispro resulted in a prolonged half-life of insulin as well, yet due to concerns regarding its liver safety and local lipohypertrophy and lipodistrophy, further development of this compound was terminated. Insulin formulations remain a major topic of research and development including combinations of ultra-long acting basal insulin with short acting insulin, as well as with GLP-1 receptor agonists recently launched. Novel methods of further enhancing insulin action, or creating "smart" glucose-responsive insulins are being explored and hopefully the future will hold better, safer and more efficient methods of insulin treatment.

S28-3
New era in insulin therapy: the ultra-fast acting insulins
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Insulin had its evolution throughout the years since its discovery in 1921. The introduction of insulin analogs allowed flexibility with before meal time insulin injections and improved after meal blood sugars. Despite the advances in the field of insulin therapy, the rapid acting insulin analogs are not fast enough to control after meal blood sugars. Moreover, the prolonged and late effects of rapid acting insulins lead to the undesirable late hypoglycemic episodes hours after an insulin bolus. The late and slow insulin action remain important obstacles for achieving a fully automated artificial pancreas systems. If the ultimate goal of developing insulin analogs is to recapitulate the physiologic pattern of insulin secretion and action from a healthy beta cell, it is fair to say that the evolution of insulin is not complete yet. Advances in newer insulin formulations with improved pharmacokinetics (PK) and pharmacodynamics (PD) will galvanize artificial pancreas insulin therapy system research and overcome challenges in daily management of diabetes to restore near-physiologic glycemic control. This talk will summarize implications of slow action of insulin analogs and highlight the results of key studies on new generation ultra-fast acting insulins, innovative insulin delivery devices and their impact on the artificial pancreas systems.

S28-4
Development of glucose-responsive "smart" insulin
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The development of exogenous insulin to treat diabetes has dramatically improved overall patient survival for people with diabetes. However, although currently available insulin analogs reduce blood glucose levels, this blood glucose lowering action is not regulated in a glucose dependent fashion. Insulin analogs can cause severe hypoglycemia and remain bioactive even in low glucose levels. Thus, hypoglycemia is the rate-limiting step in the insulin therapy. To reduce the risk of hypoglycemia, a glucose-responsive insulin (GRI) analog is needed that is active when blood glucose levels are high, yet is inactivated when blood glucose levels start to decline. Such a "smart insulin" will eliminate the barrier of hypoglycemia for insulin-treated people with diabetes. We developed a novel GRI through manipulation of the C-terminus of the insulin

B-chain with a phenylboronic acid (PBA), a chemical group known to bind to glucose. Lead candidates were further evaluated in mouse models of diabetes. This approach has several advantages over previous approaches to develop GRI. First, the binding between PBA and glucose has a fast binding profile, which is needed for fast responses to elevated blood glucose. Second, PBA-containing insulin analogs could achieve glucose-responsive behaviors without the injection of foreign biomaterials and their associated risk of immunogenicity. Furthermore, the circulating insulin analogs could be inactivated at low blood glucose levels, which reduce the risks of hypoglycemia. This promising strategy may lead to major breakthroughs and represents a truly novel paradigm shift in the treatment of diabetes.

Closed-Loop System and CGM

S33-1

The use of closed loop in outpatient/home studies

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Type 1 diabetes is one of the most common endocrine problems in childhood and adolescence persisting into adulthood and remains a serious chronic disorder with increased morbidity, mortality and reduced quality of life. Research over past decades showed that good blood glucose control dramatically lowers the risk of serious diabetes complications. Yet, studies reveals that even the best controlled patients spend less than 50 percent of their day within the normal blood glucose range, especially overnight, when patients are most vulnerable to episodes of low glucose levels.

Continuous glucose monitoring devices and insulin pumps can be combined to form a closed loop apparatus, also known as the Artificial Pancreas, an emerging medical device which may transform management of type 1 diabetes. This promising approach differs from conventional insulin pump therapy through the use of a control algorithm which directs subcutaneous insulin delivery according to sensor glucose levels. Closed-loop prototypes have been tested extensively under controlled laboratory conditions in youth, adults and in pregnancy demonstrating reduced risk hypoglycaemia and increased time in target glucose range. Pioneering transitional and home studies have been performed to demonstrate benefits in target settings. Exercise and meal consumption present particular challenges owning to rapid changes in glucose excursions and may require user involvement, co-administration of hormone counteracting insulin action or faster insulin analogues. Focused academia-industry collaboration is required to exploit closed-loop technologies, to bridge gaps, and to accelerate transition to clinical practice. Scalability, low biological risk and innovation potential are the main appeal.

S33-2

Redefining diabetes management by technology in children with diabetes: from insulin pumps and continuous glucose monitors to the artificial pancreas system

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The incorporation of new technology into diabetes treatment provided diabetologists with additional tools such as glucose sensors, smart insulin pumps, and the promise of closed loop insulin therapy (a.k.a the artificial pancreas project), a mechanical solution for diabetes management to restore near-physiologic glycemic control automatically. Such a system consists of three main elements: insulin delivery, continuous glucose sensing, and a controller or algorithm that, similar to the beta cell, regulates the proper amount of insulin delivery at the proper time. The continuous glucose monitor (CGM) technology allowed real time glucose monitoring, detection of patterns and determination of rapid drop or rise in glucose levels with continuous stream of data. The integration of the CGM in to the insulin pump therapy introduced the sensor augmented pump therapy (SAP). While the benefit of CGM and SAP use to lower HbA1c levels has been clearly shown in adults with diabetes, it has been challenging to achieve the same success with children and adolescents. This talk will provide finer details of the CGM technology and summarize results of the key studies regarding CGM and SAP use in children and adolescents with diabetes. We will discuss unique limitations of CGM and SAP use in the pediatric population and potential solutions to overcome these challenges. The CGM and SAP technology of the near future with new models that are in the pipeline and new developments in the artificial pancreas system research will be presented.

Obesity and Diabetes

S13-1

Roles for adipose ceramides in metabolic homeostasis

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Adipocytes package incoming fatty acids into triglycerides and other glycerolipids, with only a fraction spilling into a parallel biosynthetic pathway that produces sphingolipids. During obesity, the excessive entry of lipid into this pathway leads to the aberrant accumulation of biosynthetic intermediates such as ceramides that impair tissue metabolism and function. Notably, genetic or pharmacological inhibition of enzymes that drive ceramide synthesis (e.g. serine palmitoyltransferase, dihydroceramides desaturase, etc.) in mice ameliorates virtually all complications of obesity including insulin resistance, steatosis, diabetes, hypertension, cardiomyopathy, and atherosclerosis. To dissect the tissue-specific roles for ceramides in nutrient homeostasis, we have produced mice lacking serine palmitoyltransferase, the rate-limiting enzyme in the ceramide biosynthesis cascade, in various body locales. Using these mice, we determined that newly-synthesized adipocyte sphingolipids drive profound changes in the adipose phenotype to influence whole-body energy expenditure and nutrient metabolism.

S13-2

Roles of G6PD in ROS and inflammatory responses of obese adipose tissue

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Glucose-6-phosphate dehydrogenase (G6PD), a rate-limiting enzyme of the pentose phosphate pathway, plays important roles in redox regulation along with *de novo* lipogenesis. Recently, it has been demonstrated that abnormal increase of G6PD in obese adipose tissue mediates insulin resistance due to imbalanced energy metabolism and oxidative stress. However, it remains elusive whether the G6PD deficiency *in vivo* may relieve obesity-induced insulin resistance. In this study, we have shown that hematopoietic G6PD defect alleviates insulin resistance in obesity, accompanied with reduced adipose tissue inflammation. Compared to WT littermates, G6PD-deficient mutant ($G6PD^{mut}$) mice were glucose tolerant

upon high fat diet (HFD) feeding. Intriguingly, the expression of NADPH oxidase genes to produce ROS was alleviated whereas that of anti-oxidant genes was enhanced in adipose tissue from HFD-fed G6PD^{mut} mice. In diet-induced obesity (DIO), adipose tissue of G6PD^{mut} mice decreased expression of inflammatory cytokines, accompanied with down-regulated pro-inflammatory macrophages. In accordance with these, macrophages from G6PD^{mut} mice greatly suppressed LPS-induced pro-inflammatory signaling cascades, leading to enhance insulin sensitivity in adipocytes and hepatocytes. Furthermore, adoptive transfer of G6PD^{mut} bone marrow into wild type mice attenuated adipose tissue inflammation and improved glucose tolerance in DIO. Collectively, these data suggest that down-regulation of macrophage G6PD would ameliorate insulin resistance in obesity through suppression of pro-inflammatory responses.

S13-3

Obesity, inflammation and diabetic kidney disease

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Obesity has become an epidemic, globally. In parallel with this is a rapid surge in the prevalence of both type 2 diabetes mellitus and its related complications. Although mortality from macro-vascular complications like coronary heart disease and stroke has improved with the advent of potent statins, the incidence of diabetic kidney disease is still on the rise and it remains a major cause of end-stage renal failure worldwide.

Obesity causes dysfunction of adipose tissue, resulting in chronic inflammation and an imbalance of various adipokines. Over the past decade, the role of inflammation in diabetic kidney disease has been increasingly recognized. These have facilitated not only the improved understanding of the complex pathogenic mechanisms of diabetic kidney disease, but also the development of novel therapeutic strategies in tackling this devastating complication of diabetes.

In this short talk, the association between inflammation and diabetic kidney disease will be discussed. Furthermore, as some adipokines or obesity related markers, such as adipocyte fatty acid-binding protein and fibroblast growth factor 21, have been recently investigated as renal biomarkers, their roles as potential useful candidate markers of diabetic kidney disease will also be presented.

S13-4

The relationship between obesity and insulin resistance in Asian patients

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Obesity and insulin resistance are key pathophysiologic features of type 2 diabetes (T2D). Obesity and insulin resistance are correlated. However, insulin resistance and features of the metabolic syndrome are manifest a relatively low levels of body mass index in Asians than they are in populations of European ancestry. It has been suggested that this relates to the fact that body mass index under-estimates the degree of adiposity in Asians. Others have suggested that this relates to the relatively greater proportion of visceral fat related to total adiposity in Asians. We have found that the ethnicity modulates the relationship between obesity and insulin resistance. In South Asians, insulin resistance is present even at low body mass index, suggesting that in this ethnic group, insulin resistance does not require the presence of obesity. In contrast, while Chinese and Malays are very insulin sensitive when they are lean, with increasing levels of obesity, insulin sensitivity rapidly declines so that at a BMI in the region of 27–28 kg/m^2, there is no difference between Chinese, Malays and South Asians in relation to insulin sensitivity. This suggests that obesity may have a greater impact in Chinese and Malays than in South Asians. This provides unique opportunities to dissect out obesity dependent and obesity independent pathways leading to insulin resistance.

S13-5

17β-hydroxysteroid dehydrogenase-13 is a lipogenic lipid droplet-associated protein and is regulated by an LXRα-SREBP1c axis in the liver

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Nonalcoholic fatty liver disease (NAFLD) is characterized by a massive accumulation of lipid droplets (LDs). By using 2D LC-MS/MS, we identified a novel liver-specific lipid droplet-associated protein, 17β-hydroxysteroid dehydrogenase-13 (17β-HSD13). 17β-HSD13 expression was significantly upregulated in the livers of patients and mice with NAFLD. Increased hepatic 17β-HSD13 and its LD surface location were confirmed in type 2 diabetic db/db (diabetic) mice and high-fat diet-fed mice. Adenovirus-mediated hepatic overexpression of human 17β-HSD13 induced a fatty liver phenotype in C57BL/6 mice, with a significant increase in mature sterol regulatory element-binding protein 1 (SREBP1) and fatty acid synthase levels. These findings demonstrate that 17β-HSD13 is a pathogenic protein in the development of NAFLD. To further characterize the molecular mechanisms involved in the regulation of *17β-HSD13* gene expression, we determined the effect of liver X receptors on 17β-HSD13 expression. We found that treatment with T0901317, a non-specific LXR agonist for both LXRα and LXRβ, increased both 17β-HSD13 mRNA and protein levels in cultured hepatocytes. It also significantly upregulated hepatic 17β-HSD13 expression in wild-type (WT) and LXRβ$^{-/-}$ mice but not in LXRα$^{-/-}$ mice. Basal expression of 17β-HSD13 in the livers of LXRα$^{-/-}$ mice was lower than that in the livers of WT and LXRβ$^{-/-}$ mice. Moreover, induction of hepatic 17β-HSD13 expression by T0901317 was almost completely abolished in SREBP-1c$^{-/-}$ mice. Bioinformatics analysis revealed a consensus sterol regulatory element (SRE)-binding site in the promoter region of the *17β-HSD13* gene. A *17β-HSD13* gene promoter-driven luciferase reporter and ChIP assays further confirmed that *17β-HSD13* gene was under direct control of SREBP-1c. Collectively, these findings demonstrate that 17β-HSD13 is a lipogenic lipid-droplet protein which expression is regulated by the LXRα-SREBP1c axis. 17β-HSD13 may represent a potential therapeutic target for the treatment of NAFLD.

Adipocyte Biology and Insulin Resistance

S20-1

Lipid dynamics in brown fat-mediated thermogenesis and energy metabolism

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Obesity is a pandemic and major contributor to metabolic disorders. Increased adiposity is the main characteristic of obesity. In mammals, there are two functionally distinct types of fat tissue: white adipose tissue (WAT), which is specialized for energy storage, and brown adipose tissue (BAT), which dissipates energy for thermogenesis via uncoupling protein 1 (UCP1). In addition to the classical brown adipocytes, UCP1-positive "beige" or "brite" adipocytes can be recruited within

WAT upon cold exposure. Increasing the amount or activity of brown/beige fat has been considered as an appealing approach for the treatment or prevention of obesity and related metabolic disorders. The energetic processes executed by BAT require a readily available fuel supply, which includes glucose and fatty acids (FAs). FAs become available by cellular uptake, de novo lipogenesis, and from release of fat stored in multilocular lipid droplets in brown adipocytes. BAT also possesses a great capacity for glucose uptake and metabolism, as well as an ability to regulate insulin sensitivity. I will discuss our recent findings on cold-induced lipid dynamics in brown and white adipose tissue of mice using highly sensitive liquid chromatography coupled with mass spectrometry lipidomics analyses.

S20-2

HOXC10 suppresses browning of white adipose tissues

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As increased thermogenesis in white adipose tissue (WAT), or browning, promotes energy expenditure, significant efforts have been invested to determine the molecular players involved in this process. Here, we show that HOXC10, a homeobox domain-containing transcription factor expressed in subcutaneous (SubQ) WAT, is a suppressor for genes involved in the process of browning. Ectopic expression of HOXC10 in adipocytes suppresses brown fat genes. Conversely, depletion of HOXC10 in adipocytes and myoblasts increases expression of brown fat genes. HOXC10 protein level inversely correlates with brown fat genes in SubQ WAT of cold exposed mice. Expression of HOXC10 in mice suppresses cold-induced browning in SubQ WAT and abolishes the beneficial effect of cold exposure on glucose clearance. HOXC10 exerts its effect, at least in part, by suppressing PRDM16 expression. Taken together, we propose that HOXC10 is a key negative regulator of the process of browning in WAT.

S20-3

Inactivation of the E-Prostanoid 3 receptor gene causes adiposity and insulin resistance via altering white adipose tissue metabolism

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Prostaglandins E2 (PGE2) is the predominant prostaglandin produced in white adipose tissue (WAT) and plays an important role in adipogensis and adiposity. Among four PGE2 receptors, the EP3 receptor is most abundantly expressed in WAT. In mice, the EP3 gene gives rise to three isoforms, namely EP3α, EP3β and EP3γ, which differ only at their C-terminal tails and are produced by alternative splicing. To date, the role of the EP3 and each of its isoforms in the regulation of WAT remains incompletely characterized. In the present study, we found that the expression of all EP3 isoforms were significantly down-regulated in WAT of several obese murine models including db/db mice and high-fat diet-induced obese mice. Genetic ablation of total EP3 receptor gene (EP3-/- mice) or selective deletion of the EP3α and EP3γ isoforms (EP3β mice) led to an obese phenotype, with increased food intake, decreased motor activity, reduced insulin sensitivity and imbalanced lipid metabolism featured as enhanced adipogenesis. Terminal differentiation of preadipocytes and mouse embryonic fibroblasts (MEFs) was markedly facilitated by either pharmacological blockade of the EP3 receptor or genetic targeting of the EP3α and EP3γ isoforms. The inhibition of adipogenesis by the EP3 and the EP3α and EP3γ was mainly through the cAMP/PKA/CREB pathway. In addition, the EP3-/- and EP3β mice also exhibited increased lipolysis in WAT, which is mainly mediated by the suppression of the cAMP/PKA/HSL pathway. Taken together, the EP3 receptor is critical for the maintenance of normal WAT function, where inactivation of the EP3 promotes adiposity via facilitating adipogenesis and increases insulin resistance via enhancing lipolysis.

S20-4

Regulation of hepatosteatosis and obesity by sphingolipids

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Sphingolipids are implicated in etiology of chronic metabolic diseases including cardiovascular diseases and diabetes. In this study, we investigated whether *de novo* sphingolipid biosynthesis is associated with development of adipose tissues. SPTLC2, a subunit of serine palmitoyltransferase, was transcriptionally upregulated in adipose tissues of obese mice and during differentiation of 3T3-L1 cells. SPTLC2 knockdown suppressed expression of adipogenic genes and lipid accumulation in 3T3-L1 cells. To confirm this, we have developed adipocyte-specific SPTLC2 deficient (aSPTLC2 KO) mice that have lipodystrophic phenotype even with high fat diet feeding. The cell size and mass of adipocyte tissue were reduced dramatically and expression of adipogenic genes was down-regulated. Whereas, the fatty acids destined to the adipose tissue were accumulated by increased uptake into liver and caused hepatic steatosis. aSPTLC2 KO mice fed a high fat diet did not increase the body weight but fasting glucose levels were elevated and developed systemic insulin resistance. Although adenoviral SPHK2 overexpression in liver did not recover lipodystrophic phenotype, the floxed mice showed increased fat mass. This is in part due to downregulation of S1P receptor 1 in adipose tissue of aSPTLC2 KO mice and SPTLC2-suppressed 3T3-L1 cells. Collectively, our observations suggest that tight regulation of *de novo* sphingolipid biosynthesis and S1P signaling plays an important role in adipogenesis and hepatosteatosis.

S20-5

Targeting fat metabolism and energy expenditure in metabolic disease

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Excess fat accumulation in peripheral tissues is a risk factor for insulin resistance and type 2 diabetes. Calorie restriction and exercise are the safest and most effective ways to decrease excess lipid storage; however, poor patient compliance and disability limit the effectiveness of these approaches. Therefore, there is an unmet medical need to develop drugs that promote fat loss. My laboratory has investigated three approaches to reduce fat mass including increasing fat oxidation, reducing lipogenesis, and increasing energy expenditure. We have found that increasing fat oxidation or reducing lipogenesis by targeting acetyl-CoA carboxylase enzymes is not sufficient to promote fat loss because tissues compensate by altering carbohydrate metabolism and fat uptake. However, increasing energy expenditure by mitochondrial uncoupling represents a viable approach if safety can be improved through the development of mitochondria-specific small molecule mitochondrial uncouplers.

Hot Topics in Diabetes and Obesity (I)

S24-1

Molecular mapping of insulin action and insulin resistance

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We have utilized global unbiased phosphoproteomic analysis of insulin responsive tissues to construct a large scale map of the insulin regulated signaling network. This has revealed key regulatory nodes together with novel substrates of major insulin regulated kinases such as Akt. Using machine learning we have discovered several new Akt substrates that have revealed novel aspects of insulin action, several of which will be discussed. We have also applied similar approaches to examine changes in insulin signaling and the total proteome in adipocytes rendered insulin resistant using a range of physiological perturbations. These studies have revealed novel insights into the mechanism of insulin resistance, which appears to involve the induction of an insulin sensitive pathway in adipocytes that impairs insulin regulated glucose metabolism.

S24-2
The metabolic consequences of fecal microbiota transplantation (FMT) in mice

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Background: The gastrointestinal microbiota is a community of microorganisms that reside in the digestive tract. Studies have suggested that the microbiota composition may contribute to the development of obesity and the metabolic syndrome. Exercise has been shown to alter the microbiota composition by increasing diversity and altering specific bacteria species. We tested whether fecal microbiota transplantation (FMT) from exercise-trained mice to recipient mice alters body composition and metabolism.
Methods: C57BL6/J mice were fed a chow or high fat diet (HFD) for 4-weeks to induce obesity and insulin resistance. Mice were further divided into sedentary or exercise training groups (treadmill training for 6-weeks) while maintaining their respective diets (four groups of donor mice; chow sedentary or exercised and HFD sedentary or exercised). Recipient mice were inoculated with the faeces from the respective donor groups once a week for 6-weeks and body composition and metabolism assessed.
Results: While the HFD led to glucose intolerance and obesity, exercise training resulted in a small decrease in body fat and improved glucose tolerance. FMT from the donor groups did not alter body composition (weight, fat mss, lean mass) in any of the recipient groups. Unexpectedly given the lack of an effect on adiposity, glucose tolerance was disrupted in the mice inoculated with faeces derived from mice on a HFD irrespective of exercise status and this was associated with a decrease in insulin-stimulated glucose clearance into white adipose tissue and the large intestine.
Conclusion: FMT can transmit HFD-induced aspects of disrupted glucose metabolism to recipient mice independently of any change in adiposity. However, FMT from exercise trained donor mice appears to elicit no beneficial effect.
Disclosure: No conflict of interest.

S24-3
Chronic exercise alleviates obesity-related metabolic dysfunction by enhancing FGF21 sensitivity in adipose tissues

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Chronic exercise has beneficial effects on protecting against obesity-related metabolic dysfunction. However, the underlying molecular mechanisms are incompletely understood. Fibroblast growth factor 21 (FGF21) is a hormone mainly derived from liver and acts on adipocytes by activating the FGF21 receptor complex (FGFR1 and β-Klotho)-mediated intracellular signalling. FGF21 has pleiotropic effects on regulating glucose homeostasis, lipid metabolism and insulin actions. Here we show that chronic exercise improves FGF21 sensitivity by upregulating the expression of FGFR1 and β-Klotho in adipose tissues of diet-induced obese mice. FGF21 knockout mice were refractory to several benefits of chronic exercise, including alleviation of glucose intolerance and insulin resistance. Exercised FGF21 knockout mice show augmented lipolysis and free fatty acids (FFA) accumulation in liver and muscle compared with the wild type littermates. Furthermore, the effects of chronic exercise on enhancement of adiponectin production and fatty acids oxidation were abrogated in FGF21 knockout mice. Additionally, adipose tissue β-Klotho specific knockout mice are also refractory to the beneficial effects of exercise on attenuating diet-induced systemic lipotoxicity, glucose intolerance and insulin resistance. Collectively, chronic exercise-induced improvement of FGF21 sensitivity in adipose tissues can prevent excessive FFA influx and promote FFA oxidation in liver and muscle, leading to reduced lipotoxicity and enhanced systemic glucose tolerance and insulin sensitivity.

S24-4
Laparoscopic sleeve gastrectomy versus Roux-en-Y gastric bypass for the treatment of type 2 diabetes: 12 month results of a double-blind, randomised trial

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Introduction: It is unclear which of the two most commonly performed types of bariatric surgery, laparoscopic sleeve gastrectomy (LSG) or laparoscopic Roux-en-Y gastric bypass (LRYGB), is most effective for obese patients with type 2 diabetes (T2D).
Objectives: To examine the comparative *ad interim* effectiveness of LSG or LRYGB at 1 year in achieving improvement in T2D using different HbA1c thresholds.
Methods: Single-centre, double-blind (assessor and patient), parallel, randomized, clinical trial conducted in Auckland, New Zealand. Eligibility criteria included age 20–55 years, T2D of at least 6 months duration and BMI 35–65 kg/m^2 for at least 5 years. Recruitment of 114 patients completed in October 2014. Randomization 1:1 to LSG (n = 58) or LRYGB (n = 56) used random number codes disclosed to the operating surgeon after induction of anesthesia. A standard medication adjustment schedule was used during post-operative metabolic assessments scheduled for 5 years when primary outcome of T2D remission defined by HbA1c <42 mmol/mol without diabetes medications, is to be analysed.
Results: *Ad interim* analysis at 1 year showed 109/114 completed 12 month follow up. Participants included 17% Maori, 8% Pacific and 55% were women. Mean (±standard deviation) HbA1c pre-operatively was 63 mmol/mol±16 with 29% on insulin therapy and 65% on oral glucose lowering therapy alone. Proportions achieving HbA1c <39 mmol/mol, <42 mmol/mol, <48 mmol/mol, or <53 mmol/mol without the use of diabetes medication in LSG vs LRYGB were 43% vs 38% (p = 0.56), 49% vs 52% (p = 0.85) and 72% vs 75% (p = 0.83), and 77% vs 80% (p = 0.82) respectively. Mean (±standard deviation) weight loss at 1 year was less after LSG than after LRYGB: 34.0 ± 13.1 kg and 39.6 ± 11.6 kg respectively, (p = 0.02).
Conclusions: LSG and LRYGB achieve similar prevalence of T2D remission despite significantly greater weight loss at 1 year after LRYGB. Longer term follow up is required to determine the durability of these results.

Incretin/Islet Biology and Insulin Secretion

S30-1
β-cell glutamate signaling in insulin secretion: the physiological and pathophysiological roles

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Insulin secretion from pancreatic β-cells plays the central role in the maintenance of glucose homeostasis; impaired insulin secretion contributes to the pathogenesis and pathophysiology of diabetes. Glucose-induced insulin secretion (GIIS) is the primary mechanism of insulin secretion, in which glucose metabolism in β-cells is prerequisite. In addition to GIIS, neuro-hormonal amplification of insulin secretion is also critical in normal regulation of insulin secretion. Incretins such as glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), which are released from enteroendocrine cells in response to meal ingestion, potentiate insulin secretion primarily through cAMP signaling in pancreatic β-cells. The glucose-dependent action of incretin in insulin secretion provides the basis for the recently developed incretin-based anti-diabetic drugs. However, the mechanism of the link between glucose metabolism and incretin/cAMP action in insulin secretion was not clear. Using a metabolomics-based approach, we recently found that cytosolic glutamate produced through the malate-aspartate shuttle links glucose metabolism to cAMP action in insulin release, acting as a key cell signal in incretin-induced insulin secretion (IIIS). We also investigated the pathophysiological role of glutamate signaling in insulin secretion using various rat models of diabetes and obesity. The insulin secretory responses to glucose and the incretins GLP-1 and GIP were assessed by batch incubation of isolated pancreatic islets. Contents of glutamate isotopomers were measured by ^{13}C-enrichment analysis with uniformly-labeled [U-^{13}C]-glucose as a substrate using capillary electrophoresis mass spectrometry (CE-MS). Pancreatic islets of control Wistar rats exhibited both GIIS and IIIS. However, in islets of Goto-Kakizaki (GK) rats, a model of diabetes with impaired insulin secretion, GIIS was markedly decreased while IIIS was somewhat retained. In contrast, in Zucker fatty (ZF) rats, a model of obesity, GIIS was evident, but there was no IIIS. The islets of Zucker fatty diabetes mellitus rats (ZFDM, a model of diabetes with obesity) at 11 weeks of age were found to comprise a mixture of relatively larger and smaller islets. Interestingly, while the smaller islets (<100 μm in diameter) exhibited IIIS, the larger islets (>300 μm) did not. Glutamate production in GK islets was slightly but significantly increased by glucose stimulation. In contrast, glutamate production in neither ZF islets nor the larger ZFDM islets was increased by glucose stimulation, although it was increased in the smaller islets of ZFDM rats. These data indicate that IIIS is well correlated with glutamate production by glucose in β-cells. Our findings serve to clarify the mechanism of impaired IIIS in type 2 diabetes and to suggest novel therapeutic strategies.

S30-2
Intracellular membrane trafficking and insulin secretion

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My lab has been interested in defining the underlying mechanisms governing membrane trafficking in mammalian cells. Over the years, we have identified over half of mammalian SNARE proteins, defined several SNARE complexes and identified downstream effectors for small GTPases Arl1, Rab34 and Rab7. In addition, we have discovered that PX domain is a novel motif capable of interacting with phosphoinositides. Other regulators of membrane trafficking such as BIG3 and p125A and Tom1L1 were discovered. In addition to the overview of the research, I will discuss our work on VAMP8 and BIG3 in insulin secretion.

S30-3
Sorcs1: From diabetes quantitative trait locus to cellular function

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Type 2 diabetes occurs when pancreatic β-cells are unable to produce enough insulin to meet the increased demand for insulin brought about by insulin resistance. Most of the genetic loci that have been discovered through genome-wide association studies in humans point to defects that affect β-cell mass or β-cell function. Using mouse genetics, we positionally cloned a diabetes susceptibility locus and identified the causal gene, *Sorcs1*. Subsequent studies show that Sorcs1 is involved in type 2 diabetes and diabetes complications in humans. *Sorcs1* is a member of the Vacuolar protein sorting-10 (Vps10) gene family. Vps10 was originally discovered in yeast where it is a receptor for carboxypeptidase Y and is essential for its transport to the yeast vacuole (equivalent to the mammalian lysosome). We derived a mouse with a deletion of the *Sorcs1* gene. When made obese, the mouse develops severe diabetes. This is due to a defect in the production of insulin granules and a dramatic increase in the post-translational degradation of insulin. Our preliminary studies point to a second vps10 protein, which plays an important role in post-translational degradation of proteins, by targeting to the lysosome. We are currently investigating the role of this second vps10 family member on insulin degradation in pancreatic β-cells. In this seminar I will describe the methods we used to identify *Sorcs1* as a T2D gene and describe what we have learn from the phenotype of the Sorcs1 KO mouse and our preliminary data on receptor mediated degradation of insulin in pancreatic β-cells.

S30-4
New insights into mechanisms regulating insulin secretion

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The capacity of β-cells to secrete insulin is reduced during the development of type-2 diabetes but the mechanisms regulating insulin secretion in response to glucose and incretins remains only partially understood. This presentation will describe our evidence indicating that β-catenin and proteins that associate with it represent an important component of the nutrient responsive insulin secretory mechanism. We find that β-catenin is necessary for insulin secretion in response to both these glucose and GLP-1. What is more we find β-catenin levels change in β-cells in response to changes in glucose levels indicating this is part of the way β-cells regulate insulin secretion in response to changes in glucose. A potential role for this *in vivo* is supported by the finding that number of SNPs associated with increased risk of type-2 diabetes have been identified in genes that regulate β-catenin function (e.g. TCF7L2, CTNNA2, BTRC, IGFBP2 and MAGI1). Our mechanistic information suggests that β-catenin is acting as rheostat to regulate the amount of insulin that can be secreted at any one time. This presentation will describe the evidence supporting this.

S30-5
Role of Activin B/FSTL3 axis in the control of glucose homeostasis

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Activins, members of TGFβ superfamily proteins, are known to play a pivotal role in the reproductive and developmental processes and their variety of functions have recently been explored in many cells and tissues, while the role in glucose metabolism is poorly understood. Here we show that administration of Activin B, which is mainly produced in liver in the fasted state, significantly reduces blood glucose levels in both obese diabetic mice and insulin deficient diabetic mice, while this effect is completely canceled by co-administration of FSTL-3, known as an inhibitory molecule for TGFβ superfamily proteins. Activin B exerts glucose lowering effects through suppression of gluconeogenesis, induction of FGF21 and increased insulin secretion. Although expression of Activin B is not altered by obesity, expression of FSTL-3 in adipocytes, strongly correlates with BMI and insulin resistance in mice and humans. Indeed, suppression of FSTL-3 markedly improves glucose homeostasis in obese mice. Thus, Activin B produced by the liver contributes to the maintenance of glucose levels and insulin sensitivity under the lean condition and obesity increases the production of FSTL3 thereby suppressing the functions of Activin B leading to insulin resistance and dysregulation of glucose homeostasis.

Hot Topics in Diabetes and Obesity (II)

S35-1

Role of CRTC2 in the control of glucose metabolism

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Liver plays a major role in maintain glucose homeostasis in mammals. Under the starvation, glucose production is increased in the liver to provide enough fuels for critical organs such as brain and red blood cells. Short-term fasting mainly activates glycogenolysis in the liver, and a longer-term fasting triggers the activation of gluconeogenesis that utilizes various non-carbohydrate precursors such as lactate, amino acids, and glycerol to meet the body's need for glucose. Interestingly, activation of gluconeogenesis is in large part achieved by a transcriptional mechanism in response to pancreatic hormone glucagon and adrenal glucocorticoid. While glucocorticoid signals through a nuclear receptor glucocorticoid receptor, glucagon elicits its effects by inducing cAMP-dependent pathway in the liver, utilizing CREB and CREB regulated transcription coactivator 2 (CRTC2) as proximal transcriptional complex. Increased hepatic glucose production under insulin resistance or type 2 diabetes is one of the major causes for hyperglycemia, and it was shown that hyperactivation of CREB/CRTC2 signals could be in part responsible for such phenomenon. In this talk, we would like to delineate the mechanistic insight into the role of CRTC2 in the control of hepatic glucose metabolism by using in vivo mouse models.

S35-3

Significance of adiponectin accumulation in vasculature

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Our group discovered adiponectin from human fat tissue in 1996 and established the measurement of circulating adiponectin concentration by using ELISA in 1999. Adiponectin is characterized as follows: (1) Plasma concentration range from 1 to 30 μg/mL in human adults, which is 10^3- to 10^6-fold higher than the levels of ordinary cytokines and hormones. (2) Circulating adiponectin levels paradoxically decrease in obesity, especially in visceral fat-accumulated obesity. Clinical and experimental studies evidently showed that adiponectin directly effects on cardiovascular tissues and exhibits cardiovascular protective function, suggesting the direct axis of fat and cardiovascular system. Importantly, we recently demonstrated the existence of adiponectin protein in the cardiovascular tissues and its localization was changed when these tissues were injured. However, molecular mechanism for the adiponectin accumulation in cardiovascular tissues has not been fully understood. Lodish's group previously demonstrated that T-cadherin is a receptor for multimeric forms of adiponectin (Hug C et al. PNAS 2004). T-cadherin is an atypical glycosylphosphatidylinositol (GPI)-anchored cadherin cell surface glycoprotein. Interestingly, T-cadherin knockout mice mimick the adiponectin knockout cardiovascular phenotype (Denzel MS et al. JCI 2010). In this symposium, I would like to talk about recent advances of adiponectin research in view of the cardiovascular protective action of adiponectin via T-cadherin.

S35-4

Hypothalamic inflammation in high fat diet-induced obesity

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A prolonged consumption of high fat diet (HFD) leads to hypothalamic inflammation in rodents. HFD-fed rats displayed increased expression of proinflammatory cytokines [interleukin-1 (IL-1), IL-6 and tumor necrosis factor-α (TNFα)] and activation of inflammatory signaling [c-Jun N-terminal kinase (JNK) and the IκB kinase-β/nuclear factor-κB (IKKβ-NFκB)] in their hypothalamus. Activation of hypothalamic inflammatory signaling pathways is suggested as an important mechanism underpinning overnutrition-induced leptin and insulin resistance. While it is evident that HFD induces hypothalamic inflammation, a relative contribution and interactions of neurons, glial cells, and immune cells in this process are not largely unveiled. A recent study has reported a rapid activation of hypothalamic microglia upon HFD feeding, which is evidenced by morphological changes and increased number. In my talk, I will present our recent data which suggest a critical contribution of hypothalamic macrophages in hypothalamic inflammation observed in HFD-induced obesity.

Hot Topics in Diabetes and Obesity (III)

S38-1

Feeding-induced activation of beta-catenin/TCF signal transduction in hypothalamic neurons

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Polymorphisms in the TCF7L2 gene are associated with increased risk of type-2 diabetes and obesity. TCF7L2 is a transcriptional co-factor that binds with β-catenin to promote gene transcription in the canonical Wnt/β-catenin pathway, and studies have focused on this pathway in the pancreas as a causal link to type-2 diabetes. The role of the brain in glucose homeostasis is increasingly recognised, however, and impaired neuronal Wnt signalling may contribute to development of diabetes. Here, we investigated whether the Wnt/β-catenin pathway is regulated in the hypothalamus during the normal physiological responses to food intake. We observed that feeding acutely induced stabilisation of β-catenin in neurons in specific hypothalamic nuclei involved in metabolic regulation, associated with increased

transcription of TCF-responsive genes. The effect of feeding was mimiced by specific metabolic hormones, including GLP1 and insulin. Finally, experimental modification of β-catenin levels in a hypothalamic cell line altered neuropeptide secretion. The data suggest that both transcriptional and non-transcriptional effects of β-catenin in the hypothalamus might be involved in the regulation of body weight and glucose homeostasis, and highlights the potential role of altered hypothalamic function in contributing to the risk of diabetes conferred by specific genetic polymorphisms of TCF7L2 in human populations.

S38-2

Insulin signaling in adipocytes and metabolic control

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Insulin signaling in adipocyte is thought to play a key role in the control of energy metabolism in living animals. The pathophysiological significance of insulin resistance in adipocyte remains ambiguous, however. To understand the physiological impact of insulin resistance in adipocytes in living animals, we have generated mice lacking PDK1, a key molecule in insulin signaling, selectively in adipocytes. Insulin-induced biological actions in adipose tissue, including the stimulation of glucose uptake and lipogenesis as well as the inhibition of lipolysis, were almost completely prevented in adipocyte-specific PDK1 deficient mice (A-PDK1KO mice). The mass of adipose tissue as well as the plasma levels of adiponectin and leptin were decreased in A-PDK1KO mice. A-PDK1KO mice manifest severe insulin resistance, glucose intolerance, and dyslipidemia under normal chow feeding. Moreover, A-PDK1KO mice naturally develop nonalcoholic steatohepatitis (NASH) within ~35 weeks of age. A transcription factor FoxO1 is a negative regulator of insulin action. Insulin-induced phosphorylation of FoxO1 was abolished in the adipose tissue of A-PDK1KO mice, indicating that the FoxO1-dependent pathway is constantly activated. To investigate whether the activation of the FoxO1 pathway contributes to the metabolic abnormalities of A-PDK1KO mice, we have additionally disrupted FoxO1 selectively in adipocytes in A-PDK1KO mice. The additional disruption of FoxO1 markedly ameliorated metabolic abnormalities in A-PDK1KO mice including insulin resistance, glucose intolerance and NASH without affecting the mass of adipose tissue, the plasma levels of the adiponectin and leptin. Our results suggest that the impairment of insulin action in adipocytes contributes not only to the pathogenesis of insulin resistance and glucose intolerance, but also to that of NASH. Furthermore, the FoxO1-dependent transcriptional pathway appears to be greatly attributable to these pathological conditions. Further analysis of the PDK1-FoxO1 pathway in adipocytes may shed light on the pathogenesis of NASH and may lead to the development of a novel therapeutic approach for this global health problem.

S38-4

Role of mitochondrial quality control in hyperglycemic neuroprotection

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Population based studies have identified a link between Diabetes mellitus (DM) and the risk of developing Parkinson's disease (PD). The duration of prior DM has emerged as an independent risk factor for PD suggesting that dopaminergic neurons are susceptible to repeated hyperglycemic insults. Recent large-scale studies in the Taiwanese population have strengthened this association and further suggested that selected oral anti-hyperglycemic agents offer partial protection. However, the molecular mechanisms underlying DM-associated PD risk remain unclear. One possibility is that both diseases share common genetic and environmental risk factors. Alternatively, exposure to hyperglycemic conditions may trigger neurodegeneration in susceptible individuals. We have developed cell and animal (zebrafish) models to investigate the role of PD-associated mitochondrial quality control pathways in the neuronal response to hyperglycemia using unbiased proteomic approaches. As the repertoire of anti-hyperglycemic agents expands it will be essential to identify which drugs offer additional neuroprotective benefit to aging populations.

Nutrition and Exercise in Diabetes

S19-2

Alternative health eating index and the Dietary Guidelines from American Diabetes Association both may reduce the risk of cardiovascular disease in type 2 diabetes patients

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Type 2 diabetes mellitus (T2DM) is associated with an increased risk of cardiovascular disease (CVD) and is considered to represent a primary risk factor for coronary heart disease (CHD). Diet is crucial for disease prevention and treatment, and the risk of chronic disease is more highly correlated with overall diet than with a single nutrient. In the general population, healthy dietary patterns have been documented as reducing CVD risk. The Alternate Healthy Eating Index (AHEI), developed on the basis of the Dietary Guidelines for Americans, is designed to reduce chronic disease risk. In 2012, Chiuve et al. released AHEI-2010, an updated version of the index that includes additional dietary suggestions for reducing risk of chronic disease, such as consuming legumes and avoiding sugar-sweetened beverages. A higher AHEI-2010 score has been demonstrated to predict a 27–44% lower cardiovascular disease (CVD) mortality in the general Chinese population. The American Diabetes Association (ADA) have provided dietary recommendations to enable patients with DM to reduce their risk of CHD. We developed an ADA dietary score according to the ADA dietary recommendations. The ADA dietary score contained 10 components, namely seven adequate components and three moderate components. The total ADA dietary score was the sum of the scores for the 10 components. A score of 0 or 1 was assigned for the components: (i) proportion of whole grains; (ii) vegetables; (iii) fruit; (iv) low-fat dairy; (v) protein foods; (vi) seafood and plant protein; (vii) fatty acids ratio; oils; (ix) empty energy; and (x) sodium. The AHEI-2010 scores are calculated and detailed descriptions provided in the Chiuve's (2012) literature. In brief, a higher AHEI-2010 score indicates a higher intake of vegetables, fruit, whole grains, nuts and legumes, polyunsaturated fatty acids (PUFA) and long-chain (n-3) fats, in addition to a moderate intake of sugar-sweetened beverages and fruit juice, processed meat, sodium, trans fat and alcohol. The AHEI-2010 scores range from 0 to 110. A prospective study, the 24-h dietary recall of 124 adult T2DM patients without nephropathy or chronic kidney disease was conducted. The CVD risk factors were collected at baseline and at 6-month follow-up. Compared with lower ADA and AHEI-2010 score participants, the higher score participants exhibited a significantly lower waist circumference, serum low-density lipoprotein cholesterol level and 10-year risk of CHD. Participants with higher ADA dietary scores had a significantly reduced risk of central obesity and systolic blood pressure >140 mmHg. Higher AHEI-2010 scores were significantly related to a reduced risk of serum low-density lipoprotein cholesterol

>100 mg/dL. Cardiovascular disease is the primary cause of death among T2DM patients. Hyperglycaemia, dyslipidaemia and hypertension are the most critical risk factors for CVD. After additional adjustments for BMI, the ADA dietary score was still significantly inversely associated with SBP, serum LDL-C, HbA1c and 10-year risk of CHD. Previous studies have reported that the dietary composition of the ADA dietary score was associated with reduced CVD risk factors, and the association was independent of BMI. Conclusions: Patients with T2DM who adhere to the ADA dietary recommendations or with higher AHEI-2010 scores exhibited significantly reduced CVD risk factors, including lower central obesity, hypertension, poor control of blood glucose and dyslipidaemia. Effects other than BMI contributed to the beneficial effects of the ADA dietary recommendations on CVD risk in the present study. ADA dietary score and AHEI-2010 score might both exhibit reduced risk factors of CVD in T2DM patients.

Diabetes Education: Patient Centered Approach

S29-1

Personalised diabetes care: What is it, and does it 'work'?

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Personalised care requires effective relationships among people with diabetes, communities and the individual's support people. It can help people set relevant care goals and gain control over their care, which improves satisfaction, physical, psychological and other outcomes, and can reduce costs and unnecessary presentations to health services.

Health professionals require specific knowledge and competencies to deliver effective personalised care including how to recognise the assets and values individuals bring to consultations about their care. Personalised care is delivered in different ways, but productive conversations about what matters to the *individual* and the supportive and inhibitory factors that could affect their preferences is essential to developing personalised care plans and goals. Effective personalised diabetes care should encompass proactive conversations about changing needs, be coordinated, clearly documented and communicated to relevant care providers.

The presentation will discuss the intended outcomes of personalised care, the factors that affect decision-making, values and preferences such as experience, culture, health literacy and risk perception. The core skills and knowledge health professionals need to cogenerate personalised care plans with individuals with diabetes, will be outlined. It will touch on factors such as the human Genome studies, epigenetics, pre- and probiotics and the role these initiatives might play in future understandings and application of "personalised diabetes care."

S29-2

Going even further, from counselling to motivating: a universal patient-centered approach to provoke behaviour modifications in your patients

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Behaviour change: Behavioural changes (physical activity, diet, medication adherence, smoking cessation…) are fundamental for prevention and active treatment of diabetic patients.

The traditional approach identifies the behaviours that (*we* think) the patient should change, aim to convince about the Why and give instructions on the How to change (a Professional-Oriented directive approach).

Patients, however, don't change!

In response to this problem, we present a practical universal (Patient-Centered) intervention tool (identical for all professionals and all behaviours) that leads to behavioural change.

This targeted intervention uses recognition of the apparent Stage of Change (Prochaska's model), confirmed by the Conviction level, to develop one of three specific intervention scenarios with the proper closing technique for each scenario.

It uses a variation of the "Motivational Interviewing" communication technique. Through the skilful use of open questions, it provokes, reinforces and accelerates progress along the path to change rather than directing it.

Used by different members of the same therapeutic team (physicians, nurses, pharmacists, nutritionists…), it creates a synergy that increases the acceleration of patient progress as they move from one professional to the next.

Across the spectrum of medical interventions, we have spent more than 30 years focusing on the WHY of changing patient behaviours – the time has now come to promote the HOW!

Peer Leaders in Diabetes Management

S34-2

Effectiveness of peer leaders in diabetes self-management support

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Diabetes is a chronic and multisystem disease which can affect physical and psychological health. There is growing evidence showing the bidirectional associations between depression and diabetes which is associated with reduced adherence and increased risk of complications. Leaving aside possible biological links between diabetes and depression, misconceptions and anxiety about the nature of diabetes and its possible complications, side effects of medications, demands on self-discipline in changing lifestyle, regular medical visits and long term medications are some of the factors that can cause distress, anxiety and depression in people with diabetes. With the onset of complications and disabilities, these negative emotions can further intensify. Given the interlinking nature between cognition, psychology and behavior, education and empowerment aiming to increase self-efficacy can reduce negative emotions and promote positive behaviors. However, time contact is one of the most important determinants in patient education. Here, knowledge transfer from doctors to other personnel including nurses, dietitians, care assistants and community workers are effective measures to engage and empower patients. Supported by the medical team, the paramedical personnel can identify and train peer leaders who can provide practical tips to their peers on daily living with diabetes, such as food choices, interpretation of results of self-monitored blood glucose and ongoing social support. Research studies have supported the benefits of peer support on metabolic risk factors, psychological and behavioral factors as well as health care utilizations, especially in settings where health care provision is less well-coordinated. Furthermore, by supporting their peers, peer leaders may also improve by being more positive and engaged with stable glycemic control. That said, more studies are needed to define the attributes of peers and peer leaders and dynamics between peer and peer leaders to increase the impacts of these holistic programs. Pending such results, establishing infrastructures such as community-based Diabetes Centres or Patient-Centred Homes may improve the efficiency and effectiveness of these complex interventions

with linkage to the health care system in order to meet the pluralistic needs of patients with diabetes.

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S34-3

Experiences of peer support for diabetes in China: from urban to rural

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China, with 113.9 million diabetic patients, is leading the world when it comes to the number of patients with the disease. The challenge for China is to find ways to help diabetic people to delay and prevent diabetic complications, consequently survive longer with better quality of life. But the current healthcare systems are not able to provide sufficient resources to manage and/or treat such a large number of people with diabetes. Thus, it is extremely important to develop a low-cost, flexible, and sustainable diabetes self-management support approaches to complement the limitations of healthcare professionals.

Peer support, defined as the provision of support from an individual with experiential knowledge based on sharing of similar life experiences, has been used in various chronic diseases (including diabetes) worldwide, with positive clinical and/or psychological outcomes. It was introduced in China in 2010 and expanded rapidly nationwide.

In the last 5 years, with help from "peer for progress" (PfP) and Prof. Fisher from University of North Carolina, we have organized 5 workshops and trained over 500 physicians and nurses to develop peer support programs, including peer leader selecting, training. The trained people have developed several programs in Beijing, Tianjin, Hefei, Guilin and Nanjing, and more than 10,000 diabetic patients have received help from the 500 peer leaders.

In Nanjing, with a cluster randomized controlled trial involving 400 type 2 diabetic patients from 8 urban communities, peer support was shown to be superior to conventional diabetes self-management education in reducing diabetes distress, improving glycaemic control and providing long-term health education support. In Guilin and Jiangsu, the rural cultural specific peer support program was initiated in 2014. In Jiangsu, a rural community hospital based, community physician headed and village doctor joined peer support model was built recently and the efficacy, acceptability and feasibility will be tested in 6 sites.

Using Health Information Technology for Diabetes Care

S37-2

The use of internet health education for prevention of diabetes in the workplace: From the perspectives of human beings and living processes

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Information technology (IT) has become a part of our daily life nowadays. Wearable device products have also spread around the world. How to best utilize the convenience of IT to grasp individual patterns of behavior and recognition is still a developing issue. Wearable devices able to provide numerical assessments – such as heart rate, steps walked or calories consumed – only provide us with daily life outcomes. However, understanding what an individual thinks, why they do so, and how they decide upon and pursue their behaviors are crucial considerations for health care teams to provide effective approaches. Therefore, as a profession, we need to grasp not only the outcomes but also the processes of individuals' daily lives.

The general theory of human beings developed by Usui Hiroko – one of the founders of the Nursing School at Chiba University, as well as the founder and president of Miyazaki Prefectural Nursing University – can assist care health teams with uncovering these processes involved in individuals' patterns of behavior and recognition.

In Usui's "Scientific Nursing Theory" (*Kagakuteki Kangoron*), she states, "In order to avoid viewing human beings from a flat, fragmented and linear understanding, we need to move towards a higher level of abstraction, so as to grasp the essence of human beings." Usui explains that is essential to recognize that a human being is a biological living entity but at the same time a socially constructed living entity framed within human relationships. In other words, if one does not comprehend a human being as a unified entity consisting of these two dimensions, it cannot be said that one has grasped the full meaning of what a human being truly is.

Another concept, which Usui inherited from Florence Nightingale, is "Disease as a Reparative Process." Based on this concept, if we know what living processes cause people to become ill, then as a profession we can help them to arrange their living processes so as to prevent recurrences of the disease and apply this principle to all. This is the nursing strategy employed by Preventive Medicine.

This presentation will discuss how to apply the general theory of human beings and the concept of "disease as a reparative process," as formulated by Usui, to analyze individual patterns of behavior and recognition in two cases of Type 1 and Type 2 diabetic patients. This will be helpful for the prevention of diabetes in the workplace.

S37-3

The evaluation of patients' use of tele-health program

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Tele-health has always been considered when talking about caring for people with chronic disease conditions, while some known limitations made it still not widely adopted for care delivery today. One of the mostly discussed limitations is that most people with chronic disease, especially diabetes, are aged, and using IT products such as smart devices is often thought as obstacle for them. Also the motivation from people with diabetes and healthcare providers is usually key metrics to decide if a tele-health program can continue. The motivation of the people with diabetes can come from the ease of access to the tele-health solution, increased awareness on self-management, or improved outcome. For healthcare providers, whether the tele-health solution can help the team deliver care in more efficient way is essential, also a sustainable model will need to be created to support continuous investment of relevant resource.

A mobile App and web-based management platform are used to evaluate how people with diabetes will accept to use a mobile app as tool for blood glucose management and connected to their healthcare provider team, and the effectiveness of such intervention. How to integrate the solution into a health system's actual practice to maximize the values for both the healthcare provider team and people with

diabetes is also a subject to probe. Evaluation results will be presented during the sharing.

Associations of Life Events/Life Stress with Diabetes Control

S27-1

Diabetes control in the life context: Support for reconciling self-management and lifestyle

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People with diabetes perform self-management of diabetes in their lives. There are many stressful life events and daily activities, therefore, people with diabetes have difficulties of self-management in dealing with those events and activities. I am in charge of patient education on an outpatient clinic in the general hospital as a CNS and CDE. So far in one year, I had intake one hundred patients.

I analyzed factors in poor glycemic control of the 80 patients among them. I figured out the factors of the patients who did not succeed in control. I classified the factors into the patterns of typical behaviors. The common behavior patterns are classified as follows; the insufficient exercise (24.6%), overeating (20.3%), meal 2 hours before going to bed (14.5%), many snacks (18.8%), and low compliance of insulin (11.6%).

I have to recognize some background factors in each behavior such as the insufficient exercise and overeating. The insufficient exercise and late dinner were related to long work and night shifts. There were also some relations between late dinner and many snacks with family-centered life. However, I found no specific factors in injection compliance.

Patients may not have the economic flexibility to lead their lives, and may be overwhelmed with shift work and long work. In addition, housewives with diabetes often give priority to that of the family than that of their own. Furthermore, conflicts between wives and mothers-in-law sometimes happen as well.

Key points of consultations are reconciling their lifestyles and self-management. People often attach value to things in their lives and they also have preferences. Stress arises when diabetes self-management behaviors conflict with what patients value in life. Expert nurses support patients to reconcile treatment methods and their lifestyles, while trying to understand the meaning of the lives of patients as "people". In this session, I will explain several cases that I consulted the patients at my clinic. I will emphasize three key points; to become more manageable by changing family-centered life to oneself-centered life, to change the way of thinking about taking care of their bodies, and to reconcile while working. However, there is a limitation to reconcile self-management with work, exampling when blue-collar workers do shift works, they have difficulties in incorporating treatment regimen.

S27-2

Perceived control of patients with diabetes in Taiwan: Exploring the relationships among illness attributions, illness representations, and self-care behavior

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Background: Control representation relates to patients' consistent self-care behavior. However, the factors that affect control representation are not yet known clearly.

Purpose: This study explores the impact of illness attributions on control representation and discusses the concept of control in Chinese culture.

Methods: In this study, 146 participants with type II diabetes were recruited at an outpatient clinic and were assessed with self-report questionnaires about illness representations and self-care behavior. Illness attributions were also included in the questionnaire on illness representations.

Results: Four factors of illness attributions were extracted: "psychosocial attributions", "environment", "lifestyle", and "physical attributions". Lifestyle and environment attributions had positive and negative impacts on control representations, respectively, and both affected self-care behavior through control representations.

Conclusion: The relationships among illness attributions, illness representations, and self-care behavior are discussed. The existence of a holistic, harmonious control concept in Chinese culture is postulated.

Association of Daily Problem Solving/ Coping/Social Supports with Diabetes Control

S32-1

Impact of the peer counseling for dissolving a negative cognition toward diabetes

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The global Diabetes, Attitudes, Wishes and Needs (DAWN) survey in 2001 showed that psychosocial problems can be barriers to achieving adequate glycemic control, and that people with diabetes lack psychological support and that interdisciplinary care teams need to promote chronic illness care. Among the psychosocial problems in DAWN survey, people with type 1 diabetes had depression and anxiety and those with type 2 diabetes had sense of sin when diabetes was diagnosed. Such psychosocial problems can induce poor glycemic control, which may cause a negative cognition toward diabetes (absence of a reason for living, burden of diabetes, district toward medical tretent, watching and meddling by surrounding people, sense of alienation, rejection of antidiabetic drugs or insulin, and pressure related to diabetes self-management).

We started a group meeting held in Tokyo three times per year for young-aged diabetic patients since 2008, in which around 20 patients and 20 medical staffs were recruited through Web site for people with diabetes. People who want to participate the meeting are registered in the order to receipt. In the group meeting, we assist all of the patients to talk about negative cognitions toward diabetes and all of medical staffs to listen to what the patients talk to.

From 2008, the total of more than 150 patient-participants (mostly, type 1 diabetes) aged 20–40 years old had the various durations: from the 2 months to more than 30 years. A total of 80 medical staff-participants consisted from all but nurse and several % of physicians. The family, father, mother, and sons/daughters sometimes attended this meeting together. A half of patient-participants attended more than twice. The patients gave us their sentiments that they were able to share cognitions of others which relieved themselves, realized the presence of their own diabetes, got new skills for insulin injection and monitoring of blood glucose from other patients, and learned the earnest attitude from the medical staffs.

Every meeting has more than 50 participants, which will be held without interruption.

S32-3

The relationship between coping strategies of DM and diabetes control

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By definition, chronic illness demands a patient of life-long coping. So, besides coping against the illness conditions at present, the patient should cope continuously the illness for a relatively long period of time. It means that there are two kinds of coping process when analyzing chronic illness adjustment. An expended model of coping toward chronic illness was designed to integrate "immediate coping process" and "long-term coping process" as to cover the whole picture of the coping of chronic illness. And we had carried out a 3-year study of coping strategies of DM and diabetes control based on this expended model.

The model prescribes to collect information since first diagnosed as a DM patient and include the whole coping processes until here and now. The proper research method will be case study with semi-structured in-depth interview. 15 DM patients were interviewed. The results showed that it was better to divide the long-term coping process into following themes:

(A) **Diagnosis**. Includes: The description of how the illness was noticed, how the necessary examinations were completed, and the way that diagnosis of DM was confirmed; During the diagnostic process, what were the reactions and/or feelings she/he had toward the medical team and/or the hospital environment; What were the life stresses she/he had, besides DM, when diagnostic process was carried on.

(B) **Reactions to the Diagnosis/the Illness**. Includes: Was there any strong emotional reaction, or catastrophic reaction? Did the patient accept the illness as a problem she/he must face, or reject it and try to fight against it? What was the belief, knowledge, thought induced by this illness? What was the influence from her/his worldview, life goal, value system, religious thinking to this reaction? How was the motivating power of facing this illness derived from the above-stated reactions? How was the influence from life stressors on these responses?

(C) **Reactions to the Treatment** (and the Medical team that prescribed the treatment): Did the patient trust, depend on, the medical team, especially the doctor? Was the patient understand the treatment (and why prescribe the treatment) correctly? What was the thinking induced by the treatment? Was there any change of belief/knowledge/thought because of the understanding of the treatment? How was the execution of the treatment? How was the result of the treatment? How was the coping to the result? How was the influence from life stressors on treatment execution?

(D) **Coping Strategies and Methods:** Obtaining information and knowledge so as to understand what DM is. Comparing own experience of DM with others' and the past experiences of illness of my own so as to understand DM more thoroughly. Searching the causes of why becomes a DM patient. Seeking social support from friends as well as from medical team members and patients with DM. Talking out and/or writing out the painful feelings within one's own mind so as to relieve the stressful burden of being ill.

(E) **Adjustment of life schedule, life goal, life style**. Did the coping of DM integrated into life schedule, life goal, or life style?

(F) **Adjustment of worldview**. Did the coping of DM induced changes in worldview?

(G) **Showing Gratitude**. Did the patient give suggestions, which were learned from the successful coping with DM, for medical team as well as patients with DM, or serve as a volunteer worker for helping patients with DM.

Although the coping strategies and methods stated above were important indicators of successful coping, there were four kinds of transformation which best related to good DM control:

1. Transformation of daily living schedule: Assimilation/accommodation of treatment, including taking medicine regularly, adjusting food taking properly, doing exercise properly, into daily living schedule with the treatment as the most, or one of the most important events when designing the schedule.
2. Transformation of life style and/or life goal(s): Modification of life style and/or life goal(s) based on successfully carrying out the treatment.
3. Transformation of worldview and/or expectation(s) of life: Modification of worldview and/or expectation(s) of life by taking the chronic illness as one of the natural happenings as life goes on.
4. Transformation of attitude toward the illness by showing gratitude: Not only developing a positive attitude toward DM but also reckoning it as a gift from the medical team/relatives/friends/god and returning the kindness by giving suggestions, which were learned from the successful coping with DM, for medical team as well as patients with DM, or serving as a volunteer worker for helping patients with DM.

Association of Psychosocial Factors with Diabetes Control

S36-1

Mental states of individuals with type 2 diabetes by psychological assessment

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We evaluated the mental states of subjects with type 2 diabetes using BUKK-questionnaires.

Stress levels in type 2diabetes were similar to those in healthy subjects; however, levels of well-being in type 2 diabetes were much lower than those in healthy subjects.

This result suggested that type 2 diabetic patients worry about loss of identity in the second half of their lives.

To support the self-management of diabetes, it is necessary for health professionals to understand patients' personalities and mental states as well as to perform the medical education of the disease. However, patients' lifestyles are too heterogeneous to be fully understood. When considering the proper support, it is not easy for others to establish the rapport with the patients in the short term. In order to establish the rapport, health professionals need to understand the patients' mental states directly from what they say or express. Many psychological assessment measures have been developed to provide such evidence, but most of them were experimental and not practical to establish the rapport leading to the education for the patients. Therefore, we developed BUKK-questionnaires consists of the two superscales, stress and well-being, which were determined by factor analyses. This study aimed to examine the efficacy of BUKK-psychological assessment to evaluate and understand the patients' mental states, and its application to self-management of diabetes.

We hypothesized that the interaction between stress and well-being would affect the condition of diabetes in each patient. Well-being is a positive total mood consisting of self-esteem,

affirmation, euphoria, fulfillment, lively feeling, and independence. Patients positively having well-being could conduct their own activities towards achieving self-management of diabetes. This indicates that their successful experience of self-management is one of the important factors to support healthy feelings.
The results revealed that the score distribution of the diabetic group was different from those of the control group and the neurologic group. There were no significant differences in the mean scores of stress between the diabetic group and the control group. These results strongly suggested that the improvement of well-being among the patients would support the self-management of diabetes.
Due to the increased average life expectancy to the age of 90, identity has become increasingly critical in the 40s and 50s, the transition stages of life, as well as in the puberty. Poor physical functioning, climacteric disturbance, psychological decline, socio-occupational instability in life stages may force persons to change their lifestyles.
As suggested by Jungian psychology, we believe that considering lifestyles after the age of 40 may provide the new possible way of living. The results of the present study have shown possible benefits to patients with diabetes in addressing the future challenges to verify the hypothesis on mental states of the patients through longitudinal and cross-sectional studies.

Taiwanese Diabetes Care 3.0 – Improving Efficiency through Automation

SP02-2

Improving self-management and diabetes education programs through analytics and automation

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For decades, diabetes self-management and shared care programs have been recognized as an integral part in improving patient outcomes. The success of self-care is often credited to structured education and empowerment of the patients.
While studies around the world have repeatedly shown positive outcomes with structured care programs, low coverage rates of patients have not been resolved. In many parts of the world, including Taiwan, UK and the United States, the coverage rates are only at 15% to 25%. Known barriers from the perspective of both patients and providers have caused low coverage rates. Low patient involvement may be categorized into those who "don't know", "can't go" and "won't go" (Vivien Coates, 2015); while providers face issues mainly related to limited resources and time in midst of ever rising patient census. Considering different countries have different systems (finance, resources), it is often difficult to replicate the effective care programs across the borders.
Over the past 18 months, an online diabetes management solution (including a mobile app for patients and a web-based patient management platform for care providers) was deployed to over 2,000 diabetes patients in Taiwan. The clients connected to one of the varying degrees of educator engagement or service: (1) none at all, (2) passive, and (3) proactive. We examine the effectiveness of this solution in terms of varying degrees of educator involvement. Furthermore, we will also discuss how the online system leverages analytics and automation for self-management; (1) how the platform brings new delight to patient engagement, support, and (2) how it supplements for the lack of diabetes educator resources and in some extent compensate each of the five levels of diabetes educators.* At the end, we will also discuss how the online solution collects and analyzes data; enables care providers to interpret results, deliver tailored messages, and take action to change practice.

*American Association of Diabetes Educators (AADE) (2011). Scope of Practice, Standards of Practice, and Standards of Professional Performance for Diabetes Educators

Level 1 – Non-healthcare professional
Level 2 – Healthcare professional non-diabetes educator
Level 3 – Non-credentialed diabetes educator
Level 4 – Credentialed diabetes educator
Level 5 – Advanced level diabetes educator/clinical manager

SP02-3

Assessment of the cost-effectiveness and clinical outcomes of a fourth generation synchronous telehealth program for the management of chronic cardiovascular disease: A longitudinal study

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Background: Telehealth program is a growing field for the care of patients. The evolution of information technology has resulted in telehealth becoming a fourth generation synchronous program. The long-term outcome and the cost-effectiveness analysis of such program have not been reported in patients with chronic cardiovascular diseases.
Objectives: We conducted this study to assess the clinical outcomes and cost-effectiveness of a fourth generation, synchronous telehealth program for patients with chronic cardiovascular diseases.
Methods: We retrospectively analyzed 576 patients who had joined a telehealth program and compared them with 1,178 patients matched for sex, age and Charlson comorbidity index. The program included: (1) instant transmission of biometric data; (2) daily telephone interview; and (3) continuous decision-making support. Data on hospitalization, emergency department (ED) visits and medical costs were collected from the hospital's database, and were adjusted to the follow-up months. A Cox proportional hazards model was fitted to analyze the impact of risk predictors on all-cause mortality. The model adjusted for age, sex, and chronic comorbidities.
Results: The mean age was 64.5 years. The numbers of monthly ED visits (0.06 vs. 0.09, $p < .001$), hospitalizations (0.05 vs. 0.11, $p < .001$), length of hospitalization (days, 0.77 vs. 1.4, $p < .001$) and intensive care unit admissions (0.01 vs 0.036, $p < .001$) were lower in the telehealth group. The monthly costs of ED visits (US$20.9 vs US$37.3, $p < .001$), hospitalizations (US$386.3 vs US $878.2, $p < .001$) and all medical costs (US$587.6 vs US$1,163.6, $p < .001$) were lower in the telehealth group. The intervention costs were US$224.8 per month. There were 53 (9.27%) deaths in the telehealth group and 136 (11.5%) deaths in the control group. A Cox's regression model with time-varying covariates results showed an estimated HR of 0.866 (95% CI 0.837–0.896, $p < 0.001$; number needed to treat at one year = 55.6, 95% CI 43.2–75.7, based on HR of telehealth program) for telehealth program on all-cause mortality after adjusting for age, sex, and comorbidities.
Conclusions: Better cost-effectiveness and clinical outcomes were noted with the use of a fourth generation synchronous telehealth program in patients with chronic cardiovascular diseases. Such telehealth program is also associated with less all-cause mortality compared with usual care, after adjusting for chronic comorbidities.

Using Big Data for Research and Care in Diabetes

SP03-1

Big data from bench to bedside to population in diabetes care

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The future in diabetes care promises to move from a more generic form of care to treatment that is better tailored toward the individual. To achieve this it is essential to begin to define the principles that govern individual responsiveness to the environment (i.e. food and exercise) as well as to drugs so that health practitioners can better match optimized treatments with improved long term health. This will require analysis of multiple layers of metabolic systems such as the genome, the transcriptome, the proteome and the environment using a range of model systems as well as interdisciplinary approaches to define the underlying features that determine key biological outcomes. This will include advances in accurate data acquisition, better ways of integrating data from different labs/centres and across different omic platforms and advances in data analysis and visualization. I will describe our efforts to map individual diversity in response to diet using different genetic strains of flies, mice and humans. I will describe omics analysis in both Drosophila and mice of different genetic backgrounds that clearly highlight the immense complexity of the gene-diet interaction. By marrying these data with longitudinal analysis of humans it should be feasible to develop a suite of biomarkers that predict future health outcomes and optimal prevention strategies for individuals. Such a venture will necessitate a move toward "big data" medical care where individuals are empowered with personalized data that provides them with better options for long term health.

Key Collaborators:

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WPR Disaster Program

SP04-1

IDF WPR natural disaster program: What next?

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The International Diabetes Federation Western-Pacific Region (IDF-WPR) Disaster Program aims to help each member country develop disaster preparation and medical care strategies, and thus minimising the effects of disaster events on the lives and health of diabetic patients by preparing and publishing an important guideline for disaster management. Since the WPR is known as the "Epicenter of the Diabetes Epidemic" because 8 of the top 10 countries with the highest prevalence of diabetes are from the Western Pacific Region. It is not only significantly affected by the diabetes epidemic, it has also the most frequently occurring natural disasters and many people's lives and health, with or without diabetes, are affected by the disasters. After these disasters, not only do mortality and morbidity rates immediately increase, but the stress, infections, lack of food, water, and medications can all lead to worsening of chronic illness, and may seriously impact their disease management. A better disaster management plan for preparation, action, response, and recovery is essential to reduce the effects of a disaster incident. It is well recognised that major disasters have a significant impact on diabetes, both in the short and long terms. Some of the information which are mentioned in the IDF-WPR Region Program for Diabetes Management in Natural Disaster are: For diabetes care providers, and related organisations, and governments, should: (i) develop a disaster guideline for emergency with periodic rehearsal assessments before a disaster, (ii) cooperate and communicate closely with coordination of medical resources during a disaster, and (iii) review the response after the disaster events. The IDF-WPR Disaster Committee aims to assist each country to create a national SOP for diabetes management in natural disasters. The SOP includes: (1) Educating diabetic patients and their family members to prepare for disasters. Conducting a registry of the diabetic populations most vulnerable after disaster events. Developing a disaster diabetes care program for medical staff. Conducting surveys on the quality and quantity of medical resources for diabetic care, and creating guidelines for coordinating donations of equipment and medicine from other countries. Cooperating and communicating with governments and various relief organisations. Establishing an information network to support diabetic patients. (2) Facilitating the sharing and exchange of information among researchers and educators throughout WPR-Asia. (3) Through relationships with the IDF and other collaborative organisations, providing education to support diabetic people and aid their recovery from disaster situations. The program also has flow diagrams for disaster preparation and response at certain timelines: 1**. For patients with diabetes**: Up-dated lists at all times: Medications and other major health problems, emergency food supply, emergency medical supply kit. Planning: Create a personal evacuation plan and evacuate early if authorities advise evacuation, learn stress-management skills and complete education projects, physician and emergency contact information, such as phone number, e-mail address, and name of contact persons. Response during disaster: Adhere to usual medications and recommended diet and lifestyle as much as possible, regularly self-monitor blood glucose and blood pressure, and perform other forms of self-management, such as wound care. Resolution and recovery: Ensure that appropriate meals are provided to diabetic patients (meals in shelters can be inappropriate for diabetes patients and impaired glucose control), ensure that diabetic patients maintain their daily activities and prevent becoming bedridden, which would reduce quality of life. **2. For diabetic medical staff:** *Before disaster*: Make an emergency plan: Appoint a leader and deputy to oversee preparation and operations, procure and maintain emergency equipment and supplies with standardised resource request correctly, periodic rehearsal and assessment. Guideline development and staff training and preparation: Develop training projects for medical and paramedical staff, including physicians, nurses, dieticians, pharmacists, and social workers, etc. Organise multidisciplinary medical teams for diabetes care. *Response during disaster*: Help network coordination and assist to provide comprehensive care, including mental health support, to patients, manage glucose, blood pressure, and evaluate and manage acute and chronic diabetic complications and other related medical problems, educate patients on self-management. *Resolution and recovery:* Support people recovering from disaster situations, and assist to provide long-term, continuous, and comprehensive care, regularly evaluate the health of each diabetic patient and provide support to prevent the acute complications and worsening of chronic conditions. **3. For government and diabetes organisation:** *Before disaster:*

Planning: Help survey diabetic populations particularly vulnerable in disaster events, develop a special care program. Addressing needs: Evaluate the quality and quantity of medical resources for diabetic care, establish guidelines for coordinating the donation of equipment and medicine from other countries. Communications: Regularly preview with relief organisations (such as the Red Cross) and various government agencies, Conduct periodic rehearsals. *Response during disaster:* Provide information to people with diabetes, caregivers, and the media and direct patient medical care, Contact relief organisations to obtain information and statistics and ascertain the type of assistance required, Contribute to identifying resources of medication supplies, Assist to organise multidisciplinary medical teams. *Resolution and recovery:* Review and discuss diabetes management strategies for diabetic people during and after a disaster, and revise the guideline program as necessary. In 2014 WPR council meeting in Singapore, members met to hear the synthesis of the program and a decision was made to review the guideline after 3–5 years, and individuals who prepared the original sections were invited to review and update their section taking into consideration new evidence and new treatments. This initiative need further steps to be taken. As a follow up, we need to look for resource persons, creating teams to prepare workshop topics and organising training centres regionally, and financial supports. The suggestion is that it could be organised after the next IDF WPR meeting in Taipei 2016. People with diabetes, health providers, and official emergency departments should always be prepared, and by way of such preparedness the impact an emergency may have on their condition will be lessened.

SP04-3

Disasters and patients with diabetes – an endocrinologist's experience in missions in Africa and the Philippines

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Diabetes is termed the modern epidemic of our times and plaques not only developed countries but also developing ones. It is predicted to increase exponentially in the next couple of decades, especially in Asia. Healthcare systems to combat diabetes are suboptimal in many places, not only with regards to prevention but also its detection and management of the disease itself and its complications. What is worse, many of such places might themselves be affected by disasters – man-made or natura – and this would impact on the already weak health infrastructure to further detriment diabetic patients and their treatment. This talk touches on the reality of such situations, drawing on experience in missions in both Africa as well as in Asia, namely the Philippines. It showcases a field worker's take of the situation, who happens to also be an endocrinologist.

Integration of Diabetes Management in Taiwan

S39-1

Overcoming difficulties and pursuing excellence

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The aim of the present study is to provide practical guidance on improving diabetes care through highlighting the need for: (1) increasing patients' understanding of type 2 diabetes and reaching glycemic goals (2) sharing responsibility/common philosophy for achieving glycemic goals, and (3) building a multidisciplinary team approach to treating type 2 diabetes. In order to overcome the barriers of achieving good glycemic control and share better understanding and mutual agreement regarding good glycemic control among members in the multidisciplinary team, establishing a good rapport with the patients and motivating them to achieve and maintain glycemic control are extremely essential. The methods of motivating and supporting patients to change their lifestyle are carried out by: (1) providing practical and realistic advices on implementing and sustaining lifestyle changes; (2) discussing steps that can be implemented punctually; (3) involving, where possible, other members of the diabetes care team, particularly family and friends; and (4) emphasizing the role of the multidisciplinary team. There are two key functions of the multidisciplinary team. The first is to provide continuous, accessible and consistent care focusing on the needs of individuals with type 2 diabetes, including collections of information concerning diagnosis of conditions and continually thereafter, agreements of care standards, discussions on rational therapeutic suggestions, monitoring guideline adherence in accompany with short-term outcomes, and avoiding early complications or providing timely intervention to decrease diabetes-related complications. The second is to enable patients' long-term self-management. A multidisciplinary team can reduce 62% annual cost of treatment. Other than this, the benefits of a multidisciplinary team approach to type 2 diabetes care include: (1) improving glycemic control, (2) increasing patient follow-up, (3) lowering risk of complications, (4) improving quality of life, (5) increasing patients' sense of satisfaction[1] and (6) decreasing healthcare costs.

S39-2

Diabetes case management: Improvement measures at Changhua Christian Hospital

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With an ever-growing population of people with chronic diseases, it is estimated that Taiwan now has over 1.5 million diabetic patients. The crippling burden of diabetes on health expenditure is felt in healthcare institutions large and small as well as in governmental levels. At our hospital, a tertiary care medical center in central Taiwan, well over 10,000 patients are regularly treated for diabetes. With the majority of the patients enrolled in a diabetes share-care program, it has been a constant challenge to deliver comprehensive care to the patients while complying with the regulations and requirements of national health insurance reimbursement and meeting the quality standards imposed by the share-care program. Fortunately, with the full support of the hospital's administrative office, much resource and planning have been invested in diabetes case management at our hospital. Under constant supervision, various improvement measures have also been implemented to facilitate case management over the years. Indispensable among them are a constantly evolving information system which not only keeps comprehensive patient information in a robust, easy to access database but also provide physicians and case managers helpful guidance and reminders to guard against errors and oversights, a patient-friendly environment and arrangements that make each visit as hassle-free as possible, and various communication and standardized procedures to ensure coordinated and integrated teamwork in the delivery of care. Such efforts have earned us much recognition for the present. However, the growing burden of diabetes and the increasing complexity of its treatment and management will undoubtedly demand continual evolvement of our case management system.

S39-3

Experience of diabetes management in an integrated polyclinic of Taiwan

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Diabetes a lifelong condition that is essentially need self-managed but requires regular monitoring. The standard of care in diabetes includes emphasis on self-management

education provided through professional teams. The implementation of patient-centered care in diabetes can include diet and exercise, treatment-taking, psychological stress, self-monitoring of blood glucose, and sick-day management to reduce the risk of long-term complications, such as kidney disease, coronary artery disease, stroke, blindness and amputation. Diabetes self-management education/support access to a multidiscipline team, care planning discussions, reminding, informatics and annual checks are important procedures to identify necessary changes to treatment regimens and refer to specialist services. Integrated diabetes care is both integration of a health care system and co-ordination of services around a patient. Integration of services around the patient and across the community becomes more robust and effective as evidenced by many scientific reports. Our polyclinic specific on diabetes care constitute of diabetologist, neurologist, ophthalmologist, nephrologist, hepatologist, psychologist, and certified diabetes educators that serving over 5,000 patients with diabetes. Our experience on integrated care specific on diabetes management may suggest higher quality of management would be observed if patients are managed under the system. However, challenges and barriers of quality improvement in diabetes care still exist and need to be conquered by wisdom and encouragement.

Self-Management of Diabetes Education

S40-1

The role of shared decision making in diabetes education

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Patient-centered care has been found to be associated with improved patient outcomes, including improved self-management, patient satisfaction, and medication adherence. A patient-centered care is defined as: providing care that is respectful of and responsive to individual patient preferences, needs, and values and ensuring that patient values guide all clinical decisions. Shared decision making is one of practical and well-described methods to accomplish patient-centered care.

Shared decision making has been defined as: "an approach where clinicians and patients share the best available evidence when faced with the task of making decisions, and where patients are supported to consider options, to achieve informed preferences". In shared decision making the clinicians' role is to help patients understand what the reasonable options are, clarify treatment options, and integrate patients' informed preferences as they relate to the available options. Usually a patient has more than one reasonable treatment option, informed preferences are an optimal goal because the decisions made will be better understood, based on more accurate expectations about the negative and positive consequences and more consistent with personal preferences. In other words, individual self-determination is a desirable goal and clinicians need to support patients to achieve this goal.

The model of how to do shared decision making is based on choice, option and decision making. Three key domains of shared decision making are (1) Information-Sharing, Clinicians help patients participate by providing high quality information and also need to elicit what patients already know, and whether it is correct. (2) Deliberation, Clinicians support patients to full disclosure of treatment options, and explore their reactions to information. (3) Decision-making/implementation, Clinicians support patients to consider preferences and decide what is best. Patients and clinicians arrive at a treatment plan. Barriers and facilitators to shared decision making in diabetes education also will be mentioned.

S40-2

A diabetes self-management education/support structured program built for patients with poor glycemic control

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Diabetes self-management education/support (DSME/S) refers to the education and support that is required for implementing and sustaining coping skills and behaviors needed to self-manage on an ongoing basis. It is well established that diabetes self-management education (DSME), a complex health intervention, is generally effective at enhancing self-care behaviors, improving glycemic control, lowering health care costs, and improving quality of life. We thought that the theoretical basis and framework of the behavior change approach for the structured educational intervention among patients with type 2 diabetes (T2DM) in poor glycemic control is essential.

Focus group education approach such as Conversation Map™ (CM), an innovative visual tool grounded in several learning and behavior change theories, may be a promising toolkit for DSME. In contrast to traditional DSME provided by a one-to-one didactic method, CM is performed in a small group and allows patients to learn about key concepts through interactive discussion and choose what they can change in their daily diabetes care. In the meantime, instead of as inculcators, diabetes educators can work as facilitators by providing information to participants and helping patients to set personalized action goals to improve their diabetes care. To date, the content of CM has been recognized by several professional societies (e.g., the American Diabetes Association (ADA), International Diabetes Federation (IDF), Canadian Diabetes Association and Taiwan Association of Diabetes Educators (TADE).

Despite CM having been distributed worldwide for the past few years, scientific evidence is limited and its clinical value may also be challenged. We thought it should be noted that the delivery of DSME largely depends on the resources of the healthcare system and the clinical scenario. Hence, we design the program with CM in in our routine focus group education every Tuesday afternoon and share the experience to you.

Lunch Seminar – LG Life Science

LN02-1

Optimizing glucose control with gemigliptin in type 2 diabetes

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Type 2 diabetes is a complex and progressive disease which requires continuous medical care with multifactorial risk reduction. Glycemic variability and chronic sustained hyperglycemia are the main components of dysglycemia in diabetes. Because even short periods of hyperglycemia increase the risk of micro- and macrovasular complications, a more proactive approach is required to get patients to achieve their glycemic goals sooner.

DPP-4 inhibitors are well suited for the use in a wide range of patients with T2DM, due to their ease of use, low risk of hypoglycemia, weight neutrality and favorable tolerability. However, they differ widely in their binding to the DPP-4 enzyme, potency, and selectivity as well as their pharmacokinetics profiles because the class is heterogeneous regarding chemical structure.

Gemigliptin is a potent, selective, and long-acting DPP-4 inhibitor and also effective and well tolerated in patients with type 2 diabetes mellitus (T2DM) as either in monotherapy or in combination therapy. In addition, it is more effective in reducing glycemic variability than sitagliptin or SU as initial combination therapy with metformin in drug-naïve patients with T2DM. Various studies have shown that gemigliptin is optimized with having potent efficacy, reliable safety and compliance benefits for T2DM. In this talk, I will review the key characteristics of gemigliptin and discuss its potential benefits in the treatment of type 2 diabetes.

Lunch Seminar – Servier

LN04-1

Update on existing therapy – with a focus on SUs

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Metformin is recommended, in most guidelines, as first line treatment for overweight patients with type 2 diabetes. Sulphonylureas (SU) remain an initial option for non-obese patients and are useful second line therapy because they are effective and well tolerated. However, there is a common misconception that SU are inferior to modern agents such as DPP4 inhibitors in terms of complications prevention, cardiovascular (CV) risk and durability of control. Apart from metformin, SU are the only oral diabetes therapies to have shown clear reductions in microvascular complications in long term end-point trials. SGLT 2 inhibitors show promise with a recent study suggesting CV protection, but further studies are awaited. Also, these agents are not effective in patients with reduced renal function and are expensive. The effect of intensive glycaemic control with gliclazide (Diamicron MR®) was studied in the ADVANCE trial. 11,140 subjects were randomised to intensive therapy aiming for an HbA1C of <6.5%, or standard care, for 5 years. The intensive group attained an HbA1C of 6.4% vs. 7.0% in the control group. Intensive control reduced microvascular endpoints by 14% and had no adverse effect CV endpoints. These results were consistent with the effects of SU therapy seen in a previous end-point trial, the UKPDS. In that study, an HbA1C reduction of 1% resulted in a 25% reduction in microvascular endpoints over a 10 year follow up period. Gliclazide has been shown to cause less hypoglycaemia than comparable SU's, and it is interesting to note that the rate of hypoglycaemia in ADVANCE was much lower than that of comparable studies.

In the ADVANCE-ON study, 84% of the ADVANCE cohort (8,494 people) were followed for a further 5.4 years after the original trial finished. The difference in HbA1C between the intensive and control groups disappeared by the first post-trial visit, and remained similar at the end of ADVANCE-ON (intensive 7.2%, control 7.4%). End-stage renal disease resulting in death or dialysis was reduced by 64% ($p = 0.007$), suggesting a persisting microvascular benefit from earlier intensive glucose control with a gliclazide MR based regimen.

Diabetes is a progressive process and β cell function declines gradually over time. In the UKPDS, β cell function declined at a similar rate in SU, metformin and insulin treated patients. Interest has focused on the possibility that newer diabetes drugs might preserve β cell function. The ADOPT study compared the effects of metformin, glyburide and rosiglitazone on glycaemic control over 5 years. Although rosiglitazone initially appeared to delay the progression of diabetes, by 5 years the decline in β cell function was similar in all 3 groups. Only short-term data exists for the DPP4 inhibitors, but studies to date suggest durability of control is very similar to SU's.

There have, over many years, been concerns about the effect of SU's on the risk of cardiovascular complications. One possible mechanism is that many of these drugs prevent the opening of myocardial K^+-ATP channels, thereby increasing the effects of ischemia on the myocardium. Gliclazide does not have this effect and, in the ADVANCE and ADVANCE-ON trials, there was no adverse effect on cardiovascular end-points. Also, gliclazide appears to have some unique properties not shared by other SU's. We have found that gliclazide, but not other SU's or metformin, inhibited the oxidation of LDL and reduced markers of oxidative stress in diabetic patients. In another study, both metformin and gliclazide but not glibenclamide inhibited the progression of the intima-media thickness of the carotid artery, an index of the progression of atherosclerosis.

SU's, and particularly gliclazide (Diamicron MR®) are effective and well tolerated agents for the treatment of type 2 diabetes and their use is well validated by large scale end-point studies. SU's differ in their propensity to cause hypoglycaemia and in their vascular effects, and this should be taken into account when prescribing. Sulphonylureas are likely to retain a major role in diabetes treatment algorithms for the foreseeable future.

Lunch Seminar – Boehringer-Ingelheim

LN09-1

New horizons for managing type 2 diabetes

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Type 2 Diabetes Mellitus (T2DM) is a complex cardio-metabolic disorder characterized by insulin resistance, pancreatic beta cell dysfunction and hyperglycaemia. Due to the progressive nature of T2DM, maintaining glycemia as close to normal as possible can significantly reduce microvascular complications. Long-term reduction in macrovascular disease was also observed, if the glycemic control was implemented soon after diagnosis. Current treatment guidelines emphasize the importance of individualizing patient care with regard to both goals and therapies. A number of different diabetes therapies exist, allowing for personalized therapy regimens. Engage patients by involving them in healthcare decisions and selecting therapies that fit with their needs and preferences, which may enhance adherence to therapy. As the disease progresses, changes in β-cell function and insulin resistance can limit the ability of certain oral antidiabetic agents to reduce blood glucose levels.

Sodium glucose cotransporter 2 (SGLT2) inhibitors are a new class of antidiabetic agents through insulin independent pathway that reduce hyperglycemia in patients with T2DM by reducing renal glucose reabsorption and thus increasing urinary glucose excretion (UGE). Most recent guidelines have already included SGLT2 inhibitors as one of the dual or triple therapy options, even concomitantly treatment with insulin. Drugs within the class of SGLT2 inhibitors have shown various clinical, mechanistic and theoretical effects on cardiovascular pathways and some of the cardiovascular outcome studies have been conducted to assess whether any of the individual SGLT2 inhibitor compounds has an impact on cardiovascular outcomes.

Based on the placebo-controlled phase III trials in T2DM patients taking empagliflozin (one of the SGLT2 inhibitors), improved hemoglobin A1c (HbA1c) has been noted in monotherapy or add-on therapy with a low risk of hypoglycemia, reduced body weight and blood pressure, without increases in heart rate. Further investigations have also revealed the efficacy and safety data of empagliflozin in patients with certain range of impaired renal functions. In addition, empagliflozin has also been reported to reduce other CV risk markers such as visceral fat mass, uric acid, arterial stiffness and glomerular hypertension. With the positive results

observed from EMPA-REG OUTCOME, more and more studies will be implemented to confirm the potential benefits and safety in patients with cardiovascular and renal disease.

LN09-2
EMPA-REG OUTCOME®: Macrovascular and microvascular outcomes
Ele FERRANNINI[1,2]. [1]*University of Pisa School of Medicine and CNR (National Research Council) Institute of Clinical Physiology, Pisa, Italy;* [2]*University of Texas Health Science Center, San Antonio, Texas, USA*

People with type 2 diabetes (T2D) are at increased risk of vascular morbidity and mortality. Cardiovascular (CV) disease remains a major complication and is the leading cause of death associated with diabetes. While intensive glucose control reduces the risk of microvascular complications, its relationship to CV outcomes remains unclear. The management of T2D is therefore complex and necessitates treatment considerations beyond glycaemic control.
In the context of these current challenges, Professor Ele Ferrannini from the University of Pisa, Italy, and the University of Texas Health Science Center in San Antonio, USA, will provide an overview of EMPA-REG OUTCOME®, the first CV outcomes trial in T2D to demonstrate improved CV outcomes in patients at high CV risk. In EMPA-REG OUTCOME®, the SGLT2 inhibitor empagliflozin was found to significantly reduce CV death compared with placebo in patients with T2D and established cardiovascular disease.[1]
Professor Ferrannini will begin by outlining the baseline characteristics of the trial population, background standard of care and trial endpoints. He will then explore the CV outcomes, heart failure outcomes and renal findings from the study. The trial safety findings, including those relevant to patients with renal impairment or heart failure at baseline, will also be reviewed during his presentation. Finally, Professor Ferrannini will consider the wider clinical implications of the EMPA-REG OUTCOME® trial results for future diabetes care.

Reference

1. Zinman B *et al*. Empagliflozin, cardiovascular outcomes, and mortality in type 2 diabetes. *N Engl J Med* 2015;373:2117.

Lunch Seminar – Takeda

LN10-1
Collaborations & combinations: Spotlight on high CV risk and T2D patients in Asia

Cardiovascular outcome trials (CVOT) are increasing our understanding of how we can optimize the way we manage type 2 diabetes (T2D) patients.
We want to have a conversation about what this means for endocrinologists and cardiologists treating high CV risk and hypertensive patients with T2D mellitus in Asia.
This unique symposium will look at the challenges – and discuss the potential solutions – to help improve and optimize the treatment of specific patient populations in Asia.
Professor Fen-Yu Tseng and Professor Bob Chilton will talk about the importance of collaboration from the perspective of endocrinologists and cardiologists – including strategies to help optimize multidisciplinary collaboration.
We will spotlight the epidemiology of high CV risk and hypertensive patients, focus on CVOTs and discuss why they are important. We will present the individual trials in detail – including EXAMINE, LEADER, EMPA-REG and PROactive. We will then look at what these clinical data mean for patients and clinicians.
Professor Bob Chilton and Professor Stefano Genovese will discuss the azilsartan and alogliptin treatment families. We will examine the clinical data and look at the specific patient populations for whom these treatments and treatment combinations are most appropriate.
Now is the time to have a conversation about how we improve and optimize the management of high CV risk patients with T2D in Asia.
Please come join us and collaborate in this symposium.

Lunch Seminar – Ascensia

LN11-1
Accuracy and user performance evaluation as key factors in self-monitoring in diabetes patients
Guido FRECKMANN[1]. [1]*Institute for Diabetes-Technology Research and Development Corporation, Germany*

For people with diabetes, self-monitoring of blood glucose (SMBG) is an essential part in the maintenance of glycemic control. Particularly for patients with intensified insulin therapy or insulin pump therapy, the availability of reliable and accurate glucose results is crucial to adequately adjust insulin doses.
The international standard ISO (International Organization for Standardization) 15197 defines various requirements for SMBG systems, concerning safety and reliability, analytical performance (e.g. system accuracy), information supplied by the manufacturer and performance in the hand of lay-users. The currently applicable version of the standard is ISO 15197:2013, its predecessor was ISO 15197:2003.
Regarding system accuracy, ISO 15197:2013 describes the following minimum criteria: Criterion A: At least 95% of a system's measurement results shall fall within ±15 mg/dL of the comparison measurement results at blood glucose (BG) concentrations <100 mg/dL and within ±15% at BG concentrations ≥100 mg/dL. Criterion B: At least 99% of individual measurement results shall fall within Consensus Error Grid zones A and B. Criterion A is also applicable for user performance evaluation.
A number of accuracy evaluation studies performed in recent years have reported that not all available SMBG systems show sufficient measurement quality to comply with ISO 15197 requirements. However, there are qualitative differences even among SMBG systems that comply with ISO 15197 requirements. Simulation studies show that higher accuracy leads to clinical benefit. User performance evaluation studies showed that SMBG systems showing high accuracy when used by trained professionals do not necessarily also showed high accuracy in the hands of lay-users. This underlines the importance of patient education and training, not only to avoid meter-independent factors like contamination of hands, but also to highlight meter-specific details. A reliable and accurate SMBG system is an important aspect in optimizing insulin-dependent patients' therapies.

Lunch Seminar – AstraZeneca

LN14-1
Is there a unifying hypothesis to explain the cardio-renal benefit of SGLT2 inhibitors? – Spotlight on the role of ketone bodies
Sunder MUDALIAR[1,2,3]. [1]*University of California,* [2]*Director Diabetes Clinic, VA San Diego Healthcare System,* [3]*Director Special Diagnostic and Treatment Unit, VA San Diego Healthcare System, San Diego, CA, USA*

Type 2 diabetes causes excessive morbidity and premature cardiovascular (CV) mortality. Although tight glycemic control improves microvascular complications, its effects on macrovascular complications have been mixed. In the ACCORD study, tight glycemic control was associated with increased CV and all-cause mortality, despite a significant reduction in non-fatal myocardial infarction (MI). Some diabetes medications like the glitazones and saxagliptin (a DPP-4 inhibitor) have been associated with an increase in the risk of hospitalization for heart failure, despite improving glucose control. In the recent EMPA-REG OUTCOME study conducted in patients with type 2 diabetes at high cardiovascular risk, treatment with empagliflozin (an SGLT2 inhibitor) was associated with impressive reductions in CV/all-cause mortality and also hospitalization for heart failure without any effects on classic athero-thrombotic events (MI and stroke). Equally impressive was the effect of empagliflozin on renal outcomes. Compared to placebo, empagliflozin treatment was associated with a 39% relative risk reduction in the occurrence of incident or worsening nephropathy, defined as progression to macroalbuminuria, doubling of serum creatinine, initiation of renal replacement therapy, or death due to renal disease. Of note, these cardio-renal benefits occurred in the setting of more than 80% of the patients being on statins and ACEi/ARB agents. However, what is puzzling about the above CV and renal benefits is the fact that the curves for heart failure hospitalization, renal outcomes and CV mortality begin to separate within 3 months and were maintained for more than 3 years. It is unlikely that modest improvements in glycemic, lipid or blood pressure control contributed significantly to the beneficial cardio-renal outcomes within three months. Other known effects of SGLT2-inhibitors on visceral adiposity, the vascular endothelium, natriuresis and neuro-hormonal mechanisms are also unlikely major contributors to the cardio-renal benefits. We postulate that that the cardio-renal benefits of empagliflozin are due to a shift in myocardial and renal fuel metabolism away from fat/glucose oxidation, which are energy inefficient in the setting of the diabetic heart and kidney and towards an energy efficient "super" fuel like ketone-bodies which improve myocardial/renal work efficiency and function. Even small beneficial changes in energetics on a minute-to-minute basis translate into large differences in efficiency and improved cardio-renal outcomes over weeks to months and continue to be sustained. Well planned physiologic and imaging studies need to be done to characterize this "fuel energetics" based mechanism for the cardio-renal benefits.

Lunch Seminar – Zespri

LN15-1

Kiwifruit – A double agent for glycaemic control and nutrient enhancement

John MONRO[1]. [1]*The New Zealand Institute for Plant & Food Research, New Zealand*

A ripe kiwifruit is a luscious, sweet, carbohydrate-rich food – the kind of food that would be expected to raise blood glucose concentrations. However, kiwifruit is also nutrient dense and capable of promoting health in numerous ways.
We therefore faced two questions:

1. What is the true glycaemic potency of whole kiwifruit – the capacity of the whole fruit to raise blood glucose?
2. What effect does the interaction of kiwifruit with other components of a meal have on the meal's glycaemic impact?

We addressed these questions in a research sequence involving in vitro and human intervention studies, and found:

(a) The non-digested dietary fibre remnants from kiwifruit that had been digested in vitro occupied about four times their original volume in the intact fruit. They would therefore surround and extensively interact with other foods in the limited volume of the gut.
(b) Within the dispersion of pre-digested kiwifruit remnants several processes important to the glycaemic response were substantially retarded in vitro, including:
- Digestion
- Sugar diffusion
- Mixing of intestinal contents

(c) In a human intervention study we found the glycaemic impact of kiwifruit to be relatively low; 100 g of kiwifruit would have about the same effect on blood glucose as only 6 g of glucose.
(d) The low in vivo glycaemic impact could be partly attributed to the carbohydrate in kiwifruit being fruit sugars, but the kiwifruit also caused changes in the blood glucose response curve that indicated improved homeostatic blood glucose control due to factors other than sugar, consistent with effects of kiwifruit remnants on intestinal processes indicated by the in vitro studies above (in c).
(e) Analysis of the effects of equal carbohydrate, partial substitution of kiwifruit for highly glycaemic foods – such as those based on cereal starch – showed that it is an effective strategy for improving intake of nutrients such as vitamin C, with the added benefit of reducing glycaemic impact.

Lunch Seminar – Boehringer-Ingelheim

LN17-1

Translation into clinical practice: New findings in linagliptin

Per-Henrik GROOP[1]. [1]*Helsinki University Central Hospital, Finland*

Cardiovascular (CV) and kidney disease remain significant clinical challenges, and are key considerations in the management of patients with type 2 diabetes (T2D). In addition to reducing the risk of developing complications, treatment selection for patients with T2D is also influenced by individual patient factors, including the risk of hypoglycaemia, the presence of renal impairment, and requirements for dose adjustment within a multi-drug regimen.
Professor Per-Henrik Groop from the University of Helsinki, Finland, will begin his presentation by providing an overview of the use of DPP-4 inhibitors for glucose control in patients with renal dysfunction, including recent data for linagliptin in this patient population. He will present data on the efficacy and safety of linagliptin in patients with T2D and co-morbid kidney disease, and will discuss how these data may translate into clinical practice.
Professor Groop's presentation will then describe the potential effects of linagliptin beyond glucose control, discussing data from the MARLINA-T2D™ trial in patients with T2D at early stages of diabetic kidney disease. In addition, he will discuss the longer-term CARMELINA® trial, designed to investigate the potential renoprotective effects of linagliptin treatment in patients with more advanced diabetic kidney disease, and the CAROLINA® trial, which will evaluate CV safety in patients with T2D at elevated CV risk, including patients with chronic kidney disease.

LN17-2

Reality of insulin initiation in Type 2 Diabetes Mellitus

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Prevailing evidences indicated that diabetes-related vascular complications are highly preventable through intensive glycaemic control, and that achieving blood glucose targets early in the disease trajectory translates to latent benefits for decades beyond. Maintenance of optimal glycaemic control requires successive up-titration of anti-diabetic drug treatment, and insulin is necessary for the majority of patients due to natural progressive decline in pancreatic β-cell function. Whilst international guidelines strongly advocate basal insulin upon failing 2 or 3 non-insulin anti-diabetic drugs, initiation of insulin therapy is often delayed as a result of clinical inertia and resistance by patients.

Psychological insulin resistance is a phenomenon that describes barriers to starting insulin therapy and/or to adhere to prescribed treatment, and is a common reaction in up to 40–70% of people with diabetes. It encompasses a range of psycho-cognitive factors including fear of injection, fear of hypoglycaemia and/or weight gain, poor self-efficacy about the skills required to administer insulin, anxiety over interferences with daily living, anticipated social stigmatization, and misconception about the rationale and efficacy of insulin therapy. Of the latter, patients may perceive insulin therapy as a form of punishment for their personal failure to manage their diabetes, whilst others may have concerns that insulin causes harm.

Despite high prevalence, psychological insulin resistance is often under-recognized and inadequately addressed. Culture, age, and gender are variables that may influence the scope of psychological insulin resistance, which is also linked to underlying depression. Failure to initiate insulin therapy in a timely manner and to comply with the recommended injection doses and schedule are key factors leading to low rates of glycaemic target attainment. Health care professionals should be alerted to the multi-dimensional nature of this problem and encourage acceptance of insulin therapy by exploring underlying issues and managing patients' concerns in a positive manner.

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International Diabetes Federation

Oral Presentations

Epidemiology and Prevention of Diabetes

OL01-2

Characteristics of abnormal oral glucose tolerance test in GDM diagnosis

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Objectives: To describe characteristics of abnormal OGTT values in GDM diagnosis and their clinical correlation. In addition, the effects of omitting any OGTT value on GDM diagnosis were evaluated.
Methods: A total of 415 women diagnosed with GDM were included. GDM screening and diagnosis results were extracted from medical records. Detailed analysis of OGTT values at the time of GDM diagnosis was performed, including prevalence of abnormalities of each value, number of abnormal values. In addition, relationship between abnormal OGTT values and maternal characteristics and clinical characteristics were also evaluated.
Results: Mean age was 32.9 years, 46% were nulliparous, and 39% were overweight. Mean gestational age at diagnosis was 19.2 weeks and 42.4% were diagnosed during 24–28 weeks. Insulin therapy was indicated in 12% of cases. Most common abnormalities were found in the 2nd and 3rd values (85.3% and 96.6% respectively). In terms of number of abnormal OGTT values, abnormal 2 values was found in 42.9% while abnormal 3 or 4 values were found in 34.2% and 22.9%, respectively. Detailed analysis revealed that 16.7% of GDM would be missed if the 4th OGTT was omitted, including 2 cases who required insulin therapy. Number of abnormal OGTT values were significantly higher among overweight women ($p = 0.02$) and those who required insulin therapy ($p < 0.001$), but not related to timing of diagnosis. Mean birth weight and rate of macrosomia were also comparable between different numbers of abnormal OGTT values.
Conclusion: Among GDM women, 57.1% had abnormal 3 or 4 OGTT values. Number of abnormal OGTT values were positively related to overweight and insulin requirement. Omitting the 4th OGTT value would result in unacceptable 16.7% undiagnosed GDM.

OL01-3

Increased risk for diabetes development in subjects with large variation in total cholesterol levels in Koreans

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Background: Recent studies suggest the role of hyperlipidemia on development of diabetes. However, statins are reported to increase the risk for diabetes development. We analyzed the relationship between the variations of total cholesterol (TC) levels and the risk of type 2 diabetes in data from a Korean nationwide population-based study.
Methods: In 2,827,950 Korea examinees in general health check-up database (DB) as a sub-dataset of Korean National Health Insurance Service (NHIS), in whom at least two health check-up data were available between 2002 and 2006, and did not have diabetes at baseline, the variations of TC between the examinations were calculated. The examinees were divided into 10 groups according to deciles of TC variation and the hazard ratio for diabetes development from 2007 to 2013 were analyzed.
Results: During the follow-up period, 3.4% of the examinees developed diabetes. The subjects with the highest decile of TC variation (32.5%) showed the highest incidence rate for diabetes among the decile groups of TC variation (5.24%), and the incidence rate for diabetes showed J-shaped curve with fourth decile group showed the lowest incidence rate for diabetes. The highest decile group of TC variation showed increased hazard ratio for diabetes development after adjustment for confounding variables (1.16; 95% CI 1.14–1.18). These results were similarly observed in either group with or without hyperlipidemic medication.
Conclusions: The subjects with large variation of TC showed increased risk for diabetes development, independent to the medication of hyperlipidemic agents. These results suggest the possibility of contribution of variation in TC level, not the medication itself that affects the risk for diabetes development.

OL01-4

Central blood pressure and insulin sensitivity after an oral glucose loading

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Background: Although peripheral blood pressure (BP) is generally used to guide therapeutic decisions, recent

meta-analysis reported that central arterial pressure can be a more useful predictor of cardiovascular disease. Postprandial metabolic and hemodynamic responses are not fully studied. We aimed to examine the changes and associations between central BP and insulin sensitivity during an oral glucose tolerance test (OGTT).
Research design and methods: Subjects without diabetes history underwent a 75-g OGTT from November 2011 to June 2015 while those taking anti-hypertensive medications were excluded. A validated oscillometric BP monitor was used to measure and calculate brachial systolic BP (SBP-b), brachial diastolic BP (DBP-b), central SBP (SBP-c) and central DBP (DBP-c) at the timings of 0, 30 and 120 min, respectively, during the OGTT while plasma glucose and insulin concentrations were measured at these timings. Percentage of each change (presented as %Δ) after OGTT was calculated by subtracting pre-OGTT measurement as (post-OGTT–pre-OGTT)/pre-OGTT. The relationships between changes in BP and glucose and Matsuda insulin sensitivity index (ISIM) during OGTT were analyzed.
Results: Sixty-four adults (43 men and 21 women, mean age of 56 ± 14 years) were enrolled and baseline (0 min) SBP-b, DBP-b, SBP-c, DBP-c were 122 ± 11, 74 ± 8, 120 ± 11, and 69 ± 7 mmHg, respectively. Fasting glucose was 93 ± 11 mg/dL. Percentage change of glucose at 30 min (%ΔGlu 30′) negatively correlated to %ΔSBP-b 120′ ($r = -0.367$, $p = 0.003$) and %ΔSBP-c 120′ ($r = -0.283$, $p = 0.02$), respectively. In addition, the more SBP-c increment from 0′ to 30′ (%ΔSBP-c 30′), the higher log-transformed ISIM was measured ($r = 0.265$, $p = 0.03$). Results of multivariable linear regression analysis, adjusted of age, sex, body mass index, smoking status, heart rate and glucose tolerance status, identified %ΔSBP-c 30′ but not %ΔSBP-b 30′ was an independent determinant of log-transformed ISIM ($p = 0.02$, 95%, CI: 0.183–1.714).
Conclusion: Metabolic and hemodynamic responses including BP, glucose and insulin sensitivity after an oral glucose loading varied greatly. We present the subtle changes during short-term postprandial phase that elevated SBP-c was associated with one's enhanced insulin sensitivity. The detailed mechanisms and long-term BP variability on cardiovascular outcomes require further investigation.

OL01-5
High diagnosis lag in diagnosis of type 2 diabetes mellitus: Need of the hour
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Background and objectives: Type 2 Diabetes Mellitus is often characterized by an asymptomatic phase of around 4–7 years between the onset of diabetes and its clinical diagnosis. Diabetic retinopathy is the one to be observed as an early sign of microvascular complications. The objective of the present study is to investigate the time lag between the onset of hyperglycemia and clinical diagnosis of T2DM.
Methods: The present cross-sectional study was done at an outpatient setting of an endocrinology clinic. According to inclusion criteria, Consecutive patients subjects of either sex with T2DM either newly diagnosed at the time of first encounter with study investigator or previously diagnosed with any duration of T2DM were eligible to be recruited in the present study. A weighted linear regression analysis was performed to estimate the prevalence of retinopathy at each time point. The period at which the prevalence of retinopathy was zero is back extrapolated from the graph to get onset of diagnosis.
Results and interpretations: A total of 1407 patients with T2DM are included in present analysis. 52% (n = 725) were females and mean (SD) age was 54.3 (10.1) years. The prevalence of diabetic retinopathy was found to be 13.7% (n = 194) at the time of clinical diagnoses. Prevalence of retinopathy increased linearly with duration of T2DM. Estimated the actual onset of time of diabetes was found to be 11.4 (95% CI, 9.5–15) years before the patients were clinically diagnosed with T2DM.
Conclusions: High diagnostic lag was observed in present study. It indicates that there is a need for continues education, counseling of high risk population on diabetes mellitus and its complications to increase awareness of diabetes and reduction of diagnostic lag.

OL01-7
The influence of oral contraceptives on the prevalence of diabetes in postmenopausal women: 2007–2012 KNHANES
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Background and aims: There is little information on whether past use of oral contraceptives (OCs) at childbearing age influences the incidence of diabetes and insulin resistance (IR) after menopause. This study aimed to evaluate the association of past use of OCs with the development of diabetes and IR in post-menopausal women.
Materials and methods: This cross-sectional study was based on data from the Korea National Health and Nutrition Examination Survey from 2007 to 2012. Of the 50,405 participants, 6554 postmenopausal women were selected and included in the analysis. The long-term effects of OCs use on the prevalence of diabetes in post-menopausal women were examined using multivariate logistic analysis. In addition, fasting glucose and insulin levels were measured in 3338 non-diabetic post-menopausal women, and the association between IR and OCs was examined by analysis of covariance.
Results: The prevalence of diabetes was significantly higher in post-menopausal participants who had taken OCs for more than 6 months than in those who had never taken OCs. The association remained significant after adjusting for multiple confounding factors (odd ratio, 1.379; 95% CI, 1.115–1.707; P = 0.003). The duration of OCs use was also positively associated with the prevalence of diabetes. Furthermore, taking OCs for more than 6 months led to a significant increase in fasting insulin levels and HOMA-IR in non-diabetic participants.
Conclusion: Past use of OCs for more than 6 months led to a significant increase in the prevalence of diabetes in post-menopausal women, and increased IR in non-diabetes participants. These results suggested that prolonged use of OCs at a reproductive age is an important risk factor for developing diabetes in post-menopausal women.

Pathogenesis of Obesity, Diabetes, and Diabetic Complications

OL02-1
Possible role of hepassocin in chronic social defeat-induced metabolic disturbance
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Background: Several stress-induced psychiatric illnesses, including social defeat are associated with an increased risk of developing metabolic disturbances. The stress of social defeat activates the sympathetic nervous system, and recruits the hypothalamic-pituitary-adrenal axis (HPA) to change the neurotransmitter release in several brain regions, and might result in long-lasting physiological changes, including metabolic disturbances such as obesity and metabolic syndrome. Although the relationship between metabolic disturbances and stress were well established, the mechanisms linking social defeat and metabolic disorders remain obscure. Hepassocin is an interneukin-6-regulated hepatokine, and exerts an activity to induce insulin resistance through an ERK-dependent pathway. In addition, the expressions of hepassocin were increased in social defeat animal model. Thus, the aim of this study is to investigate the role of hepassocin in stress-induced insulin resistance.
Material and methods: The chronic social defeat model was established with C57BL/6J and CD-1 mice. C57BL/6J mice that are repeatedly subjected to bouts of social defeat by a larger and aggressive CD-1 mouse for 10-day results in the development of a depressive-like syndrome. Insulin sensitivity and glucose utility in animals were assessed by insulin and glucose tolerance tests, as well as HOMA-IR. The concentrations of interleukin-6, cortisol, and hepassocin were measured by commercialized ELISA kits. The expressions of hepassocin and interleukin-6 receptor were determined by western blots.
Results: In the present study, we found that chronic social defeat not only induced glucose intolerance, but also aggravated high fat diet induced insulin resistance in C57BL/6J mice. In addition, chronic social defeat in mice increased the plasma concentrations of hepassocin, cortisol, and interleukin-6. Treatment of cortisol increased the translocation of interleukin-6 receptor to cell membrane, and interleukin-6 increased the expression of hepassocin in hepatocytes. Furthermore, co-treatment of cortisol, and interleukin-6 synergically facilitated the expression of hepassocin, and thus contributed to the development of insulin resistance.
Conclusion: Chronic social defeat increased the concentrations of both cortisol and interlekin-6 in circulation to synergically increase the expression of hepassocin. The elevated hepassocin levels in circulation further contribute to systemic insulin resistance.

OL02-2
The role of casein kinase 2 in ER stress associated pancreatic β cell failure

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Objective: During the development of type 2 diabetes, endoplasmic reticulum (ER) stress not only leads to insulin resistance but also causes pancreatic β cell failure. We have revealed that ER stress affected the pancreatic β cell mass. Recently, casein kinase 2 (CK2) inhibitors have attracted attention as anticancer drugs. CK2 inhibitors suppress proliferation and induce apoptosis in cancer cells, but do not affect non-cancer cells. The difference of ER function between cancer cells and normal cells has been attributed to one of these mechanisms. Furthermore, inhibition of CK2 is reported to have protective function in diabetic nephropathy, and promote beige adipocyte biogenesis. This implies that CK2 inhibitors might be a promising approach to prevent or treat diabetes and impaired glucose tolerance. However, the effect of CK2 on pancreatic β cells remains to be elucidated. Therefore, we analyzed the role of CK2 in ER stress-associated pancreatic β cell failure.
Methods: The function of CK2 in MIN6 cells and isolated islets of mice were evaluated by molecular biological approach. CK2 inhibitor, emodin, was administered to pancreatic β cell-specific C/EBPβ transgenic (TG) mice, which is our original diabetic model mice that exhibit reduction of pancreatic β cell mass associated with ER dysfunction and present with mild hyperglycemia without insulin resistance (JCI, 2010).
Results: Under normal conditions, CK2α was mainly localized in the nucleus and CK2β was mainly localized in the cytoplasm in MIN6 cells. However, under conditions of ER stress, CK2β translocated to the nucleus and colocalized with C/EBPβ. Furthermore, in C/EBPβ-overexpressing MIN6 cells and the isolated islets of TG mice, both CK2α and CK2β were also colocalized with C/EBPβ in the nucleus. Moreover, pull-down assay with GST-C/EBPβ and recombinant CK2 revealed that C/EBPβ directly combined with CK2 in vitro. Unfolded protein response, indicated by expression of C/EBPβ, CHOP, and phospho-c-Jun, was suppressed by deletion of CK2β in MIN6 cells. The CK2 inhibitor, emodin, had no effect on blood glucose levels and body weight in TG mice ad libitum. However, intraperitoneal glucose tolerance test revealed that emodin treatment remedied glucose intolerance in TG mice.
Conclusion: We confirmed that CK2 interacts with C/EBPβ under ER stress, and suggest that CK2 inhibitors might reduce insulin resistance and play a protective role in pancreatic β cells.

OL02-3
A surge of appetite regulating hormone, ghrelin, and its relevance to motivation for the initiation of voluntary exercise in mice

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We previously reported that voluntary exercise contributed to an amelioration of abnormal feeding behavior with a concomitant restoration of ghrelin production in obese rats, suggesting a putative relationship between exercise and ghrelin. Because ghrelin is related to higher motivation and hyperactivity as an exploring behavior for food, we investigated the relevance of ghrelin as an initiator of voluntary exercise as well as feeding behavior.
The animals were housed under a 12 h light dark cycle (light on 7:00–19:00). Four-week-old male wild type (WT) mice were either fed control chow diet (WT-CD) or high fat diet (60 kcal% fat: WT-HFD) for 12 weeks. Ghrelin knockout mice at the same age were fed CD for the same period (GKO-CD). At 16weeks old, they were moved individually into acrylic metabolic chambers equipped with running wheel for the measurement of food intake (FI) and wheel running count (COUNT) as voluntary exercise performance on a minute by minute basis. After all measurements, they were sacrificed under isoflurane anesthesia and blood samples were collected at 8 time points during the day for the measurement of plasma active ghrelin concentrations by RIA.
WT-HFD revealed an obvious weight gain and abnormal feeding behavior as an increase of FI during light phase compared to WT-CD. Plasma ghrelin levels in WT-CD showed a bimodal diurnal rhythm with its peaks at 7:00 and 19:00. In

WT-HFD, however, those peaks shifted to 13:00 and 1:00, respectively. In WT-CD, a marked increase of COUNT was observed both at the beginning and at the end of dark phase concomitant with an increase of FI in these periods. These increases were weakened in WT-HFD and markedly reduced in GKO-CD. To verify a role of ghrelin as an initiator of voluntary exercise, we further tested effects of ghrelin agonist (GHRP6) injection (ip) on COUNT in GKO-CD at 16 weeks old. A single injection of GHRP6 (1 mg/kg) at 18:30 for 2 weeks brought about a significant enhancement of COUNT during dark phase in spite of no effect of continuous administration of this agent by osmotic pumps at the same dose.
It was thus clearly demonstrated that ghrelin surges at 7:00 and 19:00 observed in WT-CD play a crucial role in the initiation and motivation of voluntary exercise in these periods. Because diurnal ghrelin rhythm were disturbed in WT-HFD concomitant with the decrease of COUNT, therapeutic properties of this peptide are to be further elucidated in future investigations.

OL02-4

Attenuation of high fatty acid-induced hepatic lipotoxicity and insulin resistance by induction of miR-302

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Non-alcoholic fatty liver disease (NAFLD) is a very common disorder and characterized by the accumulation of excess fat in the liver. Hepatic insulin resistance is a typical feature of NAFLD, which represents the precursor stage of type 2 diabetes. Increased lipid accumulation leads to interfere with hepatic metabolism, which in turn stimulates oxidative stress and lipotoxicity and subsequently induces hepatic damages including inflammation, senescence and apoptosis. As a result, inhibition of hepatic fatty acid formation and accumulation represents a valid therapeutic strategy for the treatment of NAFLD. Recently, many studies have demonstrated that several microRNAs (miRNAs) contribute to the pathogenesis of NAFLD. Particularly, miR302 is predicted as a repressor in fatty acid synthesis by targeting at elongation of very long chain fatty acids-6 (Elovl6), a key enzyme produces long chain fatty acids in the liver. Elovl6 regulates the composition of fatty acid in cells and affects some inflammatory factor activity, which influences the occurrence and development of NAFLD and hepatic insulin resistance. In addition, we have previously demonstrated that upregulation of miR302 is able to alleviate neuronal insulin resistance by slowing aging process, suggesting miR302 may exert potential benefits in preventing NAFLD. As both hepatic insulin resistance and cellular senescence are two major factors in the pathogenesis of NAFLD, we speculate that miR302 may display protective roles in NAFLD. However, the detailed molecular mechanisms underlying miR302 in NAFLD pathogenesis are still largely unclear. In the present study, we demonstrated that palmitic acid and oleic acid mixture can induce the formation of fatty acid, total lipid and triglyceride (TG), which close resemble to NAFLD. However, overexpression of miR-302 may attenuate fatty acid-induced lipid accumulation. Moreover, overexpressed miR-302 not only attenuates lipotoxicity, but also prevents insulin resistance, oxidative stress, senescence and mitochondria dysfunction by targeting to Elovl6 in HepG2 cell. In conclusion, our results provided some details of miR302 at molecular basis involved in the pathogenesis of NAFLD. Accordingly, restoration of hepatic insulin signaling by upregulation of miR302 may display potential implications to develop novel preventive, diagnostic, or therapeutic strategies in NAFLD.

OL02-5

One-year post-transplant hyperglycemia aggravated kidney function in diabetic patients

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Background: The efficacy of kidney transplantation in diabetic patients is well known; however, immunosuppressive treatment with steroids after surgery contributes to insulin resistance, bulimia, obesity, and hyperglycemia. Furthermore, functional kidney recovery contributes to an increase in the required amount of insulin, and more antidiabetic medications are needed after transplantation in some cases.
Objective: This retrospective study included 12 chronic renal failure patients who underwent kidney transplantation between 2008 and 2014 in Shizuoka General Hospital.
Changes in HbA1c, GA, urine albumin, and eGFR levels were assessed at 6 months, 1, and 2 years after transplantation.
Results: One patient was diagnosed with acute rejection, requiring dialysis soon after transplantation. Therefore, we assessed the 11 remaining patients: 8 men and 3 women, one with type 1 and 11 with type 2 diabetes, and average age of 48.5 ± 11.7 years.
Before surgery, 4 patients used injectable insulin (average, 20.5 U/day), 2 patients took oral antidiabetic medication (DPP4 inhibitors), and 5 did not take diabetic medication.
One year later, all patients were being treated with diabetic drugs: 8 with injectable insulin (mean, 32.3 U/day) and 3 with oral antidiabetic medication.
Although, the treatment of diabetes was more intensive than before surgery, blood glucose controls worsened after surgery (HbA1c: pre, 6.6 ± 1.1%; 1 year later, 8.0 ± 1.8%; GA: 19.1 ± 3.9%, 25.7 ± 9.7%).
The eGFR levels were improved by transplantation (5.3 ± 2.1 mL/min/1.73 m^2, 43.6 ± 7.3 mL/min/1.73 m^2). Urine albumin was detected 1 year later (average, 91.0 ± 119.0 mg/g•Cr), including 5 patients (45%) above 30 mg/g•Cr.
There was a correlation between urine albumin at 1 year and glycemic control markers (GA at pre-transplantation: $r = 0.80$, $p = 0.03$; HbA1c at 1 year: $r = 0.86$, $p = 0.006$).
There was no correlation between eGFR at 1 year and glycemic control markers.
Mental disease (e.g., developmental disorders, hysteria, and depression) is a risk factor of aggravation of renal function.
Discussion and conclusion: Post-transplant hyperglycemia affected kidney function at 1 year in diabetic patients in this study.
As previously reported, the pathological recurrence of diabetic kidney disease can appear as early as 2 years after kidney transplantation.
Patients with psychiatric problems occasionally are noncompliant for glycemic control, pre- and post-transplantation, which contributes to rapid progression of kidney failure.
We need to carefully consider diabetes self-management ability and education before kidney transplantation.

OL02-6

Abrogation of Toll-like receptor 4 (TLR4) mitigates obesity-induced insulin resistance and glucose intolerance through reducing mitochondrial ROS in visceral fat

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Obesity-induced excessive visceral fat (VF) accumulation is associated with insulin resistance and systemic oxidative stress and chronic inflammation. Toll–like receptor 4 (TLR4) plays an important role in innate immunity and chronic

inflammation. Here we investigate the role of TLR4 knockout (TLR4KO) on insulin resistance, glucose intolerance, mitochondrial reactive oxygen species (ROS), oxidative stress, mitochondrial biogenesis in VF using a high fat high sugar (HFHS) diet-induced obesity mouse model. C57BL6 (B6) and TLR4KO mice were fed with either control diet (CD) or HFHS for six months, totally four experimental groups: B6 + CD, B6 + HFHS, TLR4KO + CD and TLR4KO + HFHS. Compared to B6 + CD, B6 + HFHS demonstrated significant increase in bodyweight (BW), VF accumulation, VF oxidative damage, VF mitochondrial ROS level, VF inflammation markers and development of insulin resistance as well as glucose intolerance. TLR4KO + CD did not show differences in all physiological and biomarker measurements from B6 + CD. In contrast, TLR4KO + CD showed markedly increased BW and subcutaneous fat (SF), but no difference in VF compared to B6 + CD. On the other hand, TLR4KO + HFHS mice presented significant improvement in VF oxidative damage and VF mitochondrial ROS, insulin resistance and glucose intolerance, as compared to B6 + HFHS. The TLR4KO + HFHS mice also presented increased BW as compared to B6 + HFHS. Notably, SF contributes higher proportion than VF in the increase of BW of TLR4KO + HFHS mice. In addition, TLRKO hindered HFHS-induced increasing mtDNA content in VF over time. Also, TLR4KO mice exhibited decreased HFHS-induced inflammatory markers in VF. Taken together, despite showing higher BW, abrogation of TLR4 gene mitigates obesity-induced insulin resistance and glucose intolerance via reducing mitochondrial ROS level, which is associated with induction of mitochondrial biogenesis and inflammation in VF. Thus, our study provides a critical insight in linking innate immunity to prevention of insulin resistance. That paves the way to developing novel therapeutic strategy for diabetes mellitus.

OL02-7
Interaction of TET-1 and OGT enzymes regulates epigenome modification and high-glucose induced renal proximal tubular cell injury

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Diabetic kidney disease is a leading cause of chronic kidney disease (CKD) and end-stage renal disease (ESRD) in Taiwan and worldwide. Currently, available therapies have not been fully effective in the treatment of CKD and ESRD, suggesting that further understanding of the molecular mechanisms underlying the pathogenesis of diabetic nephropathy (DN) is necessary. Epigenetic mechanisms may underlie the renal cell injury and the progression of diabetic kidney disease. Aberrant DNA methylation has been observed in the renal proximal tubules of diabetic mice. However, the mechanism is not fully understood. Ten-eleven translocation (TET) enzymes can oxidize the 5-methylcytosine (5-mC) of DNA to generate 5-hydroxymethylcytosine (5-hmC) and dynamically regulate global or locus specific 5-mC and 5-hmC levels by facilitating active DNA demethylation. TETs are also found to interact with O-GlcNAc transferase (OGT) for regulating histone modification. Thus far, the function of TETs in kidney has not been investigated. We hypothesize that high-glucose may influence DNA demethylation and histone modification via TETs in renal proximal tubular cells. In this study, we demonstrated that 5-mC was decreased and 5-hmC was increased in a time-dependent manner, indicating an active DNA demethylation occurred in the human renal proximal tubular HK-2 cells under 25 mM D-glucose stimulation. By real-time PCR, we observed TET-1 mRNA was significantly upregulated after high glucose stimulation. These results are consistent with the immunohistochemistry data that showed TET-1 protein was upregulated in the renal proximal tubules of db/db mice. We also found methylation level of histone 3 lysine 4 (H3K4me) was increased in high-glucose stimulated HK-2 cells and in renal proximal tubules of db/db mice. After treated the HK-2 cells with TET-1 or/and OGT siRNA, we found increase in high-glucose induced H3K4me and 5-hmC were reversed. In addition, TET-1 and OGT could be co-immunoprecipitated with either TET-1 or OGT antibody in HK-2 cells treated with HG. The result suggests these two proteins may have interaction in response to glucose stimulation. TET-1 and OGT siRNA downregulated cleaved-caspase-3 protein level that suggests an interaction of TET-1 and OGT may involve in regulating tubular cell apoptosis induced by high glucose. Our study reveals TET-1 may be a novel pathological molecule in modifying epigenome in diabetic kidney disease.

OL02-8
Astaxanthin prevents and reverses insulin resistance and steatohepatitis: A comparison with vitamin E

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Objective: Nonalcoholic steatohepatitis (NASH) and insulin resistance frequently coexist in subjects with obesity and type 2 diabetes. Hepatic insulin resistance and NASH could be caused by excessive hepatic lipid accumulation and peroxidation. In our previous study, we developed a cholesterol- and saturated fatty acid-induced model of lipotoxic NASH and revealed that hepatic oxidative stress and insulin resistance promoted hepatic inflammation and fibrosis. To date, vitamin E has become a standard treatment for NASH. However, additional more effective therapies are needed. Astaxanthin is a carotenoid compound that is known to be approximately 500 times more potent in inhibiting lipid peroxidation than vitamin E in vitro. In this study, we compared the preventative and therapeutic effects of lipophilic antioxidants, astaxanthin and vitamin E, in a lipotoxic model of NASH.
Methods: C57BL/6 mice were fed a high-cholesterol high-fat (CL) diet or CL diet either containing 0.02% astaxanthin (CL + AX) or 0.02% vitamin E (CL + VE). Liver histology, insulin sensitivity, and intrahepatic immune cell numbers were examined.
Results: After 12 weeks on the CL diet, astaxanthin treatment alleviated excessive hepatic lipid accumulation by reducing hepatic TG, TC, and NEFA by 25%, 24%, and 31%, compared that of 12%, 10%, and 23% by vitamin E. Although both of astaxanthin and vitamin E suppressed lipid peroxidation assessed by TBARS equivalently, by 37% and 33%, astaxanthin reduced the accumulation of Kupffer cells and inhibited the activation of hepatic stellate cells and fibrogenesis (hydroxyprolin content 10.4 ± 0.7 vs 7.1 ± 0.5 nmol/mg protein, $P < 0.05$), in the liver of NASH to extents greater than did vitamin E. Flow cytometry analysis revealed that CL + AX and CL + VE mice exhibited a 56% and 33% reduced CD11c + CD206− (M1) macrophages, respectively, whereas the number of CD11c−CD206 + (M2) macrophages was increased by 3.7- and 1.5-fold, respectively. These effects resulted in an M2-dominant shift of macrophages/Kupffer cells in the livers of both CL + AX and CL + VE mice, with a reduction of hepatic CD4 + and CD8+ T cell recruitment, which contributed to improved insulin resistance and steatohepatitis. Importantly, astaxanthin reversed insulin resistance as well as hepatic inflammation and fibrosis, in pre-existing NASH more potently than did vitamin E.
Conclusions: Overall, astaxanthin was more effective at preventing and treating NASH compared with vitamin E in mice, suggesting that astaxanthin might be a novel and promising treatment for NASH.

Diabetes Complications: Epidemiology and Biomarkers

OL03-1

Examination of sleep disorders of 1023 type2 diabetic outpatients

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Objective: Diabetic neuropathy can cause sleep disorders. Sleep disorders, meanwhile, increase insulin resistance, and affect leptin and ghrelin which enhance appetite. This study examined the relationship between diabetes mellitus (DM) and sleep disorders in type-2 DM (T2DM) patients, using a cross-sectional design.

Methods: The participants in the study were 1033 Japanese outpatients with T2DM (age, 62.9 ± 13.1 years; M/F, 710/323 persons; DM duration, 16.3 ± 16.7 years; Hemoglobin A1c [HbA1c], 7.4 ± 1.3%) who visited our hospital in February 2014. We investigated sleep disorders, quality of life (QOL), and depression (assessed by the Pittsburgh Sleep Quality Index [PSQI], the Center for Epidemiologic Studies Depression Scale [CES-D], and the SF-8 Health Survey [SF-8]). We then compared the results with the data of 572 age- and sex-matched people from the general population without a diabetes history.

Results: The mean PSQI score (cutoff ≥5.5) was 5.6 ± 3.3 (mean ± SD) in the participants, and 454 patients (44%) had PSQI scores of ≥5.5. Patients with a lower PSQI score tended to be obese. However, PSQI scores were not significantly correlated with glycemic control, diabetes duration, and insulin intake, respectively. In terms of CES-D (0–11 normal, 12–20 moderate, 21–36 severe), 929 patients (90%) were categorized as normal, 73 (7.1%) moderate, and 29 (2.9%) severe. PSQI scores and CES-D scores showed a positive correlation, whereas PSQI scores and SF-8 scores showed a negative correlation.

In comparison with the non-diabetic population (n = 572), the diabetic group (n = 572) had significantly higher PSQI scores (5.7 ± 3.2 vs 5.2 ± 2.8) with significantly shorter sleep duration and lower sleep efficiency. Similarly, on SF-8, the diabetic group scored significantly lower in the Physical Functioning (PF), Role Physical (RP), Body Pain (BP), General Health (GH), and physical summary components. We observed no significant difference in CES-D scores between the two groups.

Discussion: This study showed that many patients with T2DM suffer sleep disorders. Sleep quality is associated with depression and deteriorated QOL. While it is quite difficult to assume whether the diabetic patient has a sleep disorder through their patient characteristics, BMI – both the present and past maximum – had a correlation, pointing to the importance of noting patients' body weight history. Sleep disorders should be widely recognized as a diabetic complication: intervention in the disorders can alleviate depression, and improve QOL and probably blood glucose control as well.

OL03-2

Global and Chinese prevalence of diabetic foot

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Background: Diabetic foot is a severe public health issue worldwide and in China, and updating its epidemiologic characteristic is beneficial for future policy, prevention strategy and care management. However, there is a lack of studies to investigate the epidemiologic characteristics of diabetic foot. Here we performed a systematic review and meta-analysis to generate global and Chinese diabetic foot prevalence.

Methods: In the systematic review and meta-analysis of global diabetic foot prevalence, we searched Pubmed, EMBASE, ISI Web of science and Cochrane and identified 67 studies. In the study of Chinese diabetic foot prevalence, we searched Pubmed, EMBASE, ISI Web of science, and Chinese databases: Chinese Biochemical Literature on Disc, Wanfang data resource and China National Knowledge Infrastructure database and included 39 studies. Random effects model meta-analysis was used to obtain the pooled prevalence of diabetic foot. Subgroup analysis and meta regression were also conducted to evaluate the sources of heterogeneity.

Results: Global diabetic foot prevalence was 6.9% (95%CI: 5.9–7.8%). North America had the highest prevalence (13.0%, 95% CI: 8.2–15.9%), and Oceania's prevalence was the lowest (3.0%, 95%CI: 0.9–5.0%). The prevalence in Asia, Europe and Africa was 6.2% (95%CI: 5.2–7.2%), 5.7% (95%CI: 4.5–6.8%) and 8.8% (95%CI: 6.2–11.4%), respectively. Diabetic foot was more prevalent in males (4.5%, 95%CI: 3.7–5.2%) than in females (3.5%, 95%CI: 2.8–4.2%), and more prevalent in type 2 diabetes (9.4%, 95%CI: 6.4–12.4%) than type 1 diabetes (5.6%, 95%CI: 3.6–7.6%). Patients with diabetic foot were older, with longer diabetic duration, higher HbA1c, larger percentage of smokers, hypertension and diabetic retinopathy as well as lower body mass index when compared with patients without diabetic foot. Chinese diabetic foot prevalence was 5.7% (95%CI: 4.9–6.5%), which was higher in eastern region (6.9%, 95%CI: 5.6–8.2%) than in western region (4.2%, 95%CI: 3.0–5.4%), and higher in males (6.6%, 95%CI: 2.1–11.2%) than in females (4.8%, 95%CI: 1.9–7.8%).

Conclusion: We for the first time demonstrated that overall diabetic foot prevalence was 6.9% worldwide and 5.7% in China as well as its epidemiologic characteristics. Prevention of diabetic foot may include glycemic control and quit smoking. Our findings provide evidence for future policy making in diabetic foot, and thus alleviate the economic burden.

OL03-3

Bilateral atrophy of extensor digitorum brevis muscle may be useful for diagnosis of diabetic polyneuropathy in Japanese diabetic men

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Aims: We aimed to evaluate validity and reliability of observation of extensor digitorum brevis muscle (EDB). EDB atrophy for diagnosis of diabetic symmetric polyneuropathy (DPN). Firstly, we examined the relations between EDB atrophy and neurological findings in regional population-based Japanese subjects (Study I). Secondly, we investigated relations between EDB atrophy and quantitative neurological findings in the hospital-based diabetic patients (Study II).

Methods: Study I. 548 non diabetic persons who received medical screening program were subjected. Subjective symptoms (numbness in toes and sole, pain and/or paresthesia in feet), quantitative vibratory perception at the tips of toe (QVP; using vibrometer Rion AU-02B), bilateral Achilles tendon reflexes (ATR) and EDB atrophy were evaluated. We judged EDB atrophy as positive when both EDB could not be identified by inspection and palpation. We also interviewed about Seiza habit (Japanese sit-down style with the buttocks on top of the ankles).

Study II. In 193 diabetic patients, neurological examination as same as Study I were examined. Additional 8 objective nerve function tests were evaluated. Relationships among these findings were analyzed.

Results: Study I. Prevalence (%) of EDB atrophy and Seiza habit in women (36, 73) were significantly higher than those in men

(20, 44), respectively. Prevalence of EDB atrophy in subjects with Seiza habit was significantly higher than that in subjects without Seiza habit (35 vs 20, p = 0.001). Therefore, female and male were separately analyzed. In both gender, EDB atrophy was significantly associated with ATR reduction and QVP impairment.
Study II. EDB atrophy was observed in 49% of women and in 27% of men. In both gender, EDB atrophy was significantly more prevalent in diabetic compared to non-diabetic subjects. In male diabetic patients, all items of 8 quantitative nerve tests were significantly associated with EDB atrophy. In female, only 4 items were associated with EDB atrophy. We evaluated the predictive power of EDB atrophy for diagnosing the probable DPN of Toronto consensus in diabetic men. The sensitivity, specificity and positive predictive value of EB atrophy to determine probable DPN were 48%, 92% and 83%, respectively.
Conclusion: EDB atrophy was also seen in non-diabetic subjects, but EDB atrophy was significantly associated with peripheral neuropathy. EDB atrophy was more frequent in female than male. The gender difference seemed to depend the Seiza habit. In diabetic men, EDB atrophy clearly reflected the DPN and EDB atrophy indicated the presence of DPN in approximately 90% of probability.

OL03-4

Risks of progression to end-stage renal disease among type 2 diabetic patients with albuminuric and non-albuminuric chronic kidney disease

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Diabetic kidney disease is heterogeneous in its clinical manifestation. Many patients have declined glomerular filtration rate (GFR) without preceding albuminuria and they differ in disease progression to those with albuminuric chronic kidney disease (CKD). We examined clinical characteristics and incidence of end-stage renal disease (ESRD) in a prospective cohort of Chinese patients with type 2 diabetes and CKD stratified by albuminuria status.
Between 1 July 1994 and 31 December 2004, 1,995 of 10,129 patients who were enrolled into the Hong Kong Diabetes Registry had CKD at baseline as defined by estimated GFR <60 mL/min/1.73 m^2. Albuminuria was confirmed based on urine albumin-creatinine ratio >2.5 mg/mmol in men and >3.5 mg/mmol in women. Patients were followed for new-onset of ESRD as defined by estimated GFR <15 mL/min/1.73 m^2 or dialysis.
Among 1,995 patients with CKD (mean ± standard deviation [SD] age: 68.3 ± 10.1 years, median[interquartile range] disease duration: 9[4, 15] years), 26.4% (n = 526) did not have albuminuria. Compared to patients with albuminuria (mean ± SD estimated GFR: 41.7 ± 13.7 mL/min/1.73m^2), those without albuminuria (mean ± SD estimated GFR: 50.3 ± 9.1 mL/min/1.73 m^2) were older, had shorter disease duration, and had lower blood glucose, blood pressure and cholesterol. The two groups were similar in gender ratio, smoking status and anthropometric indices. At baseline, patients without albuminuria were less likely to be complicated with diabetic retinopathy and sensory neuropathy, but did not differ in frequencies of coronary heart disease, stroke and congestive heart failure relative to the albuminuric group, who had greater prevalent use of renin-angiotensin system (RAS) inhibitors and anti-hypertensive drugs.
Over a median follow-up period of 9.1 (interquartile range: 5.6, 12.6) years, 19.1% of non-albuminuric and 57.2% of albuminuric patients without ESRD at baseline, developed ESRD. Multivariate Cox regression was performed to estimate hazard ratios (HRs) of non-albuminuric and albuminuric CKD stratified by baseline use of RAS-inhibitors for incident renal events. After adjustment for age, gender, disease duration, body mass index, blood pressures, HbA1c and GFR, patients with albuminuria had increased hazards of progressing to ESRD with HRs 3.23 (95% confidence interval [CI]: 2.42–4.30, p < 0.001) in those using RAS-inhibitors and 2.70 (95% CI: 2.03–3.59, p < 0.001) in those not using RAS-inhibitors, relative to reference group of no albuminuria and non-use of RAS-inhibitors at baseline.
In conclusion, patients with non-albuminuric CKD were less likely to have other microvascular complications and had lower risk of advancing to ESRD than patients with albuminuria, although rates of renal deterioration remained very high in both groups.

OL03-5

High prevalence of cardio-renal complications among Chinese subjects with Type 2 diabetes – The Hong Kong Diabetes Biobank

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Aims: Type 2 diabetes is associated with increased risk of diabetic complications, in particular cardiovascular and renal complications, which account for a significant proportion of the healthcare burden associated with diabetes. There is limited data on the epidemiology of diabetic complications in a contemporary cohort. Our aim is to establish a territory-wide registry and biobank of subjects with type 2 diabetes (T2D), in order to study the epidemiology of diabetic complications and to utilize samples for biomarkers discovery and replication.
Methods: We recruited subjects at the time of regular comprehensive diabetes complication screening at participating diabetes centres in major public hospitals in Hong Kong. All subjects were consented for collection of clinical information, baseline characteristics, biospecimens for archiving, genetic and biomarker research and follow-up for development of different diabetes-related outcomes. All specimens were collected and processed through a standardized protocol. Coronary heart disease is defined as history of myocardial infarction or coronary revascularization procedures. Chronic kidney disease is defined by eGFR <60 mL/min/1.73 m^2 by the Chinese modified MDRD equation.
Results: Recruitment commenced in March 2014. To date, more than 7,700 subjects with type 2 diabetes have been recruited, with more than 23,100 primary samples processed and archived. Mean age of recruited subjects was 60.5 ± 10.8 years (male 58.6%), mean duration of diabetes 10 years. Mean baseline HbA1c was 7.6 ± 1.4%. Retinopathy was present in 27.7% at recruitment and 34.1% were on insulin treatment. A significant proportion have established chronic kidney disease (defined as eGFR <60 mL/min/1.73 m^2, 796 out of 6293, 12.6%) and coronary heart disease (934 out of 6270, 14.9%). Subjects

with established CHD at baseline were significantly older, had more male subjects, longer duration of diabetes, lower eGFR, but had comparable HbA1c and % with retinopathy compared to subjects without CHD. Subjects with CKD at baseline were older, had longer duration of diabetes, had higher BMI, higher HbA1c, lower eGFR, higher urine alb/creat ratio, and higher percentage with retinopathy (all $p < 0.001$). Co-existing CHD and CKD was present in 3.1% of subjects.

Conclusions: We have established a contemporary cohort and biobank of Chinese patients with type 2 diabetes for epidemiology research and biomarker discovery. This revealed an alarmingly high prevalence of cardio-renal complications among Chinese patients with type 2 diabetes. The identification of risk factors and biomarkers associated with cardio-renal complications may facilitate the early identification of high-risk subjects.

Acknowledgment: Funded by a Theme-based Research Scheme from the Research Grants Council of the Hong Kong Administrative Region, China (Project no: T12-402/13-N)

OL03-6

The relation between urinary albumin excretion rate (AER) and peripheral artery disease in Taiwanese diabetic patients

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Objective: We wanted to find out the relation between the urinary albumin excretion rate (AER) and peripheral artery disease in Diabetes Mellitus patients.

Methods: A total of 1233 diabetic patients whose age more than 18 years old from outpatient clinic in single center hospital were included. Peripheral artery disease was diagnosed as ankel branchial index (ABI) <0.9. Urinary albumin excretion rate were divided into 3 groups, normal (AER < 30 μg/mg), microalbuminuria (AER: 30–299 μg/mg) and macroalbuminuria (AER > 300 μg/mg). We had analysed the relation between urinary albumin excretion rate and peripheral artery disease in Taiwan diabetic patient by student T test and logistic regression.

Result: There were 95 diabetic patients (male: 47, female: 46) with peripheral artery disease and 1138 diabetic patients (male: 525, female: 613) without peripheral artery disease. Patients with peripheral artery disease had higher urinary albumin excretion ratio (AER 560.68 μg/mg) than patient without peripheral artery disease (AER 199.99 μg/mg) ($P = 0.014$). The proportion of normal, microalbuminuria and macroalbuminuria in diabetic patients with peripheral artery disease was 43.5%, 28.2%, 28.2%, respectively, 65.7%, 23.2%, 11% in the diabetic patients without peripheral artery disease ($p < 0.001$). The simple logistic regression analysis revealed Ln AER significant associated with the mean of bilateral ABI with a p value of 0.012 ($\beta = -0.074$).

Conclusion: The correlation between urinary albumin excretion rate (AER) and peripheral artery disease was significant. Urinary albumin excretion rate could be a predict factor of peripheral artery disease in diabetic patients.

OL03-7

Characteristics of Korean T2DM patients with diabetic retinopathy and macular edema: A Study based on a standardized clinical data

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Objective: This study was carried out as a national project to secure standardized biomedical resources of Korean subjects with type 2 diabetes mellitus (T2DM). It was conducted as a part of the Korea Biobank Project, which was launched by the Korea National Institute of Health. It was designed as a fundamental study to identify the clinical characteristics of diabetic retinopathy and macular edema in Korean T2DM patients.

Methods: From September 2014 to July 2015, in a single university hospital in Korea, clinical data and samples were collected prospectively from T2DM subjects whose duration of DM was over 20 years. Data and samples were collected according to the common data element and the standard of procedure which was developed by the Korean Diabetes Association research council for the standardization of clinical data. The presence of diabetic retinopathy and macular edema was evaluated with multi-field funduscopy and optical coherence tomography performed by ophthalmologic specialists.

Results: Among 198 patients enrolled in the first year of the study, 183 patients completed the evaluation on diabetic retinopathy and macular edema. Mean age of the participants was 66.8 years, median duration of DM was 22.6 years, and 49.7% were male. When the characteristics of the patients were analyzed according to the presence of diabetic retinopathy and macular edema, various clinical characteristics showed significant difference between two groups. Age, fasting glucose level, duration of T2DM, family history of chronic disease, use of sulfonylureas or insulin were identified as independent risk factors for DM retinopathy. Sex, age, height, weight, duration of DM and the use of insulin were confirmed as independent risk factors for macular edema.

Conclusion: In this study, we identified various clinical features that are associated with the development of DM retinopathy and macular edema. Additional longitudinal observation and multi-omics based experiments are being conducted to understand the pathophysiology of DM related complications in Korean patients with T2DM.

OL03-8

A novel scoring system for detecting diabetic kidney disease predicts renal function decline in patients with type 2 diabetes

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Background: Diabetic kidney disease (DKD) is one of the leading causes of chronic kidney disease (CKD) and end-stage renal disease (ESRD) worldwide. Despite being the diagnostic criteria for DKD, the predictive value of urinary albumin-to-creatinine ratio (UACR) on the progression toward advanced CKD is limited, due to the heterogeneous disease nature. DN_Score is a scoring system generated from the profiles of DNlite, a urinary biomarker panel composed of alpha2-HS-glycoprotein precursor (AHSG), alpha-1-antitrypsin (A1AT) and acid-1-glycoprotein (AGP). Cross-sectional study has shown significant correlations between DN_Score and traditional indicators of DKD. In this prospective cohort study, we evaluated the potential of DN_Score for predicting decline of renal function in patients with type 2 diabetes (T2DM).

Material and methods: 308 patients with T2DM were enrolled in this study. Each participant was followed-up at 6-month interval over a period of 2.5 years. Estimated glomerular filtration rate (eGFR), UACR and DN_Score were recorded at baseline and each visit.

Results: A total of 282 participants completed the 2.5-year follow-up. With a baseline cutoff level of 11.4, the overall mean difference in change of eGFR (%) in participants with the higher and the lower DN_Score was −3.68 and 1.32, respectively (between-group difference $P < 0.01$). In participants with baseline eGFR < 60 mL/min/1.73 m^2, DN_Score also predicted a

rapid decline in renal function (10% decline of eGFR, area Under ROC Curve 0.86).
Conclusions: Higher baseline DN_Score is associated with a significantly decline of renal function in patients with T2DM over a period of 2.5 years. Further investigations with a larger study population and longer follow-up period will be necessary for better validations of the predictive role of DN_Score on the progression of DKD.

Genetics and Epidemiology

OL04-3
The association of GIPR variants with fat accumulation in Chinese Han populations

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Objectives: Obesity, particularly central obesity which is considered as the culprit of obesity-associated complications such as type 2 diabetes, metabolic syndrome and cardiovascular disease, imposes serious medical and economic burdens. Compared with body mass index (BMI), waist circumference and waist to hip ratio, visceral fat area (VFA) and subcutaneous fat area (SFA) is more precise as a measurement of obesity. Genetic variants of glucose-dependent insulinotropic polypeptide receptor (GIPR) relevant to BMI and glucose metabolism have been uncovered using genome-wide association studies (GWAS). We aimed to test the association of GIPR with fat distribution in Chinese Han populations.
Methods: A total of 2884 community-based individuals with Chinese Han ancestry were genotyped for four tag single-nucleotide polymorphisms (SNPs) of GIPR. Linear analysis was applied to test the associations of these variants with VFA and SFA quantified by Magnetic Resonance Imaging (MRI) as well as glucose related traits.
Results: We replicated the effects of several loci of GIPR on BMI, waist circumference as well as glucose related traits in Chinese Han populations (P range from 9.46×10^{-5} to 0.028). In the search for fat distribution variants, we found rs11671664 in GIPR was associated with VFA and SFA in total subjects ($p = 0.018$ and 0.020, respectively). In a subgroup analysis stratified by gender, rs11671664 showed the association with VFA in males ($p = 0.030$), whereas displayed the borderline association with SFA in females ($p = 0.049$). However, after adjusting for BMI, the association disappeared. Analysis of linkage disequilibrium (LD) revealed no association between the GIPR haplotype block (rs2334255 and rs2287019) and fat distribution, while we observed that the GT and GC haplotypes of rs2334255 and rs2287019 were associated with higher glucose and insulin level as well as higher insulin sensitivity assessed with Gutt index (P range from 1.90×10^{-5} to 0.045).
Conclusion: Our results suggest that the association between rs11671664 and visceral fat distribution might be mediated by BMI in Chinese Han populations.

OL04-4
Impaired pancreatic beta cell compensatory function is the main cause of type 2 diabetes in individuals with high genetic risk

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Aims/hypothesis: We aimed to evaluate the combined effects of type 2 diabetes risk variants on predicting deterioration of blood glucose and progression of beta cell function and insulin sensitivity in a 9-year prospective cohort from the Chinese population.
Methods: We constructed a weighted genetic risk score (GRS) model based on 40 variants associated with type 2 diabetes validated in an established cross-sectional Chinese population (n = 6,822). The weighted scores were categorised into tertiles to assess the predictive capacity for incidence of type 2 diabetes and impaired glucose regulation (IGR), as well as for changes in Stumvoll first- and second-phase insulin secretion indices and Gutt's insulin sensitivity index (ISI) in a community-based 9-year prospective cohort (n = 2,495), including 2192 individuals with normal glucose tolerance and 303 with IGR at baseline, through logistic and multiple linear regression tests.
Results: Weighted GRS predicted the incidence of type 2 diabetes and IGR in logistic regression (OR 1.236, 95% CI 1.100, 1.389, $p = 0.0004$) after adjusting for age, sex, BMI, smoking and alcohol status at baseline. Moreover, we observed that weighted GRS was able to predict deterioration in beta cell function ($\beta = -0.0480$, $p = 9.66 \times 10^{-5}$ and $\beta = -0.0303$, $p = 3.32 \times 10^{-5}$ for first- and second-phase insulin secretion, respectively), but not insulin sensitivity ($p = 0.3815$), during the 9-year follow-up period.
Conclusions/interpretation: The weighted GRS predicted blood glucose deterioration arising from change in beta cell function in the Chinese population. Individuals in the intermediate- or high-weighted GRS group exhibited progressive deterioration of beta cell function.

OL04-5
Computational analysis of type 2 diabetes associated SNPs and genes identified by GWASs

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Type 2 diabetes (T2D) is characterized by chronic hyperglycemia due to insulin resistance of peripheral tissues and insufficient compensatory insulin secretion by pancreatic beta cells. Until 2007, genetic study of T2D was mainly achieved by genome-wide familial linkage analyses and candidate gene association studies with limited success. Progress in identifying common variants associated with T2D has since been accelerated primarily by Genome-wide association studies (GWASs). By the end of 2014, 43 GWASs and 13 meta-analyses reported 116 genes and 161 SNPs (Lead SNP) that were associated with T2D at the stringent threshold of 5×10^{-8} for genome-wide significance. Functional characterization and mechanistic elucidation of these SNPs and genes action are the next major challenge. We conducted multiple computational analyses to explore function and mechanisms of T2D GWAS-associated SNPs and genes, including SNP conservation analysis and functional annotation (influence of SNPs on protein phosphorylation and miRNA binding, eQTLs), gene ontology analysis, pathway enrichment analysis and protein-protein interaction analysis.
Functional annotations using GWAS3D and RegulomeDB show that most of the SNPs were located in the non-coding region with multiple regulatory functions. Thirty-eight lead SNPs had the long-range regulatory signals. Comparative genomic analyses showed that 9 SNPs are highly conserved. A total of 1174 proxy SNPs ($r2 \geq 0.80$) were identified by SNAP based on genotype data from the International HapMap Project(v3) and the 1000 Genomes Pilot 1 Project with the CEU population panel. Some T2D GWAS associated SNPs were located at protein binding sites (identified through CHIP-seq), including CTCF, EP300, HNF4A, TCF7L2, FOXA1 and FOXA2, which are required for normal pancreatic development and maintaining β-cell function. Two T2D GWAS lead SNPs and 29 proxy SNPs were identified as miRNA related SNPs (miR-SNPs) that might

influence the binding of miRNAs, and 4 T2D lead SNPs and 8 proxy SNPs were identified as PhosSNPs that might affect protein phosphorylation. The effect of these T2D-associated GWAS SNPs on miRNAs and transcription factor binding are currently being experimentally tested in our lab.
GO analysis showed that most of the T2D related genes were enriched in the biological regulation process and binding function. Pathway enrichment analysis confirmed 2 well-known maturity onset diabetes of the young and T2D pathways. PPI network analysis identified highly interconnected "hub" genes TCF7L2, MTNR1B, SLC30A8, CDKAL1, IGF2BP2, CDC123 and KCNJ11 and FTO, HHEX and HNF1B THADA, JAZF1, CAMK1D and WFS1 and TSPAN8 that created 2 tight subnetwork

OL04-6

Association between GWAS-identified variants with CKD in Chinese with Type 2 Diabetes: The Hong Kong Diabetes Registry

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Background and objectives: Chronic kidney disease (CKD) is an important complication in patients with diabetes and significant heritability has been noted. Recent genome-wide association studies (GWAS) have identified a number of single nucleotide polymorphisms (SNPs) associated with CKD and renal function traits. However, the majority of these variants were identified from studies involving Caucasians and African Americans, with few studies conducted in Asians or involving patients with diabetes. We conducted a replication study to examine whether these SNPs are associated with the risk of developing CKD in Chinese patients with type 2 diabetes (T2D).
Subjects and methods: We performed a nested case-control study within the Hong Kong Diabetes Registry. Genome-wide genotyping was conducted for each subject using the Illumina Omni 2.5+ exome array and genotype data was imputed using minimac 3 with the 1000 Genomes Project phase 3 v5 as reference panel. After standard quality control, a total of 5730 Chinese type 2 diabetic patients were included, including 2881 patients were with pre-existing or incident CKD, and 2849 free of CKD. Through literature review, a total of 77 GWAS-identified SNPs were retrieved from previous publications as being significantly associated with CKD or renal function traits. We conducted in silico look-up to investigate associations between these known SNPs and CKD in T2D utilizing logistic regression and an additive model.
Results: The mean age of all subjects was 57.5 ± 12.9 years, 45.7% male, median duration of diabetes was 6 [interquartile range: 2–11] years, and 29% had diabetic retinopathy at baseline. After adjustment for age, gender and principal components, among the 77 known SNPs, the directly-genotyped variant rs881858 near VEGFA (OR = 0.886, 95% CI 0.805–0.974, P = 0.012) was significantly associated with CKD in Chinese T2D patient. An imputed SNP rs266734 also showed significant association with CKD (OR = 0.695, 95% CI 0.522–0.925, p = 0.012). The observed effect was consistent with the direction from previous reported findings. Excluding 8 SNPS with poor quality of imputation, the remaining 67 SNPs did not exhibit significant associations with CKD in Chinese with T2D.
Conclusions: Among 77 known GWAS-identified SNPs for kidney diseases, we identified significant association between rs881858 and CKD in Chinese patients with T2D. The discrepancies may be related to different ethnicity as well as the group of subjects being studied (general population vs. subjects with T2D). Our results highlight the need to perform studies in the relevant ethnic group in order to uncover the genetic susceptibility of diabetic kidney disease.

OL04-7

Genome-wide association study in Chinese identifies new susceptibility loci associated with chronic kidney disease in type 2 diabetes

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Background and aims: Diabetic kidney disease is a major complication of diabetes and the leading cause of end-stage renal disease in most parts of the world. Although a few common susceptibility variants have been identified by several genome-wide association studies (GWAS) recently, much of the inherited predisposition to diabetic kidney disease remains unexplained. To unravel the genetic basis of this important complication, we performed a nested case-control study for chronic kidney disease (CKD) in type 2 diabetes (T2D) from the Hong Kong Diabetes Registry (HKDR).
Materials and methods: More than 8,000 patients with T2D and prospective follow-up were included in the HKDR. eGFR was calculated according to the Chinese Modification of Diet in Renal Disease (MDRD) equation. CKD was defined (i) Diabetes with renal manifestations (ICD-9 code: 250.4), chronic kidney disease (ICD-9 code: 585), or unspecified renal failure (ICD-9 code: 586) or (ii) dialysis (ICD-9 procedure code: 39.95) or peritoneal dialysis (ICD-9 procedure code: 54.98) or (iii) eGFR < 60 mL/min per 1.73 m^2 during follow-up period. Samples were genotyped using the Illumina Omni 2.5+ exome array and genotype data was imputed using minimac 3 with the 1000 Genomes Project phase 3 v5 as reference panel. After standard quality control, ~8 million common SNPs were included in the final analysis. Association analysis was adjusted for age, gender, and principal components.
Results: After sample QC, we included 2881 case subjects with T2D and CKD, and 2849 control subjects with T2D duration of >10 years but free of CKD in the genome-wide association analysis (mean age of all subjects 57.5 ± 12.9 years, 45.7% male, median duration of diabetes 6 [interquartile range: 2–11] years, and 29% with retinopathy at baseline). We identified 22 SNPs with suggestive association with CKD in T2D ($p < 10^{-5}$), with one of the strongest signal from a SNP on chromosome 9, OR 0.73 (95% CI 0.65–0.83, $p = 9.98 \times 10^{-7}$), with other top suggestive association signals from loci on chromosomes 1, 2, 4, 7, 11, 14, 16, 17, 18, 19.
Conclusions: Our study has identified a number of novel regions associated with CKD in T2D. Additional genotyping and integrative analysis together with methylation data are currently in progress.
Funding acknowledgment: Supported by a Theme-based Research Scheme from the Research Grants Council of the Hong Kong Administrative Region, China (Project no: T12-402/

13-N), and the Focused Innovations Scheme of the Chinese University of Hong Kong.

OL04-8
Identification of a mutation associated with early-onset diabetes in the intron of INS gene with whole-exome sequencing

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Whole-exome sequencing is a new technology for mutation detection in genetic disorders. We explored the gene responsible for a family with early-onset diabetes using this method. In the family, the proband was diagnosed with hyperglycemia at the age of 3 years and has been treated with insulin immediately after diagnosed. Her two daughters were also diagnosed with hyperglycemia at the age of 12 months and 18 months, respectively. They have been also treated with insulin immediately after diagnosed. All exons and flanking regions of human genome shown in the consensus coding sequence project database were captured with specific probes (Agilent SureSelect XT Human All Exon V4 kit) and the products were sequenced with next generation sequencer (HiSeq2000). The generated reads were annotated with reference sequences in UCSC Genome Brower hg19 and two databases of variants (dbSNP 135 and 1000 Genomes). We checked the result for twenty-six known early-onset diabetes (MODY and/or neonatal diabetes) genes and a heterozygous intronic mutation c.188-31G > A in the INS gene, which is not registered in two databases, was identified in the genomic DNA of the proband. The mutation was also identified in her two daughters, but not in her son without diabetes. The substitution is located 31 bp proximal from exon 3 in the intron 2 of the INS gene. It is predicted to create an ectopic splice site leading to insert 29 nucleotides of intron 2 as exonic sequence in the transcript. The abnormal insulin would induce pancreatic beta cell apoptosis by the endoplasmic reticulum stress. This mutation has been previously described in three reports for analyzing the gene of neonatal diabetes. Our result suggests that the intronic mutation c. 188-31G > A is a hot spot of causal mutation for diabetes in the INS gene.

Treatment of Diabetes

OL05-1
Medicine-related factors that could impact on the safety and outcomes of glucose lowering medicines (GLM) in aged care home

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Background: The McKellar Guidelines consist of 18 guidelines and five risk assessment tools including Glucose Lowering Medicine-related Adverse Risk Assessment and Hypoglycaemia Risk Assessment.
Aim: To identify medicine-related factors that could impact on the safety and outcomes of glucose lowering medicines (GLM) in five Victoria regional and rural aged care homes.
Method: The study was part of a larger study to develop, implement and evaluate the McKellar Guidelines. Data were collected from an audit of medical records of residents with diabetes (n = 74), researchers informally observing staff practice during visits to the care homes and interviews with registered nurses and other care staff.
Findings: Several issues that affect medicine safety were identified. Blood glucose testing was not related to GLM onset or peak action and was not regarded as important unless the person was on insulin. GLM administration times did not always correspond with meal times. Staff did not realise neuroglycopaenic symptoms predominate in older people with low blood glucose or that hypoglycaemic unawareness is common in older people. Thus, hypoglycaemia is often missed or mistaken for confusion or delirium. Some GPs appeared to regard hyperglycaemia as a benign condition. "Reportable blood glucose range" ranged from 2.5 to 25 mmol/L. No evidence was cited to support the reportable ranges and they were not related to Guideline recommendations. Top up doses/sliding insulin scales were used to manage hyperglycaemia despite the fact they are contraindicated and do not treat the underlying cause. Staff focused on administering medicines rather than the overall process of managing medicines and monitoring their effects.
Conclusion: Managing medicines in aged care homes is complicated, especially when older people with diabetes are prescribed High Risk Medicines. Several issues were identified that put older people at risk of medicine-related adverse events and errors.

OL05-2
Changes in body composition during SGLT2 inhibitor treatment and their relevance to the improvement of insulin sensitivity

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Background and aims: Selective sodium glucose co-transporter type 2 (SGLT2) inhibitors decrease renal glucose reabsorption, which results in reductions in plasma glucose and body weight. Although body weight decreases soon after the initiation of SGLT2 inhibitor therapy, it is not clear whether the early weight loss is caused by body fat reduction or fluid loss secondary to osmotic diuresis. Furthermore, skeletal muscle could be reduced by the consumption of muscle amino acids by gluconeogenesis. In this study we assessed changes in clinical parameters and body composition together with changes in insulin sensitivity during a week of tofogliflozin treatment and analyzed factors contributing to the improvement of insulin resistance.
Materials and methods: The subjects included 13 male and 12 female patients with type 2 diabetes. The mean age was 47 ± 14 years with a mean BMI of 29.6 ± 6.8 kg/m^2. Tofogliflozin was administered at a dose of 20 mg/day without changing the doses of other drugs. Insulin sensitivity was quantified by determining the steady state plasma glucose (SSPG) concentration. Body compositions were measured via multi-frequency bioelectrical impedance analysis using InBody720. iPro2 continuous glucose monitoring (CGM) devices were used to monitor subcutaneous glucose levels
Results: Fasting plasma glucose and 24-h average glucose determined by CGM decreased from 175 ± 43 mg/dL to 117 ± 25 mg/dL and from 185 ± 44 mg/dL to 137 ± 29 mg/dL, respectively. No hypoglycemia was detected during the study period, and mean amplitude of glycemic excursion (MAGE) was reduced from 97.0 ± 33.9 mg/dL to 72.7 ± 27.4 mg/dL ($p = 0.01$). The subjects lost 1.7 ± 0.8 kg of body weight, and body fat mass was reduced by 1.38 ± 1.03 kg. No significant change was observed in muscle mass, skeletal muscle mass, or total body water, although lower limb muscle mass was slightly but significantly decreased. SSPG was reduced from 288 ± 81 mg/dL to 237 ± 77 mg/dL ($p = 0.0003$), indicating an improvement in insulin resistance. Changes in body fat mass and serum

cholinesterase were significantly correlated with the reduction of SSPG.

Conclusion: Short-term tofogliflozin treatment significantly improved 24-h glucose profiles. The decline in body weight primarily resulted from the decrease in body fat. However, the risk of dehydration was not excluded because the subjects of this study were urged to drink adequate water during the treatment. Insulin sensitivity significantly improved likely due to the decrease in body fat mass. In addition, the improvement of hepatic steatosis may be involved in the amelioration of insulin resistance.

OL05-3

Efficacy and safety of once-weekly semaglutide vs exenatide ER after 56 Weeks in subjects with type 2 diabetes (SUSTAIN 3)

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Semaglutide is a glucagon-like peptide-1 (GLP-1) analog in development for the treatment of type 2 diabetes (T2D). This study evaluated the efficacy, safety and tolerability of once-weekly subcutaneous semaglutide versus exenatide extended-release (ER) in subjects with T2D inadequately controlled on 1–2 oral antidiabetic drugs (OADs: metformin, sulfonylureas and thiazolidinediones).

In this phase 3, open-label study, 813 adults with T2D (HbA1c 7–10.5%) were randomized 1:1 to once-weekly semaglutide 1.0 mg or once-weekly exenatide ER 2.0 mg for 56 weeks. The primary endpoint was change in HbA1c from baseline to Week 56. Secondary efficacy endpoints included change in body weight (BW), blood pressure and other glycemic parameters.

Baseline characteristics were similar in both arms; overall mean age 56.6 years, duration of T2D 9.2 years. Mean HbA1c (overall baseline mean 8.3%) was reduced by 1.5% with semaglutide and 0.9% with exenatide ER (estimated treatment difference vs exenatide ER [ETD] –0.62%; $p < 0.0001$). HbA1c <7% was achieved by 67% of semaglutide-treated subjects versus 40% with exenatide ER; 47% and 22% achieved HbA1c ≤6.5%, respectively. Mean BW (overall baseline mean 95.8 kg) was reduced by 5.6 kg with semaglutide and 1.9 kg with exenatide ER (ETD –3.73 kg; $p < 0.0001$).

Adverse event (AE) rates were comparable between groups: 75.0% and 76.3% of subjects reported AEs with semaglutide and exenatide ER, respectively. Serious AEs were reported by 9.4% of subjects receiving semaglutide and 5.9% of subjects receiving exenatide ER (spread over multiple system organ classes). Two fatal events were reported in the semaglutide arm (both advanced stage neoplasms considered unrelated to treatment). The proportion of subjects discontinuing treatment due to AEs was 9.4% for semaglutide and 7.2% for exenatide ER. The most frequent AEs were gastrointestinal (GI), which were mainly mild or moderate in severity. GI AEs were reported by 41.8% and 33.3% of subjects receiving semaglutide and exenatide ER, respectively; 22.3% and 11.9% for nausea, 11.4% and 8.4% for diarrhea and 7.2% and 6.2% for vomiting. The proportion of subjects reporting nausea diminished over time in both groups. Injection site reactions were reported by 1.2% of subjects receiving semaglutide and 22.0% of subjects receiving exenatide ER.

In conclusion, once-weekly subcutaneous semaglutide 1.0 mg was superior to exenatide ER 2.0 mg in improving glycemic control and reducing BW in subjects with T2D inadequately controlled on 1–2 OADs. Semaglutide was well tolerated, with a safety profile similar to that of other GLP-1 receptor agonists.

OL05-4

Efficacy and safety of once-weekly semaglutide versus once-daily insulin glargine in insulin-naïve subjects with type 2 diabetes (SUSTAIN 4)

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This trial evaluated the efficacy and safety of subcutaneous (s.c.) semaglutide versus insulin glargine (IGlar) in insulin-naïve subjects with T2D.

In this phase 3a, randomized, open-label study, 1082 adults with T2D (HbA1c 7–10%) received semaglutide 0.5 mg (n = 362) or 1.0 mg (n = 360) once weekly or IGlar (n = 360; starting dose 10 IU/day) once daily for 30 weeks, added to stable metformin +/– sulfonylurea (SU). Investigators were instructed to titrate to a pre-breakfast self-monitored plasma glucose (SMPG) target of 4.0–5.5 mmol/L. Primary endpoint was change in HbA1c from baseline to Week 30.

Mean HbA1c (baseline 8.2%) was reduced with semaglutide 0.5 and 1.0 mg by 1.2% and 1.6% versus 0.8% with IGlar (estimated treatment difference versus IGlar [ETD] –0.38% and –0.81%; $p < 0.0001$ for both). Mean IGlar dose at Week 30 was 29.2 IU/day. HbA1c <7% was achieved by 57.5% and 73.3% of 0.5 and 1.0 mg semaglutide-treated subjects, respectively, versus 38.1% with IGlar. HbA1c ≤6.5% was achieved by 37.3%, 54.2% and 17.5% of subjects, respectively. Mean fasting plasma glucose (baseline 9.7 mmol/L) was reduced with semaglutide 0.5 and 1.0 mg by 2.1 and 2.7 mmol/L versus 2.1 mmol/L with IGlar (ETD 0.07 mmol/L [$p = 0.7$] and –0.61 mmol/L [$p = 0.0002$]). Mean 8-point SMPG (baseline 10.9 mmol/L) was reduced by 2.4, 2.9 and 2.4 mmol/L, respectively (ETD –0.07 mmol/L [$p = 0.6$] and –0.58 mmol/L [$p < 0.0001$]).

Mean body weight (BW; baseline 93.4 kg) decreased with semaglutide 0.5 and 1.0 mg by 3.5 and 5.2 kg versus a 1.2 kg increase with IGlar (ETD –4.62 kg and –6.34 kg; $p < 0.0001$ for both).

Proportions of subjects reporting adverse events (AEs) were 69.9%, 73.3% and 65.3% with semaglutide 0.5, 1.0 mg and IGlar, respectively; 6.1%, 4.7% and 5.0% reported serious AEs. Fatal AEs were reported in 4 semaglutide subjects and 2 IGlar subjects. Discontinuation due to AEs occurred in 5.5%, 7.5% and 1.1% of patients, respectively. The majority of discontinuations with semaglutide were due to gastrointestinal (GI) AEs; mild, transient GI AEs were the most common AEs with semaglutide. Proportions of subjects reporting GI AEs were: 21.3%, 22.2% and 3.6% for nausea; 16.3%, 19.2% and 4.4% for diarrhea; and 6.6%, 10.3% and 3.1% for vomiting.

In conclusion, semaglutide (0.5 and 1.0 mg s.c. once weekly) provided superior glycemic control and BW reduction versus IGlar in patients with T2D treated with metformin +/– SU. Semaglutide was well tolerated with a safety profile similar to other GLP-1 receptor agonists.

OL05-5

Effects of SGLT2 inhibitor luseogliflozin under different dietary formula in type 2 diabetes: A randomized, controlled exploratory trial

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Effects of SGLT2 inhibitors (SGLT2i) under different dietary formula need to be investigated as a case of ketoacidosis due to SGLT2i use under strict carbohydrate restriction was reported. This study was designed to determine safety and efficacy of SGLT2i luseogliflozin under 3 different dietary formula in patients with type 2 diabetes. Twenty four patients with type 2 diabetes were randomly assigned to tree groups and received either one of the three different delivery meals for 14 days (i.e. Day 1 to Day 14) [Group A, high glycemic index meals with 55% energy from carbohydrate; group B, low glycemic index meals with 55% energy from carbohydrate; and group C, high glycemic index meals with 40% energy from carbohydrate]. The patients in all three groups also received luseogliflozin once daily for last 7 days (i.e. Day 8 to Day 14). Daily glycemic profiles were analyzed during Days 6–7 and 13–14 using continuous glucose monitoring devices; and changes of biochemical parameters were investigated using blood samples withdrawn on Days 8 and 15. Luseogliflozin improved mean (mg/dL) [A 142.9 to 127.7*; B 129.9 to 115.2*; and C 130.4 to 111.4* (*, $p < 0.05$ hereafter)] and AUC (mg/dL x min) [A 6849 to 6121*; B 6226 to 5521*; and C 6247 to 5340*] in all groups, while it has little effects on SD (mg/dL) [A 39.5 to 35.2; B 31.9 to 30.6; and C 27.7 to 27.6]. Levels of glucagon (pg/mL) [A 152.6 to 154.6; B 144.4 to 142.9; and C 152.0 to 150.3] were unaffected by luseogliflozin. Total ketones (μmol/L) [A 590.5 to 752.3*; B 596.9 to 689.8; and C 599.1 to 744.7*] were increased by luseogliflozin but comparable among three groups. Of 23 patients who received luseogliflozin, 2 mild adverse events, frequent urination and drowsiness occurred in one patient in A. These results suggest SGLT2i can be safely and effectively used under mild carbohydrate restriction and low glycemic index, while long-term safety and efficacy of SGLT2i, in association with different dietary formula, need to be determined.

OL05-6

Use of the Japanese health insurance claims database to assess safety of SGLT2 inhibitors in the management of diabetes

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Aims: A considerable number of serious adverse events (SAEs) were reported in patients receiving SGLT2 inhibitors (SGLT2i) clinically in Japan during the early stage of their use. These included urinary tract infections (UTI), genital infections (GI), hypoglycemia and dehydration in addition to acute myocardial and cerebral infarctions (MI and CI). While announcement of the recommendations for appropriate use of SGLT2i seemingly reduced SAEs substantially in Japan, safety of SGLT2i remains to be shown in actual clinical practice.

Methods: Incidence of UTI, GI, hypoglycemia, dehydration, MI and CI was compared in patients receiving SGLT2i or other OADs. The index date was defined as the prescription date of the first claim for a new OAD during the target period from April, 2014 through May, 2015. An anti-diabetic drug was considered new if there were no claims for the medication during the prior 6 months. The observation period started on the index date and ended at the occurrence of one of the following events, whichever was earliest: (i) UTI, GI, hypoglycemia, dehydration, MI and CI, (ii) initiation of another new antidiabetic drug, insulin or GLP-1, (iii) end of observation period and (iv) end of eligibility.

Results: Cox proportional hazard models (CPHM) comparing the adjusted risk of UTI and GI with age and gender as independent variables revealed that SGLT2i was associated with higher hazard risks (HR) of UTI [SGLT2i n = 2,615 and other OADs n = 6,250; HR 1.4 (95%CI 1.1–1.9), p = 0.0122] and GI [SGLT2i n = 2,675 and other OADs n = 6,390; HR 2.5 (95%CI 1.6–3.8), $p < 0.0001$]. CPHM comparing the age- and gender-adjusted risk of hypoglycemia revealed no significant increase in HR of all hypoglycemia [SGLT2i n = 2,711 and other OADs n = 6,492; HR 1.6 (95%CI 0.3–9.5), p = 0.6203]. CPHM comparing the age- and gender-adjusted risk of dehydration revealed that SGLT2i was associated with higher hazard risks (HR) of dehydration [SGLT2i n = 2,646 and other OADs n = 6,293; HR 1.4 (95%CI 1.0–1.9), p = 0.0239], while CPHM comparing the adjusted risk of MI and CI with age, gender, and risk comorbidities as independent variables revealed that SGLT2i did not significantly elevate HR of MI [SGLT2i n = 2,686 and other OADs n = 6,450; HR 1.3 (95%CI 0.4–4.7), p = 0.6868] and CI [SGLT2i n = 2,657 and other OADs n = 6,324; HR 1.0 (95%CI 0.4–2.2), p = 0.9488].

Conclusion: The announcement of the recommendations reduced SAEs such as hypoglycemia, MI and CI substantially in Japan. However, UTI and GI should be screened and appropriately treated, if exist, in all patients receiving SGLT2i.

The Pancreatic Islet and Bariatric Surgery

OL06-1

Clock gene dysregulation induced by chronic endoplasmic reticulum stress disrupts β-cell function

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Wolfram syndrome, caused by the WFS1 mutation and characterized by insulin-dependent diabetes mellitus, is one of the prototypical human endoplasmic reticulum (ER) diseases. In addition, recent studies have suggested that glucotoxicity and lipotoxicity induce ER stress responses resulting in β-cell failure. One environmental condition that is gaining greater appreciation as a risk factor for type 2 diabetes (T2DM) is circadian rhythm disruption, and various animal studies support the concept that clock genes have an essential function in the endocrine pancreas. Herein, we demonstrate potential mechanisms whereby chronic ER stress can predispose β-cells to failure via clock gene dysregulation. To newly identify mechanisms underlying the β-cell dysfunction in diabetic Wfs1-/- Ay/a mice, we performed microarray analyses and discovered a decrease in albumin D-element binding protein (Dbp) expression and an increase in nuclear factor interleukin 3 (Nfil3)/E4 binding protein 4 (E4bp4) expression in Wfs1-/- Ay/a islets as compared to non-diabetic Ay/a islets. As expected, Ddit3 (Chop) expression was up-regulated in Wfs1-/- Ay/a islets as compared to Ay/a islets. No other clock genes, including Arntl (Bmal1), showed altered expressions. The Quantitative real-time PCR analysis of isolated islets revealed that levels of Dbp and Nfil3/E4bp4 expression had decreased about 3-fold and increased about 3-fold, respectively, in Wfs1-/- Ay/a as compared to WT islets. MIN6 cells treated with 1 μM thapsigardin (TG) for 24 h showed a marked

decrease in Dbp mRNA and a marked increase in Nfil3/E4bp4 mRNA. Meanwhile, Chop mRNA increased 24-fold as compared with the level in controls. Isolated islets treated with 0.5 μM TG for 24 h or 2 μg/mL tunicamycin (TM) showed very similar changes in the expressions of clock genes and Ddit3. Overall, chronic ER stress should decreases DBP transcriptional activity in β-cells. To explore the role of DBP transcriptional activity in ER stress-induced β-cell dysfunction, we created transgenic mice expressing E4BP4 under the control of the mouse insulin I gene promoter (MIP), in which E4BP4 should β-cell-specifically compete for D-box, with DBP and suppress the expressions of the targets of DBP. We analyzed insulin secretion in the perfused pancreas. MIP-E4BP4 mice had markedly reduced and delayed insulin secretion during perfusion with 16.8 mM glucose. In pathophysiological settings, our data indicate that chronic ER stress disrupts this circadian alignment leading to β-cell failure. Elucidating the role of circadian clocks in ER stress-induced β-cell failure could introduce novel approaches to treating diabetes.

OL06-2
Effect of heparan sulfate proteoglycan Syndecan-4 on the insulin secretory response

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Objectives: Heparan sulfate (HS) proteoglycans (PGs) comprise a core protein to which extracellular glycosaminoglycan chains are attached. We recently found that HS is localized exclusively around β-cells in the islets of adult mice and is required for islet morphogenesis, β-cell proliferation and insulin secretion. Furthermore, we found that the 3-*O*-sulfate groups of HS are necessary for maintaining glucose-induced insulin secretion (GIIS). So far it is not known, however, which core proteins are crucial in this process and how they function to modulate β-cell function. The aim of this study was to identify the core protein(s) which are critical for insulin secretion, and to clarify the effect of the core protein(s) on insulin secretion.
Methods: To investigate the participation of HSPGs in the insulin secretion mechanism, MIN6 cells, a mouse pancreatic β-cell line, were subcloned by limiting dilution method. The subcloned MIN6 cells were selected based on their insulin secretion level following stimulation with glucose or KCl. Furthermore, we examined the expression of HS and core proteins in the subclones. Using silencing and overexpression of the core protein which involved in insulin secretion in cultured subclones, we examined changes of disaccharide composition of HS, GIIS and expression of the genes related to insulin secretion.
Results: Syndecan-4 (Sdc4), one of the major HS-containing core proteins, is distributed on the cell surface. The results from our screening experiments indicated that only Sdc4-expressing subclones are able to secrete insulin in response to glucose. While, Sdc4-lacking subclones had significantly low GIIS response and no HS from cell surface PGs. Silencing of Sdc4 by RNA interference reduced GIIS by about 50% at 25 mM glucose ($p < 0.001$), whereas the overexpression of Sdc4 increased the insulin secretory response by approximately 2- to 8-fold as compared with control cells. Based on HPLC analysis, the amount of HS had increased in Sdc4-overexpressing cells by approx. 5.5- to 29-fold. In Sdc4-overexpressing cells, Glut1 or Gck mRNA levels were elevated, suggesting that these genes have enhancing effects on insulin secretion pathway.
Conclusions: Our data indicate that the HSPG Sdc4 plays important role(s) in the GIIS response of pancreatic β-cells. However, there exists the differences in glucose responsiveness and expression levels of GIIS-related genes among the Sdc4-overexpressing subclones. The further investigation is necessary to clarify the mechanisms in the relationship between Sdc4 and GIIS.

OL06-3
Elucidation of mechanism of human pancreatic beta-cell maturation with hiPSC reporter line

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After the discovery of human induced pluripotent stem cell (hiPS), regenerative therapy with hiPSCs for patient with insulin-dependent diabetes mellitus (IDDM) has been expected, but there are still several tasks to clarify before we perform transplantation of hiPSC-derived insulin secreting cells in future.
One of the difficulties comes from unknown mechanism of human pancreatic beta-cell maturation. The mechanism has been clarified gradually as it has been reported that several transcriptional factors play an important role in beta-cell maturation such as Pdx1, MafA, NeuroD, Nkx6.1, GLP-1R and Rfx6, but the difference between species has been pointed out in some reports, so more accurate mechanism in human still remains to be elucidated.
EGFP knock-in artificial gene, that express EGFP in a downstream of the promoter region of the target gene, enables us to detect when it expresses and when it does not. Therefore, we consider the reporter line is suitable to evaluate the function of target gene.
Our group has already constructed Insulin(INS)-GFP reporter line with this method and we are now establishing hiPSC-reporter line of several transcriptional factors. Among the transcriptional factors, MafA (V-maf musculoaponeurotic fibrosarcoma oncogene homolog A) attracts our attention for its expression synchronized with beta-cell maturation so that we are working especially on MafA-EGFP reporter line.
Cloning method we use is called Red-ET recombination system with bacterial artificial chromosome (BAC) which contains target gene.
To validate the accuracy of the reporter line, we are planning to perform in vitro and in vivo assay of the reporter line. As to in vitro assay, we are going to check the marker of undifferentiation and pluripotency and then follow several methods of hiPS differentiation and evaluate when and how much the target genes are expressed, and evaluate the ability of glucose-sensitive insulin secretion (GSIS). In the point of in vivo assay, we will transplant the undifferentiated cell colonies to mice to make tumor with ectoderm, mesoderm and endoderm to certify its pluripotency, and transplant semi-differentiated cell colonies to trace its destination in vivo compared to in vitro, and transplant differentiated cell colonies to check in vivo function of GSIS. We are considering that this research can contribute to more accurate hiPSC regenerative therapy in future for IDDM patients. In this presentation, we will report our latest findings of our reporter line.

OL06-4
The effect of caveolin-1 on the process of proliferation and apoptosis and function regulation in beta cell

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Beta cell loss is a hallmark in all forms of diabetes mellitus. Strategies to prevent beta cell loss and dysfunction are urgently needed. Our study aims to access the influence of caveolin-1 on the beta cell's apoptosis and function. We knockdown the expression level of caveolin-1 in both NIT-1 cell and islet isolated from C57BL/6J mice by RNA interference technique which realized by transfer a shRNA vector target

caveolin-1 mRNA into the NIT-1 cell and islet through the latent virus infection then purified the positive infection cell by puromycin containing(10 ug/mL) medium. First, we identified the change of gene expression profile in islet by mouse gene expression microarray when the expression level of caveolin-1 is down regulated and those pathways related with beta cell proliferation and pancreatic secretion function were found influenced much. Then we found the same result in the NIT-1 cell strain. The differences of cell proliferate and apoptosis among the caveolin-1 knockdown cell, the scramble vector infection cell and the wildtype NIT-1 cell were compared, and the effect of caveolin-1 on the cell's proliferation and apoptosis were analyzed. The results of flow cytometry and MTT show that knockdown the expression level of caveolin-1 in NIT-1 cell could promote proliferation as well as increase the resistance to palmitic acid's lipotoxicity. The result of Real-time fluorescence quantification PCR show that the expression level of casepase7 and caspase12 that mediated the apoptosis process caused by endoplasmic reticulum stress was downregulated according the down-regulation of caveolin-1 expression in palmitic acid treated NIT-1 cell strain. These findings suggest that caveolin-1 which involved in the process of apoptosis and function regulation in beta cell may serve as target for the development of novel therapies for diabetes mellitus.

OL06-5

Disruption of peripheral clock gene Nocturnin leads to defective islet beta cell function and glucose intolerance

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Nocturnin is one of the circadian rhythmic "output gene", encodes a deadenylase – ribonuclease that specifically removes the poly (A) tails from mRNAs. We investigated the difference of glucose homeostasis, beta cell function, and mRNA microarray between wild type (WT) and Nocturnin knockout (NOC-/-) mice.

Body weight (BW), oral glucose tolerance test, insulin tolerance test, isolated islet perifusion study, intrapancreatic insulin content, immunohistochemical stain of insulin to measure beta cell mass, micro-array of mRNA and microRNA were performed and compared between wild type (WT) and NOC (-/-) mice. Neither BW nor beta cell mass and insulin content were different between WT and NOC (-/-) mice. NOC (-/-) mice are more glucose intolerant but more insulin sensitive than WT mice. Oral glucose-stimulated insulin secretion in 30 min is much less in NOC (-/-) mice than in WT mice. During isolated islet perifusion study, the glucose stimulated insulin secretion was much less in NOC (-/-) mice than in WT mice. According to microarray study of mRNA of purified islets, the gene expression levels of G protein coupled receptor 18 (GPR 18), and hexokinase I (HK I) were much less in NOC (-/-) mice than in WT mice. In islets from WT mice, gene expression of GPR18 and HK1 showed prominent circadian rhythm (night time >day time), which is compatible with the circadian rhythm of Nocturnin gene expression. However, the rhythmic change of these two genes was dysregulated in NOC (-/-) mice. We also found the glucose-stimulated insulin secretion (GSIS) was impaired in GPR18 knock-down MIN6 cells. Furthermore, we also found the GPR18 agonist, N-Arachidonylglycine (NAGLy) enhanced GSIS in islet perifusion study of WT mic.

In conclusion, NOC plays a role in regulating glucose homeostasis. Knock-out NOC gene leads to glucose intolerance with impaired glucose-stimulated insulin secretion. The differences may attribute to the down-regulation and dysregulation of GPR18 and HKI genes. It warranted to further investigate the mechanism of GPR18 regulated by NOC and the role of GPR18 on glucose homeostasis.

OL06-6

Durability of diabetes remission after bariatric surgery: A 5-year prospective follow-up in a multi-ethnic Asian population

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With the advent of bariatric surgery, diabetes remission has taken on a new perspective. One-year post-bariatric surgery remission rates of type 2 diabetes mellitus (T2DM) have been reported to be as high as 95%. Longer-term follow-up suggests that relapse of DM in those who have remitted, is common. However, such data is lacking, especially in Asia. We hereby report the longer-term outcome of Asian T2DM patients, who have undergone bariatric surgery.

Method: The prospective data of 100 patients with T2DM who have undergone bariatric surgery at the Singapore General Hospital with at least 2 years' follow-up is analyzed. Complete and partial DM remission are defined as HbA1c <6.0% and <6.5% respectively without the use of DM medications. DM is considered to have relapsed if the HbA1c rose to > 6.5% or if any DM medication was used regardless of HbA1c.

Results: Of the 100 patients who underwent bariatric surgery (sleeve gastrectomy 25%; gastric bypass 75%), 57% of them were women and 47% were Chinese. Mean age was 50.0+/−9.2 years with a mean preop BMI of 39.1+/−7.6 kg/m^2. At 1 year post-op, 80% achieved remission (71% complete, 9% partial). Of those who have achieved DM remission at 1-year post-op, 12% had DM relapse in the 2nd year, 25% in the 3rd year, 30% in the 4th year and 37% by the 5th year. At the end of 5 years, only 36% remained in complete remission while 7% were in partial remission with 57% either never achieving remission or had DM relapse. Compared with those who achieved DM remission at 1-year post-op but relapsed into the DM range subsequently, those who achieved sustained DM remission for at least 2 years, had lost significantly more weight (mean weight loss 27.3+/−9.6% vs 9.3%+/−0.8%; p = 0.001), and pre-operatively, had significantly shorter mean duration of DM (55+/−59 months vs 157+/−120 months; p = 0.032) and lower HbA1c (7.9+/−1.3% vs 8.6+/−1.1%; p = 0.012), without any significant differences in pre-op BMI.

Conclusion: Bariatric surgery in T2DM patients is associated with sustainable DM remission in a substantial proportion. However, prospective long-term follow-up is crucial as up to 50% of those who achieve DM remission at 1-year post-op may develop DM relapse at 5 years post-op. Patients with longer DM duration, poorer glycemic control preop and those who attain less weight loss post-op seem to be at higher risk for relapse.

OL06-7

Metabolic surgery for Type 2 Diabetes Mellitus in young-onset patients

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Background: The prevalence of young onset Type 2 Diabetes Mellitus (T2DM) is increasing and it is known to respond poorly to medical treatment. Metabolic Surgery has been well recognized for its effectiveness in remission of T2DM but its effectiveness and durability on remission of diabetes in young onset T2DM has not been explored so far.

Methods: In this cohort study of Taiwanese patients with BMI above 25 who underwent metabolic surgery to ameliorate T2DM between 2007 to 2013, 558 patients (339 young onset and 219 late onset T2DM patients) with minimum of one year follow up were included. Preoperative, peri-operative and post-operative follow up clinical and laboratory data were prospectively collected and compared between two groups. Diabetes remission rate (HbA1c <6.0% without anti-glycemic medication) was primary outcome measure.
Results: Young-onset patients had higher preoperative BMI and HbA1c profiles than late-onset patients. Distribution of surgical procedures and major complications were similar between two groups. At one year, young onset group achieved greater weight loss even though it was not statistically significant. A higher complete diabetes remission rate was observed in young onset patients (57.3% vs. 50.2%, p = 0.019). At 5-year, young-onset patients still maintained a higher weight loss (11.8% versus 11.7%, p = 0.002) and higher remission rate (65.3% versus 54.2%, p = 0.04) than late-onset patients. Age at operation, duration of diabetes and C-peptide level were independent predictors of diabetes remission. Remission rate was directly related to extent of weight loss. Multivariate analysis confirmed higher DM remission rates in young-onset group.
Conclusion: This report describes the largest, long-term study examining metabolic surgery for young-onset diabetic patients. Metabolic surgery may achieve better and more durable glycemic control in selected young-onset than those with late-onset T2DM patients and early treatment is preferred.

OL06-8

Metabolic surgery for diabetes treatment: A comparative study of sleeve gastrectomy and gastric bypass

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Background: Bariatric surgery has gained reputation for its metabolic effect and is increasingly being performed to treat type 2 diabetes mellitus (T2DM). However, there is still a grey area regarding the choice of surgical procedure according to patient characteristics due to inadequate evidences. We aim to compare the efficacy of two most commonly performed bariatric/metabolic surgeries, sleeve gastrectomy (SG) and gastric bypass (GB) with regards to remission of T2DM after surgery.
Methods: Outcomes of 579 (349 women and 230 male) patients who underwent SG (109) or GB (470) for the treatment of T2DM with one year follow-up were assessed. The remission of T2DM after SG or GB surgery was evaluated in matched groups using the ABCD scoring system. The ABCD score is composed of the age, BMI, C-peptide levels and duration of T2DM (years).
Results: The weight loss of the SG patient at one year after surgery was similar to the GB patients [26.3(1.1) % vs. 32.6(1.2) %; p = 0.258]. The mean BMI decreased from 35.7(7.2) to 28.3 (3.7) Kg/m^2 in SG patients at one year after surgery and decreased from 36.9(7.2) to 26.7(4.5) Kg/m^2 in the GB patients. The mean HbA1c decreased from 8.8% to 6.1% of the SG group and from 8.6% to 5.9% of the GB group. Sixty-one (56.0%) patients of the SG group and 300 (63.8%) of the GB group achieved complete remission of T2DM (HbA1c < 6.0%) at one year after surgery without statistical difference. However, GB exhibited significantly better glycemic control than the SG surgery in groups stratified by different ABCD score. At 5-years after surgery, GB had a better remission of T2DM than SG (53.1% vs. 35.3%; p = 0.055).
Conclusions: In conclusion, although both SG and GB are effective metabolic surgery, GB carries a higher power on T2DM remission than SG. ABCD score is useful in T2DM patient classification and selection for different procedures.

Laboratory Medicine for Diabetes

OL07-1

Time-dependent sensor performance is sustained during 4 years: Accuracy measurement with mean absolute difference (MAD) in continuous glucose monitoring (CGM)

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Background: Mean absolute difference (MAD) is a numerical accuracy measures which is defined as closeness between continuous glucose monitoring (CGM) and corresponding in-time reference blood glucose (BG) measurements 1). However, possible factor affected to MAD is not well documented so far 2).
Methods: During May 2012 and March 2016, 55 diabetic patients were unintentionally collected in a single institute and consecutively recorded 96 CGMs with iPro2 (Medtronic MiniMed, Northridge, CA) 2). Analyzed CGMs were assigned to Term 1 (n = 30), 2 (n = 29), and 3 (n = 30) by record starting day [May-Dec 2012,-Nov 2013,-Mar 2016]. Among terms, patient's age, recoded duration days, sensored BG, effective calibration times by metered BG reference were set as independent variables and MAD was as dependent. Factorial ANOVA was performed with SPSS Statistics version 22.0 (IBM, Chicago, IL).
Results: Of consecutive 96 CGM recodings from 55 patients (51.9+/−13.5 years old), 7 were excluded from this study due not to assessed relative coeffficient (r) of MAD; 89 recordings, type 1(45), type 2 (27), fulminant type 1 (13), tumor (insulinoma, etc) peri-operation (3), SPIDDM (1), were subjected to this study. Of total 102,934 times sensored in 89 recordings (1,156.6+/−439.9 times sensored per record), sensor BG was 9.5 +/−2.5 mmol/L, and effectively calibrated 1,706 times by meter BG reference; MAD was 12.24+/−1.51%, r was 0.917+/−0.075. Among three terms [T1, T2, vs T3], patient number was [30, 27, vs 29], patient age was [55.3+/−14.0, 52.4+/−12.5, vs 48.0+/−13.3] years old, and record duration was [4.1+/−0.4, 4.7+/−1.2, vs 6.7 +/−0.7] days per recording. Sensored BG was [9.8+/−2.4, 9.9 +/−2.9, vs 8.7+/−1.9] mmol/L, which was calibrated effectively in [14.7+/−3.3, 17.4+/−7.0, vs 25.4+/−5.5] times per recording; MAD was [11.09+/−2.77, 11.61+/−2.97, vs 13.3+/−5.03] %, and it's r was [0.932+/−0.114, 0.923+/−0.240, vs 0.905+/−0.173]. Both sensored BG 3) and MAD were not statistically different throughout Terms, whereas patient was younger, record duration was longer, and calibration was most frequent in Term 3.
Discussion: Former and no experience users was not different in MAD 4). Relationship between age and frequency of discontinuation 5) was not investigated in this study; Patient's level of numeracy, literacy, and cognitive function, and poor reimbursement was not investigated.
Conclusion: MAD is not affected by patient's numerical characteristics; within favorable values during 4 years.

OL07-3

Validation of a new formula (SMART2D) for estimation of LDL cholesterol in patients with and without diabetes

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Background: The Friedewald formula, widely used in clinical laboratories to estimate LDL cholesterol (LDL-C), tends to

underestimate LDL-C especially at high triglyceride levels and low LDL-C levels. This is especially seen in patients with diabetes due to abnormalities in lipoprotein composition and hypertriglyceridemia. A study from our institution derived a new formula (SMART2D formula) from a cohort of patients with type 2 diabetes for estimation of LDL-C. The aim of this study is to validate the use of the SMART2D formula to estimate LDL-C in patients with and without diabetes.

Methods: We examined 54639 lipid profiles from January 2011 to December 2014 at a Regional General Hospital. LDL-C calculated using the Friedewald formula (F-LDL-C) and the SMART2D formula (SMART2D-LDL-C) were compared with direct LDL-C measurement (M-LDL-C) by an automated assay (Roche Cobas C501). The agreement in classification into National Cholesterol Education Program defined LDL levels was also studied.

Results: In patients with diabetes, the mean difference between M-LDL-C and F-LDL-C was 0.381 ± 0.253 mmol/L and between M-LDL-C and SMART2D-LDL-C was −0.148 ± 0.201 mmol/L. Bland Altman plots showed better agreement between SMART2D-LDL-C and M-LDL-C (B = −0.02, p = 0.160) than between F-LDL-C and M-LDL-C (B = 0.027, p = 0.00). By Friedewald formula, 28.7% of patients with M-LDL-C ≥ 2.6 mmol/L were classified as F-LDL-C < 2.6 mmol/L. (Kappa: 0.389) With the SMART2D formula, 5.3% of patients with M-LDL-C ≥ 2.6 mmol/L were classified as SMART2D-LDL-C <2.6 mmol/L. (Kappa: 0.828) In patients with TG > 2.2 mmol/L, 45.3% were misclassified with Friedewald formula, while 8.6% were misclassified with the SMART2D formula.

In patients without diabetes, the mean difference between M-LDL-C and F-LDL-C was 0.361 ± 0.231 mmol/L and between M-LDL-C and SMART2D-LDL-C was 0.001 ± 0.182 mmol/L. Bland Altman plot showed positive bias for the SMART2D formula (B = −0.004, p = 0.00) and negative bias for the Friedewald formula. (B = 0.008, p = 0.00) By Friedewald formula, 33.6% with M-LDL-C ≥ 2.6 mmol/L were classified as F-LDL-C < 2.6 mmol/L. (Kappa: 0.451) With the SMART2D formula, 6.3% with M-LDL-C ≥ 2.6 mmol/L were classified as LDL-C < 2.6 mmol/L. (Kappa: 0.837) In patients with TG > 2.2 mmol/L, 54.2% were misclassified with Friedewald formula, while 11.4% were misclassified with the SMART2D formula.

Conclusion: The SMART2D formula, as compared to the Friedewald formula, provides a more accurate estimate of LDL-C and reduces misclassification in patients with and without diabetes.

OL07-5

Elevated hemoglobin A1c levels are associated with increased arterial stiffness in a Taiwanese population

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Introduction: Studies have shown that diabetes mellitus increased brachial-ankle pulse-wave velocity (baPWV), but the impact of two pre-diabetes conditions, impaired fasting glucose and impaired glucose tolerance, remains controversial. Recently, another surrogate for the diagnosis of diabetes and pre-diabetes has been suggested from an oral glucose tolerance test to hemoglobin A1c (HbA1c). The aim of this study was to investigate the impact of different HbA1c status on baPWV in a relatively healthy Taiwanese population.

Methods: We enrolled 4938 apparently healthy subjects after excluding those who were under medications for diabetes, hypertension or hyperlipidemia; or had a history of cardiovascular disease; or had diagnosed anemia and peripheral atherosclerosis with ankle brachial index (ABI) <0.95 in the health examination center of the National Cheng Kung University Hospital from Oct. 2006 to Aug. 2009. The baPWV values to assess arterial stiffness were calculated as the distance traveled by the pulse wave divided by the time taken to travel the distance. The participants were classified into three groups based on 2011 report by an International Expert Committee, American Diabetes Association: normal glucose tolerance (NGT) (HbA1C <5.7%, n = 2973), pre-diabetes (HbA1C 5.7–6.4%, n = 1817) and newly diagnosed diabetes (NDD) (HbA1C ≥6.5%, n = 148).

Results: The mean values of baPWV were 1265.2 ± 195.0, 1386.7 ± 241.2, 1488.5 ± 278.7 cm/s in NGT, pre-diabetes and NDD groups, respectively. Both pre-diabetes and NDD groups had a higher baPWV value as compared with NGT group (p < 0.001). In multiple linear regression with the reference group of NGT, both pre-diabetes (β = 13.96, p = 0.002) and NDD (β = 25.76, p = 0.002) groups had a significantly higher baPWV values after adjustment for age, sex, body mass index, current smoking, alcohol consumption, habitual exercise, systolic blood pressure, cholesterol and high-density lipoprotein cholesterol.

Conclusions: Diabetic subjects with HbA1c ≥6.5% exhibit a greater arterial stiffness, even in pre-diabetes with HbA1C of 5.5–6.4%.

OL07-6

Urine albumin/creatinine ratio is a significant predictor for incident diabetic peripheral neuropathy in patients with Type 2 Diabetes: 3-year prospective study

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Introduction: Diabetic peripheral neuropathy (DPN) is a common complication of Type 2 Diabetes (T2D). Apart from hyperglycemia, its pathogenesis is poorly understood. DPN can develop despite intensive glucose control, suggesting that other risk factors are involved in the pathophysiology of DPN. In this study, we aim to determine baseline predictors of incident DPN.

Methods: We consecutively enrolled patients (n = 2058) with T2D (21–90 years old), seen our institution's Diabetes Centre and a primary care polyclinic in Singapore (August 2011–March 2014). From 2014, 684 of the participants made a repeat visit 3-year from first visit. The prospective data collection is still on-going. Anthropometric data, fasting blood, urine were collected for biochemistry and urine albumin/creatinine measurements (uACR). Systolic and diastolic blood pressure (SBP and DBP) was taken from participants using an automated blood pressure monitor. Carotid-femoral Pulse wave velocity (PWV) was determined using SphygmoCor equipment and software. Neuropathy was considered present if an abnormal finding in monofilament (<8 of 10 points) or neurothesiometer testing ≥25 volts on at least one foot.

Results: Baseline characteristics of 684 patients are: Age: (57.2 ± 10.4) years, 50.1% males, ethnicity: 53.8% Chinese, 20.9% Malay, 21.5% Indian and 3.8% of others, duration of T2D: (11.1 ± 8.6) years and HbA1c (7.71 ± 1.26) mmol/L. In these 684 patients, 599 had no DPN at baseline. On a 3-year follow-up, 48 (8%) of them developed DPN. Patients with incident DPN (n = 48) versus controls who did not develop DPN (n = 551), were older [(60.4 ± 8.0) vs (56.9 ± 10.6)]years (p = 0.026), had longer duration of diabetes [(14.6 ± 10.2) vs (10.4 ± 8.2)] years (p = 0.007), increased SBP [(148.4 ± 16.5) vs (136.6 ± 17.6)] mmHg (p < 0.0001) and DBP [(81.1 ± 9.1) vs (77.7 ± 9.4)] mmHg (p = 0.017), increased PWV [(10.8 ± 2.5) vs (9.6 ± 2.6)] m/s (p = 0.002), lower eGFR [(75.7 ± 34.8) vs (90.5 ± 29.7)] (p = 0.001), worse uACR [18.0(6.0–63.8) vs 51.0(20.0–334.0)] mg/g (p < 0.0001) at baseline. There were no significant difference for patients, with incident DPN vs those without, in their baseline HbA1c [(7.81 ± 1.35) vs (7.65 ± 1.25)] mmol/L and fasting glucose [(7.88 ± 2.43) vs

(7.89 ± 2.77)] mmol/L. In generalized linear model, baseline uACR (B = 0.412, p = 0.044) and SBP (B = 0.021, p = 0.032) remained significant independent predictors of future risk of DPN, after adjustment for age, gender, ethnicity, eGFR, PWV and duration of diabetes.
Conclusion: In patients with T2D followed up for 3 years, baseline uACR and blood pressure are significant predictors of incident DPN. While our data allows identifying patients at risk of future DPN, further studies are needed to see if improvements in these predictors will result in lower incidence of DPN.

OL07-7
Relationship between blood neutrophil–lymphocyte ratio and chronic kidney disease in overweight and obese adult population
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Background: Obesity-associated inflammation has a potential role in the pathogenesis of chronic kidney disease (CKD). Neutrophil-to-lymphocyte ratio (NLR) is increasingly recognized as a marker of systemic inflammation. We investigated the association between NLR and renal function in an adult population.
Methods: For cross-sectional study, 2965 apparently healthy adults (1824 men and 1141 women) who attended health examination from August 2000 to April 2002 at a medical centre in central Taiwan were included. We collected anthropometric measurements, fasting blood test results, lifestyle habits and medical history. Renal insufficiency (RI) was defined as estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2 calculated by using the CKD-EPI equation. Body mass index (BMI) was calculated by dividing body-weight by the square of height (kg/m^2). Weight status was categorized according to the criteria of the Ministry of Health and Welfare, Taiwan.
Results: There were 485 obese participants (BMI ≧ 27, M:F = 342:143), 942 overweight participants (24 ≦ BMI < 27, M:F = 676:266), and 1538 normal weight or underweight participants (BMI <24, M:F = 806:732). Higher prevalence rates of RI were observed in obese and overweight participants, compared to participants with BMI < 24, in women (14.7% vs. 9.4% vs. 5.7%, p for trend = 0.0001) but not in men (14.4% vs. 14.4% vs. 15.8%, p for trend = 0.602). In overweight and obese participants, multivariable logistic regression analysis revealed that higher NLR (per 1 unit) was independently associated with higher risk of RI in both women [OR = 1.85 (95% C.I.: 1.16–2.97), p = 0.010] and men [OR = 1.41 (95% C.I.: 1.08–1.84), p = 0.013], after adjusting for age, BMI, smoking, alcohol consumption, systolic blood pressure, total cholesterol, triglyceride, HDL-cholesterol, fasting plasma glucose, and serum total bilirubin.
Conclusions: In both men and woman with BMI ≧ 24, higher NLR was associated with higher risk of RI. As NLR is an inexpensive and readily available marker, it may be potentially useful for CKD risk assessment in overweight and obese populations.

OL07-8
The risk factors for asymptomatic pyuria among the patients with type 2 diabetes
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Introduction: Although urinary tract infections are common in diabetic patients, there have been only a few studies that investigated the relationships of pyuria in type 2 diabetic patients with patient background, laboratory data and diabetes complications. We aimed to elucidate the risk factors for asymptomatic pyuria among the patients with type 2 diabetes.
Methods: We retrospectively investigated the patients with type 2 diabetes who visited the Department of Internal Medicine because of diabetes for the first time from December 2010 to November 2012. The study protocol was approved by institutional review board. We excluded the patients who had cystitis or pyelonephritis or who had antibiotics within 1 month. We collected the information about patient characteristics, laboratory data, and diabetes complications. We examined the coefficient of variation of R-R interval (CVR-R) of electrocardiogram for the evaluation of autonomic function. Pyuria was defined as the presence of more than 10 leucocytes/High Power Field in a random urine sample. We used t-test and chi-square test to compare the variables between patients with and without pyuria. Values were expressed as mean ± Standard Deviation.
Result: Among 121 eligible cases, 52 cases were female. Mean age, BMI, and duration of diabetes were 63.2 ± 13.4 years old, 26.0 ± 5.7 kg/m^2, and 5.1 ± 7.5 years, respectively. Forty-eight cases had mental illness. Mean HbA1c, plasma glucose, and CVR-R were 8.5 ± 2.1%, 195 ± 95 mg/dL and 3.0 ± 2.0%, respectively. Pyuria was found in 19 cases (16%). Prevalence of pyuria was significantly higher in female than male (30.8 vs 4.3%). Patients with mental illness had significantly higher prevalence of pyuria than those without mental illness (25.0 vs 9.6%). Patients with pyuria had significantly lower mean CVR-R than those without pyuria (1.8 ± 1.1% vs 3.2 ± 2.0%). In the sub-analysis limited to female, mental illness and lower CVR-R were significantly associated with the presence of pyuria. Age, HbA1c, retinopathy were not associated with pyuria.
Conclusion: In addition to female sex, the presence of mental illness, and low CVR-R values were significantly associated with the asymptomatic pyuria in diabetic patients. We need to carefully manage these patients for the risk of urinary tract infections.

Nutrition, Diabetes Education and Management Systems

OL08-1
Whole grain intakes are associated with better ABC control in patients with type 2 diabetes in Taiwan
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To study the association of whole grain intake with ABC control in patients with type 2 diabetes, a cross-sectional survey by using food frequency questionnaire was conducted 2011 in Taiwan. A total of 677 adults type 2 diabetes were enrolled. Whole grain included brown rice and mixed grains, and participants reported the intake frequency and the amount of whole grains, including brown rice and mixed grains, during the past month on a daily, weekly, and monthly. Whole grain group was defined as intake of one of the brown rice or mixed grains at least once a day and no whole grain group was less than once a day. Only one third of diabetes patients (n = 214) ate at least once a day whole grain (31.6% vs

68.4%). There were no differences in calories, protein, fat, and carbohydrate intake between those two groups. We found that fiber intake (19.6 ± 9.7 vs. 15.5 ± 7.8 g/day, $p < 0.01$), magnesium (341 ± 158 vs. 223 ± 101 mg/day, $p < 0.001$), phosphate (1239 ± 478 vs. 945 ± 379 mg/day, $p = 0.001$), folic acid (149 ± 82 vs. 129 ± 54 mg/day, $p < 0.001$), niacin (19.3 ± 7.8 vs. 12.2 ± 5.1 mg/day, $p < 0.001$), calcium (631 ± 422 vs. 452 ± 298 mg/day, $p < 0.001$) and iron (16.5 ± 7.9 vs. 12.6 ± 6.2 mg/day, $p < 0.01$) intake were significantly higher in the whole grain group, while sodium intake (1054 ± 628 vs.1197 ± 811 mg/day, $p < 0.01$) was significantly lower in the whole grain group. Values of SBP, DBP, total cholesterol, HDL and triglyceride were not different between whole grain and no whole grain groups. Levels of HbA1c (7.5 ± 1.3 vs. 7.6 ± 1.5%, $p = 0.02$) and LDL-cholesterol (96.2 ± 25.2 vs. 101.3 ± 30.3, $p = 0.036$) were also significantly lower in the whole grain group. Percentages of those who attained the ABC goals in the whole grain group were 13.5% compared with 8.5% in the no whole grain group ($p = 0.058$). Furthermore, when vegetables (at least once a day) and fruit (at least once a day) intake were added with whole grain group together, the percentages of those who reached the ABC goals were significantly higher in all intake at least once a day compared with those no intake(15.9% vs. 8.6%, $p = 0.017$). In conclusion, nutrients intake of the whole grain (at least once a day) group and glycemic controls were better than those who did not take any whole grain group, We have to encourage diabetes patients to take whole grain food to increase the nutrients intake and maintain a better diabetes control.

OL08-2

Chinese physician–patient communication at T2D diagnosis and links between patient-perceived communication quality and patient outcomes: Insights from the IntroDia™ study

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Effective communication between physicians and type 2 diabetes (T2D) patients may improve patient self-care and outcomes. IntroDia™ is a global survey investigating physician-patient conversations in early T2D diagnosis and treatment and the potential impact on patient self-care and self-reported outcomes. As part of IntroDia™, 3628 T2D patients from 26 countries were surveyed about conversations with physicians at diagnosis.

A total of 886 T2D patients from China on 1 oral antidiabetes drug completed an on-line survey on conversations with physicians at diagnosis. Parameters examined included the conversation's content (via a 43-item version of PACIC modified for T2D diagnosis), conversation quality (using CAHPS, TIPS and IPC scale items to ascertain patient-perceived communication quality [PPCQ]), current psychosocial status (WHO-5, DDS) and self-care behaviour (SDSCA).

Four statement types were identified by factor analysis on a global level – Collaborative (e.g. "Gave me choices about treatment to think about"), Encouraging (e.g. "Told me that a lot can be done to control my diabetes"), Discouraging (e.g. "Told me that diabetes gets harder…") and Recommending Other Resources (ROR) (e.g. "Referred me to a dietician, health educator, nurse or counselor"). In China, PPCQ was positively associated with Encouraging ($\beta = 0.72$, $p < 0.001$) and Collaborative ($\beta = 0.53$, $p < 0.001$), negatively associated with Discouraging ($\beta = -0.53$, $p < 0.001$) and not significantly associated with ROR ($\beta = -0.11$, $p = 0.157$).

In turn, PPCQ was significantly associated with better self-care behavior (SDSCA – general diet: $\beta = 1.84$, $p < 0.001$; specific diet: $\beta = 1.54$, $p < 0.001$; exercise: $\beta = 1.47$, $p < 0.001$; medication: $\beta = 1.77$, $p < 0.001$), poorer general well-being (WHO-5: $\beta = -0.19$, $p < 0.001$), and not significantly associated with diabetes distress (emotional DDS: $\beta = 0.08$, $p = 0.176$; regimen DDS: $\beta = 0.02$, $p = 0.718$).

Physicians' use of collaborative and encouraging conversation elements at T2D diagnosis may improve physicians' communication with patients, leading to slightly less general wellbeing but overall better patient self-care behaviour. Conversations using discouraging elements, however, may be counterproductive.

OL08-3

Multidimensional effects of a diabetes management program in a Taipei community hospital – a 7-year prospective follow-up study

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Background: Multidisciplinary diabetes management program has often been deemed as the important strategy to improve quality of diabetes care. However, value-added effects of the embodied health education remain unclear. We therefore used a 7-year longitudinal diabetes cohort to demonstrate the effects of usual medical care and the additional benefits to diabetes control after implementing an accredited diabetes management program in a community hospital.

Methods: We used descriptive statistics and trajectory analyses to investigate the changes of diabetes care indicators in two time periods: before and after implementation of the diabetes management program. The investigated diabetes care indicators included fasting blood glucose, HbA1c, blood pressure, triglyceride, total cholesterol, low-density lipoprotein cholesterol (LDL-C), smoking rate and frequency of exercise per week.

Results: Since 2006, the investigated community hospital has implemented a diabetes management program, strengthening dietetic consultation, health education, and case management. The data surveillance center has currently recorded 300 enrollees to this program. Of the enrollees, 52.7% were male, 52.0% had education level ≦6 years, mean age was 61.2 ± 10.4 years at the first visit, and diabetes duration was 8.6 ± 8.0 years upon participating in the program. Compared to one year before participation, the following indicators had been significantly improved one year after recruited in the diabetes management program: diastolic blood pressure (75.5 vs. 74.0 mmHg; $P = 0.001$), fasting blood sugar (148.9 vs. 135.0 mg/dL; $P < 0.001$), HbA1c (8.0 vs. 7.4%; $P < 0.001$), total cholesterol (192.6 vs. 181.4 md/dL; $P < 0.001$), LDL-C (121.2 vs. 113.4 mg/dL; $P = 0.007$), triglyceride (181.2 vs. 152.3 mg/dL; $P = 0.011$), male smoking rate (30.1 vs. 25.8%; $P = 0.032$), and regular exercise (3.7 vs. 4.1 times per week; $P < 0.001$). Inspecting the 7-year trajectory pattern, we found systolic and diastolic blood pressure, total cholesterol, and LDL-C had continuously been reduced since the patients received usual medical care; however, glycemic control, triglyceride level, male smoking rate, and frequency of exercise have not been improved until the diabetes patients were recruited in the diabetes management program.

Conclusion: Our results indicate the healthy behaviors modification, an essential component in diabetes management, can be effectively strengthened by multidisciplinary care in the accredited diabetes management program. Without health education and dietetic consultation, the usual medical care provided by physicians alone is hard to optimize diabetes care, especially in bettering glycemic control, normalizing triglyceride level and changing healthy lifestyle.

OL08-5

Intervention outcomes from a randomised controlled trial of diabetes prevention: Mothers after Gestational Diabetes in Australia Diabetes Prevention Program (MAGDA-DPP)

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Incidence of gestational diabetes mellitus (GDM) and type 2 diabetes (T2DM) is increasing worldwide posing an immense burden to healthcare systems. Women with GDM diagnosis have a life-time risk exceeding 70% of developing T2DM. The Mothers after Gestational Diabetes in Australia (MAGDA) study was a randomised controlled trial aiming to assess the effectiveness of a group-based lifestyle modification program for women with GDM diagnosis in their first postnatal year. A total of 573 women were randomised to either the intervention group (n = 284) receiving a structured diabetes prevention program or the control group (n = 289) receiving usual care. The diabetes prevention intervention comprised of 1 individual and 5 group face-to-face sessions delivered by trained healthcare professionals followed by 2 additional follow-up telephone calls.

The primary outcome was changes in diabetes risk determined by weight, waist and fasting plasma glucose (FPG). The secondary outcomes included changes in behavioural goals, depression score, and cardiovascular disease risk factors. These outcomes were assessed at baseline and 12 months for all participating women and additionally at 3 months for the intervention participants only. At baseline, 28% and 38% of participants were overweight or obese respectively, while only 10% participants had impaired glucose tolerance (IGT) and 2% impaired fasting glucose (IFG). Results of intention to treat (ITT) analysis show, at 12 months, the intervention groups' average weight loss was 0.23 kg (95% CI −0.89, 0.43) compared with weight gain of 0.72 kg (95% CI 0.09, 1.35) in the usual care control group. The change difference between groups over 12 months was statistically significant, with 0.95 kg weight loss in the intervention group (95% CI −1.87, −0.14, group by treatment intervention $p = 0.04$). At three months, the intervention group had lost 0.92 kg ($p = 0.001$) compared to the baseline levels. Other significant outcomes at three months were reduction in waist circumference, total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) (all $p < 0.001$) in the intervention group. Reduction in waist circumference, total cholesterol and LDL-C were maintained at 12 months, but not the reduction in weight and HDL-C. The MAGDA-DPP study demonstrates a modest effect of the intervention in women with prior GDM diagnosis. Although 1kg weight difference is likely to be significant for reducing diabetes risk, the engagement effort required during the first postnatal year is not sustainable in routine health services. It is recommended to implement annual diabetes screening until post-GDM women develop IGT or IFG, before offering an intervention.

OL08-6

Program engagement in a randomised controlled trial for diabetes prevention: Mothers after Gestational Diabetes in Australia Diabetes Prevention Program (MAGDA-DPP)

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Women with gestational diabetes (GDM) are at sevenfold increased risk of developing type 2 diabetes compared with women without GDM. The Mothers after Gestational Diabetes in Australia (MAGDA) study was a multicentre randomized controlled trial assessing the effectiveness of a structured diabetes prevention program (DPP) for women with previous GDM in their first postnatal year.

The MAGDA-DPP intervention comprised 1 individual and 5 group sessions delivered by trained healthcare professionals, with 2 follow-up telephone calls. Women aged over 18 years diagnosed with GDM in their most recent pregnancy were recruited using multiple strategies: (i) an antenatal clinic appointment approach (4 metropolitan hospitals); (ii) a postnatal private obstetrician invitation letter; and (iii) a postnatal invitation letter through the National Gestational Diabetes Register (NGDR) to selected postcodes.

NGDR-recruited participants were older ($p < 0.001$) and the babies of women recruited antenatally were younger than the other recruitment methods ($p < 0.001$). On average, recruiters spent 22 minutes per woman assessing interest and eligibility. ANOVA results showed no difference in recruitment efforts (number of contacts, time and staff cost) across different recruitment strategies. Recruitment success rates did differ; with the NGDR being the most successful strategy (149/191, 74%), followed by postnatal invitation (36/77, 47%) and antenatal approach (402/1972, 20%) ($p < 0.001$). Among women randomized to the intervention (n = 284), 66% (n = 188) completed ≥1 session. More specifically, 13% had only an individual session (IS) (n = 37), 53% completed the individual session plus ≥1 group session(s) (GS) (program minimum standard, n = 149), with only 10% completing all 6 sessions (n = 28). 34% of women randomised had no exposure (n = 96), despite an average of 4 contact attempts made by facilitators. On average, group facilitators spent 18 minutes per intervention participant arranging and reminding women about intervention sessions. Of those participants achieving the program minimum standard, the average attendance was 3 sessions, with facilitators averaging 20 minutes with 10 contacts to achieve this. ANOVA tests showed no difference in retention efforts between intervention participants recruited by different strategies. Program attendance by women recruited through antenatal approach, however, was significantly lower than other recruitment methods [IS only ($p = 0.04$), IS plus ≥1 GS ($p = 0.01$), and IS plus ≥3 GS ($p < 0.001$)].

Engaging women in a postnatal DPP is very challenging and resource intensive. Despite substantive engagement effort, the MAGDA-DPP experienced a low overall participation rate. The improved recruitment and retention of older women, however, suggests an intervention timed for post-GDM women with older children may be more appropriate.

OL08-7

Clinical application of a self-reported diabetic-behavior assessment computerized program in management of patients with type 2 diabetes mellitus

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Objective: Diabetes self-management education/support (DSME/S) is obligatory in long-term management of diabetes because of a complex health intervention, is generally effective at enhancing self-care behaviors. This study aimed to evaluate the effectiveness of a self-reported diabetes-related behavior dashboard computer program on clinical management of patients with diabetes mellitus.
Materials and methods: A Chinese version of computerized assessment system was constructed to evaluate diabetes self-management behaviors, including health eating, taking medication, exercise, blood glucose self-monitoring behaviors. Furthermore, to assess the psychological stress, a short-form Chinese version of PAID and WHO 5 well-being index questionnaire were also build into the system. There were 3,404 patients with type 2 diabetes mellitus (T2DM) received the behavior dashboard evaluation at baseline and re-evaluated again 12-months later.
Results: The computer program content validity index was calculated by experts' ratings of item relevance. The CVI was 0.866~1.0. The inter-rater reliability, involved the process of inter-rater reliability assessment to test the rating consistency among observational ratings was 0.816–0.965 ($p < 0.001$). The test-retest reliability of intra-class correlation coefficient was 0.752 ($p < 0.001$). The baseline and 12-month HbA1c, BMI, LDL cholesterol, and e-GFR levels correlated well with the correspondent behavior scores of eating, medication, exercise, self-blood glucose monitoring, the PAID and WHO-5 scores, and the total scores. The difference in baseline and 12-month HbA1C level was significantly associated with the difference of baseline and 12-month total score and a model predicting the 12-month HbA1C level was also constructed.
Conclusion: Diabetes behavior assessment program could be a precise, convenient computer-based system to evaluate the diabetes related behavior that associated with glycemic control in patients with T2DM.

OL08-8

Fidelity: The missing dimension in structured diabetes education around the globe

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Background: Client centred structured education programs with focus on the quality development of facilitators are a proven method to enable supported self-care in diabetes.
Group programs for type 2 diabetes are conducted worldwide. However, few can be delivered with sufficient fidelity to ensure client outcomes.
DESMOND is the collaborative name for a family of group self-management education modules, toolkits and care pathways for people with, or at risk of, type 2 diabetes. It breaks the mould of the traditional train the trainer model with its focus on measuring the quality of the facilitator of the program. In doing so facilitators strongly orientated in a medical model are moved along a pathway and provides them with the tools to empower their patients. The DESMOND collaborative has crossed international borders and is delivered in the UK, Ireland, Qatar, Australia and New Zealand.
Aim: Based on solid evidence, quality diabetes structured education provides a blueprint to maximise time spent problem solving self-care behaviours among peers and ensuring the development of personalised action plans under the guidance of skilled facilitators.
Method: There are agreed criteria on what constitutes quality structured group education:

– An underpinning philosophy
– Evidence-based theories linked with outcomes
– Using a structured curriculum
– Delivered by trained educators
– Quality assured, with an ongoing audit

DESMOND UK has worked with international partners to adapt the program to enable translation into other countries.
Results: DESMOND across the globe is building the diabetes workforce beyond its traditional medical model by delivering a consistent dose of quality education.
Aware of national health targets and messaging, the DESMOND program has been adapted to reflect these differences, whilst maintaining the core elements of the program. Cultural adaptions and modifications have been taking place ahead of rolling out DESMOND in Qatar and in the Australian Aboriginal and Torres Strait Islander Communities. The changes include translating the participant resources into Arabic as well as making the resources culturally acceptable.
The South Island of New Zealand has trained DESMOND educators and the program is firmly embedded in their diabetes care pathways.
Discussion: DESMOND has demonstrated how international collaboration can share best practice between countries to improve health outcomes. It is possible to transcend cultural and geographical barriers with an evidence-based structured education program. The training and quality development pathway for facilitators has maintained the fidelity of the program and ensured that the same "dose of DESMOND" is given across the globe.

Novel Treatment for Diabetes and Diabetic Complications

OL09-2

GLP-1 action attenuates breast cancer growth and progression

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Incretin therapy has emerged as one of the most popular treatment for type 2 diabetes. GLP-1R agonist, Exendin-4(Ex-4), has received much attention, because of its tissue protective effects beyond glycemic control, such as weight reduction and vascular protection. We have previously reported vascular protective effects (Diabetes 2010, BBRC 2011) and anti-prostate cancer effect (Diabetes 2014, PLOS ONE 2015) of Ex-4. On the other hand, breast cancer is one of the most popular cancers in female with patients with type 2 diabetes and obesity. Then, we next examined whether GLP-1 action could attenuate breast cancer in the present study.

First, we observed abundant GLP-1R expression in early stage breast cancer (Stage I) tissue extracted from patients without diabetes, but not advanced breast cancer (Stage IIb). In human breast cancer cell lines, MCF-7, MDA-MB-231 and KPL-1 cell, GLP-1R was expressed abundantly. 0.1~10 nM Ex-4 treatment significantly decreased cell number of breast cancer cells in growth curve, in dose-dependent manner. Although Ex-4 did not induce apoptosis in breast cancer cells, BrdU assay revealed that Ex-4 attenuates cell proliferation of breast cancer cells in dose dependent manner. If we transplanted MCF-7 cells into non-diabetic nude mice subcutaneously and treated them with 300 pM/kg/day Ex-4 for 6 weeks, we observed decreased tumor size of MCF-7 in Ex-4-treated mice, in both male and female mice with no change in body weight and blood glucose level. Immunohistochemistry with Ki67, a marker of cell proliferation, revealed that breast cancer cell proliferation was significantly decreased in tumor extracted from mice treated with Ex-4. Further, 60% high fat diet significantly increased breast cancer size and weight in nude mice. Further, Ex-4 treatments decreased tumor size and weight in high fat fed mice similar to that of control diet level.

These data suggest that GLP-1 action could attenuate breast cancer via inhibition of breast cancer cell proliferation.

OL09-3

Activation of heat shock response improves glucose metabolism and inflammation in obese subjects with type 2 diabetes

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Decreased heat shock response (HSR) is reported to be associated with insulin resistance in type 2 diabetes. Activation of HSR improves accumulated visceral adiposity and metabolic abnormalities in type 2 diabetes. This study was designed to identify the optimal intervention strategy of the activation of HSR provided by mild electrical stimulation with heat shock (MES + HS) in obese type 2 diabetes patients. We have previously reported that MES + HS improved HbA1c by −0.43% in male subjects with obese type 2 diabetes.

This study was a prospective, frequency-escalating, randomized, open-label, triple-arm trial. A total of 60 obese type 2 diabetes patients were randomized into three groups of two, four, or seven times treatments per week for 12 weeks.

No adverse events were identified. In comparison to the baseline, MES + HS treatment over time significantly improved visceral adiposity (−11.69 cm^2. $p < 0.001$), glycemic control (HbA1c: −0.36%: from 7.64% to 7.28%. $p < 0.001$), insulin resistance (HOMA-IR: −1.09. $p < 0.001$), systemic inflammation (TNF-α: −0.40 pg/mL. $p < 0.001$. CRP: −663.6 ng/mL. $p = 0.008$), renal function (eGFR: +2.96 mL/min/1.73 m^2. $p < 0.001$), hepatic steatosis (AST/ALT: +0.06. $p = 0.007$) and lipid profiles (triglyceride: −30.02 mg/dL. $p = 0.015$). The clinical target of HbA1c less than 7.0% was achieved by 38.3% (n = 23) of participants after MES + HS treatment. The reduction in HbA1c was significantly greater in 4 per week (−0.36%. $p = 0.036$) or 7 per week (−0.65%. $p = 0.001$) than that in 2 per week (−0.10%) of treatment. The decrease in the visceral fat area showed similar trend of changes (−5.37, −14.24, −16.45 cm^2 by two, four, seven per week, respectively), indicating that the beneficial effects depend on its frequency. More pronounced effects were observed in males (HbA1c: −0.44%. from 7.70% to 7.25%. $p < 0.001$) than those in females (HbA1c: −0.17%. from 7.50% to 7.33%. $p = 0.140$).

This research provides additional lines of evidence to support the positive impacts of MES + HS in improving metabolic outcomes in obese type 2 diabetes patients. Those who do not reach the glycemic control goal of HbA1c less than 7.0% could be offered additional personalized medical care including MES + HS treatment.

OL09-7

Dipeptidyl peptidase-4 inhibitor prevents diabetic nephropathy through STRA6 signaling

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We recently found that O-GlcNAcosylation of RBP4 receptor (STRA6) with a decrease of RBP4 binding activity suppressed CRBP-1 and RARα expression and thereafter activate apoptosis and fibrosis in high-glucose cultured renal cells and in the kidneys of diabetic mice. Dipeptidyl peptidase-4 inhibitors (DPP-4i) was reported to capably ameliorate kidney fibrosis in diabetic mice. We hypothesized that DDP-4i can produce its pleiotropic action to prevent kidney damage beyond glycemic control.

STRA6, CRBP1, RARα, caspase 3, collagen 1 and fibronectin was measured by Western blot analysis for protein and PCR for mRNA expression in the kidney in normal fat diet(NFD)-fed, high fat diet(HFD)-fed mice and sitaglitipin-treated HFD-fed mice. We aimed to investigate whether the reciprocal appearance of STRA6 cascade down-regulation and fibrosis increase in the kidney of HFD-fed mice, and whether DPP4i reverses these alterations beyond glycemic control.

The expression of STRA6, CRBP1 and RARα protein and mRNA expression remarkably decreased, while caspase 3, collagen 1, and fibronectin significantly increased in kidney of HFD-fed mice as compared with NFD-fed mice. All these changes in the aorta of HFD-fed mice were reversed in sitaglitipin-treated HFD-fed mice. The blood glucose values in HFD-fed mice and sitaglitipin-treated HFD-fed mice are not different, but are higher than NFD-fed mice.

We conclude that DDP-4 inhibitor can produce its beneficial action to prevent HFD-induced fibrosis and apoptosis in kidney of HFD-treated mice by reversing the suppression of RBP 4 receptor/CRBP-1/RARα signaling beyond its glycemic control.

OL09-8

Trans-S-1-propenyl-l-cysteine sulfoxide from *Allium cepa* (onions) has appreciable antidiabetic potential in streptozotocin-induced diabetic mice

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Previous researches have shown that *Allium cepa* (onions) possess appreciable antidiabetic effects in both animals and human beings. Among the active compounds in A. cepa, Alk (en) yl cysteine sulfoxides (ACSO) are believed to play a major role in the onion's pharmacological properties. Since trans-S-1-propenyl-l-cysteine sulfoxide (PeCSO), is the major ACSO in onions, our study was aimed at evaluating antidiabetic potential of PeCSO in streptozotocin (STZ) induced diabetic mice. To isolate PeCSO, onion bulbs were macerated and subjected to a series of chromatographic techniques to obtain PeCSO with a yield of 1.65 mg/g fresh weight and purity of 98%. Type 1 diabetic mice was induced by a single high dose STZ i.p injection while type 2 diabetes was induced by a combination of high fat diet (HFD) and single low dose STZ.

Oral administration of purified PeCSO in type 1 diabetic mice for 4 weeks reduced blood glucose to an average of 189 mg/dL. In contrast, diabetic control mice that received saline had their blood glucose exacerbate to 553 mg/dL, suggesting that PeCSO was either suppressing the effects of, or ameliorating the damage caused by STZ. Oral administration of the onion extract in type 2 diabetic mice tended to decrease the elevated blood glucose levels and to improve insulin sensitivity. To determine the possible mode of action, we evaluated in vitro antioxidant effect of PeCSO by monitoring its 2,2-diphenyl-1-picrylhydrazyl (DPPH) and H2O2 scavenging abilities. At high concentration of 50 mg/mL, PeCSO appeared to be an excellent scavenger of DPPH radical when dissolved in DMSO, with a DPPH radical formation inhibition ability of 91%, much higher than that of N-Acetyl cysteine (NAC), a potent antioxidant, which was 51%. The result suggest that one possible mode of action of the observed antidiabetic effect is by scavenging reactive oxygen species in the body. However, PeCSO did not show any significant H2O2 scavenging ability. From bioavailability assay, the highest concentration of PeCSO in blood was observed 1 hour post oral administration and was also detectable 2 and 3 hours after administration. Although more studies are needed, our results suggest that PeCSO possess appreciable antidiabetic potential, probably by acting as an antioxidant and thus promoting insulin sensitivity.

Novel Biomarkers for Diabetes

OL10-2
Pre-beta HDL in type 2 diabetes mellitus

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Introduction: Cellular cholesterol efflux is the first step of reverse cholesterol transport and the efficiency of this process is determined partly by the concentration of extracellular cholesterol acceptors like HDL. Pre-beta HDL mainly composes of apolipoprotein (apo) AI and phospholipids, and serves as the preferred acceptor of cellular cholesterol efflux mediated by the ATP-binding cassette transporter A1 (ABCA1). We have evaluated whether there are changes in pre-beta HDL concentration in type 2 diabetic patients independent of the levels of HDL cholesterol (HDL-C) and the effect on cholesterol efflux.
Methods: 500 type 2 diabetic patients and 360 non diabetic controls matched for age, gender and serum HDL-C levels were recruited. Subjects on lipid lowering agents were excluded. Plasma pre-beta HDL was measured by ELISA. In a random subgroup of subjects (115 diabetic patients and 70 control subjects), cholesterol efflux to serum mediated by ABCA1 was determined by measuring the transfer of [3H]cholesterol from Fu5AH cells expressing ABCA1 (induced by 22(R)-hydroxycholesterol and 9-cis-retinoic acid) to the medium containing the tested serum.
Results: There were no significant differences in the age and in the proportions of male/female subjects between the 2 groups. Despite the diabetic subjects having similar HDL-C levels (1.25 ± 0.35 mmol/L) and apo AI (1.32 ± 0.23 g/L) as controls (HDL-C: 1.25 ± 0.27 mmol/L, apo AI: 1.35 ± 0.22 g/L), serum pre-beta HDL was significantly lower in the diabetic patients [190.4 (123.0–260.5) ug/mL vs 201.6 (135.7–293.6) respectively, median (interquartile range), $p < 0.01$]. Cholesterol efflux to serum mediated by ABCA1 was reduced in diabetic patients compared to control (1.40 ± 0.40% vs 1.72 ± 0.45 respectively, $p < 0.05$). In the diabetic patients, cholesterol efflux mediated by ABCA1 correlated with log (pre-beta HDL) ($r = 0.30$, $p < 0.05$) but not with HDL-C.
Conclusion: Low HDL-C level is common in patients with type 2 diabetes. However, even when type 2 diabetic patients were compared with a group of non-diabetic control subjects with similar HDL-C levels in our study, plasma pre-beta HDL level was significantly decreased in diabetic subjects and was associated with a reduction in cholesterol efflux to serum mediated by ABCA1 ex vivo. Our data therefore suggest that low pre-beta HDL level in type 2 diabetes might cause impairment in reverse cholesterol transport.

OL10-3
The association among cardiotrophin-1, insulin resistance and nonalcoholic fatty liver disease

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Nonalcololic fatty liver disease (NAFLD) is the most common cause of chronic liver disease worldwide. The disease is characterized by a wide spectrum of histological abnormalities ranging from simple hepatic steatosis, to nonalcoholic steatohepatitis, to liver fibrosis, and to cirrhosis. Although the precise mechanism of NAFLD remains incompletely understood, the most accepted pathophysiologic model for NAFLD is the "two-hit hypothesis".
Cardiotrophin-1 is one member of the interleukin-6 family cytokines. In the liver, previous studies demonstrated the hepato-protective effects of cardiotrophin-1 in different models of acute liver injury. Moreover, cardiotrophin-1 was found to be upregulated in human and murine steatotic livers, and chronic administration of recombinant cardiotrophin-1 eliminated hepatic steatosis in obese mice.
Recently, one animal study suggested that cardiotrophin-1 may be a promising therapy for insulin resistance and linked metabolic disorders. Although cardiotrophin-1 protects liver against acute injury, it is unclear whether cardiotrophin-1 is involved in the pathogenesis of NAFLD. Therefore, the aim of this study is to clarify the association between cardiotrophin-1 and NAFLD.
We recruited 287 subjects with (n = 148) or without (n = 139) NAFLD. All subjects received a health checkup and completed a structured questionnaire, and those who did not have a medical history of diabetes received a standard 75-g oral glucose tolerance test. Subjects with the following conditions or diseases were excluded: (1) alcohol consumption ≧20 g/day in the last year; (2) a positive test for hepatitis B surface antigen or hepatitis C antibody or other causes of liver disease; (3) serum creatinine >1.5 mg/dL; (4) any acute or chronic inflammatory disease as determined by a leukocyte count >10000/mm^3 or clinical sighs of infections; (5) any other major including generalized inflammation or advanced malignant disease.
Individuals with NAFLD had significant higher body mass index (BMI), systolic and diastolic blood pressure, fasting plasma glucose, homeostatic model assessment-insulin resistance (HOMA-IR) index, triglyceride, and high density lipoprotein (HDL) levels than those without it. Furthermore, subjects with NAFLD had significant higher cardiotrophin-1 concentrations than those without it. The results of multivariate linear regression analysis showed that NAFLD was positively associated with cardiotrophiin-1 after adjusting for age, gender, BMI, HOMA-IR, systolic blood pressure (SBP), creatinine, triglyceride, HDL, hsCRP, smoking, and habitual exercise.
Subjects with NAFLD had significant higher cardiotrophin-1 concentrations than those without it. Furthermore, NAFLD an independent predictor of cardiotrophin-1 levels after adjusting for age, gender, BMI, HOMA-IR, SBP, creatinine, triglyceride, HDL, hsCRP, smoking, and habitual exercise. Cardiotrophin-1 may be a surrogate biomarker of NAFLD.

OL10-5

The role of irisin in components of metabolic syndrome, insulin secretion and resistance in schoolchildren

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Background: The prevalence of obesity worldwide has increased rapidly in recent decades, leading to increased morbidities and mortalities. Different from white adipose tissue, brown and beige adipose tissues contain abundant mitochondria, and help burn energy and create non-shivering thermogenesis. Enriching brown and beige adipose tissue may have potential as an anti-obesity strategy. Irisin, shaved from fibronectin type III domain containing 5 (FNDC5) in muscle tissue, increases after exercise and is believed to be the crucial factor in converting white adipose tissue to beige adipose tissue. In the present study, we explored the relationship between irisin levels and components of metabolic syndrome, fibrinolytic proteins, insulin secretion and resistance in schoolchildren in Taiwan.
Methods: There were 369 children (172 boys and 197 girls), aged 10.3 ± 1.5 years, enrolled from Taiwan elementary schools in our study. Irisin, anthropometry, metabolic syndrome components, insulin secretion, and resistance were measured. Subjects were divided into normal, overweight, and obese groups for evaluation of irisin in obesity. Finally, the relationship between irisin level and metabolic syndrome in boys and girls was analyzed.
Results: In boys, irisin levels were not associated with BMI percentile, body fat, blood pressure, lipid profiles, insulin secretion or resistance. The irisin levels in boys were associated, however, with age and fasting plasma glucose. After adjusting for age, the irisin level in boys was negatively related to fasting plasma glucose ($r = -0.21$, $p = 0.006$) and weakly positively related to soluble plasma activator receptors ($r = 0.135$, $p = 0.046$). In girls, the irisin levels were associated with age and body fat. However, after adjusting of age, the irisin levels in girls were only positively related to fasting plasma glucose ($r = 1.49$, $p = 0.038$). In both genders, irisin levels were similar among normal, overweight, and obese groups, and between subjects with and without metabolic syndrome.
Conclusion: The irisin levels were not associated with metabolic syndrome and obesity in either boys or girls in Taiwan. However, we found that the irisin levels were negatively related to fasting plasma glucose in boys and positively related to fasting plasma glucose in girls. The contrary relationship between irisin and fasting plasma glucose in boys and girls needs further exploration in the future.

OL10-6

Association between 1,5-anhydroglucitol and early-phase insulin secretion in Chinese patients with newly diagnosed type 2 diabetes mellitus

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Objective: Glucose monitoring plays a key role in comprehensive management of diabetes. Insulin secretion deficiency and insulin resistance are involved in both the onset and progression of diabetes mellitus. The goal of this study was to probe into the relationships of glycated hemoglobin A1c (HbA1c) and 1,5-anhydroglucitol (1,5-AG) with insulin sensitivity and secretion in patients who were newly diagnosed with type 2 diabetes mellitus.
Methods: A total of 302 patients with newly diagnosed type 2 diabetes mellitus (166 men and 136 women; age range, 27–79 years old) were enrolled in this study. The homeostasis model assessment of insulin resistance (HOMA-IR) and homeostasis model assessment of β cell function (HOMA-β) were calculated to evaluate the basal insulin sensitivity and secretory function, respectively. Insulinogenic index (IGI) was used for assessment of early-phase insulin secretion. HbA1c was detected by high-performance liquid chromatography. Serum 1,5-AG was assayed using the enzymatic method.
Results: When the subjects were stratified according to HbA1c quartiles, the trends analyses showed an upward trend for HOMA-IR and downward trends for both HOMA-β and IGI with increasing HbA1c quartiles (all P for trend <0.001). Increased 1,5-AG quartiles were accompanied by a decreasing trend in HOMA-IR and increasing trends in HOMA-β and IGI (all P for trend <0.001). Multiple stepwise regression analysis revealed that the independent correlations of HOMA-IR (standardized $\beta = 0.525$) and HOMA-β (standardized $\beta = -0.673$) with HbA1c were present (both $P < 0.001$) when HbA1c was defined as the dependent variable. Moreover, 1,5-AG was not only independently associated with HOMA-IR and HOMA-β (standardized $\beta = -0.349$ and 0.232, both $P < 0.01$), but also exhibited an independent and positive association with IGI (standardized $\beta = 0.242$, $P < 0.001$).
Conclusions: 1,5-AG level was not only correlated with basal insulin sensitivity and secretion, but also closely associated with early-phase insulin secretion in Chinese patients with newly diagnosed type 2 diabetes mellitus.

OL10-7

Increases in urinary N-acetyl-β-D-glucosaminidase excretion are associated with increased arterial thickness and presence of carotid plaques in type 2 diabetes

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N-acetyl-β-D-glucosaminidase (NAG) present in high concentration in lysosomes of proximal renal tubular cells is released into the urine after renal proximal tubule injury. Recently, urinary NAG has gained considerable attention because of its clinical implications as a sensitive and specific biomarker for early stage diabetic kidney disease. Several studies on associations between urinary NAG and micro-/macrovascular complications of diabetes have been reported. However, there is no data on association between urinary NAG and carotid intima media thickness (IMT) in patients with type 2 diabetes mellitus (T2D). The aim of this study was to investigate whether increases in urinary NAG are associated with arterial atherosclerosis assessed by carotid IMT. In this retrospective cross-sectional study, a total of 343 participants with T2D who had been tested for urinary NAG, carotid IMT, and gluco-metabolic parameters were enrolled. Demographic factors including age, sex, body mass index, smoking habit, blood pressure, duration of diabetes, and history of cardiovascular events were recorded. Mean age and duration of diabetes were 59.9 and 11.6 years, respectively. The participants with above median level of urinary NAG (11.4 (8.72–16.7) U/gCr) showed significantly higher values of mean and maximum carotid IMT (0.72 (0.60–0.84) vs 0.67 (0.58–0.77) mm and 0.90 (0.74–1.06) vs 0.82 (0.70–0.97) mm, respectively) than

participants with median level of urinary NAG and below (4.89 (3.70–6.21) U/gCr). In participants with carotid plaques, the levels of urinary NAG were significantly higher than those without plaques (7.53 (5.24–12.0) vs 6.35 (4.40–8.35) U/gCr). In the multiple regression analysis, age (STD $\beta = 0.22$), hypertension (STD $\beta = 0.13$), and above median level (7.21 U/gCr) of urinary NAG (STD $\beta = 0.13$) predicted higher values of maximum carotid IMT. Odds ratio for presence of carotid plaques after adjustment for age, hypertension, albuminuria, serum cholesterol, and estimated glomerular filtration rate was 1.86 (95% CI, 1.02–3.38) for increase in urinary NAG. In conclusion, urinary NAG was independently associated with carotid atherosclerosis in patients with T2D.

OL10-8

Validation of a novel biomarker panel, DNlite, for management of renal complication in type 1 diabetes

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Background: In the previous studies, we have developed a novel biomarker panel, DNlite, for detecting kidney disease in patients with type 2 diabetic mellitus (T2DM). We also establish a novel scoring system, diabetic nephropathy score (DN_Score). DN_Score is a composite score built from fitting several urinary biomarkers, including alpha2-HS-glycoprotein precursor (AHSG), alpha-1-antitrypsin (A1AT) and acid-1-glycoprotein (AGP) in DNlite, to a statistical model that correlates highly with the stage of kidney disease in T2M. However, the development of diabetic nephropathy (DN) of T2DM is not as straightforward as it is in type 1 diabetic mellitus (T1DM) where there is a clear progression from normal renal function to hyperfiltration after about 5 years. In order to strengthen the application of DNlite, we conduct a large scale validation of DNlite in patients with T1DM.

Material and methods: 447 patients with T1DM were enrolled and tested with DNlite. There were 206 male and 241 female participants. The mean age was 21.15 ± 9.5 years. Related clinical parameters were well recorded. To access the severity and risk of kidney disease, patients were further categorized by GFR and albuminuria (KDIGO 2012 Clinical Practice Guideline).

Results: The difference between patients with normo- and clinical albuminuria was very significant ($p < 0.0001$), and diagnostic accuracy using AUROC is up to 0.92. The DN_Score and stage in KDIGO is highly correlated. The difference of DN_Score between the low risk (1 if CKD) and the high risk (1–4+) is very significant ($p < 0.0001$). We also evaluated the correlation of DN_Score with metabolic variables. DN_Score was highly correlated with BMI, blood pressure, fasting plasma glucose, HbA1c and plasma triglyceride level.

Conclusion: DN_Score is correlated significantly with the traditional indicators of DN in all stages of the disease in Type 1 DM. The application of DNlite in T1DM for detecting of DN has been demonstrated in this study. Furthermore, the application of DNlite for managing the DN prognosis in T1DM is under investigation.

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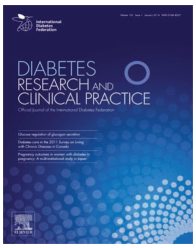

Poster Presentations

Early Screening and Intervention of Prediabetes and Diabetes

PA-01

The impact of age on fasting plasma glucose-based screening algorithms for gestational diabetes mellitus

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Objective: Screening methods based on fasting plasma glucose (FPG) have been proposed to reduce oral glucose tolerance tests (OGTT) in the diagnosis of gestational diabetes mellitus (GDM) by the IADPSG criteria. Since these methods are developed in countries where women get pregnant at younger ages, they may not be applicable in countries where women get pregnant at older ages. In this study, we investigated the impact of maternal age on diagnosis of GDM.
Research design and methods: In 2011, 948 pregnant women who received a 75 g OGTT to diagnose GDM at National Taiwan University Hospital were included. FPG-based screening algorithms considering age or not were developed. Another 375 pregnant women were recruited in 2013–2015 as a validation cohort for the algorithms.
Results: Using FPG criteria only, more GDM were missed in women ≥35 years old than in women <35 years old (13.3% vs. 5.8%, $p < 0.001$). Among GDM women ≥35 years old, 62.5% had normal FPG. The sensitivity, specificity, and the percentage of women who received OGTT (OGTT%) of the FPG-based screening algorithm were 92.1%, 100%, and 77.6%, respectively. Another algorithm was developed with age-specific cutoffs for FPG, which reduced OGTT% to 59.2%, with good sensitivity (91.3%) and specificity (100%). Similar reduction in OGTT% was found in the validation cohort (87.0% to 70.1%). In the simulation, if the percentage of women ≥35 years old were between 30% and 70%, algorithms considering age can reduce OGTT% by 15.4–19.9%.
Conclusions: Algorithms considering age can reduce the need of OGTT in the diagnosis of GDM.

PA-02

Improvement on risk factors of metabolic syndrome by community activities in small to medium hospital-study from local hospital in Kaohsiung

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Objective: Metabolic syndrome is a cluster of conditions included high blood pressure, high fasting blood sugar, abnormal cholesterol and obesity. The more risk factors in metabolic syndrome, the higher morbidity occurred in cardiovascular diseases and diabetes mellitus. In 2014, the major diseases among the top ten leading causes of death were chronic diseases such as heart diseases, diabetes mellitus and cerebrovascular diseases in Taiwan. The prevalence of metabolic syndrome in population of age over 20-year-old is 19.7%. This study aimed to connect the small to medium hospital with diversified community activities to improve life patterns and decrease metabolic syndrome.
Methods: We recruited participants with metabolic syndrome from the medical examination center, screen activities, inpatients and outpatients. The participants were randomized to experiment group and control group. Community activities were provided for experiment group. The biochemistry test and satisfaction of the community activities were collected after the intervention.
Results: The analysis was done using SPSS 12.0 statistical package. The satisfaction of the community activities was 92.7%. In the experiment group, the systolic blood pressure (decreased 21.61 ± 17.81 mmHg), the fasting blood sugar (decreased 21.49 ± 32.26 mg/dL) and triglyceride (decreased 87.33 ± 194.58 mg/dL) showed significantly improvement. The waistline of female participants decreased 4.11 ± 3.59 cm and 6.08 ± 3.90 cm in male participants. In control group, systolic blood pressure (decreased 5.87 ± 21.2 mmHg), triglyceride (decreased 36.94 ± 122.98 mg/dL) and high-density lipoprotein (increased 3.59 ± 6.12 mg/dL) showed the significance. There are significantly improved in systolic blood pressure, triglyceride and the waistline of both male and female participants between experiment and control group.
Conclusions: After the diversified community activities in experiment group, the risk factors of metabolic syndrome such as blood pressure, fasting blood sugar, triglyceride and waistline improved significantly. It is effective for the small to medium hospital to connect with the diversified community activities to improve the risk factors of metabolic syndrome.

PA-03

Effects of exercise program on normal responsiveness of serum GDF15 in middle-aged women

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Background: Protective effects of exercise on the chronic inflammatory disease such as metabolic disease and cardiovascular disease is emerging as one of very important field of medical research. Growth differentiation factor 15 (GDF15) is well-known as stress-induced cytokine association with metabolic disease. GDF15 play a role in body weight by higher

regulation of glucose and fatty oxidative metabolism in animal models. The effects of GDF15 on metabolism have similarities with the muscle fiber-derived or cytokines or peptides called as "mytokine". However, the study whether exercise have effects on the plasma level of GDF15 has not been reported. Therefore, we examined the change of GDF15 level with metabolic parameters, including glucose and various kinds of cholesterol after regular exercise.

Methods: We enrolled the 20 subjects to be able to do aerobic and strength exercise at least 3 times a week during 12 weeks. All subjects had baseline records, including age, body mass index (BMI), waist to hip ratio, body fat percentage. Blood samples were collected the fasting, 2 and 4 hour after taking the high calorie mixed meal at the starting and ending time of study.

Results: Two people excluded the study because of anemia and laboratory errors. Total 18 subjects were enrolled and women with average age of 37 ± 10 years. 4 subjects were glucose intolerance (22.2%). 7 subjects had dyslipidemia (38.9%). Body weight, BMI, waist to hip ratio, and body fat percentage had no difference. Metabolic parameters in fasting state, including glucose, insulin, cholesterol, HOMA-IR, and HOMA-β had no difference. We investigated the differentials between fasting and 2 hr postprandial glucose level (2 hr postprandial glucose – fasting glucose, ΔGlu 2-0) and between fasting and 2 hr postprandial GDF15 level (2 hr postprandial GDF15 – fasting GDF15, ΔGDF 2-0) in subgroup according to glucose intolerance. ΔGlu 2-0 showed significantly higher variation in Subjects with glucose intolerance than in subjects with normal glucose tolerance at time before exercises. However, two groups showed no difference in ΔGlu 2-0 at time after exercise. ΔGDF 2-0 in subjects with normal glucose tolerance showed positive values at all of times before and after exercise. However, in subjects with glucose intolerance showed negative ΔGDF 2-0 at times before exercise, but positive ΔGDF 2-0 at times before exercise.

Conclusion: Our data suggested that exercise in subjects with glucose intolerance could result in recovery of GDF15 response at postprandial times with improvement of postprandial glucose level.

PA-04

Association between serum white blood cell counts and hemoglobin A1c in a Korean adult population

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Few studies have investigated the clinical effect of subclinical inflammation on the use of the hemoglobin A1c (HbA1c) as a screening parameter for diabetes or prediabetes. We investigated the association between serum white blood cell counts (WBC) within normal ranges as a marker of subclinical inflammation and HbA1c levels in a Korean adult population. Among 11,472 adults (>/=19 years old) who participated in the 2011–2012 Korea National Health and Nutrition Examination Survey, participants with anti-diabetes/anti-hypertensive/anti-lipid drugs, or history of previous cancer, or the presence of chronic kidney disease, or positivity of HBsAg, or abnormal WBC (<4000 micro/L or >10000 micro/L) were excluded. Finally in 7116 participants, we investigated the association between quartile (Q) of WBC and HbA1c. After adjusting for age, sex, fasting plasma glucose (FPG), the presence of college graduation, smoking history, the presence of hypertension, serum total cholesterol, serum triglyceride, and the presence of anemia, the level of HbA1c increased with increase of WBC (HbA1c, mean+/−SEM, 5.55+/−0.01% in Q1, 5.58+/−0.01% in Q2, 5.60+/−0.01% in Q3, and 5.65+/−0.01 in Q4, $p < 0.001$). After adjusting for above mentioned covariates, the proportions (%) of an HbA1c level of >/=5.7%, and >/=6.5% were also higher in participants with the increase of WBC (proportion of >/=5.7%, 30.9+/−1.0% in Q1, 34.1+/−1.0% in Q2, 36.6+/−1.0% in Q3, and 39.3+/−1.0% in Q4, $p < 0.001$; proportion of >/=6.5%, 3.1+/−0.4% in Q1, 2.9+/−0.4% in Q2, 4.1+/−0.4% in Q3, and 4.1+/−0.4% in Q4, $p = 0.022$). In logistic regression analyses with above mentioned variables as covariates, the proportions of an HbA1c level of >/=5.7%, and >/=6.5% increased with increase of WBC (odds ratio [95% CI] for HbA1c level of >/=5.7%, 1.20 [1.02–1.42], $p = 0.028$ in Q2, 1.37 [1.16–1.62], $p < 0.001$ in Q3, and 1.59 [1.35–1.89], $p < 0.001$ in Q4; for HbA1c level of >/=6.5%, 0.85 [0.45–1.63], $p = 0.632$ in Q2, 1.79 [1.01–3.18], $p = 0.048$ in Q3, and 2.03 [1.13–3.64], $p = 0.018$ in Q4). Our study showed that serum WBC count within normal ranges, marker of subclinical inflammation, are associated with the increase of HbA1c after adjusting for several covariates including FPG. The data suggested that the subclinical inflammation need to be considered before using HbA1c as a screening test for prediabetes or diabetes.

PA-05

Incidental risk for diabetes according to the change level of body mass index in Korean men

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Objective: Although accumulated evidence implies that change of body mass index (BMI) have deep relation with diabetes, there is little information about longitudinal relationship between the BMI change and diabetes in Asian. Therefore, this study was conducted to evaluate the incidental risk of diabetes according to the change of body mass index

Research design and methods: Cohort of 31,138 middle aged nondiabetic Korean men was followed-up annually or biennially from 2005 to 2010. On the basis of BMI in 2005, study participants were categorized into 5 groups according to their change levels of BMI for follow-up period from the lowest quintile to the highest quintile (1stquintile – 5thquintile). The incidence and adjusted hazard ratios (HRs) for diabetes were evaluated in 5 quintiles.

Results: During 120,785.3 person-years of follow-up, 1,687 (5.3%) incident cases of diabetes developed between 2006 and 2010 (quintile 1: 6.6%, quintile 2: 4.3%, quintile 3: 4.0%, quintile 4: 5.0%, quintile5: 7.2%). When quintile 3 was set as a reference, in adjusted model, the adjusted hazard ratios for diabetes showed the J-shaped relationship with the levels of BMI change [quintile 1: 1.52 (1.27–1.82), quintile 2: 0.85 (0.70–1.04), quintile 3: 1 (reference), quintile 4: 1.27 (1.05–1.53), quintile 5: 2.85 (2.39–3.40), respectively].

Conclusions: In this study, J-shaped relationship pattern was demonstrated between risk for diabetes and the change levels of BMI. This finding indicates that the risk of diabetes can paradoxically increase not only by decreased BMI and but also by increased BMI in Korean men.

PA-06

Elevated circulating plasma miRNA27b-3p in type 2 diabetes and reduced miRNA3195 in diabetic nephropathy

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Diabetic nephropathy (DN) is the most common chronic microvascular complication in diabetes, in particular the type 2 diabetes (T2DM). But DN is always neglected by diabetic patients. It is need to find a simple, sensitive and specific marker for early detection, diagnosis and treatment of DN. The unique circulating microRNAs (miRNAs) observed in patients with early DN are candidates as new biomarkers. In this study, we first applied miRNA microarray techanology and identifified four miRNAs, miR27b-3p, miR215, miR3195, and miR4298, which were increased more than 1.5 folds in pooled (n = 20 per each group) plasma samples from DN and T2DM patients, as compared to normal control (NC) subjects. To validate these miRNAs as biomarkers, we measured and analyzed their plasma levels by quantitative real-time PCR in 205 subjects including 65 T2DM patients with early DN, 70 patients with T2DM without DN and 70 NC. And the area under the curve for circulation miRNAs was determined using Receiver Operator Characteristic analysis. We found that the plasma concentrations of miRNAs, miR-27b-3p was significantly increased among the patients with early DN, T2DM without kidney disease and normal controls (NC) ($p = 0.007 < 0.01$), within two groups that miRNA27b-3p was significantly increased in T2DM and DN compared with NC ($p = 0.021 < 0.05$ and $p = 0.037 < 0.05$, respectively), but there is no significant between DN and DM ($p = 0.852 > 0.05$). The plasma concentrations of miRNA3195 was no significantly among the patients with early diabetic nephropathy and type 2 diabetes (without kidney disease) and normal controls ($P = 0.068 > 0.05$), within two groups that miRNA3195 was significantly decreased in DN compared with T2DM and NC ($p = 0.043 < 0.05$ and $p = 0.043 < 0.05$, respectively). While miR-215, miR-4298 were no significantly among the three groups. According to the regression analysis, the concentrations of miRNA27b-3p was correlation with BMI ($r = 0.163$, $p = 0.020$) and HbA1c ($r = 0.170$, $p = 0.015$). The concentrations of miRNA27b – 3p was still increased among the three groups when BMI, HbA1c was not considered. The area under ROC curve of miRNA27b-3p, miRNA215, miRNA3195, and miRNA4298 were 0.406, 0.400, 0.318 and 0.500, respectively), while combined miRNA27b-3p and miRNA3195, The area under ROC curve is 0.7057 ($p = 4.206 \times 10^{-6}$). Our results demonstrated that the applications of circulating miR27b-3p as a potential biomarker for DN/T2 DM and miR3195 for DN, and thus can be used in clinical monitoring,or the combination of elevated miR27b-3p and reduced miR3195 as biomarkers for DN warrant further investigations.

PA-07

The presence and the extent of gastric atrophy are inversely associated with incident diabetes

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Objective: Gastric atrophy results in low plasma ghrelin, vitamin B12 deficiency, and a change in gut microbiota because of decreased gastric acid secretion, which may lead to the incidence of diabetes. Helicobacter pylori infection is a major cause of gastric atrophy and is associated with diabetes in some reports. Since there is no study which investigates the impact of gastric atrophy on diabetes, we conducted a prospective cohort study to examine the relationship between H. pylori infection, gastric atrophy, and incident diabetes.
Research design and methods: From 2006 to 2012, we enrolled 855 subjects without diabetes. Serum antibodies against H. pylori were measured at baseline. Gastric atrophy was defined as serum pepsinogen (PG) I ≤70 ng/mL and PG I/II ratio ≤3. PG I/II ratio was used as a measure for the extent of gastric atrophy.
Results: At baseline, 283 (36%) subjects were positive for H. pylori infection and 78 (9%) subjects were diagnosed as gastric atrophy. Serum PG I/II ratio was inversely correlated with HOMA2-IR, HOMA2%B, and H. pylori IgG titer (all $p < 0.05$). During an average of 3.4-year follow-up, 73 subjects (9%) developed diabetes. Subjects with gastric atrophy had a lower risk of incident diabetes (HR 0.28, 95%CI 0.09–0.91, $p < 0.05$), adjusting for risk factors of diabetes, blood pressure, and lipid profiles. Serum PG I/II ratio predicted incident diabetes (adjusted HR 2.06, 95%CI 1.11–3.84, $p < 0.05$). However, H. pylori infection was not associated with incident diabetes ($p > 0.05$).
Conclusions: The presence and the extent of gastric atrophy are inversely associated with incident diabetes.

PA-08

Changes in lifestyle habits and subsequent risk of type 2 diabetes in males and females

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Objectives: Several lifestyle factors have been associated with an increased risk of type 2 diabetes (T2D). However, whether changes in lifestyle factors are related to the subsequent type 2 diabetes risk remains unknown. The aim of the present study was to evaluate the association between changes in lifestyle habits during a one-year period and the subsequent 5-year risk of type 2 diabetes.
Methods: A prospective study of 59,400 non-diabetic participants aged from 40 to 74 years (29,253 males and 30,147 females) was performed using the Specific Health Check and Guidance System in Japan. Inclusion criteria included being aged 40–74 years. Exclusion criteria included diabetes, hypertension, hyperlipidemia, and chronic kidney disease treatment. The height and weight of the subjects were measured, and information concerning lifestyle habits (eating speed, physical activity, exercise habits, gait speed, alcohol drinking, smoking, and restorative sleep) was obtained using a self-administered questionnaire in 2008 and 2009. Incident cases of T2D were defined based on FPG ≥ 7.0 mmol/L, postprandial glucose ≥11.1 mmol/L, glucose HbA1c ≥ 6.5%, and the use of anti-diabetic agents. Cox proportional hazard models were used to calculate hazard ratios (HRs) and 95% confidence intervals (CI) with adjustment for age, BMI, and initial and changes in lifestyle factors.
Results: Over a mean follow-up period of 3.9 years, 1,223 males (4.2%) and 427 females (1.4%) newly developed T2D. In males, never smokers had significantly lower T2D risks compared with the reference group (HR 0.65, 95% CI 0.57–0.74). In males with changes of lifestyle factors, skipping breakfast was significantly associated with an increase of T2D (HR 1.46, 95% CI, 1.06–1.99). In females, never smoking and faster gait speed were significantly associated with a decrease of T2D (HR 0.53, 95%CI 0.36–0.79; HR 0.76, 95%CI 0.58–0.98). In females with changes of lifestyle factors, slower eating speed was significantly associated with a decrease of T2D (HR 0.72, 95%CI 0.56–0.93).
Conclusions: These findings suggest that several changes of lifestyle factors were associated with an increased or decreased rate of T2D. Lifestyle modification targeting these factors is required to prevent T2D in the future.

PA-09

Gender differences in plasma growth arrest-specific protein 6 levels in adult subjects

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Background: Growth-arrest-specific 6 (Gas6) is recognized as a secreted vitamin K-dependent protein, as it interacts with receptor tyrosine kinases of the TAM (Tyro-3, Axl, Mer) family. The plasma Gas6 are important to the inflammatory process, and are involved in diverse human diseases. Few studies have shown plasma Gas6 concentration varies with genders. Hence, the aim of this study was to determine whether plasma Gas6 levels are associated with sex hormones in both genders.
Methods: A total of 589 adult subjects, including 361 male and 228 female were recruited. Plasma Gas6 concentration, biochemical, testosterone, estradiol (E2), sex hormone-binding globulin were assayed. The index of free androgen (FAI) and free E2 (FEI) were calculated.
Results: Our results showed that significantly higher Gas6 levels were observed in adult male rather than female ($P < 0.05$). In univariate regression analysis, plasma Gas6 levels were positively associated with FAI in male ($\beta = 0.167$, $P = 0.002$) and both E2 and FEI in female ($\beta = 0.384$, $P < 0.001$ and $\beta = 0.292$, $P < 0.001$, respectively). Otherwise, Gas6 levels were inversely associated with ages in both genders ($\beta = -0.234$, $P < 0.001$ in male and $\beta = -0.226$, $P = 0.001$ in female, respectively). In multivariate regression analysis, only age in male and E2 in female were independent variables to determine the plasma Gas6 levels ($\beta = -0.231$, $P = 0.002$ and $\beta = 0.458$, $P = 0.001$).
Conclusions: These results suggest that plasma Gas6 is associated with sex hormones in female and ages in male, indicating a potential role of sex hormones and ages involving the Gas6/TAM system.

PA-10

Glucose-dependent insulinotropic peptide level is associated with the development of type 2 diabetes mellitus

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Introduction: Incretin hormone levels as a predictor of type 2 diabetes mellitus have not been fully investigated. Therefore, we measured incretin hormone levels to examine the relationship between circulating incretin hormones, diabetes, and future diabetes development in this study.
Materials and Methods: A nested case-control study was conducted in a Korean cohort. The study included the following two groups: the control group (n = 149), the incident diabetes group (n = 65). Fasting total glucagon-like peptide-1 (GLP-1) and total glucose-dependent insulinotropic peptide (GIP) levels were measured and compared between these groups.
Results: Fasting total GIP levels were higher in the incident diabetes group than in the control group (32.64 ± 22.68 pmol/L vs. 25.54 ± 18.37 pmol/L, $P = 0.034$). There was no statistically significant difference in fasting total GLP-1 levels between groups (1.14 ± 1.43 pmol/L vs. 1.39 ± 2.13 pmol/L, $P = 0.199$). In multivariate analysis, fasting total GIP levels were associated with an increased risk of diabetes (odds ratio, 1.005; $P = 0.012$) independent of other risk factors.
Conclusion: Fasting total GIP levels may be a risk factor for the development of type 2 diabetes mellitus. This association persisted even after adjusting for other metabolic parameters such as elevated fasting glucose, hemoglobin A1c, and obesity in the pre-diabetic period.

PA-11

The relationship between body composition, glycemic index, and glycemic response of foods in healthy Indonesian adults

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Previous study showed that body composition could influence glycemic response in healthy subjects. However, only a small number of respondents were included in the study. The objective of the current research was to study the relationship between body composition, glycemic index, and glycemic response of food in healthy Indonesian adults. Seventy-eight adults (BMI: 22.8 ± 3.4 kg/m^2) were recruited to participate in the study. Body weight and composition were determined by body composition analyzer (Inbody 720). Capillary finger stick blood sample were analyzed for glucose concentration at –0, 15, 30, 45, 60, 90, and 120 minutes and the resulting 2 h iAUCs following consumption of a 50-grams glucose beverage and noodles in two separated days were calculated. Study results were analyzed in different BMI and gender categories. The current study showed that glycemic index of noodles was not correlated with body composition. However, skeletal muscle mass (SMM) was negatively correlated with iAUC of glucose (r: –0.29, P: 0.009). In overweight subjects (n = 9) (BMI 23.0–25.0 kg/m^2), a strong significant negative correlation between iAUC of glucose and waist-to-hip ratio (WHR) (r: –0.83, P: 0.006) was observed. In obese subjects (n = 19) (BMI > 25.0 kg/m^2), iAUC of glucose was moderately positively correlated with visceral fat (r: 0.59, P: 0.007) and iAUC of noodles was moderately positively correlated with WHR (r: 0.61, P: 0.005). Subgroup analysis showed that iAUC of glucose and noodles were negatively correlated with SMM (r: –0.42 and –0.37, P: 0.01 and 0.024) only in male adults (n = 37). However, there was no correlation observed between body composition to glycemic response of foods in female adults. This study showed that muscle mass might be a potential determinant of glycemic response of food in Indonesian adult subjects.

PA-12

Chronic kidney disease and peripheral artery disease in type 2 diabetes

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Background: To examine the association of chronic kidney disease (CKD) with the peripheral artery disease (PAD) in type 2 diabetic subjects.
Materials and methods: A total of 212 type 2 diabetic patients (64 ± 13 years, 135 males) were enrolled and divided into two groups: one with a presence of CKD (eGFR < 60 mL/min/1.73 m^2, n = 74) or one without (n = 138). We recorded clinical and biochemical data as well as ankle brachial index (ABI) for comparisons. Data are reported as mean ± SD.
Results: The patients with CKD was older and had had diabetes mellitus (DM) longer, had higher systolic blood pressure (BP), higher albumin to creatinine ratio (ACR) than those without CKD. The patients with CKD also had more prevalence of hypertension and dyslipidemia. Lower mean ABI was noted in those with CKD than without (1.08 ± 0.15 vs 1.14 ± 0.10, p = 0.001). The occurrence of PAD (defined as one ABI < 0.9) was

also more in those with CKD (17.6% vs 3.6%, p = 0.001). We found mean ABI was positively correlated with eGFR (γ = 0.184, P = 0.007), and negatively correlated with age (γ = –0.326, P < 0.001), duration of DM (γ = –0.386, P < 0.001), and systolic BP (γ = –0.200, P = 0.003). Multivariate regression analysis revealed that age and duration of DM were correlated with mean ABI.

Conclusions: Type 2 diabetic patients with CKD are associated with higher prevalence of PAD than those without. Moreover, older age and longer duration of DM account for the highest risks. Routine performance of ABI for early detection of PAD is indicated in these patients.

PA-13

The relationship between hyperglycemic clamp and low dose graded glucose infusion in quantifying second phase insulin secretion

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Aim: First phase insulin secretion usually disappears even in pre-diabetic stage. Thus, maintaining glucose control after occurrence of diabetes must rely on the existence of second phase insulin secretion (SPIS). There are several methods to quantify SPIS, such as oral glucose tolerance, low dose graded glucose infusion (LDGGI) and hyperglycemic clamp (HC). In the same time, whether to use c-peptide and deconvolution to estimate "true" insulin secretion was also suggested to have some influence on the measurement. If we take the HC as the gold standard, it is interesting to note that LDGGI has never been validated against HC. In the same time, whether to use deconvolution is also interesting.

Methods: Fourteen subjects (3 with normal glucose tolerance, 8 with pre-diabetes and 3 with diabetes) were enrolled. They received both 120 min HC and 200 min LDGGI proposed by Polonsky et al. Four different SPIS were measured. Two from the HC, i.e., plasma insulin level (PIclamp) and insulin secretion rate (ISRclamp, by using deconvolution) between 80 and 120 min. Similarly, the other two were from the LDDGI, plasma insulin level (PILDDGI) and ISR (ISRLDDGI) by deconvolution during the whole test. Simple correlation was used to evaluate their concordance.

Results: Both PILDDGI and ISRLDDGI were highly correlated with PIclamp (r = 0.851, 0.748, p = 0.000). It should be noted that the r value is higher for the PILDDGI than that of ISRLDDGI. In the same time, the PIclamp and ISRclamp is also highly correlated (r = 0.886, p = 0.000).

Conclusion: Our results showed that if we take clamp as the gold standard, PILDDGI could be used as another accurate method to measure SPIS. In the same time, to use deconvolution is not mandatory in order to have precise estimation

PA-14

Clinical pictures associated with borderline heteroplasmy rate of 3243 mitochondrial tRNA Leu (UUR) mutation in type 2 diabetes

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Approximately 0.5–2.8% of Japanese diabetic patients population is estimated to have mitochondrial DNA (mtDNA) mutation at position 3243 in the blood. However, the cut-off limitation for detecting the mutation in blood differs depending upon the judgements of researchers. In general, using the ordinary polymerase chain reaction (PCR) method, the threshold is around 1% of the heteroplasmic rate. A new technology using real-time PCR with a TaqMan Probe was introduced, which can quantify as little as 0.001% of the 3243 mtDNA mutation in blood cells. By using this method, we examined the association of low borderline heteroplasmic rate with clinical pictures in cross sectional study of type 2 diabetes.

189 patients with type 2 diabetic were subjected. The profile of the 189 subjects was 142 males and 47 females. Their ages were 59.4 ± 10.2 years and diabetes duration was 12.1 ± 7.9 years. BMI 22.9 ± 4.0 and HbA1c 8.2 ± 1.3% (mean ± SD).

In result, the heteroplasmy rates were about six times higher than the healthy controls (aged 20–60 years, n = 186). In all the type 2 diabetes subjects, the mathematical mean and SD of heteroplasmy rate was 0.041 ± 0.018%. When logarithmically converted, the data were seemingly distributed normally. By the data, the mean was –1.408, and SD was 0.142. "Mean + 2SD" was –1.124, which corresponds to 0.075% of the heteroplasmy rate. Therefore, we regarded the patients with over 0.075% heteroplasmic rate as having a high level among type 2 diabetes patients.

As the result, five patients were positioned over 0.075%. Interestingly, all the five had clinical pictures associated with mitochondrial dysfunction, such as juvenile cataract (Subject-1: 0.090% of heteroplasmy rate), ophthalmoplegia and lipoma (Subject-2: 0.102%) and high lactate levels in the blood (Subject-3: 0.172% and Subject-4:0.115%). Subject 5 (heteroplasmy rate: 0.127%) had a maternal inheritance of diabetes and cerebellar atrophy. The details of Subjects 1 and 2 have been described in Diabetologia 2004 and Diab.Res.Clin, Prac. 2004 63(3): 225–9

Thus, when we define the upper-borderline level of heteroplasmy rate to be 0.075% among type 2 diabetes patients, five patients were found to have a high heteroplasmy rate. Interestingly, the five patients had one or two mitochondria-associated characteristics. They did not have hearing loss.

Therefore, we propose that clinicians should not overlook the important features of mitochondrial diabetes, even when the result of examination for 3243 mtDNA mutation is negative by ordinary PCR method and even when hearing loss is absent.

PA-15

The correlation between lifestyle factors and subclinical neuropathy in patients with type 2 diabetes

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Background: Little is known regarding correlation between the lifestyle factors and asymptomatic neuropathy in patients with type 2 diabetic (T2D) in Taiwan. The aim of the study was to evaluate which lifestyle factors were associated with increased risk of subclinical diabetic neuropathy.

Method: We conducted a prospective cross-sectional study at Chia-Yi Christian Hospital, Taiwan. 153 T2D patients with subclinical neuropathy, which was diagnosed by using neuro-electrophysiology, 2-point discrimination, and pressure threshold measurement were enrolled. Questionnaires including food frequency questionnaire (FFQ) and Douleur Neuropathique 4 (DN4) questionnaire were obtained.

Results: Of 153 participants, 38 (24.8%) patients were diagnosed to have subclinical neuropathy. Comparing the lifestyle factors between the two groups, T2D patients with neuropathy had significant lower amounts of daily vegetable intake

(1.97 ± 1.1 vs. 2.49 ± 1.0, p = 0.01) and higher amounts of smoking (0.45 ± 0.5 vs. 0.16 ± 0.37) than T2D patients without neuropathy. In addition, T2D patients with neuropathy had significantly higher levels of HbA1C, microalbuminuria, and urine albumin to creatinine ratio. In a multivariate logistic regression model, smoking, HbA1C and presence of microalbuminuria were significantly associated with increased risk of neuropathy in DM patients.
Conclusion: Decreased vegetable intake and habit of smoking were lifestyle factors to develop neuropathy in T2D patients. Therefore, daily vegetable intake and smoke cessation should be strongly recommended in T2D patients.

PA-16
Insulin significantly changes the expression of T1DM mice's circulating microRNA
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Background and objective: the circulating miRNA spectrum of patients with Type 1 Diabetic Mellitus (T1DM) is expected to early screening and diagnosis, but the patients involved in the clinic trial usually use the treatment of insulin, which needs us to understand the influence of insulin to T1DM circulating miRNA.
Method: We measured circulating miRNA expression by microarray and quantitative RT-PCR in plasma samples of streptozotocin (STZ)-treated C57BL/6 mice after 4 weeks glargine intervention.
Result: compared with blank control group and diabetic control group, insulin improves the expression of miR-320a (1: 2.65: 10.71, p < 0.01), miR-26b (1: 1.42: 3.95, p < 0.05), let-7b (1: 2.88: 39.77, p < 0.01) in serum.
Conclusion: Confirmation of the change of TiDM circulating miRNA by insulin is helpful for the early diagnosis of T1DM.

PA-17
The differences of metabolic syndrome in elderly subgroups: A special focus on young-old, old-old and oldest old
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Background: Metabolic syndrome (MetS) is known to be correlated to future diabetes and cardiovascular disease. Due to the aging society, the increasing prevalence of MetS in the elderly is an important health issue. However, there were few studies focusing in this field. We investigated the changes of MetS components in the subgroups of the elderly.
Methods: Subjects aged above 65 years old who underwent routine health checkups in Taiwan (N = 18916) were divided into three groups (young-old: ≧65 and < 75, old-old: ≧75 and <85 and oldest-old ≧85). By using multiple logistic regressions, the odds ratio (OR) of subjects with abnormal MetS components to have MetS were evaluated.
Results: For men, the systolic blood pressure (SBP) and high-density lipoprotein cholesterol increased as the age got older. On the contrary, the diastolic blood pressure and triglycerides (TG) decreased. In women, the waist circumference and SBP increased significantly from the young-old to the oldest-old groups. The highest percentage having MetS was 35% in old-old men and 62% in oldest-old women. Finally, subjects with high TG had the highest and BP had the lowest ORs for having MetS in both genders except oldest-old women.
Conclusions: In the elderly, the MetS and its components have different patterns not only in young-, old- and oldest-old groups but also in men and women. Moreover, among the five components, hypertension was always the most prevalent one. Finally, subjects had high TG had the highest OR to have MetS compared to other components.

PA-18
Diabetes nurse case management: Improving the health of diabetes high-risk groups
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In recent years, diabetes prevalence has been gradually increasing worldwide. This research was aimed to investigate the effect of diabetes nurse case management for diabetes high risk patients in improving their health self-management.
Methods: An observational method was adapted in this research. The research was performed from Jan to Sep, 2015. The study participants with high diabetes risks were referred by the Endocrinology and Metabolic department or Family Medicine department. The enrollment criteria include fasting blood glucose (FBG) of 100~125 mg/dL or total cholesterol of >200 mg/dL. The participants were given 1 to 1 individualized health education by a certified diabetes educator as a case manager. The health education content include: intensive diet and physical activity behavioral counseling program adhering to the tenets of the Diabetes Prevention Program (DPP) targeting loss of 7% of body weight and should increase their moderate physical activity to at least 150 min/week. The program was implemented for 6 months. The patients' pre- and post-intervention physical measurements, body mass index (BMI), and waist circumference, blood pressures, and blood biomarker levels were compared and their lifestyle changes monitored.
Results: A total of 75 patients were enrolled in this study, with 31 male (41.3%), 44 female (58.6%), and an average age of 57.71 ± 10.85 years. After the study intervention, 44 (58.7%) patients maintained moderate physical activity to at least 150 min/week, 17 (22.7%) patients achieved 90–150 min/week. Most patients were determined with significant weight, BMI, diastolic and systolic blood pressure, FBG, and total cholesterol improvements (p < 0.05), yet, with no change in waist circumferences.
Conclusion: The American Nation Institutes of Health Diabetes Prevention Program (DPP) and the Finland Diabetes Prevention Study (DPS) research team have reported that intensive lifestyle modification programs are very effective in the prevention or delay of type 2 diabetes. The research also indicated that high diabetes risk cases can improve their health conditions after the intervention of diabetes nurse case management. Pay for performance has become a popular approach to increase efficiency in health care. It is with hope that pay for performance in Taiwan can be implicated in the group of high risk for diabetes to increase the awareness of chronic disease and promote the health of the pre-diabetes.

PA-19
Association of uric acid concentrations and metabolic syndrome in Taiwan elderly population
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Background: Currently, uric acid (UA) is not in the definition of Metabolic syndrome (MetS), the positive correlation between UA and MetS had been shown in several studies. The aging of the general population becomes a major issue due to the progress in the public health. However, the aforementioned relationship between MetS and UA is not fully explored in elderly group. To fill up the deficient piece of knowledge, we enrolled age-difference groups in the Taiwanese elderly to shed light on the relationships between UA levels and variable

numbers of MetS component. We would like investigate UA according to the number of MetS components.
Methods: We randomly selected 36,169 subjects who were over 65 years old for 10 years and 18,907 subjects, 9,732 male and 9,175 female participants had MetS, were eligible finally. Subjects were grouped by age to be young-old (65–74 years old), old-old (75–84 years old), and oldest-old (85–94 years old). Correlations between MetS components and UA were evaluated and multivariate linear regression analysis was performed to confirm if UA is independently related to MetS components.
Results: Positive correlation between UA levels and variable numbers of MetS component in the female and male young-old and old-old groups but oldest-old groups. There were trends of correlations between UA levels and variable numbers of MetS component in young-old and old-old groups, but reversed relationships in both genders of oldest-old groups.
Conclusion: In this cross-sectional study, we found that serum UA is correlated with the elder age with MetS and age is one of the risk factors for increasing UA in the elder groups, but reversed correlation in the male oldest-old group.

PA-20

The correlation between carbohydrate food intake and nutritional knowledge, attitude, behavior and self-efficacy among community people

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Objectives: The purpose of this study is to understand the correlation between carbohydrate food intake and nutritional knowledge, attitude, behavior and self-efficacy among community people and participants enrolled in hospital reduction program. With the health intervention strategies to maintain more balanced diet, it is anticipated that subjects can reach long-term weight reduction goal.
Methods: Subjects who randomly selected from community activity and participants who joined Chimei weight reduction program were issued a self-reporting questionnaire to fill after a single instruction. Questionnaire included questions covering food frequency, nutrition knowledge, attitude and self-efficacy.
Results: A final 169 valid questionnaires (response rate 84.5%) were analyzed. The results showed a significant positive correlation between body weight and waist circumference, hip circumference, blood pressure, pasta-based intake, meal frequency and fried food frequency. There were significant negative correlations between body weight and vegetable intake, eating attitudes, as well as eating behaviors. There were significant positive correlation between nutrition knowledge, attitude, health self-efficacy, but not between nutrition knowledge and dietary behaviors. Eating behaviors were also positively correlated with health self-efficacy. Among women group, better nutrition knowledge, attitudes and behaviors were shown along with age increase. Healthy eating behaviors were negatively associated with frequency of dining out or purchase of half-cooked food. We concluded that more frequent dining out owing to busy work and school could be a major factor hindering health eating behaviors.

PA-21

Comparison of diabetes conversion rates among Chinese prediabetic population using different diagnosis criteria

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Background: The American Diabetes Association (ADA), the World Health Organization (WHO) and the National Institute for Health and Care Excellence (NICE) have different criteria for diagnosing prediabetes. However, what needs to be explored is whether these criteria result in different conversion rates to diabetes in Chinese population in order to determine which criteria should be used in the early screening or intervention of prediabetes.
Objective: The study aims to compare the diabetes conversion rates in a Chinese prediabetic population diagnosed using different criteria.
Method: A 4-year retrospective cohort (recruting1397 subjects aged 18–89 at 4 sites) was built to estimate the rates of diabetic conversion in subjects with prediabetes compared to normoglycemic at baseline. Diabetes (physician diagnosis) conversion rates were calculated in seven mutually exclusive prediabetic subgroups, including ADA specific isolated impaired fasting glucose (IFG; $5.6 \leq FPG < 6.1$ and $2hPG < 7.8$); WHO isolated IFG ($6.1 \leq FPG < 6.9$ and $2hPG < 7.8$); ADA specific combined IFG and impaired glucose tolerance (IGT; $5.6 \leq FPG < 6.1$ and $7.8 \leq 2hPG < 11.1$); WHO Combined IFG and IGT ($6.1 \leq FPG < 6.9$ and $7.8 \leq 2hPG < 11.1$); ADA isolated IGT ($FPG < 5.6$ and $7.8 \leq 2hPG < 11.1$); Rest captured by ADA specific HbA1c ($5.7\% \leq HbA1c < 6.0\%$); and Rest captured by NICE HbA1c ($6.0\% \leq HbA1c < 6.5\%$). These subgroups were compared to normoglycemia group ($FPG < 5.6$ and $2hPG < 7.8$ and $HbA1c < 5.7\%$) to assess the relative risk among these groups.
Results: The study found that the 4-year diabetes conversion rate in subjects with normoglycemia was 6.9%. Compared with normoglycemia, the rates in ADA isolated IFG, WHO isolated IFG, ADA specific combined IFG and IGT, WHO combined IFG and IGT, ADA isolated IGT, ADA specific HbA1c and NICE HbA1c subgroups were 13.8% (risk ratio, RR = 1.8; 95%CI: 1.2–2.7), 22.5% (RR = 2.8; 95%CI: 1.6–4.7), 23.9% (RR = 2.7; 95%CI: 1.5–4.8), 35.3% (RR = 4.2; 95%CI: 2.4–7.1), 22.6%(RR = 2.8; 95% CI: 1.7–4.8), 8.7% (RR = 1.1; 95%CI: 0.7–1.9), and 19.5% (RR = 2.2; 95%CI: 1.3–4.0) respectively, after adjusting for age, gender, low HDL, binge drinking and BMI.
Conclusion: The 4-year diabetes conversion rates were lower in the ADA groups than in the WHO or NICE groups. Other than the ADA specific HbA1c group, the rates in all the other groups were significantly higher than normoglycemia group over 4 years. Diabetes conversion rates were lower using ADA criteria and the ADA specific criterion diagnosing prediabetes based on HbA1c did not identify a group at higher risk converting to diabetes compared to normoglycemia group, possibly due to lower IFG or HbA1c cutoff used.

PA-22

Improvement of hemoglobin A1c by a diet adherence monitoring for diabetic inpatients ordering diabetes meals

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Background: Diabetes and its associated comorbidities increase healthcare resources utilization. Diabetes control requires long-term management, including lifestyle changes, effective self-care, and optimal glycemic control, to prevent acute and chronic complications. Eating healthful meals is pivotal for maintaining glycemic control.
Objectives: Utilize PRECEDE model as a framework to explore the behavior of compliance and relevant parameters on the impact of HbA1c among hospitalized diabetic patients.
Methods: We conducted a cross-sectional study on diabetic inpatients by using hospital therapeutic diet and a diet adherence monitoringin a teaching hospital between October 2015 and March 2016. In tota, 46 patients were enrolled. The

study used a structured questionnaire as a tool to measure patients' knowledge, behavior, and diet adherence. In addition, demographic characteristics, comorbid medical disorders, the awareness and compliance of nutritional practice, capability, attitude, self-efficacy, accessibility of medical resources, social support were into analyses.
Results: This study supported positive correlation of self-care, diet adherence and diabetes control. Patients with effective self-care and strict diet adherence were significantly lower HbA1c level. The average HbA1c for those patients after a diabetic diet adherence monitor reduced from 8.04 ± 2.74 to 6.88 ± 1.26 ($P < 0.05$).
Conclusion: Proper diet adherence monitoring and educational program are recommended in diabetes educational clinics to enhance diabetes control.

PA-23

Relationship of neck circumference to metabolic syndrome and central obesity in regional hospital employees

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Objective: Metabolic syndrome (MS) increases the relative risk of cardiovascular disease. In Taiwan, the prevalence rate is estimated to be 15–18%. Upper-body fat distribution has long recognized as related to increase cardiovascular disease risk, and neck circumference (NC) has been used as an index for risk profile, suggesting it plays an important role in metabolic risk . The aim of the study is to investigate the relationship of NC to MS and central obesity in regional hospital employees.
Methods: A cross-sectional study, participants aged between 25 and 60 yrs with mean age of 43.7 ± 7.7 yrs (mean ± SD) and criteria compatible to two or more of risk factors for metabolic syndrome combined with LDL-C ≧130 mg/dL or total cholesterol ≧200 mg/dL were included.
Results: Total of 34 participants were completed (11 male, and 23 female). Male, with a mean NC of 39.1 ± 2.1 cm, 6 cm wider than female of 33.1 ± 2.5 cm ($P < 0.01$). NC correlate positively with BMI ($r = 0.39$, $P < 0.01$). NC also correlate positively with waist circumference ($r = 0.68$, $P < 0.01$) and MS ($r = 0.65$, $P < 0.05$). Our study also showed that an NC of 38.2 cm for male and 37.4 cm for female was optimal cutoff point for central obesity, NC of 39.15 cm for male and 34.55 cm for female was the optimal cutoff point for overweight and NC of 38.2 cm for male and 35.2 cm for female was the optimal cutoff point to determine participants with MS.
Conclusion: In our study, neck circumference is positively related with BMI, central obesity, and metabolic syndrome in regional hospital employees

PA-24

The role of medical nutrition therapy on components of metabolic syndrome in community-based population

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Objective: The prevalence of obesity is rising in throughout the world, reaching 14.6% in Taiwan, and it increases with increasing age. According to American Diabetes Association guideline in 2012, medical nutrient therapy(MNT) not only decreases the complications of obesity, but also prevents the occurrence of MS. Weight reduction have shown reductions in various mediators of chronic diseases, including hyperglipidemia, hypertension, hyperglycemia, metabolic syndrome and cardiovascular disease. The aim of this study was to evaluate the effects of MNT on weight reduction and metabolic risk factors in the community-based population.
Methods: Participants aged 20–60 yrs with meanage of 45 ± 1.82 yrs (mean ± SD) and BMI ≥ 24 kg/m^2 were included. The intervention period of 8 weeks and the maintenance period of 6 weeks. Dietitians provided continuous individualized MNT to the participants for initial 8 weekly then biweekly in following 6 weeks period. We measured height at baseline and body weight, BMI, and waist circumference at baseline, 8-week, 14-week, and 24-week. We also checked blood sugar and lipid profile at baseline, 8-week, 14-week and collected KAP questionnaires of diet to estimate the effectiveness at baseline and 8-week.
Results: Total sixty participants were completed both intervention and maintenance period. There were significant reductions in body weight 3.53 kg, waist circumference 5.97 cm, BMI 1.34 kg/m^2, total cholesterol 18.3 mg/dL, LDL-C 12.06 mg/dL compared between baseline, 8-week, 14-week ($p < 0.001$) and scores of KAP questionnaires at 8-week compared to baseline ($p < 0.001$). However, there were no significant differences 14-week compared to 8-week.
Conclusion: Our study showed that it was effective on weight reduction by continuously individualized MNT, can improve metabolic syndrome and associated cardiovascular risk factors.

PA-25

Low lung function associated with type 2 diabetes risk in Chinese older people: Data from the Qingdao Aging Study

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Backgrounds: Evidence suggests that low lung function increased risk for type 2 diabetes in Europeans, but not well known in Chinese. The aim of this study was to investigate the association between lung function and type 2 diabetes based on the Qingdao Aging Study.
Methods: A total of 1321 individuals aged 50–78 years was randomly selected to investigate in the current study. Forced vital capacity (FVC) and forced expiratory volume in 1 s (FEV1) were measured using standard spirometry. Newly type 2 diabetes were classified by the fasting plasma glucose ≥7.0 mmol/L and (or) 2-h plasma glucose ≥11.1 mmol/L. The odds ratios of FVC and FEV1 for prevalence of type 2 diabetes were analyzed adjusting for age, BMI, gender, residential areas, hypertension status, family history of diabetes, total cholesterol, smoking and drinking status.
Results: The mean values of FVC and FEV1 were significantly inversely associated with fasting, 2-h glucose and fasting insulin concentrations both in men and in women ($P < 0.01$ for all comparisons). The multivariable adjusted model indicated that odds ratio of FEV1 was significantly declined in prevalence of type 2 diabetes, but not for FVC. The corresponding figures were 0.66 (0.46–0.95) and 1.23 (0.95–1.59), respectively.
Conclusions: It is first time to show that the low level of FEV1, but not FVC is independently increased risk for development of the type 2 diabetes in Chinese people.

PA-26

Risk for cardiovascular diseases based on relationship between post-load and fasting plasma glucose levels in the normal range

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Background: Individuals whose 2 h plasma glucose (2hPG) levels did not return to their fasting plasma glucose (FPG) level (2hPG > FPG), increased risk of cardiovascular diseases than those whose 2hPG did (2hPG FPG) during an oral glucose tolerance test in Europeans. However, the risk for cardiovascular risk was not well known in Chinese. We will assess the risk for and prevalence of cardiovascular diseases (CVD) in relation to FPG and 2hPG levels within normoglycemic range in Chinese population.
Methods: Data from Qingdao Diabetes Prevention Program comprising 1687 men and 2568 women aged 35–74 years who had FPG < 6.1 mmol/L and 2hPG < 7.8 mmol/L was analysed in the current study. Multivariate-adjusted odds ratios (ORs) and 95% confidence interval (95% CI) for prevalence of CVD was estimated for individuals whose 2hPG > FPG as compared with those whose 2hPG ≤ FPG, controlling for age, BMI, total cholesterol, uric acid, triglycerides, smoking status, drinking status, frequency of vegetable and fruit consumptions.
Results: A total of 829 (986) individuals was classified as CVD in men (women). The prevalence of CVD was significantly higher in the Group II than in the Group I (P < 0.01). The individuals from the Group II was older and had higher BMI, diastolic blood pressure, total cholesterol, triglycerides, uric acid and insulin resistance than those in the Group I (P < 0.01 for all comparisons). The multivariate-adjusted ORs (95%CIs) for prevalence of CVD was 1.23 (1.06–1.42), 1.07 (1.06–1.08), 1.17 (1.14–1.19) and 1.43 (1.16–1.77) for Group II vs. Group I, age, BMI and drinking status, respectively. The ORs (95%CIs) for prevalence of CVD was also significant difference after additional adjustment for insulin resistance, vegetable and fruit intake in a subgroup of individuals.
Conclusions: In individuals with both FPG and 2hPG within normoglycemic range, high 2hPG was significantly associated with insulin resistance and increased risk of CVD. Studies are warranted to evaluate the causal relevance of these findings.

PA-27
The correlation of diabetic status, ischemic and atrophic burdens and cognitive decline in diabetic patients with cognitive impairment

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Background: Although the increasing number of clinical researches about diabetes and cognition, many limitations and debates have been exposed and yet revealed little. Also the contribution of Alzheimer-type and/or vascular pathology to cognitive declines has been remained unclear. The aim of this study was to evaluate the contributing factors correlated with cognitive declines in selected diabetic patients with cognitive impairments prospectively.
Methods: After interviewing 286 diabetic patients using dementia screening questionnaire in their 7thdecades, we enrolled 49 subjects who have cognitive impairment (age = 64.76 ± 3.27 (61–70), M:F = 26:23, education = 7.74 ± 4.53 years, K-MMSE = 25.37 ± 3.92, MoCA = 18.24 ± 4.69). Korean version mini-mental status examination (K-MMSE), MoCA and several laboratory examination of diabetes and lipid were tested and repeated after 6 and 12 months. All subjects were performed Brain MRI and scored visually focusing ischemia and atrophy.
Results: The fluctuation index of fasting blood glucose (FBS) and glycosylated hemoglobin (HbA1c) were negatively correlated with cognitive change (p = 0.01, p = 0.02). And low density lipoprotein (LDL) level was negatively correlated with cognitive change (p = 0.02) but high density lipoprotein (HDL) was positively (p = 0.03). MRI factors focusing on white matter hyperintensities and medial temporal atrophy are not significantly correlated with cognitive declines.
Conclusions: We concluded the fluctuation rather than mean value of blood glucose level are the possible predictor of cognitive declines in diabetic patients and suggested management strategy. There is a need for larger, quantitative, clinical-neuroimaging studies to improve knowledge of the complex contributions by vascular and Alzheimer pathologies in diabetic patients.

PA-28
Relationship between glycated albumin and glycated hemoglobin according to glucose tolerance status: A multicenter study

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Aims: To determine the relationship between glycated albumin (GA) and glycated hemoglobin (HbA1c) and to explore the association of glycated albumin/glycated hemoglobin (GA/HbA1c) ratio with glucose indices in Chinese subjects with different glucose tolerance status.
Methods: The hospital-based, cross-sectional study involved 953 participants without known diabetes from 11 centers in China. Oral glucose tolerance test (OGTT) was used to identify three groups of subjects: normal glucose regulation (n = 194), impaired glucose regulation (n = 303) and newly diagnosed type 2 diabetes group (n = 456). The GA, HbA1c and GA/HbA1c ratio were tested.
Results: GA was positively correlated with HbA1c (r = 0.832, P < 0.001). After correcting for age, sex and BMI, the correlations remained significant (r = 0.824, P < 0.001). Linear regression analysis estimated that a 1% increase of HbA1c was associated with a 2.84% increase of GA (GA = 2.843 × HbA1c–0.203; R2 = 0.692, P < 0.001). GA would be 18.3 (16.7–19.9) % and 19.7 (18.0–21.4) % with HbA1c of 6.5% (48 mmol/mol) and 7.0% (53 mmol/mol). The mean GA/HbA1c ratio was 2.81 ± 0.38, and it significantly increased with the presence of glucose intolerance (all, P < 0.05). In the total study population, GA/HbA1c was correlated with BMI, glucose levels and 30-min insulin during OGTT, the homeostatic model assessment of beta-cell function (HOMA-beta), and ΔI30/ΔG30 (all, P < 0.05). Increased glucose at 30 min (standardized beta = 0.221, P < 0.001), and decreased BMI (standardized beta = –0.114, P = 0.008) were associated with elevated GA/HbA1c ratio by multiple linear regression (adjusted R2 = 0.045).
Conclusions: The relationship between GA and HbA1c was strong. The GA/HbA1c ratio was related to acute postprandial glucose excursion and BMI level.

PA-29

Optimization of diabetes screening and diabetes risk assessment in Australian community pharmacy settings: Current evidence and future directions

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Many studies have shown that a quarter to one half of type 2 diabetes mellitus (T2DM) cases were undiagnosed in various Australian populations. Strict control and management of T2DM can delay onset of complications. Additionally, 5–10% of people with impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) progress to T2DM annually. Studies from different parts of the world have demonstrated that lifestyle modification interventions can prevent T2DM in people with IFG/IGT. Thus, early detection of T2DM, IFG and IGT is crucial in achieving long-term health benefit.

Previous research demonstrated that risk factor questionnaires followed by point of care (POC) capillary blood glucose testing in pharmacies was a superior screening strategy to that using risk assessment as a stand alone test. When biomedical profile data from three population surveys in rural south-eastern Australia were analysed using risk categories determined by the subsequently validated Australian Type 2 Diabetes Risk Assessment Tool (AUSDRISK), results indicated cut-off at AUSDRISK >=12 alone for entry to lifestyle modification intervention was too relaxed and therefore resulted in less impact on T2DM risk reduction. Although questionnaires such as AUSDRISK are inexpensive and rapid tools to screen for people at risk of diabetes, their use in conjunction with blood glucose tests or glycated haemoglobin has been recommended to improve intervention effectiveness and cost-effectiveness.

Similar findings were shown in the Melbourne Diabetes Prevention Study (MDPS), an effectiveness RCT linked to a state-wide translational diabetes prevention program (Life!) in Victoria, Australia. Eligible MDPS participants were individuals aged 50–75 with AUDSRISK >=15 and 80% of trial participants were recruited through community pharmacies. Participants randomised to the intervention arm received one individual and five structured group sessions, while the control group received usual care. The MDPS results showed modest reductions in weight (−1.13 kg) and waist (−1.35 cm) in the intervention group, due to the challenge in recruiting high-risk individuals using screening questionnaires alone, as well as the abbreviated intervention offered to individuals at low risk of progression to diabetes.

As a convenient blood test with less intra-individual variance, HbA1c has been recommended by the American Diabetes Association to be used for T2DM diagnosis. Future research should explore sequential testing by risk assessment tools followed with point of contact capillary HbA1c test, to examine the impact of community pharmacy-based screening and referral for diabetes and IFG/IGT to reduce the burden of T2DM.

PA-30

Partnering with general practitioners to improve access of diabetes education for patients and caregivers

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Background: In Singapore, 25.4% of patients with Type 2 diabetes exhibit poor glycemic control with HbA1c value at an unacceptable range of >8%. Patients with diabetes seek primary care consultation at their neighborhood general practitioners (GP) clinics have limited access to diabetes education services.

Aims: Partner with general practitioners to Improve access of diabetes education for patients and caregivers

Methodology: The Association of Diabetes Educators (Singapore) (ADES) collaborated with the GPs who were supportive of diabetes education to arrange their patients and caregivers to attend diabetes nurse educators' (DNE) service at their clinics. The iControl Diabetes Program was set up and supported a team of ADES members to provide diabetes education reaching out to the GPs' patients and caregivers. Examples of education topics provided were understanding of diabetes and its targets of control, self- management of blood glucose, self-injection, foot care, and others.

A total of 3 diabetes education sessions per patient were planned over a period of 3–6 months. The GPs identified patients for either individual or group education. The DNEs were notified by program leader of the date, time and location of GP clinics to support. The same DNE supported the same GP's patients/caregivers for next 3 visits. The DNE updated GPs or clinic assistants of activity of patient education sessions accordingly.

Results: 3 GPs attended the pre-iControl meeting with DNEs. 6 GPs were recruited for iControl Diabetes Program through program coordinator. 18 patients with caregivers (patient: N: 16; caregivers: 2) attended DNE sessions. 70% (N: 11) were Chinese patients. The age of patients ranged from 39 to 75 years old. The last HbA1c values of GP patients reported were range from 5.3% to 10.6%; POCT random blood glucose tested were range from 5.6 mmol/dL to 18.7 mmol/dL. 8 patients and caregivers attended group sessions and 9 attended individual sessions. 3 patients were taught/reviewed on injection techniques; 6 patients were taught with return demonstration on use of home glucose monitoring; 7 patients received foot examination with monofilament; all patients were informed of target glucose control, effects of medication and diet control.

Conclusion: The program achieved its purpose to provide accessibility of GP patients for DNE's service to address their diabetes care and concerns. The sustainability of this program would largely depend on the GPs' interests and effort to support their patients for diabetes education.

PA-31

Serum vascular adhesion protein-1 is associated with obesity and predicts incident diabetes

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Objective: Vascular adhesion protein-1 (VAP-1) is involved in the pathogenesis of diabetic complications. Physiologically, VAP-1 enhances glucose uptake in skeletal muscle and adipocytes. Secreted VAP-1 can act as an endocrine or paracrine hormone to induce glucose uptake in liver tissue. Since the role of secreted VAP-1 in obesity and diabetes remains unknown in human, we investigated the relationship of serum VAP-1 (sVAP-1), obesity, and incident diabetes in this cohort study.

Research design and methods: From 2006 to 2012, 600 subjects without diabetes from Taiwan Lifestyle Study were included and followed regularly. Diabetes was diagnosed by an oral glucose tolerance test. Abdominal fat areas were measured by abdominal computed tomography and sVAP-1 was analyzed by ELISA.

Results: sVAP-1 was associated negatively with body mass index (BMI, r = –0.1449, p = 0.003), waist circumference (r = –0.1425, p = 0.004), visceral (r = –0.1457, p = 0.003) and subcutaneous (r = –0.1025, p = 0.035) abdominal fat areas, and serum C-reactive protein (r = –0.2035, p < 0.0001), and positively with plasma adiponectin (r = 0.2086, p < 0.0001) and aldosterone (r = 0.1018, p = 0.041), adjusted for age and gender. After 4.7 ± 2.6 years, 73 subjects (12.2%) developed incident diabetes. Subjects with sVAP-1 in the highest tertile showed the lowest incidence of diabetes, adjusted for age and gender. Every 1 standard deviation increase in sVAP-1 was associated with a 34% decrease in the risk of incident diabetes (HR = 0.66, 95% CI = 0.5–0.88, p < 0.01), adjusted for age, gender, BMI, family history of diabetes, hemoglobin A1c, HOMA2%B, and HOMA2-IR.
Conclusions: Serum VAP-1 is associated with obesity negatively. High sVAP-1 predicts a lower incidence of diabetes in human.

PA-32
Vegetarian diet lowers the incidence of diabetes in a Taiwanese Buddhist population

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Objective: Vegetarian diet has been shown to reduce risk of diabetes in Western populations, but its impact on high risk Asians is unknown.
Aim: To examine the effect of vegetarian diet on occurrence of diabetes within a prospective cohort study.
Methods: We followed 2568 non-smoking, non-alcohol drinking Buddhists free of diabetes at baseline. All participants completed a validated food frequency questionnaire in addition to having fasting blood glucose tested at baseline. Dietary pattern, fasting glucose, and HbA1C were assessed at follow-up. Multiple logistic regression was used to assess the effect of diet on diabetes, adjusting for age, gender, education, family history of diabetes and BMI.
Results: In the 5 years of follow-up, 222 new cases of diabetes were identified. 991 vegetarians and 907 non-vegetarians stayed consistent with their diet pattern, while 74 baseline vegetarians reverted to non-vegetarians (the reverted), 596 non-vegetarians converted to vegetarians (the converted). We found lower risk of diabetes in consistent vegetarians (OR: 0.66, 95% CI: 0.48, 0.93) and the converted (OR: 0.59, 95% CI: 0.39, 0.88), compared with consistent non-vegetarians.
Conclusion: Taiwanese vegetarian diet is associated with lower risk for diabetes, independent of BMI.

PA-33
The effect of Medical Nutrition Therapy on metabolic risks patients

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Objective: Metabolic syndrome is a group of risk factors for cardiovascular disease and other health problems, such as diabetes and stroke. The aim of study is evaluate the effect of Medical Nutrition Therapy (MNT) in metabolic risks patients.
Methods: This study recruited sixty-eight metabolic risks patients who regular follow-up in outpatient service and received 2 times of MNT within 11 months. Body weight, waist circumference, fasting glucose, lipid profile were assessed. We analyzed the body position and fasting glucose and lipid profile through before and after intervention.
Results: The results showed the participants of men and women were 25% and 75% and the mean age was 57.3 ± 9.98 yr and 57.9 ± 9.35 yr respectively. Regular exercise more than 30 minutes and over five times a week was twenty-two people (33%), three to five times a week was twelve people (18%). After MNT intervention, the women group diastolic blood pressure (form 81.91 ± 3.24 mmHg decreased to 75.11 ± 5.01 mmHg), fasting glucose (form 108.96 ± 9.03 mg/dL decreased to 103.06 ± 11.68 mg/dL), cholesterol (form 227.84 ± 24.89 mg/dL decreased to 194.75 ± 12.97 mg/dL), triglyceride (form 225.12 ± 120.36 mg/dL decreased to 145.07 ± 78 mg/dL),low- density lipoprotein (form 39.18 ± 11.14 mg/dL decreased to 53.8 ± 9.26 mg/dL), and high- density lipoprotein (form 39.18 ± 11.14 mg/dL increased to 53.8 ± 9.26 mg/dL) were significant (p < 0.05).
Conclusion: To conclusion, the MNT intervention could improve the fasting glucose, diastolic blood pressure and lipid profile in women group in our study patients.

PA-35
Matsuda index and clinical indicators of insulin resistance in obese children and adolescents. Is there a correlation?

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Background: Obesity-related insulin resistance is present in obese children and Matsuda index is a method proposed to evaluate insulin resistance, using data obtained from the oral glucose tolerance test (OGTT). Early detection of children who are at risk is important.
Objective and hypotheses: To evaluate the prevalence of insulin resistance, as calculated by the Matsuda index, in children with family history of obesity and/or Type II diabetes, acanthosis nigricans and increased waist circumference and to investigate whether they could be used as selection markers for patients to undergo OGTT. Moreover, to estimate the correlation of insulin resistance with the coexistence of metabolic syndrome.
Methods: Data from 95 overweight and obese children (47 boys and 48 girls) with mean age 10.7 ± 2.2 years were analyzed. Student's t-tests were used for the comparison of means and Pearson correlation coefficients were used to explore the association of two continuous variables.
Results: Insulin resistance was found in 39.1% of the children, while the mean MATSUDA index was 3.4 (SD = 1.9). Also, the Mean Area Under the Curve (AUC) for glucose was 14211.3 (SD = 2016.5) and the mean AUC for insulin was 13484.2 (SD = 11985.3). A negative correlation of Matsuda index with TSH (r = –0.33, p = 0.003), total cholesterol (r = –0.25, p = 0.030), triglycerides (r = –0.44, p < 0.001) and LDL levels (r = –0.34, p = 0.005), as well as with HOMA index (r = –0.55, p < 0,001) was found. Moreover, the mean Matsuda index was 2.64 in cases with acanthosis nigricans (p = 0.007). Additionally, Matsuda index was significantly correlated with waist circumference (r = –0.40, p = 0.006). Furthermore, Matsuda index was lower in those with metabolic syndrome and in puberty. There was no sex difference regarding insulin resistance, while it was greater in puberty. AUC for glucose was not different according to the existence of metabolic syndrome and acanthosis nigricans, in contrast with AUC for insulin that was significantly greater in cases with acanthosis nigricans (p = 0.007) or metabolic syndrome (p = 0.006). Waist circumference was also predictive for AUC for insulin (r = 0.30, p = 0.044).
Conclusion: The clinical indicators of family history of obesity and diabetes, the presence of acanthosis nigricans and

increased waist circumference are associated with insulin resistance as measured by the Matsuda index and can be used as clinical markers to indicate that a patient should undergo OGTT. In addition, increased insulin sensitivity is associated with better metabolic profile as reflected by lower levels of triglycerides, LDL and higher HDL.

PA-36

Reduced complexity of glucose dynamics is associated with poor control patients among patients with type 2 diabetes

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Chronic sustained hyperglycemia has been shown to play an important role in the formation of diabetic complications. However, emerging evidences have suggested that acute fluctuating hyperglycemia contribute to these complications. Continuous glucose monitoring system (CGMS) is a useful tool to monitor the blood glucose fluctuation in diabetes. Complexity index (CI) derived from multiscale entropy (MSE) analysis has recently been shown to be a new parameter for the evaluation of blood glucose fluctuation in patients with diabetes receiving CGMS recording. In addition, the diabetic patients revealed a significant decrease in the MSE CI compared with the control subjects, indicating a decreased complexity of glucose dynamics in the diabetic patients. No study has investigated the MSE analysis among moderate and poor control diabetes. This study was designed to compare the complexity of glucose dynamics between moderate and poor control type 2 diabetes (T2D). Twenty moderate control and 25 age- and BMI-matched poor control patients with T2D were evaluated retrospectively from CGMS data recorded in a teaching hospital. Compared with moderate control patients, the poor control patients revealed a significant increase ($P < 0.05$) in the mean (poor control 190.7 ± 5.8 vs. moderate control 160.0 ± 6.2 mg/dL), the standard deviation (58.3 ± 2.7 vs. 46.3 ± 3.1 mg/dL), and the mean amplitude of glycemic excursions (138.4 ± 6.9 vs. 114.0 ± 6.9 mg/dL); and a significant decrease ($P < 0.05$) in the MSE CI (4.85 ± 0.23 vs. 5.45 ± 0.22). In conclusion, these findings show that the poor control diabetic patients manifest a greater fluctuating blood glucose profile and an increased regularity of blood glucose fluctuating pattern compared with the moderate control diabetic patients. Moreover, MSE CI could potentially be used as a biomarker in the monitoring of diabetes.

PA-37

The effect of medical nutrition therapy in diabetic patients with early chronic kidney disease

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Introduction: Diabetic nephropathy is a diabetic complication characterized by albuminuria, increased blood pressure and a relentless decline in renal function. It is the fourth leading cause of death in Taiwan. The aim of this study is evaluate the effect of medical nutrition therapy (MNT) in diabetic patients with early chronic kidney disease.
Methods: A total of one hundred eighteen diabetic patients with early CKD received MNT were included. Patients were divided into two groups: (1) <65 years and (2) ≧65 years. Data including weight, blood pressure, glomerular filtration rate (eGFR), serum creatinine, LDL, HbA1c and microalbuminuria were analyzed by retrospective review of the medical records. All patients were at least received MNT and followed up four times.
Results: There were significantly reductions in body weight ($P = 0.022$) and systolic blood pressure ($P = 0.050$) in all patients but not significant differences in microalbuminuria, serum creatinine and eGFR. There is also significant reduce in HbA1c ($P = 0.032$) of <65 year-old patient group.
Conclusion: Our study showed that MNT for diabetic patient with early CKD can improve body weight and systolic blood pressure in our study patients.

Diabetes Management: Gene and Environment

PB-01

Two-year efficacy and safety of moderately-low-carbohydrate diet

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Recently, many scientific organizations recommend moderately low-carbohydrate diet (MLCD) (Diabetes Care 2013) (Lancet 2014). In East-Asian population, we first reported the efficacy of MLCD in randomized controlled trial (Intern Med 2014). In this study, we assessed the 2 year efficacy and safety of MLCD (70–130 g/d) in Japanese type 2 diabetes. Two hundred type 2 diabetic patients who were advised MLCD were enrolled and 160 patients were followed for 2 years (drop-out 23, move 14, death 3). Glycemic control, body mass index (BMI), lipid profiles, liver enzymes and dose of antidiabetic drugs were assessed at baseline and after 2 years. During the 2-year follow-up period, HbA1c levels were significantly improved (baseline: 8.0 ± 1.5%, 2-year: 7.4 ± 1.2%, $p < 0.0001$), and ALT also decreased significantly (baseline: 30.1 ± 23.4 mg/dL, 2-year: 25.2 ± 18.6 mg/dL, $p = 0.003$). Body weight, LDL-C, TG, HDL-C, AST, SBP, and DBP showed non-significant improvement. UA (baseline: 5.8 ± 1.5 mg/dL, 2-year: 5.8 ± 1.4 mg/dL) and Cr (baseline: 0.8 ± 0.2 mg/dL, 2-year: 0.8 ± 0.2 mg/dL) did not change and UN slightly increased (baseline: 15.9 ± 5.2 mg/dL, 2-year: 17.0 ± 5.4 mg/dL, $p < 0.05$). Our results suggest long-term efficacy and safety of MLCD in East-Asian population.

PB-02

Comparison of epidemiological, clinical, laboratory and radiological features of diabetic and non-diabetic patients with pulmonary tuberculosis at Calmette Hospital, Cambodia

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Background: As the global prevalence of diabetes mellitus (DM) increases, especially in low-to-middle income countries such as Cambodia where tuberculosis (TB) remains endemic, we will encounter a growing number of TB patients with DM. Diabetes mellitus (DM) due to suppressive effect on cellular immunity can impact on progression of tuberculosis (TB).
Objectives: The aim of this study was to investigate the impact of DM on the epidemiological, clinical, and biological and chest x-ray of pulmonary TB patients.
Patients and methods: In this retrospective study, the informations of 120 admitted pulmonary TB patients with BK (+) in Medicine A and A4 ward of Calmette hospital in Phnom Penh from 1st January 2014 to 31st December 2015 were extracted from their medical files. The patients were divided into two groups as TB with DM (n = 56) and TB without DM (n = 64). The related data on epidemiology, signs, symptoms, biological tests, radiology and sputum smear or bronchoaveolar lavage

fluid examination in both groups were compared in STATA by using chi squared test and t-test.
Results: The mean age of TB with DM is higher than TB only (63.07 ± 13.85 vs. 54 ± 19.41 p 0.04). The Epidemiological Features and clinical signs and symptoms are similar in both groups. In diabetic group the sputum smear is positive in 64.29% while in non-diabetic group it is positive in 45.31%, which is statistically significant (p 0.04). There is no statistically difference in radiological features. And it is noted in our study most of diabetic patients are not well controlled.
Conclusions: Epidemiological, clinical and radiological features of pulmonary tuberculosis in both diabetic and non-diabetic patients are similar. The rate of sputum smear positivity in TB with DM is higher than TB without DM. The burden of diabetes mellitus is increasing worldwide. The association between diabetes and tuberculosis is the next challenge for global tuberculosis control and in particular in Cambodia.

PB-03
Metabolic endotoxemia and an alterlation in the gut microbiota composition are present in Japanese type 2 diabetes
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Recently the potential role of the gut microbiota and metabolic disorders such as obesity or type 2 diabetes has been intensively explored. Endotoxemia, a process resulting from translocation of lipopolysaccharides (LPS) of gram-negative intestinal bacteria is related to low grade inflammation associated with insulin resistance or diabetes. Data on Japanese are scarce and may be different from those of Western subjects because of the ethnicity and dietary habit. In the present study, we examined LPS-binding protein (LBP) in Japanese type 2 diabetes and investigated the relationships between LBP and various clinical indices. We also valued fecal microbiota by 16SrRNA sequence analysis.
Fifty-two consecutive type 2 diabetes patients were recruited. The exclusion criteria were those with acute illness, malignancy or pregnancy. Patients taking antibiotics or alfa-glucosidase inhibitors were also excluded. The blood samples were obtained after overnight fast. The plasma level of LBP was measured by human LBP ELISA kit (Hycult Biotech, Netherland). The average age (±SD) was 50 ± 10, BMI, 28 ± 4.4, HbA1c, 6.9 ± 1.2(%), respectively. The duration of diabetes was 7 ± 8 years. Thirty Japanese healthy adults with no history of diabetes were recruited as control subjects.
The mean LBP level was 12.3 ± 1.9 ug/mL, which was significantly higher compared to that of control subjects. LBP was positively correlated with BMI ($p < 0.001$), HbA1c ($p < 0.001$), FBS ($p < 0.001$), TG ($p < 0.05$) and ALT ($p < 0.001$), but was not associated with LDL-C.
The counts of the Bifidobacteriaceae, Clostridiales incertae sedis XIV, and Peptostreptococcaceae were significantly lower ($p < 0.05$), while the counts of the Enterobacteriaceae and Vellonellaceae were significantly higher ($p < 0.05$) in fecal samples of diabetic patients than in those of control subjects. Changes in the composition of microbiota were correlated with metabolic marker.
In conclusion, Japanese obese type 2 diabetes had metabolic end toxemia.
The next step in this research protocol is to perform interventional studies to investigate whether improvement of gut dysbiosis by the administration of probiotics or prebiotics can reduce the levels of circulatory inflammation markers and the microbiota diversity, with improvement of glycemic control. Double blind randomized intervention trial (UMIN00001234) is to be undertaken.

PB-06
High glucose induces human endothelial dysfunction through an Axl-dependent mechanism
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Background: The receptor tyrosine kinase Axl and its ligand growth arrest-specific protein 6 (Gas6) are involved in the diabetic vascular disease. The aim of this study was to explore the role of Gas6/Axl system in high glucose (HG)-induced endothelial dysfunction.
Methods: We investigated the effect of various glucose concentrations on Axl signaling in human microvascular endothelial cells (HMEC-1 s).
Results: Human plasma Gas6 value inversely correlated with glucose status, endothelial markers. HG decreased Gas6/Axl expression and increased intercellular adhesion molecule-1 (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) expression in HMEC-1 s. HG significantly decreased HMEC-1 s cell viability and tube formation and promoted monocyte-EC adhesion. Down-regulation of Akt phosphorylation was found in HG culture. Axl transfection significantly reversed HG-induced Akt phosphorylation, VCAM-1 expression and endothelial dysfunction. We also found additive changes in Axl-shRNA-infected HMEC-1 cells in HG culture. Furthermore, Axl overexpression in HMEC-1 s significantly reversed HG-induced vascular endothelial growth factor (VEGF) and VEGF receptor 2 (VEGFR2) expression. In addition, significantly lower Axl and VEGFR2 expression in arteries were found in diabetic patients as compared with non-diabetic patients.
Conclusions: This study demonstrates that HG can alter Gas6/Axl signaling and may through Akt and VEGF/VEGFR2 downstream molecules and suggests that Gas6/Axl may involve in HG-induced EC dysfunction.

PB-07
Mitochondrial diabetes associated with tRNA Leu (UUR) mutation at position 3271 and two times of GAD antibody negative conversion
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The proband has been followed up as a patient of mitchondrial diabetes associated with tRNA Leu (UUR) mutation at position 3271 for over 20 years. We first reported this case in 1996. We report here that this case has had phenomena of GAD antibody positive-negative conversion two times in his life.

1. First episode:
   When he was 54 y/o, his GAD antibody became positive, glycemic control got worse. It was transient phenomena, then, GAD antibody became negative and glycemic control improved. The etiology was unknown. To our knowledge, only seven cases were reported as mitochondrial diabetes having GAD antibody. However, among them, this case is the first as having negatively-converted GAD with insulin independent state.
   When we started sitaglipitin, DPP4-inhibitor, 50 mg/day and observed 9 months, HbA1c improved remarkably and oral glucose tolerance test showed increase of early phase insulin secretion and suppression of postprandial hyperglycemia.

2. Second episode:
   When he was 59 y/o, his GAD antibody became positive after the start of 6 months of SGLT2 inhibitor treatment. In addition, Serum amylase was elevated together with rise of CA19-9, elastase-I, lipase, tripsin and IgG4. The reassessment of the radiological diagnosis has not identified pancreatic mass as a manifestation of focal pancreatitis. Because of high IgG4, he was tentatively diagnosed as having had autoimmune pancreatitis (AIP).
3. Discrepancy:
   Interestingly, during the first episode, glycemic control got abruptly worse according to the elevation of GAD antibody titer. GAD antibody titer and HbA1c elevation had seemingly close relationship. In contrast, during the second episode, glycemic control was stable, seemingly having no relationship between GAD antibody titer and HbA1c level. While the difference of two times episodes was apparent, true aetiology was unknown.
   In conclusion, this is the first case report of mitochondrial diabetes, in which GAD antibodies were detected once positive and soon after became negative two times in life. The aetiology and pathophysiology are not fully elucidated.

PB-08

Evaluation of the web-based nutritional management program for pregnant women with diabetes mellitus

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Objective: This study aimed to evaluate the effectiveness of the web-based nutritional management program by applying to pregnant women with gestational diabetes (GDM) and type 2 diabetes mellitus (T2DM).
Methods: From June 2008 to May 2010, 96 pregnant women with GDM and T2DM were included. At entrance they were instructed to record their dietary intake using the 24-hour recall method and then received nutritional education by dietitian. Since then, they had received well designed management by the web-based program for 4 weeks. Weekly nutritional intake status was assessed using data they recorded meal diary in the web-based program. Repeated measures ANOVA were performed to compare the change of intake level.
Results: At entrance, mean weeks of gestation and energy intakes were 26.4, 12.3 weeks and 1590.7, 1620.6 kcal in the GDM and T2DM group, respectively and carbohydrate intakes compared with total calorie were highly presented in both group. After applying the web-based program for 4 weeks, the percentages of total energy from carbohydrate were decreased significantly (from 57.2% to 50.2% in GDM and from 63.7% to 51.6% in T2DM group) with increasing protein and fat intakes close to recommended levels. Also, weight management especially in the overweight/obese subjects was improved.
Conclusion: This study showed that an effective management of nutrition intake and weight control for pregnant women with GDM and T2DM will be available by using the web-based nutritional management program and it is expected to influence positively for decrease of the maternal and fetal complications.

PB-09

Study of frailty prevalence and status of elder diabetic patients in a primary care clinic

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Background: Frailty is characterized by multi-system decline and vulnerability to adverse health outcomes. Elder diabetic patients were considered to have high risk of frailty. The goal of this study was to analyze the frailty prevalence and status of those elder diabetic patients.
Methods: This pilot study was conducted in a local diabetes clinic located at Yilan County, Taiwan. A total of 181 patients aged 65 years or older were selected by randomly systematic sampling from August to December in 2015. Frailty was measured by the Chinese version of Tilburg Frailty Indicator (TFI) including 15 items. When total score was 5 or greater, they were determined to have frailty. Other baseline characteristics were evaluated by Activities of Daily Living (ADLs) scales, instrumental ADL scale, Taiwan Geriatric Depression Scale, Mini-Mental State Examination, demographic datum, and clinical parameters.
Results: 181 elder diabetic patients were included in this study. Participants' average age was 74.3 ± 5.8 years old, and the mean DM duration was 15.0 ± 9.2 years. 58.0% were male. The average A1C and BMI were 7.1 ± 1.1% and 25.3 ± 3.9 kg/m^2, respectively. Hypertension (66.3%), hyperlipidemia (72.9%), diabetic nephropathy (56.4%), retinopathy (16.0%), neuropathy (4.4%), and stroke (3.9%) were reported. The average disease number of those patients was 2.7 ± 1.5. Those patients used 3.2 ± 1.7 types of medicine. The self-reported frequency of fall and hypoglycemia of those patients were 0.6 ± 1.2 and 1.7 ± 5.2 in the past year, respectively. The frailty prevalence rate for all participants was 32.0%, for male was 27.6% and for female was 38.2%. The age-specific frailty prevalence rates were 22.9%, 40.8%, and 55.6%, for 65–74.9, 75–84.9, and ≥85 y/o respectively and significantly different among age groups ($\chi 2 = 8.63$, $p = 0.013$). Compared to patients without frailty, patients with frailty had significantly higher percentage of stroke and fall, worse physical function, higher depressive level, and worse cognitive impairment.
Conclusions: The frailty prevalence was determined to be 32.0% by TFI in a local primary care clinic. The prevalence increased with age. Patients with frailty had higher percentage of stroke and fall. They also had worse physical function, higher depressive level, and worse cognitive impairment than those patients with no frailty. More patients will be involved to verify related factors of causing frailty of elder diabetic patients in future studies.

PB-10

Association study of WFS1 rs10010131 and type 2 diabetes microvascular complication in a Chinese population

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Objective: Genome-wide association studies found WFS1 rs10010131 was associated with type 2 diabetes by affecting beta cell function. Diabetic nephropathy (DN) and diabetic retinopathy (DR) are both the common microvascular complications. Besides poor blood glucose control and long duration of the disease, genetic factors do predispose to diabetic nephropathy and retinopathy. The aim of the study is to investigate the association of WFS1 rs10010131 and diabetic nephropathy and diabetic retinopathy in the Chinese population.
Methods: The study was conducted in two stages. In the first stage, 1251 individuals with type 2 diabetes were recruited and stratified into 4 groups: 313 with diabetic retinopathy but without diabetic nephropathy, 419 with nephropathy but without retinopathy, 281 with both retinopathy and nephropathy, and 238 with diabetes of ≥10 years duration but without microvascular complications. In the second stage,

594 individuals with diabetes were recruited, including 201 with diabetic retinopathy and 393 with diabetes of ≥5 years duration but without retinopathy. GCKR rs780094 genotyping was conducted with Sequenom. The diagnose and grading of diabetic retinopathy were according to fundus examination. 24-hour urinary albumin excretion rate and estimated glomerular filtration rate were used to evaluate diabetic nephropathy.

Results: In the first stage, rs10010131 was significantly associated with diabetic retinopathy (OR = 1.629, 95% CI 1.019–2.606, P = 0.0416) after adjusting for duration of diabetes, HbA1c, blood pressure and body mass index. However, rs10010131 did not show association with Diabetic nephropathy (OR = 0.991, 95% CI 0.619–1.586, P = 0.970). In the second stage, no significant association of rs10010131 and DR was observed (OR = 0.837, 95% CI 0.408–1.716, P = 0.627). The meta-analysis showed that rs10010131 was not significantly associated with DR (OR = 1.334, 95% CI 0.901–1.977, P = 0.150).

Conclusion: WFS1 rs10010131 was not associated with diabetic nephropathy and diabetic retinopathy in the Chinese individuals with type 2 diabetes.

PB-11

In type 2 diabetes, smoking cessation is associated with deterioration in glycemic control and this is unrelated to weight gain

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Background/aims: Diabetes mellitus (DM) are closely associated with the development of cardiovascular diseases. Smoking represents one of the most important preventable risk factors for the development of atherosclerosis. In patients with DM, smoking works synergistically in increasing the risk of cardiovascular events and death.

There are some studies suggesting that diabetes control deteriorates temporarily during the first year after smoking quitting. The aims of this study were to examine whether or not quitting smoking was associated with altered diabetes control, and whether or not this association was mediated by weight change.

Patients and methods: From May 2010 to October 2014, we recruited 131 patients on medication for DM and in hope to use Varenicline for smoking cessation at the Institute for Adult Diseases, Asahi Life Foundation. Physical examinations and blood samples were taken on the day of starting administration, and every two weeks thereafter. Varenicline were administered for three months. All patients gave informed written consent. We investigated the association between a quit event, smoking abstinence duration, change in HbA1c, and the mediating effect of weight change.

Results: 97 (74.0%) quit smoking and remained abstinent for at least 1 year. The majority (89.7%) was male and the median body mass index (BMI) was 24.2 kg/m^2 (IQR 21.8–26.9).

BMI and HbA1c level showed a significant increase during smoking cessation. But this increase in HbA1c was not mediated by weight change. The changes in HbA1c during smoking cessation were not correlated with the changes in BMI, and HbA1c level increased in 75.0% of patients who decreased BMI during smoking cessation. In patients who were treated with insulin, HbA1c level increased higher than in those who were treated with oral drugs only. Patients who increased BMI during smoking cessation gained significantly more weight within the first year after quitting than those who decreased BMI during smoking cessation.

Spearman's rank correlation revealed that the white blood cell count and neutrophil to lymphocyte ratio (NLR) significantly improved immediately after smoking cessation. High-density lipoprotein cholesterol levels increased after smoking cessation, although BMI also significantly increased.

Conclusions: In type 2 diabetes, smoking cessation is associated with deterioration in glycemic control and this is unrelated to weight gain, although smoking cessation significantly and immediately decreased systemic inflammation and increased serum HDL cholesterol level in diabetic patients.

PB-12

New findings of genetic determinants of sulfonylurea efficacy from next-generation sequencing in sulfonylurea sensitive patients

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Background: The genetic determinants for sulfonylureas efficacy has not been well understood until now.

Methods: This pharmacogenetic study was divided into three stages. In the First stage, we screened a total of 747 patients with type 2 diabetes enrolled from the Xiaoke Pills Clinical Trial to select patients with extreme phenotype. We regarded "very sensitive to sulfonylurea" as an extreme phenotype, including two conditions (1) sulfonylurea treatment best responders: HbA1c level was decreased by more than 1%, and body weight increased by more than 5% during the first three months of follow up. (2) hypoglycemia occurred so frequently that the dose of glybeclamide was 1.25 mg/d during the whole follow up period as initial dose or the patient lost follow up because of hypoglycemia. In the second stage, next-generation sequencing was performed in patients with extreme phenotype. Variants with prediction of harmful were selected and validated by first-generation sequencing and re-sequenced them in subjects with normal glucose metabolism. In the third stage, we did case-control study in 340 patients treated with glybenclamide to investigate if the selected variants could really influence sulfonylurea efficacy.

Results: We selected 32 "sulfonylurea very sensitive patients'. After next-generation sequencing, we selected 48 variants (39 genes), which seem to be harmful in prediction. Then 26 variants were successfully validated by first-generation sequencing and were re-sequenced in 20 normal glucose metabolism subjects to compare genotype between patients and controls. The genotypes were similar between patients and normal glucose metabolism subjects, except rs56743379. Rs56743379 was an insert/delete mutation in exon 5 of DMKN gene. So we did case-control study in 340 patients treated with glybenclamide to investigate the association between rs56743379 and sulfonylurea efficacy. There were 35 (10.3%) homozygous with insert mutation (Ins group), 50 (14.7%) homozygous with delete mutation (Del group). And because there were 58 SNPs downstream to the rs56743379, including 3 SNPs hit on the same contig position of rs56743379. So we regarded 255 (75%) subjects as heterozygous with varying degrees of insert/delete mutation (Hetero group). There were no significant difference between genotypes and treatment failure of glybenclamide (OR = 1.488, 95%CI 0.937–2.361, P = 0.092). However, Logistic regression analysis showed that rs56743379 were significantly associated with proportion of patients with FPG < 7 mmol/L after adjustment of age and sex (OR = 0.630, 95% CI 0.405–0.979, P = 0.040).

Conclusions: Rs56743379 in DMKN gene may be associated with sulfonylurea efficacy. Further pharmacogenetic and functional studies are needed to confirm this observation.

PB-14

Impact of diabetes and Intercellular adhesion molecule-1 genetic polymorphism on coronary artery disease susceptibility in Taiwan

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Objectives: The aim of the study was to evaluate impact of diabetes and Intercellular adhesion molecule-1 (ICAM-1) genetic polymorphism on coronary artery disease (CAD) in patients received coronary angiography to assess the genetic risks and conventional risks.
Background: The prevention of CAD might be facilitated by identifying genes that confer susceptibility, as defined by conventional risk factors. The pathogenesis of CAD is atherosclerosis which is a chronic inflammatory disease on the vessel walls. Genetic variants in ICAM-1 gene have been shown to have association with a range of inflammatory diseases. Therefore, we conducted a study to investigate the association of the single nucleotide polymorphisms (SNPs) of ICAM-1with CAD.
Methods: The study population comprised 525 unrelated Taiwanese individuals who received elective coronary angiography in Chung Shan Medical University. Among all study subjects, 207 had diabetes mellitus, 364 individuals had hypertension, 183 had hypercholesterolemia, and 219 were active smokers. The single nucleotide polymorphismsof ICAM-1 were determined by real time-PCR and genotyping.
Results: Diabetes and other conventional risks were significantly associated with CAD. Our study showed that rs281432 (C8823G) was the only ICAM-1 SNP which affect the development of CAD. Multivariate analysis revealed that ICAM-1 SNP rs281432 CC/CG [$p = 0.016$; odds ratio (OR): 2.56, 95% confidence interval (CI): 1.19–5.56], male gender ($p = 0.018$; OR: 1.66, 95% CI: 1.09–2.51), aspirin use in the past 7 days ($p = 0.001$; OR: 2.05, 95% CI: 1.33–3.14), hypertension ($p < 0.001$; OR: 2.15, 95% CI: 1.42–3.25), serum cardiac troponin I elevation ($p < 0.001$; OR: 2.14, 95% CI: 1.47–3.24) and severe angina in recent 24 hours ($p = 0.001$; OR: 1.97, 95% CI: 1.31–2.95) increase the risk of CAD.
Conclusions: In conclusion, diabetes remains one of the strongest risks of CAD. And ICAM-1 SNP rs281432 is an independent factor to predict the development of CAD. ICAM-1 SNP rs281432 homozygotic mutant GG can reduce the susceptibility to the CAD in Taiwanese subjects. Genotyping of polymorphisms may prove informative for assessment of the risks of CAD.

PB-15

Gain of muscle strength in mitochondrial diabetes treated with SGLT2 inhibitors

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In 1996, we reported the first identified case of mitochondrial diabetes caused by a T-to-C transition at position 3271. The proband was a 58-year-old male. Heteroplasmy of the 3271 mutation, strongly maternal inheritance of diabetes and other evidences associated with mitochondrial dysfunction suggested this 3271 mutation to be pathogenic.
During a 20 year follow-up, in 2014, he received SGLT2 inhibitor (Sodium glucose transporter 2 inhibitor: SGLT2i), first ipragliflozin 50 mg/day for 6 weeks, subsequently luseogliflozin 2.5 mg/day for 4 weeks, dapagliflozin 10 mg/day for 4 weeks, tofogliflozin 20 mg/day for 2 weeks, and again dapagliflozin 10 mg/day for 4 weeks. The four different products of SGLT2i seemingly had similar effect on weight loss and the decrease of HbA1c. Then, he lost weight and attained improvement of glycemic control with HbA1c from 6.5% to 6.3%. Concurrently, the dose of glimepiride was adjusted to decrease from 6 mg to 1mg daily. Body weight decreased from 64.7 to 58.7 kg within three months (height 174 cm. BMI: from 21.4 to 19.4). These phenomena suggested that he relieved insulin resistance.
The patients with sarcopenia have been believed to suffer from loss of muscle power and frailty. Therefore, it is noteworthy that, in this patient, his grip strength (GS) and back strength (BS) got stronger despite robust weight loss. Before SGLT2i treatment, GS was 37.6 kg in right hand and 30.5 kg in left hand, respectively. BS was 82 kg. After three months of SGLT2i, GS of right hand grew stronger to 39.4 kg (+1.8 kg) and left hand to 32.2 kg (+1.7 kg). BS also grew stronger to 105 kg (+23 kg).
Thus the case provides a novel information in diabetes treatment and the role of mitochondria. Caloric restriction that reduces oxidative damage improves mitochondrial function. In our previous study, defective insulin secretion as well as insulin resistance is a salient feature of mitochondria diabetes. Reduced glucose flux in muscles with SGLT2i treatment possibly mitigates insulin resistance via decreased oxidative stress. Insulin resistance is one of risk factors of sarcopenia. Hence, the recovery of muscle strength after SGLT2i treatment in our patient is attributed to regained energy from restored mitochondria.
Conclusion: SGLT2i upon the patient of mitochondrial diabetes could induce remarkable weight loss within short time and decrease of insulin resistance, which seemingly compensated genetic deficit of mitochondrial DNA. This supports our previous published study.

PB-16

Mitochondrial diabetes and subjective hypoglycemia unawareness

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Mitochondrial diabetes (MtDM) usually lacks endocrinal insulin secretion from pancreas. Therefore, most patients are on insulin injection therapy. Hence, among MtDM, rare patients are free of insulin injection. We experienced two MtDM patients without insulin therapy, both of whom had never noticed subjective hypoglycemia.
Case 1: 26 y/o. women (at 2006). She was diagnosed as having diabetes at age 12 y/o. During 14 years observation, she never noticed hypoglycemia under sulfonylurea treatment. As examination, we injected rapid insulin to induce absolute hypoglycemia. In result, she never noticed symptoms even when the plasma glucose level became lower than 30 mg/dL. She was afterward diagnosed to have mitochondrial DNA (mitDNA) mutation at position 3243. Her detailed profile are described already (Diabetologia 47:592–3, 2004).
Case 2: 59 y/o. men (at 2018). He was diagnosed as having MtDM diabetes at age 33 y/o. During 26 years observation, he never noticed hypoglycemia. Though he was under glimepiride 6 mg daily treatment, he had never experience of hypoglycemia. His detailed profile are already described (Diabetes Care 19: 1304–1305, 1996).
Discussion: Some cases of Kearns-Sayre syndrome (KSS), resulting from a mitochondrial DNA deletion, associated with diabetes that presented with hyperosmolar hyperglycemia with minimal ketosis were reported. Some cases of MtDM and MELAS were reported with ketoacidosis in literature.
Ketone bodies are produced in liver, mainly from the oxidation of fatty acids, and exported to peripheral tissues for use as an energy source. They are particularly important for the brain, which has no other substantial non-glucose-derived energy

source. Especially, d-3-hydroxybutyrate (3OHB) is an alternative energy substrate for the brain during hypoglycemia. Therefore, we speculate that above two cases are unlikely to notice hypoglycemia, thanks to the protection of minimal ketosis, which could prevent the brain energy depletion and contribute to the unawareness of hypoglycemia.
In contrast, normal MtDM patients under insulin therapy have experience of hypoglycemia usually. We speculate that, because the capacity and limits of 3OHB to compensate cerebral glucose depletion during hypoglycemia is important for its potential clinical use, non-appropriate insulin supplemental treatment might block the ketone production from liver, which disturbs the exportation of ketone to brain for use as an energy source, thereby inducing the actually subjective hypoglycemia.
Conclusion: although only two case reports are not enough to have a robust conclusion, to confirm our speculation, further other parameters associated with subjective hypoglycemia unawareness should be considered with more number of various MtDM patients without insulin therapy.

PB-17

A case of diabetes with severe peripheral neuropathy who had negligible level of mitochondrial tRNA Leu (UUR) mutation at position 3243

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We previously reported that the mitochondrial tRNA Leu(UUR) mutation at position 3243mutation was found with higher frequency (9.8%) in diabetics with symptomatic neuropathy than in those without it (1.1%). To evaluate it, the ratio of heteroplasmy was screened among 195 type 2 diabetes patients by using the new technique. In result, mean ± SD of Log (heteroplasmy ratio %) was –1.364 ± 0.43. A diabetic patient whose heteroplasmy level was the lowest, almost negligible level (0.001%, –3.0 by Logarithm transormation).
The case was 59 y/o man with diabetes onset 41 y/o. Since age 18, he has continued to drink alcohol (half bottle of whisky) every day. After nine years of diabetes' diagnosis, he developed bilateral leg pain and foot numbness. He then had progressive weakness, wasting and sensory loss in both legs, and became unable to walk, being confined to a wheel chair.
At age 51, physical examination showed distal upper limb weakness, mild to moderate proximal and moderate to severe distal lower limb weakness. The legs were markedly wasted and weak diffusely, more severely distally. Pinprick sensation and vibration sensation were impaired below the low thigh. Tendon reflexes were absent in both arms and legs. Hands' muscles were markedly wasting and weak. Nerve conduction motor studies showed combinations of conduction slowing and block, prolongation of distal latencies. Motor nerve conduction velocity of median nerve was 8.09 m/sec and of tibial nerve was not evoked. On sural nerve biopsy, marked loss of myelinated fibers was seen on light microscopy. Proliferation of Schwann cells and degeneration like Onion Bulbs were found in electron-microscopy. Foot ulcer and gangrane often appeared. At age 62, giant lipoma appeared at neck (30 × 23 mm), a manifestation found sometimes in patients with mtDNA deletions or mutations.
This case suggests that heteroplasmy level of mtDNA mutation is not always related to the severity of diabetes polyneuropathy. Interestingly, he was a very heavy drinker. Acetaldehyde is a highly reactive and mutagenic substance, and mtDNA is 10–16 times more prone to oxidative damage than nuclear DNA. A high incidence of 4977-bp mtDNA deletion among alcoholic patients has been reported. Hence, it is plausible that he have a certain factor, such as mtDNA deletion, which prohibits the accumulation of 3243 mtDNA mutation. And, the certain factor impairs the mitochondrial function of nerves or Schwann cells, thereby developing severe peripheral neuropathy.

PB-18

A case of mitochondrial diabetes associated with 3243 bp tRNA Leu (UUR) mutation, who suffered from the rapid appearance of "mitochondriopathies"

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His diabetes was diagnosed at age 38. Although he was found to have mitochondrial diabetes associated with 3243 bp tRNA (Leu (UUR)) mutation, he had few complications despite the long duration of the disease. The heteroplasmy ratio was 10% in blood and 59% in muscle. At age 54 y/o., we reported that, despite long duration of glucose intolerance and high heteroplasmy rate in blood and muscle, he had been free from diabetic complications. Serum lactate was normal. There were no hallmarks of MELAS (mitochondrial encephalopathy, myopathy, lactic acidosis and stroke-like episodes). In this case, respiratory chain enzyme activities of mitochondria in biceps brachii muscle were over three times higher than the normal range. While ragged red fibers were found, focal cytochrome c oxidase deficiency was absent. We then speculated that he may have a compensative mechanism by up-regulating respiratory chain system activity, thereby delaying the occurrence of various complications. The details were reported previously in literature (Diabetes Res Clin Pract. 69:309–10, 2005).
However, after around 60 y/o, he noticed to suffer severe hearing loss. He gradually developed heart failure. At age 65 y/o, he suffered from severe hepatic and renal dysfunction. The acute renal-hepatic failure appeared abruptly, the rapidness of which was as like the stroke-like episode in MELAS. After several times of hospitalization, he died by unexplained progressive multisystem disorders.
Discussion: Mitochondriopathies (MCPs) are either due to sporadic or inherited mutations in nuclear or mitochondrial DNA located genes (primary MCPs), or due to exogenous factors (secondary MCPs). MCPs usually show a chronic, slowly progressive course and present with multiorgan involvement with varying onset between birth and late adulthood. Apart from well-recognized syndromes, MCP should be considered in any patient with unexplained progressive multisystem disorder. Although there is actually no specific therapy and cure for MCP, many secondary problems require specific treatment. This case suggests that the mitochondrial diabetes does not always progress step by step. Even when the associated phenomena were seemingly light in the beginning, the various systematic disorders can appear abruptly at any time.
Conclusion: Diabetologists should be aware of the high risk of progression from simple mild stage of mitochondrial diabetes into the serious stage of MCP. Because this mitochondrial diabetes case complicated few manifestation during long time, rapid worsening at the end stage was a big surprise.
We hope the increasing understanding of MCPs may further facilitate the diagnostic approach and open perspectives to future, possibly causative therapies.

PB-19

Two times elevation of CA19-9 in mitochondrial diabetes associated with tRNA (Leu) at position 3271

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We first reported a case of mitochondrial diabetes associated with a tRNA Leu(UUR) mutation (Mt-DM) at position 3271. So far, the case has shown several important findings in practice. He has a strong inheritance of type 2 diabetes but no hearing loss. His mother and ten relatives in maternal side had diabetes without hearing loss, suggesting the clear different expression from Mt-DM at position 3243 (hearing loss is often complicated).

In 2012, at age 57-y/o, within weeks of stopping smoking, CA19-9 was elevated up to 221 U/mL, five times higher than the normal value (normal: less than 37.0 U/mL). He noticed dull back pain. Some change in the lung's tissue level associated with emphysema was diagnosed as a plausible cause (FEV: 73.2% on spirometry and on CT). But, latent pancreatitis are also plausible, because he had a back pain, a sign of pancreatitis.

We started taurine treatment (3.06 g/day), which was conducted in clinical trial for mitochondrial diseases. Interestingly, after taurine treatment, back pain disappeared. And remarkable improvement of emphysema was noted functionally (FEV: improved to 83.4%). Accordingly, CA19-9 returned to be normal.

We previously reported that patients of Mt-DM at position 3243 are likely to have posttreatment painful neuropathy. Therefore, we speculate that Mt-DM is likely to cause ischaemia/reperfution damage, triggered by rapid environmental change as like rapid glycemic control or stop-smoking. Recently, at age 59 y/o. (at 2016), he suffered from autoimmune pancreatitis with elevation of CA19-9 (55.3 u/mL). After six months of sodium glucose cotransporter 2 inhibitor (SGLT2i) treatment, CA19-9 was elevated together with elevation of p-amylase, elastase I, and IgG4. Even after stopping SGLT2i treatment, CA19-9 was still high.

Thus, two times elevation of CA19-9 suggests that Mt-DM patients are likely to suffer from lung or pancreatic damage after the rapid change of environmental or habitual conditions. However, question whether these phenomena are reproducible in other Mt-DM patients remains to be a problem. Additionally, hereditary pancreatitis (HP) is a rare, heterogeneous familial disease. HP usually appears with an acute, a recurrent acute, and a chronic phase. Therefore, two times elevation of CA19-9 could be a reflection of a recurrent acute pancreatitis. The possibility of mitochondrial DNA abnormality as a cause of HP is the first finding in literature.

PB-20

Potential non-laboratory predictors of fitness and status of insulin resistance among young adult Futsal players

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Background: Futsal is a variant of association football and originated in Uruguay in 1930. The five-a-side football became popular after Uruguay won the 1930 World Cup. This study aims to assess the impacts of insulin resistance and non-laboratory predictive factors of fitness among Futsal player aged from 13 to 19 years.

Methods and materials: Futsal players under agreement of parent were divided into two groups according to the quadrant percentiles of fitness. Anthropometric measurements, serum glycated hemoglobin, insulin, fasting glucose were measured. Descriptive statistics, chi-square, independent-sample t-test, and multivariate logistic regression were performed.

Results: Forty eight participants completed the study. Comparing to low score ($\leq$25, n = 25) group, the group with score more than 25 presented male dominant (95.7 vs. 48%, $p < 0.001$), higher height (168.9 ± 6.15 vs. 161.7 ± 6.28 cm, $p < 0.001$), larger waist circumference (75.9 ± 3.93 vs. 71.2 ± 5.66 cm, $p < 0.01$), but lower body fat rate (12.6 ± 3.57 vs. 18.9 ± 8.31%, $p < 0.01$). The high score group also shown significant low levels of serum insulin (12.1 ± 5.91 vs. 17.9 ± 8.79 mg/dL, $p < 0.05$) and HOMA-IR (2.8 ± 1.44 vs. 4.2 ± 2.33, $p < 0.05$). The multiple linear regression models showed body fat rate and waist circumference to be potential predictive factors.

Conclusions: In our study, the participants with better fitness by quadrantile scoring showed more height, more waist circumference, but less body fat rate than the opposite ones. They also had lower serum insulin levels and lower insulin resistance index. Further study to define the impacts of sufficient physical activities on fitness and insulin resistance would be interesting.

PB-21

Presentation of type 2 diabetes in children and adolescents – A single centre experience

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Background: With the increasing prevalence of childhood obesity in Hong Kong, the number of prediabetes and type 2 diabetes is expected to be increased.

Objective: The study aims to describe the clinical presentation of type 2 diabetes in children and adolescents in a tertiary referral centre.

Methods: The study is a retrospective chart review of patients with type 2 diabetes followed up in our diabetes clinic from 2000 to 2014. Patients aged 18 years or less at onset of diabetes were included. Those with genetic and secondary diabetes were excluded. Demographic, socioeconomic, clinical and laboratory data at onset of diabetes were analyzed. Comorbidities included hypertension, dyslipidemia, non-alcoholic fatty liver disease, polycystic ovarian syndrome and obstructive sleep apnoea syndrome were reviewed.

Results: Total of 46 patients with type 2 diabetes were diagnosed from 2000 to 2014, with median age of 14.3 years (range 10.1–18.0 years). Median body mass index was 27.6 kg/m^2 (range 18.9–43.2 kg/m^2). Median weight-for-height standard-deviation-score was 2.564 (range –0.177 to 8.097). 65% of the patients was female and 96% of the cohort was Chinese. 46% of them lived in public housing. 83% of the cohort had either first or second degree relatives having type 2 diabetes. Majority of them were picked up by screening. But there was still 2% of the patients presented with diabetic ketoacidosis. Median haemoglobin A1c was 8.9% (range 5.3–15.5%). Although majority of them received metformin, there was 25% of the cohort required metformin plus add-on therapy. At presentation, 22% of the patients had coexisting hypertension, 15% had dyslipidemia, and 30% had non-alcoholic fatty liver disease. 17% of those who had undergone polysomnography were diagnosed with obstructive sleep apnoea

syndrome. Furthermore, 23% of the females had polycystic ovarian syndrome.
Conclusion: In our cohort, type 2 diabetes is more common in girls. Most of our patients are picked up by screening. Family history of type 2 diabetes is very common. And a significant portion of our patients already has comorbidities at diagnosis. There are limitations in our retrospective cohort study. A diabetes registry is the way forward to better understand the characteristics of type 2 diabetes in children and adolescents. Hence, a one-stop clinic for cardiometabolic health can be planned for our next generations.

PB-22

Association of glucokinase regulator genetic variant and metabolic syndrome in Taiwanese adolescents

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Background: Variants of the glucokinase regulator (GCKR) gene are associated with components of the metabolic syndrome (MetS). This study explores the association between a common variant of this gene and metabolic syndrome (MetS) and its related traits in a population of Taiwanese adolescents.
Methods: The prevalence of MetS and its components were compared between individuals (962 adolescents; 468 boys, 497 girls) with different genotypes or alleles of the GCKR rs780094 single-nucleotide polymorphism (SNP). Logistic regression analysis was performed to explore the independent roles of MetS and metabolic traits.
Results: Subjects with the T-allele had a higher prevalence of low HDL-C and MetS than did those with the C-allele ($p = 0.009$ and 0.044, respectively). Subjects with T-carrying genotypes had a higher prevalence of low HDL-C ($p = 0.028$) but a similar prevalence of MetS as compared to those with non–T-carrying genotypes. After adjusting for confounding factors, the odds ratio (OR) for low HDL-C in subjects with T-carrying genotypes was 1.64 (95% confidence interval [CI]: 1.07–2.53). Similarly, the OR for MetS prevalence in subjects with T-carrying genotypes was 2.79 (95% CI: 1.09–7.11).
Conclusions: The GCKR rs780094 polymorphism is associated with low HDL-C levels and MetS in a Taiwanese adolescent population.

PB-23

Potent anti-obesity effect of acetate; acetate may alter the expression of genes involved in beige adipogenesis in obese KK-Ay mice

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Potent anti-obesity effect of acetate; acetate may alter the expression of genes involved in beige adipogenesis in obese KK-Ay mice.
Recently, overweight and obesity rates have been increasing in Asian countries and Asians tend to have higher amounts of abdominal fat at lower body mass indexes. Carrying higher amounts of abdominal fat is associated with increasing risks of a number of health problems including insulin resistance, hypertension, dyslipidemia, impaired glucose tolerance, type 2 diabetes mellitus as well as cardiovascular diseases. Notably, recent animal experiments revealed that induction of "browning of white adipose tissue (WAT)" or "thermogenic beige adipogenesis in visceral WAT" appears as a powerful strategy to combat obesity and obesity-associated complications including insulin resistance and diabetes.
Among short-chain fatty acids (SCFAs), acetate is the most abundant end product generated by colonic fermentation of undigested carbohydrates, and it is detected in the systemic circulation. Oral administration of acetate has been reported to suppress weight gain and postprandial plasma glucose levels in rodents and human. Although several molecular mechanisms including activation of AMP-activated protein kinase (AMPK) as beneficial effects of acetate are proposed, its potential effects on the beige adipogenesis in visceral WAT has not been investigated.
In the present study, we examined the effects of acetate administration in KK-Ay mice, and show that acetate reduced food efficiency ratio, increased whole-body oxygen consumption rate, and improved glucose tolerance of KK-Ay mice. In both epididymal WAT from acetate-treated mice and differentiating 3T3-L1 preadipocytes incubated with acetate, the elevated mRNA expression of PRDM16, PGC1α and PPARα (all of which involve in the differentiation into beige adipocytes) and of beige-adipocyte selective markers TMEM26 and CD137 were observed. In differentiating 3T3-L1 preadipocytes, treatment with acetate did not increase phosphorylation of either AMPK or acetyl-CoA carboxylase, and an inhibitor of AMPK failed to inhibit acetate-induced elevations in gene expression mentioned above.
In conclusion, these observations suggest that acetate may alter the gene expression involved in thermogenic beige adipogensesis in an AMPK-independent manner in obese diabetic KK-Ay mice and may provide a potential therapeutic strategy to fight obesity.

PB-24

Low skeletal muscle mass is associated with increased mortality in postmenopausal women with type 2 diabetes mellitus

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Background: Diabetes mellitus is known to be associated with deteriorated quality of life as well as increased mortality. Previous studies have shown that low skeletal muscle mass is associated with all-cause mortality in elderly population. Although patients with type 2 diabetes are reported to have lower muscle mass of limbs than healthy people, little is known about the association between muscle mass reduction and mortality in type 2 diabetes. In this study, we thus examined the association between skeletal muscle mass index (SMI) and all-cause mortality in postmenopausal women with type 2 diabetes mellitus.
Methods: This is a historical cohort study with the end-point of all-cause mortality in postmenopausal women with type 2 diabetes. We recruited 141 postmenopausal women with type 2 diabetes whose appendicular skeletal muscle mass (ASM) were previously evaluated by dual-energy X-ray absorptiometry at Shimane University Hospital. Asian Working Group for Sarcopenia suggested that SMI is calculated by the following formula; ASM/height2, and its reference value in Asian women is 5.4 kg/m^2. The participants were observed up to 7 years from the start of this study, and the association between SMI at baseline and mortality rate was examined. The association between all-cause mortality and SMI was explored using the Kaplan-Meier method, the logrank test, and Cox regression analysis.
Results: At the entry of this study, mean age and duration of diabetes were 66.1 and 11.6 years, respectively. Of 141 postmenopausal women, 17 died during the follow-up period (average time: 6.2 years). Dead patients were significantly older and had longer duration of diabetes compared to survivors (74.9 ± 7.1 v.s 64.9 ± 9.6 years old, and 18.2 ± 12.1 v.s 10.6 ± 9.6 years, respectively). SMI was significantly lower in dead patients than in survivors (5.93 ± 0.94 kg/m^2 v.s 6.46 ± 0.85 kg/m^2, $p = 0.019$). Unadjusted survival analyses indicated that

patients with SMI < 5.4 kg/m^2 had higher mortality rate than those with SMI >=5.4 kg/m^2 (p = 0.014). Moreover, in the Cox regression analysis adjusted for age, duration of diabetes, HbA1c, and serum creatinine, SMI was significantly and inversely associated with the mortality (hazard ratio = 6.39, 95% confidence interval = 1.42–28.68, p = 0.016).
Conclusion: The present study showed that lower SMI was associated with the increased all-cause mortality in postmenopausal women with type 2 diabetes mellitus, suggesting that muscle mass reduction is an important complication which is involved in the risk of mortality in type 2 diabetes.

PB-25
The influence of diabetes on eradication rate of Helicobacter pylori
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Introduction: The prevalence of Helicobacter pylori (HP) infection is high in Asia. Although eradication therapy of HP has been strongly recommended to prevent gastric cancer and peptic ulcer, several studies reported the lower success rate of eradication in diabetic patients. We aimed to elucidate the influence of diabetes and glycemic control on eradication rate of HP.
Method: We retrospectively investigated the patients who underwent first line HP eradication therapy (Proton Pump Inhibitor, Clarithromycin, Amoxicillin) from January 2011 to December 2013. We excluded the patients who did not complete the eradication therapy and the assessment test of HP infection. We collected information about patient characteristics, smoking history, laboratory data, endoscopic findings, regimen of HP eradication, status of diabetes, and anti-diabetic drugs. We compared eradication success group and failure group by t-test and chi-square test, and used logistic regression model to analyze the factors associated with eradication of HP. Study protocol was approved by institutional review board.
Result: Of the 546 patients who underwent first line HP eradication from 2011 to 2013, 415 patients were eligible. Mean age was 64.2 years old and 192 patients were male. Sixty-three patients had diabetes and mean HbA1c was 6.9%. Eradication rate in total was 75.7%. Age, sex, smoking status, dose of clarithromycin, type of proton pump inhibitor, and atrophy of gastric mucosa were not significantly associated with eradication rate. Diabetic patients had significantly higher eradication rate than non-diabetic patients (85.7% vs 73.9%). In diabetic patients, mean HbA1c before eradication therapy was not significantly different between eradication success group and failure group. HbA1c and body mass index before and after eradication were similar. Multivariate analysis showed that adjusted odds ratio of successful eradication in diabetic patients was 2.00 (95% confidence interval: 0.86–4.31, p = 0.11).
Conclusion: Contrary to previous small scale studies, eradication rate was relatively better in diabetic patients. We need the prospective, larger scale study to clarify the relationship between diabetes and eradication of HP.

PB-26
The glycemic control of adult population in Nauru
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Background: Nauru is one of the countries with high prevalence of diabetes mellitus (DM). However, diabetic control among overall and newly diagnosed DM adult population had not evaluated in the past.
Methods: This is a retrospective observational cohort study. All of the data come from the Nauru Diabetes Registry database from Naeoru Public Health Center from 2011 to 2015. All patients with their hemoglobin A1C (HbA1C) will be analyzed and compared between year of 2011–2012 and 2014–2015.
Results: A total of 614 patients were enrolled for analysis with mean age of 49.8 year-old and mean diabetic duration of 10.1 years. The mean age of onset of DM is 40.4 year-old. The female population had long duration of DM than male population. The overall HbA1C levels are slightly greater in 2014–2015 than 2011–2012 without statistical significance (10.9 ± 2.7 and 10.6 ± 2.2% respectively). The HbA1C levels also do not differ among DM patients with regular outpatient visits. The mean HbA1C of newly diagnosed DM is significant higher in 2014–15 than that in 2011–2012 (11.5 ± 2.4 and 10.6 ± 2.1% respectively, p = 0.039), but not different from HbA1C levels in 2013 in DM patients who received ongoing treatment (10.9 ± 2.3%). Furthermore, HbA1C worsened significantly in 2 of the 15 districts between 2011–2012 and 2014–2015.
Conclusions: Nauru has a high prevalence rate with early onset and inadequately controlled diabetes. It needs to propose strategy to early detect and improve glycemic control early to prevent future diabetic complications.

PB-27
Association between CAG repeat length polymorphism of androgen receptor gene, cardio-metabolic risk factors and clinical outcomes in Chinese men
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Low testosterone is linked to metabolic syndrome and increased risks of cardiovascular morbidity and mortality. Cellular effects of testosterone are mediated by its binding to androgen receptor (AR), and CAG repeat length polymorphism of receptor gene correlates with its function with longer length being associated with reduced receptor sensitivity. We explored the relationship between AR CAG repeat length and cardio-metabolic parameters, total testosterone levels, and incident cardiovascular disease (CVD), chronic kidney disease (CKD) and all-cause death in a prospective cohort of Chinese men with type 2 diabetes.
From January 2008 to December 2011, 495 men with type 2 diabetes underwent structured assessment of metabolic profile and complications. DNA was extracted from whole blood and the region containing AR CAG repeat was amplified by polymerase chain reaction using primers that flank the region. Patients were followed for new-onset CVD (coronary heart disease, stroke, peripheral vascular disease), CKD as defined by estimated glomerular filtration rate (GFR) <60 mL/min/1.73 m^2, and/or death until 31 May 2016.
In this cohort (mean ± standard deviation [SD] age: 57.9 ± 12.2 years, disease duration: 14.3 ± 7.3 years), CAG repeat number ranged from 12 to 31 with median of 23 (interquartile range [IQR]: 21,25). Patients were stratified into two groups by median of CAG repeat number for comparison of risk factors and outcome. The two groups did not differ with respect to age, disease duration, total testosterone, anthropometric (body mass index, waist circumference) and glycaemic (HbA1c, fasting plasma glucose) indices, but noted that low density-

lipoprotein cholesterol was lower among men with CAG repeat ≥23 than those with CAG repeat <23 (2.4 ± 0.7 vs 2.5 ± 0.7 mmol/L, p = 0.051) at borderline significance. The group with CAG repeat ≥23 had higher urine albumin-creatinine ratio (2.7 [IQR: 0.9,21.6] vs. 1.9 [IQR:0.7,11.5 mg/mmol, p = 0.046), although mean GFR and frequencies of other baseline micro- and macrovascular complications were similar to the other group. Over mean follow-up time of 5.2 years, the incidence of CVD, CKD and death per 1,000 person-year were 31.0 and 24.6 (p = 0.354), 188.0 and 140.6 (p = 0.022), and 14.2 and 14.0 (p = 0.964) in men with CAG repeat ≥23 and those with repeat <23, respectively.
Men with longer CAG repeat length denoting diminished AR sensitivity had similar cardio-metabolic control but higher albuminuria than men with shorter CAG repeats. For comparable age and disease duration, men with longer CAG repeats had higher incidence of CKD, whilst rates of CVD and death did not differ.

PB-28

An investigation on the factors of diabetic patients' cognition of diabetic control indicators

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Background: The ABCs of diabetes (A1c, Blood pressure, Cholesterol) is promoted in international diabetes education program to strengthen diabetes management of the general public and medical professionals, reduce occurrence of diabetic complications, and decrease mortality rate.
Objectives: This study aims to investigate how diabetic patients understand diabetic control indicators and the influential predictors of diabetic control indicators.
Methods: This survey was based on pruposive sampling. The subjects were diabetic patients in a medical center in central Taiwan from November 1, 2014 to August 31, 2015. A self-designed questionnaire, verified in terms of reliability (Cronbach's α = 0.731) and validity (CVI = 0.94) was used.
Results: There were totally 1313 subjects, including 661 males (50.3%) and 652 females (49.7%). For disease type, there were 144 type I patients (11.0%), 1166 type II patients (88.8%) and 2 other types patients (0.2%). Most of the subjects were elementary school graduates. The mean age of the subjects was 58.03 ± 17.85. The mean disease duration was 11.76 ± 8.13 years. The average glycated hemoglobin was 7.35 ± 1.34%. As for the questionnaire response, 0.1% of the subjects were totally correct, 27.4% were correct regarding blood sugar, 28.7% were correct regarding blood pressure, and 0.7% were correct regarding lipid. Significant differences were noticed in terms of education level (college and unversity), disease duration (11–15 and 16–20 years), age (21–30) and disease type (type I diabetes) (p < 0.001). Age, disease duration, disease type and education level were found to be the predictors of diabetic control indicators based on regression analysis.
Conclusion: In this research, less then 1% of the subjects thoroughly understand blood sugar, blood pressue and lipid, the key diabetic control indicators of diabetes. The findings indicate the importance of diabetes health education of diabetic patients.

PB-31

Green tea but not coffee consumption is inversely associated with metabolic syndrome; An epidemiological study in Korean adults

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Background: Cumulative evidence suggests that intake of caffeinated beverages, such as coffee and green tea, may have beneficial effects on metabolic syndrome (Mets). The aim of this study was to evaluate whether or not consumption of coffee or green tea was associated with the prevalence of Mets in a Korean population.
Methods: We analyzed 15,568 Korean adults, aged 19–65 years, using cross-sectional data from the The Sixth Korea National Health and Nutrition Examination Survey (KNHANES VI-2, 2013–2015). Coffee consumption level was assessed based on food frequency questionnaire and 24-h recall. Demographic and lifestyle factors were assessed using self-administered questionnaires. Data on metabolic biomarkers were obtained from a health examination. Multivariate analyses were performed to clarify the association between coffee or green tea consumption and the components of metabolic syndrome.
Results: Among all components of metabolic syndrome, high systolic blood pressure was inversely associated with the frequency of green tea consumption (p = 0.005), after adjusting for sex, age, body mass index, smoking status, drinking status. And in female, HDL was associated with the frequency of green tea consumption (p = 0.036). However, the consumption of coffee was not significantly associated with the prevalence of metabolic syndrome or its components.
Conclusions: Green tea but not coffee consumption was inversely associated with metabolic syndrome.

PB-32

Anti-tissue transglutaminase autoantibodies and DQB1 genotypes in patients with type 1 diabetes

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Celiac disease is an immune disorder that affects the small bowel and that is triggered by ingested gluten from barley, rye, and wheat. It is characterized by small intestinal damage with loss of absorptive villi and hyperplasia of the crypts, typically leading to malabsorption. IgA and/or IgG antibodies to tissue transglutaminase (tTG) are present in the sera of patients. The prevalence of celiac disease is 3.3–10/1000 in Caucasians whose food contains gluten. However celiac disease has been rarely reported in Asian people.
Celiac disease is more frequent in Caucasian patients with type 1 diabetes (T1D) with a prevalence of 1–16%. We hypothesized that celiac disease is also less frequent in Asian patients with T1D. Therefore we investigated the tTG Abs in patients with T1D.
Material and methods: The subjects were 354 T1D patients consisting of 163 males and 191 females. Their mean (SD) age at diagnosis was 8.0 (4.8), range 0.5–40.7 years, and disease duration 11.0 (6.6), range 0.1–34.7 years. T1D was diagnosed on the basis of clinical manifestations and laboratory evidence. Patients had a HbA1c level of ≥6.5%, a fasting plasma glucose level ≥7 mmol/L at least 2 times, or a random glucose level ≥11.1 mmol/L with diabetic symptoms, and at least one of autoantibodies to islet cell antigens, glutamic acid decarboxylasee (GAD) and Islet antigen-2 (IA-2) or c-peptide level <0.7 mmol/L at random or <1.1 mmol/L at the peak by a glucagon test.
Anti-tissue transglutaminase autoantibody_IgA (tTGIgA) and anti-tissue transglutaminase autoantibody_IgG (tTGIgG) were measured by using Open tTG-ab Elisa (IgA) and (IgG) kits (Zedira, Germany). A value of >3.5 U/mL was graded positive. We genotyped DQB1 using SeCore DQB1 Locus Sequencing Kits (5341925D, 25Tests/Kit, Invitrogen/Life Technologies, Brown Deer, WI) on an ABI 3730XL DNA Analyzers (Applied Biosystems, Foster City, CA) with uTYPE6.0 SBT software (Invitrogen).

Results: 4 patients were positive for tTGIgA and 2 patients were positive for tTGIgG. Among them, one man was positive for both tTGIgA and tTGIgG. His DQB1 genotype was 02:01/03:02 and disease duration 20.5 years. The positive rate of either tTGIgA or tTGIgG was 5/354 (1.4%). DQB1 genotypes were 03:02/03:02, 02:01/03:03, and 02:01/06:01 in the remaining 3 patients positive for tTGIgA, The DQB1 genotype was 03:03/04:01 in the other patient with tTGIgG positivity. No gastrointestinal symptoms or signs were detectable clinically in the 5 patients.
Conclusion: The positive rate of tTGIgA was 1.4% in T1D patients in Taiwan and the patients with positive tTGIgA carried DQB1*02:01, *03:02, or both.

PB-33
The association of YKL-40 genetic polymorphisms with coronary artery disease in Taiwan population and diabetes subgroup

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Background: YKL-40, released by human activated macrophages, neutrophils and vascular smooth muscle cells, plays a role in the pathogenesis of endothelial dysfunction, atherosclerosis and abnormal angiogenesis. However, the association of single nucleotide polymorphisms (SNPs) of YKL-40 with coronary artery disease (CAD) has not been clear in the Taiwan population and diabetes subgroup. Materials and methods: Five hundred and seventy-six unrelated Taiwanese patients (male 397, female 179), receiving coronary angiography because of chest pain at Chung Shan Medical University Hospital were recruited from April 2007 to March 2013. The blood samples were obtained for the analysis of YKL-40 SNPs rs6691378, rs10399805, rs4950928, rs880633 using real time PCR assay from CAD case group (373 patients) and non-CAD control group (203 controls). Thereafter, we analyzed the relationships among CAD, the related clinical features and the distributions of genotype and allele of these SNPs. We assessed the demographic characteristics and the odds ratio between case group and control group. Additionally, we also analyzed the YKL-40SNPs from the diabetes subgroup(226 cases).
Results: In the female population, the frequencies of YKL-40 rs6691378 with GA/AA genotype [P = 0.008, odds ratio (OR) = 2.267] and rs10399805 with GA/AA genotype (P = 0.004, OR = 2.421,) were higher, as compared to their wild GG genotypes in CAD than non-CAD groups After multivariate analysis for YKL-40 SNPs and clinical features in the female group. In addition to, recent 24 hours severe angina and elevated cardiac enzyme, YKL-40 SNP rs10399805 GA/AA (P = 0.009, OR = 2.524, 95% confidence interval = 1.254–5.078) was an independent factors for CAD.
In the female diabetes population, the frequency of YKL-40 rs10399805 with GA genotype was higher, as compared to GG genotype in CAD female group than non-CAD female group (56.8% vs 29.6%, OR = 2.930, p = 0.047). The frequency of YKL-40 SNP rs880633 with CC genotype was lower, as compared to TT genotype in CAD group than non-CAD group [9.1% vs 25.9%, odds ratio (OR) = 0.190, p = 0.034].
Conclusion: In the Taiwanese female, YKL-40 SNP rs6691378 (-1371G/A) with GA/AA genotype and SNP rs10399805 (-247G/A) with GA/AA genotype were associated with CAD. Based on multivariate analysis, YKL-40 SNP rs10399805 (-247G/A) however was an only independent genetic factor for CAD in the Taiwanese female. Besides, in the Taiwan female diabetes, YKL-40 SNP rs10399805 (-247G/A) with GA genotype can increase genetic susceptibility of CAD. Additionally, YKL-40 SNP rs880633 (+2950 T/C) with CC genotype can protect genetic susceptibility of CAD.

PB-34
Facial flushing and blood pressure among Cambodians with T2D

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Purpose: Facial flushing is a proxy for variants of genes that encode enzymes that metabolize alcohol, and is common among Asians. The metabolic syndrome (MS) is a cluster of risk factors for type 2 diabetes (T2D) and cardiovascular disease: hypertension, hyperglycemia, abdominal obesity, and dyslipidemia. Data suggest that flushers have increased risk for MS. Rates of MS and T2D are increasing in Cambodia. Yet little is known about flushing in persons with extant T2D or from Cambodia. Data in this regard may have implications for increasing rates of MS and T2D in Cambodia and point to potential opportunities for intervention. This study investigated the relationships among flushing, glycemia, and blood pressure among Cambodians with T2D.
Methods: CDA patients were invited to participate if they were 35–80 years old, T2D >=one year, not taking insulin, no documented psychiatric disorder, and no documented long – term diabetes complications. After informed consent, trained clinic staff administered Khmer-language Alcohol Use Disorders Identification Test – Consumption (AUDIT – C). Flushing was assessed with the question, Response options were "yes" (drinker/flusher), "no" (drinker/non – flusher), or 'I don't drink' (non – drinker). Trained staff, assessed biomarkers and reviewed medications. SBP and DBP were each taken, according to JNC8 guidelines. A1c was measured. A glucometer was used to determine glucose. Data were analyzed.
Results: Fifty-nine participants were M = 56.6 (SD = 9.4) years old and 60% female, diabetes duration
M = 4.8 (SD = 3.6) years, A1c M = 9.2% (SD = 1.8%), glucose M = 153.5 mg/dl (SD = 50.3), SBP M = 130.2 (SD = 14.1) and DBP M = 82.7 (SD = 8.0) mmhg. Results remained significant after controlling for antihypertensive use and AUDIT – C scores. Non-drinkers and non – flushers did not differ from each other, p = 0.61. There were no significant differences between groups for SBP, glucose or A1c.
Discussion: Flushing was associated with higher DBP. Lack of findings for glycemic variables may suggest that flushing is associated with cardiovascular, rather than metabolic, mechanisms of MS. Other data suggest that the risk of MS among flushers rises with increasing alcohol consumption. More research is needed to determine whether alcohol actually potentiates MS in flushers, or whether flushing is a marker for a third, as yet unidentified risk for MS. Limitations include small sample, cross – sectional design, and inclusion of only select components of MS.
Conclusions: In Cambodians with type 2 diabetes, drinking despite facial flushing is associated with higher DBP.

Diabetes Performance Measures: An Update and Future Directions

PC-01
Demographic and clinical features of diabetes mellitus in Tuvalu patients

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Background: It is well recognized that diabetes is a major and increasing public health problem worldwide. Of particular

importance is the increasing prevalence of diabetes throughout the Pacific Region. In Tuvalu, the prevalence of diabetes is about 14%, and chronic diseases accounted for 67% of all deaths in 2002. The effective prevention and control of this condition remains difficult. The purpose of this study was to assess the diabetes and its co-morbidities status in Tuvalu as a foundation to help health care providers and community leaders to create culturally customized health promotion interventions.

Methods: A suitable sample of 150 (54.2%) from a total of 286 medical records of Princess Margaret Hospital adult outpatients of non-communicable disease registration, 18 or more years of age was evaluated in May to July, 2014. Anthropometric data (body height, body weight, body mass index (BMI), and waist circumference), and blood pressure were measured. Biochemistry data (fasting blood glucose, hemoglobin A1c (HbA1c), lipid profile (total-cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol and triglyceride)) were measured.

Results: This cross sectional survey consisted of a group of mean age of 57.14 ± 10.12 years old, 63% were females. The mean BMI and waist circumference were 32.30 ± 1.31 kg/m^2, and 220.68 ± 94.27 cm, respectively. Female patients had a significantly higher mean BMI than males ($P < 0.05$). In regard to ABC goal, only 18% of the patients had reached the glycemic target (A1c < 7%), 24% achieved LDL-C < 100 mg/dL, and 62% reached blood pressure goal. Large vessel disease (LVD) was observed in 14% of patients, peripheral neuropathy in 44%. Some of them were also with foot ulcer problems.

Conclusions: Inadequate glycemic and lipid controls were noticed in the majority of patients,which is probably due to demographic transition to an ageing population, modernization, lifestyle changes, non-compliance to medication, and a relatively lower proportion of patient using insulin. A large proportion of chronic diabetic complications also have significant impact on health budget.

PC-02

Targeted Active Recruitment for Intervention (TARIN) for patients with type 2 diabetes (T2DM) in general medical specialist outpatient clinics

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Introduction: In general medical specialist outpatient clinics, doctors are usually engaged with patients with multiple medical problems within very short consultation time. Referral rate of diabetes patients to structured management is low. TARIN programme has been established in Tuen Mun Hospital since January 2015 to fill the service gap.

Objective: To evaluate the outcomes of patients recruited into the TARIN programme.

Method: Patients with T2DM, whose age <65, latest haemoglobin A1c (HbA1c) >/=7% and plasma creatinine <200 umol/L were identified from CDARS. Those who received structured diabetes empowerment within two years were excluded.

A trained nurse went to target clinics to recruit patients. She provided brief introduction on the programme and arranged appointments according to patients' convenience. Patients received metabolic risk assessment (MRA) and were invited to attend an education class. A copy of MRA report was distributed to each patient in the class. Patients with eyes and feet complications were referred to podiatrist or ophthalmologist for timely interventions. In subsequent nurse clinic, they were counselled on diet and lifestyle modification, self-monitoring of blood glucose (SMBG) and had their anti-diabetic medications intensified. Treatment plans were reviewed with endocrinologists in weekly case conferences.

Results: 73 patients were recruited in January 2015 and the outcomes were analyzed in January 2016. We recruited 45 men and 28 women (mean age 56.7 ± 6.9 years; body mass index 28.3 ± 4.3 kgm^2). Ten were newly diagnosed T2DM and 63 were known diabetes with mean duration of disease 10 ± 5.2 years. All of them had MRA done, of which 4% were referred to podiatrist and 15% were referred to ophthalmologist. Mild non-proliferative retinopathy was detected in 6% of patients and they were offered follow-up MRA in 1 year to monitor the progression. On entry to programme, 19% of patients were on insulin and 19% were doing SMBG. After receiving structured care, 55% of patients were performing SMBG. Mean number of nurse clinic visits were 1.6. Thirty percent saw endocrinologist for major treatment intensification. Mean baseline HbA1c was 8.2 ± 1.1% and post-intervention 7.1 ± 0.9% (Paired t-test, $p < 0.0001$). 53.4% of patients had HbA1c < 7% after completing the programme. There was no emergency admission or death during this period.

TARIN is effective in empowering patients with T2DM in self-care and improving surrogate marker of T2DM in general medical clinics up to one year.

PC-03

Results of the comprehensive care model for the care of children with new-onset Type I diabetes

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Introduction: According to the International Diabetes Federation statistics, the prevalence of Type I diabetes in the world is 20 per 100,000 population and it is still gradually increasing. According to the Taiwan National Health Insurance database, the diabetes prevalence between 2003 and 2008 is 5.3 persons per 100,000. Thus, we can see that Type I diabetes is a common chronic disease among children worldwide. Therefore, it is also a very important topic for diabetes care.

Objective/methods: This study was aimed to investigate the care results of a comprehensive care model for children and adolescents inpatients with new-onset Type I diabetes. The two groups' average hospital stay, glycated hemoglobin (A1C) monitor rate, A1C improvement, and care satisfaction were analyzed with SPSS.

Results: The hospitalization duration prior and after the implementation of the comprehensive care model was 8.8 ± 2.2 and 6.6 ± 1.7 days ($p < 0.05$), respectively. The A1C monitor rate increased from 88.9% to 93.8%. The hospitalization and 3–4 month after discharge A1C level difference prior and after the implementation of the comprehensive care model were 3.7 ± 2.9% and 5.6 ± 2.1% ($p > 0.05$). The nursing team's satisfaction, by utilizing this care model for preparing the patient for discharge, increased from 77.1% to 84.0%. The inter-team intervention immediacy increased from 77.1% to 87.0%, and the instruction content satisfaction increased from 80% to 87%.

Conclusion: The use of the "comprehensive care model" can significantly reduce the hospitalization duration for children with Type I diabetes. Although, the A1C level difference did not exhibit a significant, however, it did show an overall improvement. Therefore, the implementation of the comprehensive care model is beneficial for the care of these patients.

PC-04

Dietary intake in elderly type 2 diabetes subjects in Taiwan

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This was a cross-sectional survey commissioned by Health Promotion Administration, Ministry of Health and Welfare, and conducted by Taiwanese Association of Diabetes Educators in year 2011. In brief, type 2 diabetic subjects who regularly visited the same Diabetes Health Promotion Institute for at least one year were invited by a method of one per every 5 consecutive visitors. Every 5 enrolled subjects were asked to fill the semi-quantitative food frequency questionnaire (FFQ). The categories listed in FFQ included a total of 10 food categories and 83 types of food. We compared elderly group (≧65 years old, n = 285, with age 72.6 ± 5.1 years (mean + SEM), and the adult group (<65 years old, n = 392, with age 54.4 ± 8.0 years). The body mass index of the elderly group was lower than the adult group (25.3 ± 3.7 vs. 26.4 ± 4.4 kg/m^2, $p < 0.05$). Values of SBP, DBP, fasting glucose, PPG, HbA1c, total cholesterol, LDL-cholesterol and triglyceride were not different between elderly and adult diabetes. There were no differences between calorie intake (1856 ± 631 vs. 1965 ± 619 kcal/day, $p = 0.80$) and protein intake (60 ± 25 vs. 65 ± 24 gm/day, $p = 0.47$) while cholesterol intake were significantly lower in elderly diabetes subjects (159 ± 124 vs. 206 ± 157 mg/day, $p < 0.01$) than adults diabetes. In general, nutrients intake were lower in women than men with the cholesterol intake reached statistically significant. The percentages of those who attained the ABC goals in the elderly group were 12.3% compared with 8.6% in the adult group ($p = 0.413$). In conclusion, nutrients intake of the elderly diabetic group are lower than the adult group. Further careful monitoring and ensure adequacy nutrients intake while maintain good diabetes control in elderly patients are clearly needed.

PC-05

Utilizing diet behavior and knowledge for improving the nutritional care of type II diabetes patients

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Objective: This goal of this project is to utilize a diabetes diet behavior and diet adjustment knowledge questionnaire assessments, twice, for motivating and improving the participants' diet behavior and knowledge. The result from this study can be utilized for educating the participant on the monitoring of fasting and postprandial blood glucose (FBG; PBG) for the improvement of blood glucose management and living qualities.
Methods: The consulting health education including the knowledge of low glycemic index foods, the use of a healthy food plate, the correct assessment of macronutrients and calories, the use of a health diary, and diabetes diet behavior and diet adjustment knowledge assessment were provided by a nutritionist to inpatients. The participant consisted of diabetic inpatient with stable conditions. The participants were enrolled from the hospitalization period until three month after discharge.
Results: The FBG and PBG levels and types of food were analyzed by a two-factor analysis of variance (ANOVA). The ANOVA analysis indicated that there is no significant blood glucose difference between the types of food. However, the blood glucose levels were determined to be significantly different between the FBG and PBG, and the types of food has an interaction with the FBG levels ($p = 0.001$). Furthermore, the glycated hemoglobin index for the control and experimental group were also analyzed by two-factor ANOVA, which exhibited significant difference between the FBG and PBG. Finally, the diabetes diet behavior and diet adjustment assessments showed an improvement in patient diet behaviors.
Conclusion: Individualized diet education and continual follow-up after hospital discharge were able to convey the importance of FBG and PBG management to the patients for improving their diet behavior and knowledge.

PC-06

Metabolic outcome for pay for performance for diabetes care – An example from a regional teaching hospital in Taiwan

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Backgrounds: Taiwan's National Health Insurance (NHI) Program implemented a diabetes pay-for-performance program (P4P) based on process-of-care measures in 2001. This research is directed primarily to those outpatients with diabetes from the Division of Endocrinology and Metabolism at Feng Yuan Hospital who have joined the "Diabetes Shared Care Model" management since 2002. We want to study the metabolic outcome among the patients.
Methods: An observational method was adapted in this research. The research was performed from 2012 to 2015. The study participants were all outpatients from the "Diabetes Shared Care" in Feng Yuan Hospital. The health education content was provided by a specialized center offering team-based care (including endocrinologist, dietitian, nurse-certified diabetes educator). The patients' baseline characteristics, annual metabolic indicators, the improvement of annual metabolic indicators were monitored and analyzed. Multifaceted efforts were arranged to maintain the quality including 1: Encourage more certified physicians to join the Diabetes Shared Care program (number increased from 9 to 12); 2: Using digital health technology in the case management; 3: Diabetes health education to enhance the knowledge of self management and enhancing the usage of waiting times.
Results: The patients number of the "Diabetes Shared Care" program increased by 15% from 56% to 71%. The percentages of subjects who had HbA1c lower than 7% increased by36.3% (from 35.22% to 71.52%), both SBP and DBP lower than 130/80 mmHg (B), and LDL cholesterol lower than 100 mg/dL increased by 38.42% from 43.99% to 82.41%) respectively.
Conclusion: The "diabetes shared care model" case management system is a system that is worth popularizing in the regional teaching hospital and it should be offered to patients to strengthen and improve diabetic knowledge and self-care skills which can be helpful to improve the life quality and to reduce the severity of the chronic complication.

PC-07

The correlation with continuity of care and diabetic foot in Taiwan

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Objective: The expense of treating Diabetes Mellitus and its complication is the 4th largest part of all in Taiwan Health insurance system. Since continuously multidiscipline team service is the best strategy for Diabetic care. This study is aimed to investigate the relationship between COC (continuity of care) and risk of diabetic foot in Taiwan.
Method: We used Taiwan National Health Insurance database to make a longitudinal study during 2001–2007. Only adult diabetes patients who had more than 4 times ambulatory records in 2001–2002 were enrolled. The outcomes from 2003 to 2007 were analyzed as following: risk of amputation, re-

amputation, and death. COC and medical expense and organization of care were counted as independent variables.
Result: Re-amputation rate is 23.26%, 1/3 amputated diabetes have been received ≧3 times amputation. The highest risk of amputation and re-amputation is high COC, which are 1.26 times ($p < 0.001$) and 1.62 times ($p < 0.001$). Amputated diabetes patient had 3 times ($p < 0.001$) risk of specific diabetes associated death. Different medical organization type was not related to the risk of amputation. Low COC was related to poorer vascular and neurological outcome.
Conclusion: We believed that diabetic foot care was a missing circle of the chain of multidiscipline diabetes care chain.

PC-08
A patient centred care service model for enhancing Diabetes Mellitus management in primary care
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Background: Diabetes Mellitus is an important disease managed in primary care setting. We have more than 40,000 DM patients with regular follow-up and management at 8 General Out-patient Clinics (GOPCs). This review aimed at assessment of the impact of this service model.
Aims: 1/ To review the clinical outcome of the service model, in term of key performance indexes [KPI] such as HbA1c,BP and LDL level
Methodology: Since March 2011, our clinics has implemented this structured integrated service model to enhance the quality care of DM patients, via structural and protocol-driven approved, provided by multidisciplinary professionals. The patients would be stratified into various risk categories for management by their usual doctors, nursing specialists, allied health professionals or experienced family physician for advance medical support such as insulin initiation and titration.
Ongoing quality data in term of various KPIs were retrieved for clinic peer review for service enhancement and patient care management.
Results: The KPIs after the implementation were promising with currently 50% of patient HbA1c < 7%, 50% of patient BP < 130/80 mmHg & 65% of patient LDL < 2.6 mmol/L.
Conclusion: This service model is well-accepted by the patients with more than 85,000 attendances and over 90% of diabetic patients have benefited from this over 5 years. With the structural model provided by the primary care team and regular KPIs review, the patients' chronic disease care improved and sustained, comparable to many international standard.

PC-09
Effects of resistance exercise in the deteriorations of cardiac contractility and mitochondrial uncoupling in cardiac muscle of diabetic animal model
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Background: Cardiomyopathy (CMP) in patients with type 2 diabetes is an important complication of long-standing hyperglycemia and known to be caused by characterized by diabetes-induced metabolic and mitochondrial disturbance. Resistance exercise (RE) has been recommended for measures of life-style modification in patients with type 2 diabetes. To date, the beneficial effects of RE in prevention of diabetic CMP and mitochondrial dysfunction of cardiomyocyte are uncertain. The aim of this study was to determine the effects of RE in the cardiac contractility and mitochondrial dysfunction in diabetic animal model.
Design and methods: Fourteen Otsuka Long Evans Tokushima Fatty (OLETF) rats were assigned to sedentary control (SC, n = 7) and resistance exercise (RE, n = 7) groups at 26 weeks of age. Long-Evans Tokushima Otsuka (LETO, n = 7) rats were used as non-diabetic control. RE rats were trained by climbing a ladder 5 days per week. Body weight, lipid profiles, and IPGTT were evaluated at the time of 12 weeks exercise. In addition, cardiac function and mitochondrial structure of cardiomyocyte were assessed by echocardiography and electron microscopy. Mitochondrial respiration and ROS production were measured.
Results: Weight gain and metabolic alterations characteristic of OLETF rats (SC) compared to LETO were reduced in RE rats despite to similar food consumption after 12 weeks of exercise. Reductions of ejection fraction and fractional shortening in SC were significantly reversed by RE. Collapsed sarcomeres and decreased number of mitochondria in SC were not observed in RE rats. In addition, decreased expression of the peroxisome proliferator-activated receptor gamma coactivator 1α (PGC-1α) and mitochondrial transcription factor A (TFAM) in SC were attenuated in RE. Higher proton leak in cardiomyocytes of SC represented by different mitochondrial oxygen consumption rate between oligomycin and antimycin A was attenuated in those of RE rats. Finally, increased production of ROS with lower mitochondrial membrane potentials were revered in SC with higher expression of mitochondrial superoxide dismutase 2 (SOD2).
Conclusion: These data suggested that RE is effective in the prevention of diabetic CMP in relation to attenuation of metabolic disturbances and mitochondrial dysfunction, which may contribute to decreased contractility of diabetic heart in animal models.

PC-11
The relationships between fasting plasma glucose and insulin resistance, first-, second-phase insulin secretion and glucose effectiveness in adolescents
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It is generally agreed that there are four factors which contribute to the occurrence of type 2 diabetes, namely, increased insulin resistance (IR), decreased glucose effectiveness (GE), first and second phase insulin secretion (FPIS, SPIS, respectively). Although these factors are studied. However, most of the literatures are non-Asian and with limited numbers of subjects. In the same time, there are no reports for adolescents. In this report, we investigated the relationships between fasting plasma glucose (FPG) and these four factors in a 18-year-old cohort.
We enrolled 507 subjects; 18-year-old adolescents. The IR, GE, FPIS and SPIS were calculated by the equations we published. In short, by using age, body mass index (BMI) and metabolic components, these for factors could be estimated. The correlation between FPG and the four factors.
Results: BMI was 20.11 ± 1.43 kg/m^2, systolic and diastolic blood pressure was 116.46 ± 12.54 and 65.00 ± 8.97 mmHg, FPG was 93.13 ± 6.50 mg/dL, triglyceride was 70.98 ± 27.30 mg/dL and HDL-cholesterol was 51.8 ± 10.7 mg/dL. The IR was 3.67 ± 0.014 mmol/L, FPIS was 61.48 ± 26.30 μU/min, SPIS was 0.0402 ± 0.0095 pmol/mmol and GE was 0.0221 ± 0.0009 min^{-1}. The correlation between FPG, IR, FPIS, SPIS and GE are 0.031, −0.132, −0.217 and −0.331 respectively. Other than the FPG and IR, all other correlations are statistically significant ($p < 0.001$).
Conclusion: In this 18-year-old adolescent cohort, elevation of FPG is mainly due to the decrease in the FPIS, SPIS and GE.

Among them, GE is the most Significant one. The role of GE in the adolescent should not be overlooked.

PC-12

Regulation of vascular BK channels in diabetes by Nrf2 signaling

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Background and objective: The nuclear factor E2-related factor-2 (Nrf2) signaling pathway has emerged as a master regulator of cellular redox status. The large conductance calcium-activated potassium (BK) channels, which are major determinants of vasodilation, are impaired in diabetes mellitus (DM) due to the downregulation of BK-β1 by reactive oxygen species-dependent mechanisms. The goal of this study is to test the hypothesis that Nrf2 signaling plays a central role in the regulation of BK channel function in DM.

Methods and results: Studies were performed combining cellular, molecular, vascular, and electrophysiological techniques. In type 2 diabetic db/db mouse aorta, Nrf2 protein expression was significantly reduced, associated with significant downregulation of BK-β1 and heme oxygenase 1 (HO-1), a known Nrf2 downstream target. Also, the muscle ring finger protein 1 (MuRF1), a known E-3 ligase targeting BK-β1, was significantly upregulated. These findings were reproduced by knockdown of Nrf2 by siRNA in cultured human coronary smooth muscle cells (HCSMC), whereas adenoviral transfer of Nrf2 gene in these cells was associated with downregulation of MuRF1 and upregulation of BK-β1 and HO-1 expression. Activation of Nrf2 by dimethyl fumarate in high glucose-cultured HCSMCs or in diabetic db/db mouse coronary arteries preserved BK-β1 expression shown by Western blot, BK channel activities using patch clamp recordings, and vascular function assessed by shear stress-mediated vasodilation in isolated mouse coronary arteries.

Conclusions: Expression of BK-β1 is closely regulated by Nrf2 through its effect on MuRF1, which regulates BK-β1 degradation, and vascular BK channel function can be restored by activation of Nrf2. Nrf2 should be considered a novel therapeutic target in the treatment of diabetic vasculopathy.

PC-13

Essential oil from sudachi peal improves glucose and lipid metabolism

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Background: According to the statement of the International Diabetes Federation, the diabetes population continues to grow around the world. The number of people associated with diabetes reaches 415 million in 2015, and one of 11 people is estimated to be a patient. It is predicted that it will increase to 642 million by 2040 if we do not take any effective measures.

Recently, the alternative medicine such as supplemental foods and aromatherapy has attracted our attention. Among them, the mechanisms of the aromatherapy are still unknown for hypoglycemic effects.

Sudachi is a citrus fruit grows in Tokushima prefecture region of Japan, and we found a suppressing effect on blood sugar level elevation by administration of its peel powder in human obese subjects. Because Sudachi has unique fragrance, we conducted a study to reveal the aromatic effects of essential oil from sudachi on the metabolic regulation.

Method: These experiments were worked using male ddY mice. We exposed vaporized oil of sudachi peal to 7–8 weeks old mice for three weeks under the fixed concentration, then body weight, food intake and water intake were measured. The intraperitoneal glucose tolerance test (IPGTT) was performed and the organ weight and plasma lipid levels were evaluated. We also analyzed expression levels of mRNA related to energy consumption. In addition, guanethidine was injected to another group to investigate involvement of the sympathetic nerve.

Result: We found weight loss involving WAT reduction without change in food intake. Triglyceride (TG) in the blood was reduced by the treatment, and glucose tolerance was also improved. The expression of hepatic PGC-1 tended to be increased compared to control. When we administered guanethidine to the sudachi treated group, the reductions of plasma TG and WAT weight were canceled.

These data suggest that vaporized sudachi oil may stimulate olfactory, resulting in the activation of the sympathetic nerve which participates in the reduction of WAT by facilitation of the energy consumption.

PC-15

Construct an IDNT-NCP computer program for clinical management of patients with Diabetes Mellitus

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Objective: Diabetic management model has been markedly changed over the past few decades especially on dietetic practice which have prompted dietitians to become more accountable and aware of treatment outcome and evaluation. Published evidence has demonstrated the numerous benefits which can be gained by application of a nutrition care process (NCP) and standardized language. However, a convenient, computerized, comprehensive tool to assess key NCP procedure is still lacking.

Materials and methods: A Chinese version of computerized International Dietetics & Nutrition Terminology (IDNT) NCP program was constructed to assess diabetes nutrition behaviors.

Results: The system is built using a Microsoft Solution based ASP.NET Web Site project template, SQL Server, and jQuery User Experience technique in rule engine. The trained Dietitians could be easily download automatically or enter patient's basic personal, anthropometric data, physical exam findings, biochemical data, and food/nutrition history into the program to complete the nutritional assessment. After completeness of nutrition assessment, the program will make inference to the rule base and make nutrition diagnosis. Dietetics professionals could then make the final diagnosis decision for the patient based on the diagnosis report generated by the web based nutrition diagnosis expert system, which involves identifying and labeling nutrition-related problems, etiology, signs and symptoms statements for conditions. The system will also set up a window for the dietitians to implement the nutrition intervention, monitoring and evaluation plan, which involves formulating goals and determining plans of action and are integrated into overall disease management and implementation.

The content validity index was calculated by experts' ratings of item relevance. The ICVI was 0.7–1.0. To understand the inter-rater reliability of system, three groups including CDEs and 5 patients, involved the process of inter-rater reliability assessment to test the rating consistency among observational ratings is 95-0.98.

Conclusion: A Chinese version of IDNT-NCP system build in a computer program may be a precise, convenient computer-based system to evaluate and follow the changes of eating behavior in patients with DM.

PC-16

Ratio of insulin cessation in patients with new onset insulin usage

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A total of 138 patients whom insulin treatment was started for glycemic regulation were enrolled into the study. Patients were hospitalised for insulin education. After 6 months, patients were evaluated again. Mean ages were 54.3 ± 11.09 years (30–78), there were 66 males (47.82%), and 72 females (52.17%). Diabetes duration was 6.7 ± 5.7 (0–20) years, initial HbA1c was % 10.9 ± 2.06 (7.9–17.7). All patients were taking 2 gr/day metformin and insulin treatment was started after cessation of other oral antidiabetics. 82 patients (59.42%) were started premix analog insulin, 16 patients (11.59%) were started long acting analog insulin and 40 patients (28.98%) were taking basal-bolus treatment. After glycemic control and education, patients were discharged from the hospital.

After 6 months, control visit was done. 93 (67.39%) patients were taking the same insulin treatment. In 17 patients (12.31%) insulin treatment regimen was changed by other doctors, 28 (20.28%) patients reported that they stopped insulin treatment after discharge. Reasons for cessation were; fear of hypoglycemia, fear of injection and fear of addiction.

As a result majority of patients who were hospitalised and started insulin treatment stopped insulin injections right after the discharge. Some patients's treatment strategies were changed by other doctors. These are factors that lead to glycemic dysregulation and chronic complications. Only continuing education can get over these barriers.

PC-17

The impact of seasonal lifestyle changes on glycemic control in T2DM – Based on Diabetes Case Management Program 2001, Taiwan

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Background and aims: In order to evaluate the impact of seasonal lifestyle changes on the glycemic control of diabetes for the ensuing development of personalized prevention program.

Materials and methods: From Jan. 2006 to Dec. 2012, 131 patients with T2DM participating randomly in DCMP 2001 with lifestyle intervention only without having any medication were under study. Accordingly, anthropometric and biochemical data were measured at least at 3-month interval and the lifestyle measurements (lifestyle I: no smoking, no alcoholic and regular exercise; lifestyle II: smoking and/or alcoholic and/or no exercise), total daily caloric intakes, macronutrient consumptions and dietary recommendations were also trimonthly recorded in each diabetes patient after seeing physician. Participants were divided into 2 groups based on the age recruited, <65 and 65 years in the DCMP 2001. The fasting blood glucose (FBS mg/dL) and A1c (%) levels were presented by Mean ± SD. Data comparison between the initial FBG and A1c level and the chronologically sequential season changes of FBG and A1c level within each group were consecutively performed in the continuous 5 years. Student-t test was used for data analysis.

Results: The general characteristics of 131 study participants with their FBG and A1c levels in 2 groups were demonstrated in Poster Table 1. The statistically significant differences of FBG and A1c level between the first recruited and sequential season changes for continuous 5 years were shown ($p < 0.05$) in Poster Tables 2 and 3.

Conclusion: The results clearly suggested that the impact of lifestyle in different seasons on the glycemic control was significantly different that was also demonstrated in different age groups. The stability of lifestyle attributed to glycemic changes was more stable in patients with age more than 65. Further study would be required.

PC-18

Geographic difference of barriers to insulin initiation in primary care physicians in Taiwan

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Aims: Insulin initiation is often delayed among type 2 diabetes patients with suboptimal glycemic control. Previous studies showed that difference in patient characteristics across countries along with physician and healthcare environment difference may contribute to the likelihood of insulin intensification. However, the geographic difference of barriers to insulin initiation in one country is not well understood. In this study, we examined the geographic difference of barriers to initiate insulin treatment among Taiwan primary care physicians.

Methods: We conducted a cross-sectional, questionnaire-based survey. The participants were categorized as follows based on their clinical practice place: Northern Taiwan, Central Taiwan and Southern Taiwan. We used a 24-item questionnaire to explore barriers for primary care physicians timely to initiate insulin. Physicians who didn't have insulin-treated patients were excluded.

Results: 240 participating physicians whose clinical setting were in Northern Taiwan (n = 85), Central Taiwan (n = 80) and Southern Taiwan (n = 75) met eligibility criteria and completed the questionnaire. After adjusting for clinical setting before private practice, specialty, participating pay for performance and number of insulin-treated patients per month, physicians in Northern Taiwan have more concerns about insulin initiation than physicians in Southern Taiwan. The difference was observed with regard to the "physician and personnel issue", "time consuming" and "concerns regarding insulin therapy" (Northern Taiwan vs. Southern Taiwan, P = 0.002; 0.003; 0.002, respectively).

Conclusions: Compared with primary care physicians in Southern Taiwan, physicians in Northern Taiwan have higher barriers to insulin initiation. Their concerns about insulin use may lead to delay of insulin treatment.

Optimizing Diabetes Therapy

PD-01

The association of glycated albumin and hemoglobin A1c with glycemic excursions in Chinese type 2 diabetic patients

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Background: Hemoglobin A1c (HbA1c) is mostly used to evaluate the long-term glycemic control and the risk for the development of complications in diabetes. Serum glycated albumin(GA) has been reported to be a useful and rapid indicator of glycemic control for diabetic patients. Postprandial glucose excursion is known to be a risk factor for diabetic micro- and macro-angiopathy in diabetic patients recently studies indicated that glycation excursion could influence

glycation reaction in albumin strongly compared with hemoglobin.
Aim: To analyze the correlation of glycated albumin (GA) and hemoglobin A1c (HbA1c) with mean amplitude of glycemic excursions (MAGE) and standard difference of blood glucose (SDBG) and to provide theoretical evidences for complete assessment of GA and HbA1c.in chinese type 2 diabetic patients.
Method: A total of 404 type 2 diabetic patients in our inpatient department of endocrinology and metabolism from August, 2013 to February, 2014 were enrolled. Fasting plasma glucose (FPG), HbA1c, GA, fasting C peptide (FCP), 2-hour postprandial plasma glucose (2hPG), 2-hour C peptide (2hCP) were examined in all the subjects. The 3 day continuous blood glucose monitoring of the enrolled subjects were performed by continuous glucose monitoring system. MAGE and SDBG were used to assess to glycemic excursions. Mean blood glucose (MBG) was used to assess overall glucose level.
Results: (1) The 404 enrolled subjects included 228 men and 176 women with mean age of (59 ± 11) years, diabetes duration of (9.1 ± 6.3) years, FPG of (7.9 ± 2.5) mmol/L, 2hPG of (13.3 ± 4.3) mmol/L, HbA1c of (8.3 ± 1.9) %, GA of (22.4 ± 6.9)%, MAGE of (5.6 ± 2.5) mmol/L, SDBG of (2.2 ± 0.9) mmol/L, MBG of (8.9 ± 2.0) mmol/L. (2) Univariate correlation analysis showed that GA had strong correlation with HbA1c ($r = 0.836$, $P < 0.01$). GA was positively correlated with FPG, 2hPG and MBG ($r = 0.604$, 0.670, 0.650, $P < 0.01$). HbA1c was also positively correlated with FPG, 2hPG and MBG ($r = 0.603$, 0.634, 0.661, $P < 0.01$). (3) Univariate correlation analysis showed that GA had positive correlation with MAGE and SDBG ($r = 0.485$, 0.529, $P < 0.01$). HbA1c was also positively correlated with MAGE and SDBG ($r = 0.417$, 0.495, $P < 0.01$). (4) Stepwise multivariate regression analysis demonstrated that GA level was independently correlated with the glycemic excursion indices including MAGE and SDBG.
Discussion: Compared with HbA1c, GA can better reflect postprandial glucose level and glycemic excursions.

PD-02
Effectiveness of diabetes quality improvement program in Chia-yi region of Taiwan

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Objective: Diabetes Mellitus is an endemic chronic disease that causes the major health issues. The population of diabetes has been doubling in the past two decades. It is found to be associated with aging, obesity and western lifestyle. Through its chronicity and multiple comorbidities, Diabetes mellitus is the most known social-economic burden in our healthcare system. This study is aim to evaluate the long-term effectiveness of diabetes quality improvement program by the national health insurance bureau.
Methods: This is a three year longitudinal follow-up study in a teaching hospital from 2009 to 2011. Totally 3217 diabetic patients receiving regular outpatient visit and entering the diabetes quality improvement program were included in the study. Medication cost of the hyperglycemia, hypertension and hyperlipidemia and the major healthcare outcome indicators were compared.
Results: The results showed that the total medication cost of the hyperglycemia, hypertension and hyperlipidemia decreased gradually and reach statistical significance ($p < 0.001$); there are also significant improvement in blood pressure ($p < 0.001$), HbA1c ($p = 0.006$), total cholesterol ($p < 0.001$), triglyceride ($p = 0.003$), HDL ($p = 0.031$) and LDL($p < 0.001$).
Conclusions: The long-term effectiveness of diabetes quality improvement program raised by the national health insurance bureau has been shown to be promising. It not only reduced the costs of pill burden but also improve the major cardiovascular outcome indicators. Through these results, we urge that the Ministry of Health and Welfare should invest more resources in the raising quality care model of chronic diseases especially the Diabetes Mellitus.

PD-03
Diabetic medications seldom deintensified in oldest old diabetic patients – Lessons from Thailand

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Background: In the recent study, older diabetes patients rarely had their medicine dosages decreased or discontinued. Little is known about medication deintensification on the growing population called the "oldest old", those in their mid-80s upwards. Therefore, the aim of this study was to describe the frequency of diabetic medications deintensification and diabetologists' attitudes toward oldest old patients.
Methods: A retrospective review was conducted on medical records of type 2 diabetes who are older than 85 years from Sep 2014 to August 2015 at Theptarin hospital which is one of the largest diabetes centers in Thailand with over 2,000 registered diabetes patients. Most diabetes patients have been treated at diabetes clinic which has 12 diabetologists and diabetes care team. Medications deintensification had been defined as reducing or discontinuing diabetic medications in the previous 180 days after the index measurement of A1C. The survey regarding glycemic target in oldest old patients and the factors they take into consideration when setting their patients' glycemic target had also been studied to understand the attitudes toward these patients.
Results: There were 143 (5.0% of total diabetic patients) oldest old diabetes patients who attended regularly during the study period. Ten patients deceased from various medical illnesses. Of the 133 active follow-up patients (median time of follow-up 15 years, range 1–30 years), 70.7% was female, and duration of diabetes was 20.1 ± 11.1 years. The mean of A1C was 6.7 ± 1.1%. Very low level of A1C (less than 6.0%), moderately low level of A1C (6.0–6.4%), safe margin of A1C (6.5–8.0%) were found in 23.3%, 22.6%, 39.8%, respectively. Regarding diabetic treatments, oral hypoglycemic agent (OHA) dual therapy was the most common treatment (26.3%) followed by OHA monotherapy (22.6%), insulin alone (19.5%), diet therapy alone (12.7%), and insulin plus OHA (8.3%). Among patients whose received diabetic medications and resulted in very low or moderately low level of A1C (less than 6.4%), only 19.6% underwent deintensification. The parameters "co-morbidity" was considered to be the most important factor in setting glycemic target while "disease duration" ranked the lowest.
Conclusions: Even though diabetologists recognized that diabetes treatment should less aggressive for older patients and those with limited life expectancy. Only less than one-fifth of oldest old patients with stable, albeit low A1C levels underwent medications deintensification. Quality-of-care initiatives should consider how to encourage appropriate deintensification in order to decrease the harm of intensive treatment and increased cost of care.

PD-04
Better improvements of indicators of β-cell function and insulin resistance with liraglutide compared to sitagliptin in Chinese T2DM patients

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Objective: To compare the effect of liraglutide and sitagliptin on β-cell function and insulin resistance improvements in Chinese patients with type 2 diabetes.
Methods: This is a post-hoc analysis of a randomised controlled clinical trial conducted from Dec. 2013 to Nov. 2014 (total 26 weeks) in China (LIRA-DPP4 CHINA). Patients aged 18–80 inadequately controlled on metformin monotherapy (HbA1c 7.0–10.0%) were included. Eligible subjects were randomised 1:1 to liraglutide 1.8 mg or sitagliptin 100 mg. Blood samples were analysed using an enzymatic assay by central laboratory during the trial for fasting plasma glucose (FPG), fasting insulin, fasting C-peptide and fasting pro-insulin. HOMA-β and HOMA-IR were calculated. The differences of above measurements and indexes between treatment with liraglutide and sitagliptin were analysed using a mixed model for repeated measurements (MMRM).
Results: 368 subjects were randomised 1:1 to liraglutide and sitagliptin, and 1 subject in liraglutide group withdrew before exposure. The baseline characteristics of the two groups were comparable. Greater reductions of fasting pro-insulin (28% vs 15%) and fasting pro-insulin to C-peptide ratio (30% vs 15%) were observed with liraglutide compared to sitagliptin, with estimated treatment ratios of 0.85 [0.75; 0.97], ($p = 0.0182$) and 0.83 [0.75; 0.91], ($p = 0.0002$), respectively. There were no statistically significant differences in fasting insulin and fasting C-peptide between the two groups after 26 weeks of treatment. Lower FPG was achieved with liraglutide (6.99 mmol/L) compared to sitagliptin (8.21 mmol/L) with statistical difference of mean changes from baseline at week 26 (−2.39 vs −1.17 mmol/L, $p < 0.0001$). An increase in HOMA-β and HOMA-IR driven by the better FPG level was achieved in both treatment groups but was more pronounced with liraglutide compared to sitagliptin (HOMA-β : 75% vs 34%; with an estimated treatment ratio of1.30 [1.17; 1.45] ($p < 0.0001$); HOMA-IR (26% vs 11%; with an estimated treatment ratio of 0.83 [0.73; 0.94], ($p = 0.0037$).
Conclusion: After 26 weeks, liraglutide resulted in significant improvements in fasting pro-insulin, fasting pro-insulin to C-peptide ratio, HOMA-β and HOMA-IR compared to sitagliptin. This indicates better improvements in β-cell function and insulin resistance with liraglutide compared to sitagliptin, both in combination with metformin, in Chinese patients with type 2 diabetes.

PD-05

Association between serum somatostatin levels and glucose-lipid metabolism in the Jino ethnic minority and Han Chinese population

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Objectives: Somatostatin has been reported as a kind of peptide hormone that inhibits the secretion of various blood glucose-regulating hormones, with its serum levels may be diverse in different populations. This study aimed to investigate the relationship between serum somatostatin levels and glucose-lipid metabolism in the Jino ethnic minority and Han Chinese population of Yunnan Province, southwest China.
Methods: A total of 224 subjects were recruited, comprising 111 subjects from Jino ethnic minority and 113 subjects from Han Chinese population. Clinical measurements analysis and glucose-lipid related metabolic traits were conducted among them. All subjects were divided into three subgroups according to blood glucose levels: subjects with abnormal fasting plasma glucose (FPG) only (n = 38 from Jino, n = 39 from Han), subjects with abnormal 2-h plasma glucose (2hPG) only (n = 37 from Jino, n = 37 from Han), and subjects with normal glucose tolerance (NGT) (n = 36 from Jino, n = 37 from Han). Serum somatostatin levels were measured via enzyme-linked immunosorbent assay (ELISA).
Results: We found significant differences in serum somatostatin levels between Jino ethnic minority and Han Chinese population ($P < 0.0001$). For further analysis, both in subgroups of abnormal FPG only and abnormal 2hPG only, significant differences were also identified between these two populations ($P = 0.0194$ and 0.0106, respectively). But no significant differences were detected among these three subgroups in Jino ($P = 0.3153$) or Han population ($P = 0.2779$) independently. After adjusting for covariates, serum somatostatin level was independently and significantly associated with FPG ($P = 0.0066$), TC ($P = 0.0041$) and LDL-C ($P = 0.0055$) in all 224 subjects. This relationship was also revealed in abnormal FPG subgroup ($P = 0.0040$, 0.0077 and 0.0161, respectively). However, none of those correlations were found in Jino ethnic minority or Han Chinese population group independently.
Conclusion: Our results suggest that serum somatostatin levels were associated with glucose-lipid metabolism and this relationship may be various in different populations.

PD-06

Efficacy and safety of SGLT2 inhibitor ipragliflozin in Japanese patients with type 2 diabetes

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Obesity and type 2 diabetes have become worldwide problem including Asian countries. Recently, average BMI of Japanese patients with type 2 diabetes reached at 25 kg/m^2. Accordingly, we need to control blood glucose level without weight gain, currently. SGLT2 inhibitor ipragliflozin is newly identified anti-diabetic agent which reduces blood glucose level by inhibition of glucose reuptake of SGLT2 in kidney. In the present study, we examined the efficacy and safety of ipragliflozin in Japanese patients with type 2 diabetes.
125 Japanese patients with type 2 diabetes were treated with 50mg ipragliflozin for 12 weeks added on existing anti-diabetic therapy. Average age was 53.9 years old, and average BMI was 29.7 kg/m^2. HbA1c was significantly decreased from 8.0% to 7.4%. Small but significant reduction of BMI was observed from 29.8 to 29.2 kg/m^2, suggesting that ipragliflozin decreased blood glucose level without weight gain. Both systolic, from 132.7 to 128.6 mmHg, and diastolic, 80.5 to 76.3 mmHg, blood pressure were significantly decreased without change of antihypertensive drug, probably because of osmotic diuresis by glucose urea. Interestingly, serum C-peptide level was significantly decreased from 2.8 to 2.5 ng/mL, suggesting that ipragliflozin reduced blood glucose level without stimulation of pancreatic beta cells. Ketone bodies, especially 3-hydroxy lactate, were slightly increased, but not statistical significant. Severe adverse effect was not observed during study period. Main adverse effects relating ipragliflozin treatment were thirsty (3.2%) and skin eruption (2.4%).
These data suggest that SGLT2 inhibitor ipragliflozin could control blood glucose level safely and effectively in Japanese patients with type 2 diabetes. In addition to blood glucose control, reduction of blood pressure, weight reduction and pancreatic beta cell protection could be expected for ipragliflozin.

PD-07

Self-perceived low-carbohydrate dieters in diabetes clinic in Japan and their actual behavior

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We have eaten rice as staple food in Japan. Even the Japan Diabetes Society has recommended getting 60% of all calories from carbohydrates.
However, the "Low-carbohydrate diet" to reduce body weight has been popular in developed countries and also cessation or decreasing carbohydrates has been recognized as being effective and an easy way to implement fair glycemic control in the relatively short-term. We investigated the influence of media and patients understanding about low-carbohydrate diets using questionnaires and face to face discussions with diabetes patients.
We administered a questionnaire of 12 questions and asked to diabetes patients to fill them in. The answers and consent were obtained from 150 patients (96 male and 54 female), average age was 68.5 (SD: 12.3) y/o, BMI was 25.6 (5.0), HbA1c 7.17 (1.05) %.
88 patients (61 male and 54 female: chi-squire test: n.s.) answered that they practiced low-carb diet. The "low-carb" group had lower HbA1c ($p < 0.04$), and BMI ($p < 0.01$). Had a longer duration of illness ($p < 0.05$), and less diet consultation with a dietitian ($p < 0.05$). The most chosen reason to practice this diet was "to improve HbA1c (93%)", however their HbA1c was not significantly better. Other reasons were "to lose weight (29%)" and "recommended on TV (11%)". People who reduced or cut staple food in "all three meals" tended to be older than those who did only "1–2 meals" ($p < 0.001$). On the other hand, people who answered "to eat fruit three times a day" were older ($p < 0.01$). Patients who did not go on a "low-carb" diet tended to choose the correct answer of carbohydrate–rich food (such as grains, fruit, and sweets)" more than those who said that they did the "low-carb" diet. 79% of all the patients answered that they did not drink vegetable juice and this is thought to be because of our educational exhibition about the amount of sugar contained in drinks". 64% of the "low-carb" dieters answered that a "low-carb" diet was effective for diabetic kidney disease.
"Low-carb" dieters had relatively good control in glucose and body weight. They were interested in diabetes control. However they received less diet consultation from dietitian. Even when they said they eat "low-carb" food, not all of them correctly answered about "carb- rich food". They were "self-perceived" low-carb dieters. Some people misunderstood "low-carb" food as good for diabetic kidney disease. They need appropriate information about diet.

PD-08

Effect of the therapy of weekly-GLP1 analog given monthly to eldery type 2 diabetes patients

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Objective: Japan is one of the world's leading nations in terms of longevity. In addition, the Japanese people are prone to diabetes. For dementia patients and for elderly patients living alone, compliance with drug therapy can be seen in many cases as risky. So, GLP1 analog formulations administered once a week has been shown as an effective treatment against type 2 diabetes mellitus in the elderly. In this study, it was evaluated when administered once a month.

Research and methods: To target type 2 diabetes mellitus patients, 13 outpatients at our hospital (5 male/8 female) over the age of 67 were administered weekly-exenatide once a month. HbA1c, 1, 5-anhydroglucitol [1, 5-AG], urine albumin-to-creatinine ratio [U-Alb/Cr], as well as a treatment satisfaction survey were also carried out. The effects of monthly administration were compared with those administered once a week with patients with type 2 diabetes in 17 people (11 male/6 female) over the age of 35.
Results:

1. Background for monthly dose group: Age 77.2 ± 6.9 (mean ± SD) years, type2 diabetes duration 20.4 ± 7.4 years, HbA1c 7.7 ± 0.4%, BMI 24.7 ± 3.7
2. After 3 months HbA1c; 7.1 ± 0.5% ($p < 0.01$)
3. After 2 months BMI; 24.3 ± 4.1 ($p < 0.05$)
4. Compared with weekly dose group (Age 64.6 ± 14.0 years, type 2 diabetes duration 17.4 ± 8.0 years, HbA1c 8.7 ± 1.2%, BMI 27.6 ± 5.5): Change of HbA1c after 3 months; −0.68 ± 0.2% vs. −1.19 ± 1.4% (n.s.). A significant difference in 1,5AG and U-Alb/Cr, in both groups, before and after administration was not observed. In the treatment satisfaction survey after the administration, no significant difference in the two groups was observed. In elderly patients with type 2 diabetes who were given a weekly GLP1 analog administered once a month, compared to the previous administration, a promising improvement in HbA1c and BMI was seen. When compared to the weekly administration group, no significant difference in the amount of change in HbA1c was observed.

Conclusions: For aged patients with type 2 diabetes, the usefulness of the method of treatment of administering a GLP1 analog monthly as opposed to weekly could be confirmed.
We will continue to follow up as part of the treatment of the elderly with type 2 diabetes.

PD-09

Insulin intensification with basal plus mealtime insulin or mid-mixture premixed insulin in type 2 diabetes in real-world clinical practice

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Insulin Intensification with Basal plus Mealtime Insulin or Mid-mixture Premixed Insulin in Taiwanese Type 2 Diabetic Patients Inadequately Controlled on Basal Insulin with or without Oral Antidiabetic Drugs in Real-World Practice.
Background: This study was performed to compare the efficacy of basal once-daily glargine plus mealtime glulisine (basal-plus group) with twice-daily mid-mixed insulin (LM50 group) in Taiwan patients with type 2 diabetes (T2D) inadequately controlled by basal insulin with or without oral antidiabetic drugs (OADs) in real-world practice.
Methods: This single-center, non-interventional, prospective, observational study enrolled T2D patients with inadequate glycemic control (glycosylated hemoglobin [HbA1c] ≥7.5%) who had been on basal with or without OADs for ≥3 months and were already decided to intensify insulin therapy by their physician prior to the start of the study. All treatment decisions were at the physician's discretion to reflect real-world practice.
Results: A total of 71 patients were included in the analysis (mean duration of diabetes, 12.8 ± 5.8 years; mean HbA1c, 9.02 ± 1.2%). After 24 weeks of insulin intensification therapy, HbA1c decreased −0.68% and −0.62% in basal-plus group and LM50 group, respectively, which was not significant. The

change of 7-point SMBG at week 24 showed that LM50 group reduced post-breakfast and post-dinner glucose concentrations more significantly compared with basal-plus group. The decrease from baseline in fasting blood glucose was significantly greater in the basal-plus group compared with the LM50 group. Body weight increased 0.95 and 1.45 kg in basal-plus group and LM50 group, respectively. Meanwhile, there was significant increase in the mean daily insulin dose of 20.4 units in LM50 group and 34.6 units in basal-plus group ($P < 0.05$). Six patients intensified their insulin to basal insulin plus two mealtime glulisine, while seven patients to thrice daily mid-mixed insulin. Overall, 15% of patients experienced at least one hypoglycemic event in both groups.

Conclusion: In a real-world setting, intensification of insulin therapy from basal failure to basal insulin plus mealtime glulisine or twice-daily mid-mixed insulin has similar effects on HbA1c reduction, hypoglycemia events and body weight change in Taiwan patients with T2D.

PD-10

Kidney function assessment based on eGFR may broaden metformin eligibility rather than serum creatinine

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Objective: When considering metformin eligibility, Japanese Diabetes Society (JDS) and US Food and Drug Administration recommend serum creatinine (sCr) as a clinical indicator, whereas Kidney Disease: Improving Global Outomes (KDIGO) guideline recommends using estimated glomerular filtration rate (eGFR). We investigated the discrepancy of the two assessment strategy and also analyzed the frequency and the clinical factors of metformin prescription.

Research design and methods: This is a cross-sectional study of 1364 diabetic patients in our hospitals. The upper threshold of sCr for metformin eligibility was 1.3 mg/dL for male and 1.2 mg/dL for female according to JDS recommendation. The lowest threshold of eGFR was 30 mL/min/1.73 m^2 according to KDIGO guideline. We first described the patients who was contraindicated by sCr but was not by eGFR. We next revealed the clinical background of these patients according to the presence of metformin prescription. Lastly, the contributing factors to metformin prescription were searched by multivariate logistic analysis.

Results: Totally 130 patients showed sCr above JDS threshold. Among these, 61(47%) patients showed eGFR over 30 mL/min/1.73 m^2, however, only 14 (23%) were prescribed metformin. The patients with and without metformin prescription were similar in gender, age and HbA1c (7.7 ± 0.7% vs 8.1 ± 1.6%, $p = 0.35$). Also the prevalence of lactic acidosis (LA) risk was not different between the groups; (1) age, (2) alcohol use, (3) coronary artery disease, (4) congestive heart failure, (5) liver disease, (6) ketosis or severe infection, (7) pregnancy and (8) insulin dependent diabetes. However, the patients with metformin prescription exceeded in BMI (28.9 ± 4.7 vs 25.6 ± 4.6, $p = 0.02$) and concomitant use of other oral anti-diabetic agent (2.5 ± 0.9 vs 1.1 ± 1.0, $p = 0.0001$). In multivariate logistic analysis adjusting covariates such as gender, age, BMI, HbA1c, every 10 mL/min/1.73 m^2 increase of eGFR, heavy alcohol use (>5 days/week), coronary artery disease, number of LA risk factors, number of concomitant oral anti-diabetic agent and insulin use, only the number of concomitant oral anti-diabetic agent was significantly associated with metformin prescription (odds ratio 4.3, 95% confidence interval 1.8–14.5, $P = 0.005$).

Conclusion: The assessment of eGFR rather than sCr may promote metformin prescription without increasing LA.

PD-11

Improving postprandial blood glucose of type 2 diabetes patients

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This study is a follow-up investigation for type 2 diabetes patients who have received basic insulin (once a day; intermediate and long-acting) treatment for more than three months, who still had fasting plasma glucose of (FPG) less than 150 mg/dL, HbA1c > 7%. These patients were transitioned to pre-mixed insulin injection twice a day. Since Feb to Aug 2015, there were 47 participants, and 42 of which have completed the follow-up. Telephone consultation was used as the health education method in this study, where 163 phone calls in total were made for the duration of this investigation. The pre- and post-transition glycated hemoglobin (GH) levels were 9.7 ± 1.58% and 8.4 ± 1.57%, respectively (overall reduction of 1.3%). The pre- and post-transition FPG and postprandial blood glucose (PBG) were 146.2 ± 47.5 mg/dL and 131.6 ± 33.2 mg/dL; and 293.0 ± 74.9 mg/dL and 204.3 ± 54.5 mg/dL, respectively. 26.2%, 31.0%, and 35.7% of the post-transition patients were determined with GH of <7%, FPG of <110 mg/dL, and FPG <180 mg/dL, respectively, indicating a significant difference in the GH, FPG, and PBG levels after the insulin treatment transition.

Individualized one-on-one interactive consultation can be used to encourage patient to monitor their blood sugar level proactively and treat FPG and PBG as equally important. The timely resolution of questions and assistance, in combination with health care education group intervention, and promote patient health and self-reliance.

PD-12

The effectiveness of diabetes care by using multiple interventions

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Project objective is to improve blood sugar and correct wrong behaviors by using multiple interventions, including individual and group health education, which guides the patient self-reaction, and share the experience of coexistence with diabetes and correct misconceptions. Recruitment is from March 1, 2015 until October 31, 2015 at someone of medical center of south of Taiwan. Recruitment of patients with HbA1c higher than 7.5 and patients agreed to participate in community health education and individual health education of more than 2 times and telephone interview at least twice. Patients follow at least three months.

Recruit in a total of 30 people, but only 28 finish final test, because one death, one person perform bariatric surgery at other hospital and not return. Weight, BMI have no significant change, HbA1C,fasting blood sugar and postprandial blood sugar, blood sugar fluctuations, eating behavior, exercise and self-monitoring of blood glucose behavior have improvement of statistical significance ($p < 0.05$; $p < 0.00$). An average score of group health education satisfaction is 4.6 points (out of 5).

PD-13

Metformin suppresses gastric cancer cell growth through inducing cell cycle arrest at G2/M phases

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The anti-diabetic drug Metformin has been shown to have the potential as a preventive and therapeutic drug for several cancers, including gastric cancer (GC). The long non-coding RNAs (lncRNAs) are non-protein coding transcripts that are more than 200 nucleotides in length. LncRNA has been reported to be dysfunction in diverse human cancers. However, its impact on metformin-induced gastric cancer cells death remains unclear. In this study, we found that metformin could suppress GC cells growth and invasion in a dose- and time-dependent manner. We also found that metformin inhibited gastric cancer cell proliferation by inducing significant cell cycle arrest at the G2/M phases. In order to identify metformin-induced lncRNAs, we performed the transcriptome profiles of HR control cell line and HR cell line treating with metformin by microarray approach (including 27958 protein-coding genes and 7419 lncRNAs). We identified 2704 genes and 2458 genes that were significantly upregulated and downregulated in the HR cells following treatment with metformin, respectively. Bioinformatics analysis showed that metformin-associated genes simultaneously participated in cell growth, cell cycles and apoptosis. Among these metformin-associated genes, we found that the expression level of Loc10050669 was significantly suppressed in dose- and time course-dependent manner after gastric cancer cells treatment with metformin. Knockdown of Loc10050669 expression could significantly suppress gastric cancer cell growth, invasion ability and induce cell cycle arrest at G2/M phases. These results implied that Loc10050669 may play a critical role on metformin-induced suppression of gastric cancer cell growth and motility. Our findings reveal a new insight for lncRNAs regulation by metformin and provide an application for gastric cancer therapy.

PD-16

Clinical effectiveness study of dapagliflozin as add-on for 33 inadequate glycemic control patients using liraglutide and OADs

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Background: Liraglutide and dapagliflozin have two different anti-diabetical action mechanisms. They have shown ability to improve the glycemic and body weight control. In this study, for those patients who used OADs and liraglutide but fail to meet the glycemic control criteria, dapagliflozin was added to evaluate the effectiveness of liraglutide on glycemic and body weight.
Methods: The design was a real-world, observational study. A retrospective case note audit of type 2 diabetes patients who were added dapagliflozin to their liraglutide regimens was performed in a diabetes clinic located at Yilan County, Taiwan. Datum of A1C, body weight (BW), and adverse events were collected to analyze the effectiveness of initiating dapagliflozin for 6 months.
Results: 33 patients were included in the final analysis. The average age at baseline was 54.1 ± 11.3 and the mean DM duration was 12.7 ± 6.6 years. 60.6% of patients were male and the average A1C and BMI at baseline were 8.0 ± 1.0% and 29.7 ± 5.7 kg/m^2, respectively. The mean duration of using liraglutide before initiating dapagliflozin was 100.2 ± 30.0 weeks. 54.5% of patients used 1.2 mg daily liraglutide and 45.5% of patients used 1.8 mg daily liraglutide at baseline. After adding dapagliflozin for 6 months, A1C has been reduced in 24 patients (72.7%), and the overall A1C has been significantly reduced by 0.71 ± 0.95% ($t = -4.33$, $p < 0.001$). A1C has been reduced by equal and more than 1% in 55.6% of 18 patients with 1.2 mg liraglutide and 26.7% of 15 patients with 1.8 mg liraglutide. BW has been reduced in 29 patients (87.9%), and the overall BW has been significantly reduced by 2.13 ± 2.24 kg ($t = -5.46$, $p < 0.001$). Body weight has been reduced by equal and more than 3 kg in 38.9% of 18 patients with 1.2 mg liraglutide and 26.7% of 15 patients with 1.8 mg liraglutide. Before dapagliflozin being initiated, the incidence of hypoglycemia was 21.2%. After using dapagliflozin for 3 months, the incidence of hypoglycemia was 15.2% (5 out of 33 patients). However, one urogenital infection case has been self-reported.
Conclusions: Dapagliflozin improved glycemic and weight control in patients who used OADs and liraglutide but fail to meet the glycemic control criteria. Reductions in A1C and body weight were not affected by the dose of liraglutide used at baseline. After using dapagliflozin for 3 months, the incidence of hypoglycemia was not increased but one urogenital infection case was self-reported.

PD-17

Clinical effectiveness of liraglutide as add-on therapy after OADs failure for two years in 77 type 2 diabetes cases

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Background: Liraglutide, a glucagon-like peptide-1 (GLP-1) analogue, has been shown to possess beneficial effects on body weight and glycemic control. The long-term effectiveness of liraglutide for type 2 diabetes patients has been evaluated in this study.
Methods: A systematic clinical case note audit of patients with type 2 diabetes who used liraglutide for two years was performed in a diabetes clinic located at Yilan County, Taiwan. After liraglutide was initiated, clinical parameters were collected at baseline, then collected every 3 months for two years. Adverse events were also investigated at the first 3 months.
Results: A total of 77 patients who were 56.2 ± 9.4 years old were selected in this study. The mean duration of diabetes was 12.5 ± 6.2 years. 54.5% of these selected patients were male. The average A1C and BMI of these people were 8.7 ± 0.7% and 29.3 ± 4.2 kg/m^2, respectively. 77.9% of patients were treated with a mixed formula that included metformin, and sulfonylurea. 77 patients have used 1.2 mg liraglutide for 2 years. A1C has been reduced in 61 patients (79.2%), and the overall A1C has been significantly reduced by 0.92 ± 0.98% ($t = -8.27$, $p < 0.001$). The body weight (BW) has been reduced in 65 patients (84.4%), and the overall BW has been significantly reduced by 2.78 ± 3.56 kg ($t = -6.84$, $p < 0.001$). In these selected patients, 30 patients used 1.2 mg liraglutide for 109.4 ± 16.9 weeks, then switched to 1.8 mg liraglutide. At the beginning of 1.8 mg liraglutide being used, their average A1C and BMI were 8.4 ± 0.8% and 29.7 ± 5.3 kg/m^2, respectively. After 3 month, A1C has been reduced in 21 patients (70.0%), and the overall A1C has been significantly reduced by 0.56 ± 0.91% ($t = -3.38$, $p = 0.002$). BW has been reduced in 22 patients (73.3%), and the overall BW has been significantly reduced by 1.47 ± 2.03 kg ($t = -3.97$, $p < 0.001$). During the first week of treatment, adverse events including nausea (29.3%) and loss of appetite (62.7%) were self-reported. However, they reduced to 5.3% and 37.3% after 3 months, respectively.
Conclusions: Long-term liraglutide treatment effectively improves glycemic and body weight control for 2 years. During the first week of treatment, adverse events including nausea and loss of appetite were self-reported more frequently, then they gradually decreased.

PD-18

An observational study of diabetes outpatients switching from glargine or detemir to degludec

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Objectives: The aim of the present prospective observational study is to assess long-term efficacy and safety of insulin degludec (IDeg) as a part of basal supported oral therapy (BOT) or basal-bolus therapy (BBT) for Japanese subjects with type 1 (T1D) or type 2 diabetes (T2D) in routine clinical practice.
Materials and methods: In this study, 93 T1D-BBT subjects and 158 T2D subjects (T2D-BOT; n = 23, T2D-BBT; n = 135) treated insulin glargine (IGlar) or detemir (IDet) were switched from their basal insulin to IDeg. The primary endpoints were the changes in HbA1c from baseline at 3, 6 and 12 months. The secondary endpoints were changes in body mass index (BMI), insulin dose and frequency of hypoglycemia.
Results: During the 1-year observation period, HbA1c levels improved significantly from 8.7 ± 1.4% at baseline to 8.4 ± 1.4% at end of study in T1D-BBT subjects ($p < 0.01$), and from 8.1 1.4% to 7.8 ± 1.3% in T2D-BBT subjects ($p < 0.001$). In T2D-BOT subjects, HbA1c level at 3 months were significantly lower than that at baseline (7.5% ± 0.8% vs 8.0% ± 1.0%, $p < 0.01$). However, there was no significant difference between HbA1c level at baseline and that at month 12. The change in HbA1c levels from baseline to 3, 6 and 12 months were −0.4%, −0.4%, and −0.3% in T1D-BBT subjects, respectively, and −0.5%, −0.1%, and −0.1% in T2D-BOT subjects, respectively, and −0.5%, −0.5%, and −0.3% in T2D-BBT subjects, respectively. BMI in T1D-BBT subjects increased significantly ($p < 0.05$), whereas that in both T2D-BOT and T2D-BBT subjects did not change. Basal insulin dose decreased significantly at 3 months after switching ($p < 0.05$), and returned to baseline dose at 12 months in T1D-BBT and T2D-BBT subjects. On the other hand, that in T2D-BOT subjects did not change during the study period. The frequency of both total and nocturnal hypoglycemia decreased significantly in both T1D-BBT and T2D-BBT subjects ($p < 0.05$). No hypoglycemia was observed before and after switching in T2D-BOT subjects.
Conclusion: In both T1D-BBT and T2-BBT subjects, switching from IGlar or IDet to IDeg led to an improvement of glycemic control with a significant reduction of hypoglycemia. As a novel basal insulin analog, IDeg might provide benefit for diabetic subjects in clinical practice.

PD-19

Different effect of testosterone and estrogen on urinary excretion of metformin via regulating OCTs and MATEs expression in the kidney

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Objective: Metformin, a commonly prescribed first-line anti-diabetic drug, is eliminated into the urine in an unchanged form, primarily secreting by the renal tubule. Membrane transporters, manly including the organic cation transporters (Octs) and multidrug and toxin extrusion proteins (Mates), have influence on the efficiency of metformin and there are gender differences in renal basolateral membrane organic cation transporter activity. The aim of this study is to investigate the effect of testosterone and estrogen on regulating Octs and Mates expression in the kidney of mice and urinary excretion of metformin.
Methods: In this study, 8 week-old male db/db mice were treated with estradiol, testosterone or olive oil with same volume. Metformin is injected to observe the difference of serum concentration and urinary excretion. Plasma, urine and tissue concentrations of metformin were determined by HPLC assay, while Western blotting and Real-time PCR analysis were used to evaluate the renal expression of Octs and Mates.
Results: After 7 days treatment, the expression of Mate1 and Oct2 in testosterone group was significantly increased than those in control group and the expression of Mate1 and Oct2 in estradiol group was significantly reduced by 29.4% and 43.3% respectively compared to those in control group, showing a good agreement with the change in mRNA level (all $p < 0.05$). In addition, the plasma metformin concentration (ng/mL) in mice treated with estradiol was significantly higher than control and testosterone group (677.56 ± 72.49 vs 293.92 ± 83.27 and 261.46 ± 79.45; $p < 0.01$). Moreover, testosterone increased the metformin urine excretion of mice while estradiol decreasing (both $p < 0.01$). Spearman correlation analysis showed that gonadal hormone was closely associated with MATE1 and Oct2 expression and metformin urine excretion in db/db mice (all $p < 0.05$).
Conclusions: Testosterone and estrogen exert reverse effect on metformin urinary excretion via regulating Octs and Mates expression in the kidney of mice.

PD-20

Comparison of acarbose versus voglibose monotherapy on GLP-1 secretion and postprandial dyslipidemia in patients with type 2 diabetes

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An α-glucosidase inhibitor (αGIs), such as acarbose, reduces the risk of impaired glucose tolerance (IGT) progressing to type 2 diabetes mellitus (T2DM), and it prevented the development of cardiovascular disease in the STOP-NIDDM trial. However, the effect of αGIs on incretin secretion and postprandial dyslipidemia remains largely unknown. In this study, we compared the effects of acarbose and voglibose monotherapy on GLP-1 secretion and postprandial dyslipidemia in patients with T2DM. The study enrolled Japanese patients who had T2DM with HbA1c levels ≤7.4% who were not taking any antihyperglycemic agents. The 30 patients (51.2 ± 11.5 years, HbA1c 6.3 ± 0.6%) were randomized to 300 mg acarbose (n = 15) or 0.3 mg voglibose (n = 15). All patients had a meal tolerance test (MTT) performed before and after 12 weeks of treatment. Twelve weeks after treatment, HbA1c decreased by 0.09 ± 0.26% with acarbose and 0.05 ± 0.61% with voglibose, and the difference was not significant. Triglyceride (TG) decreased by 17.7% with acarbose ($P < 0.02$) and increased by 5.5% with voglibose (NS). The delta active GLP-1, defined as the difference between the peak and baseline, was +6.6% (NS) with acarbose and +116.5% with voglibose ($P < 0.05$). Comparing the change in the incremental area under the MTT curves (AUC) for GLP-1 and lipids from baseline to 12 weeks of treatment, the AUC for active GLP-1 decreased by 6.1% with acrabose whereas it increased by 19.6% with voglibose, and the difference was significant ($P < 0.05$). In comparison, the AUC for triglyceride (TG) and remnant like particles cholesterol (RLP-C) decreased by 13% and 6.5% respectively, with acarbose, whereas they increased by 3.5% and 8.3% respectively, with voglibose, and the difference was significant ($P < 0.05$, respectively). In conclusion, the treatment of T2DM with voglibose resulted in a greater increase in active GLP-1 levels during the MMT than with acarbose, while acarbose significantly reduced the postprandial TG and RLP-C levels. Therefore, voglibose

enhances GLP-1 secretion, whereas acarbose improves postprandial dyslipidemia in patients with T2DM.

PD-21

Influence on urination of SGLT2 inhibitor in type 2 diabetes

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Background: Sodium glucose co-transporter 2 (SGLT2) inhibitors are new antidiabetic drugs that increase urinary excretion of glucose. They have polyuria and pollakiuria as adverse events because of their diuretic effect. Therefore we investigated influence on urinary disorder of ipragliflozin (Ipra) and tofogliflozin (Tofo).
Method: A prospective randomized study was conducted on 35 patients with type 2 diabetes [male: n = 22, female: n = 13, age: 55 ± 9, BMI: 27.9 ± 3.6, HbA1c: 7.7 ± 1.0%]. Twenty one patients received Ipra and 14 patients receiverd Tofo daily for 1 month. International Prostate Symptom Score (IPSS), overactive Bladder Symptom Score (OABSS), International Consultation on Incontinence Question- Short Form (ICIQ-SF) were evaluated at before the treatment and after 1 month.
Results: After 1 month of the treatment, body weight (75.3 ± 13.2→74.2 ± 13.2 kg, $p < 0.001$), BMI (28.0 ± 3.6→27.5 ± 4.0, $p < 0.001$), HbA1c (7.7 ± 1.0→7.5 ± 0.8%, $p < 0.001$) and γ-GTP (42.6 ± 32→36.5 ± 24.0, $p < 0.001$) improved significantly. In each total score of IPSS, OABSS and ICIQ-SF, there was no significant change. In each question of scores, there were significant increases in "How often do you usually urinate during the day?" (0.4 ± 0.6→0.7 ± 0.5, $p = 0.008$) of OABSS, "How often do you leak urine?" (0.5 ± 0.9→0.8 ± 1.3, $p = 0.031$) and "Overall, how much does leaking urine interfere with your everyday life?" (0.3 ± 0.9→0.8 ± 1.5, $p = 0.016$) of ICIQ-SF. In patients taking Ipra, there was no significant change in all scores. But in patients taking Tofo, there were significant changes in total scores of IPSS and ICIQ-SF. In the male patients with IPSS more than eight points which moderate benign prostatic hyperplasia is doubted (n = 3), there was no meaningful change in each score. In the patients with OABSS score more than 3 points which overactive bladder was doubted (n = 11), there was no meaningful change neither.
Conclusion: In type 2 diabetes, it was shown that SGLT2 inhibitors can make their glucose control better and make their body weight decrease without any urinary disorder. Some studies were shown that Ipra makes nocturia worse. However in our study, there was no significant change. We may suggest that SGLT2 inhibitors were useful for diabetes patients with and without any urinary disorder.
There are going to be more cases to present by the day of meeting.

PD-22

Assess the efficacy differences of using long-acting insulin and oral hypoglycemic agents in type 2 diabetes patients

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Background: Type 2 diabetes patients usually use two to three kinds of oral hypoglycemic agents, but the treatment effects are poor. According to the latest clinical studies that long-acting insulin and oral hypoglycemic agents can control blood sugar, decrease the risk of blood vessels, and improve quality of life in diabetes.
Objectives: This study evaluated the efficacy of five kinds of oral hypoglycemic agents with long-acting insulin.
Methods: Using retrospective mode to analyze a medical center of outpatient cases in 2014, the subjects are 65 years old with type 2 diabetes, the serum of HbA1C level greater than 7 or more, using insulin glargine and oral hypoglycemic drug to treatment. According to the oral hypoglycemic agents, we divided into five groups: glibenclamide (5 mg), glimepiride (2 mg), pioglitazone (15 mg), sitagliptin (100 mg), saxagliptin (5 mg). We used SPSS statistical software for ANOVA analysis and assessed the correlation of HbA1C level and the five groups before and after treatment.
Results: In this study, the patients have received 174 cases. We found the mean deviation of HbA1C level for the five groups before and after treatment, it had statistical significant disparity ($p < 0.05$). The HbA1C level is reduced 0.32% using insulin glargine and glibenclamide, and the HbA1C level is reduced 0.15% using insulin glargine and glimepiride, and the HbA1C level is reduced 0.49% using insulin glargine and pioglitazone, and the HbA1C level is reduced 0.51% using insulin glargine and sitagliptin, and the HbA1C level is reduced 0.79% using insulin glargine and saxagliptin.
Conclusions: We recommended the best treatment that using insulin glargine with saxagliptin (DPP-4 enzyme inhibitor) in the type 2 diabetes patients.

PD-23

The use and the appropriateness of antidiabetic agents in primary referral hospital

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Background: Diabetes mellitus (DM) is growing worldwide, especially in developing countries. The management of diabetes includes lifestyle modification, medical nutrition therapy, and life-long medication, in accordance with patient-centered approach. The caution and contraindication are highly warranted in considering the proper long term use of antidiabetic drugs. This study was aimed to identify profile and the appropriateness of antidiabetic agents in primary referral hospital.
Methods: A cross-sectional study was conducted at Cilincing General Hospital between December 2015 and February 2016. The subjects were the patients who were referred from primary health cares with clinically suspected for DM during the study. Diabetes mellitus was diagnosed according to Indonesian Society of Endocrinology guideline. The medication was listed based on the regiment given. The appropriateness was assessed by matching the antidiabetic drug and the contraindications.
Result: A total of 62 subjects were participated in the study (75.80% were females). The mean age was 59.58 ± 8.77 years old. Mean admission fasting blood sugar was 231.66 mg/dL (SD 94.01), mean body mass index was 25.23 ± 4.81 kg/m^2, and mean serum creatine was 1.27 ± 0.73. The use of oral antidiabetic agents was metformin (96.80%), sulphonylureas (64.50%), and insulin (19.40%), respectively. The regiments were given as metformin monotherapy (14.5%), sulfonylurea monotherapy (4.8%), combination of metformin and sulfonylurea (61.3%), and combination of metformin and insulin (19.4%). Of subjects who received metformin, there were 4 subjects (6.67%) with eGFR (CKD-EPI) <30 mL/min/1.73 m^2, because rejecting insulin therapy. There were 19 subjects (48.7%) receiving sulfonylurea with eGFR (CKD-EPI) <60 mL/min/1.73 m^2. No history of hypoglycemia was reported by the subjects.
Conclusion: Metformin is the most frequently prescribed drug. The use of metformin and sulfonylurea in renal dysfunction is high. The awareness and monitoring of antidiabetic drugs related their caution and contraindication are urgently needed.
Abbreviations: DM: Diabetes Mellitus / eGFR: estimated Glomerular Filtratrion Rate / CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

PD-24

Characteristics of the nutritional status of the Korean diabetic patients by the nutritional care process model

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Objectives: This study was performed to examine nutrition problems for according to the classification of nutritional care process model developed by the International Dietetics and Nutrition Terminology (IDNT).
Methods: This study was conducted to 526 diabetic patients received diet counseling visited Chonbuk National University Hospital. The patients were divided four groups, normal calorie group (NC, n = 100), over calorie group (OC, n = 135), skip meal group (SM, n = 149), and under calorie group (UC, n = 142) by their eating habits.
Results: The calorie intake of SM (1,557.86 Kcal ± 657.89) was significantly lower than the OC group (2,211.05 Kcal ± 601.24), but was significantly higher than the UC group (1,202.2 Kcal ± 319.34) ($p < 0.0001$). The body weight of SM group (69.33 kg ± 16.2) was significantly higher than the OC group (64.39 kg ± 14.74) and UC group (63.75 kg ± 14.45)($p < 0.01$). The results suggest that the body weight is a significant impact eating habits of regularly diet or skip meal diet more than total calorie intake. In the laboratory results, albumin ($p < 0.01$), lymphocyte count ($p < 0.05$), and hemoglobin level ($p < 0.05$) of the UC group was significantly lower than the OC group. These results suggest that albumin, lymphocyte count, and hemoglobin were more significantly affected by the total calorie intake than eating habits of diet.
Conclusions: Our study showed that body weight of diabetic patients was significantly affected by eating habits compare to total caloric intake. Also, laboratory results such as albumin, lymphocyte, and hemoglobin level were more affected by the total calorie intake compare to body weight.
Our study recommended that diabetic patients individualized nutrition care process is important and must be performed by the dietician who had experienced in individualization protocol, such as, IDNT.

PD-25

Empagliflozin, a sodium-glucose cotransporter 2 inhibitor, suppresses the progression of atherosclerosis in diabetic apoE-deficient mice

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Background: Cardiovascular disease is one of the leading causes of disability and death in subjects with diabetes. Recently, sodium-glucose cotransporter 2 inhibitors (SGLT-2is) were developed as a novel class of drugs for type 2 diabetes (T2D). A clinical study revealed that treatment with empagliflozin, one of the selective SGLT-2is, reduced the primary composite cardiovascular events in patients with T2D. However, it is not well known whether SGLT-2is itself can prevent the progression of diabetic macroangiopathy. In this study, we investigate whether empagliflozin suppresses progression of atherosclerosis in streptozotocin-induced diabetic apolipoprotein-E-deficient (diabetic apoE KO) mice.
Methods: ApoE KO mice were obtained from Jakson laboratory (Bar Harbor, ME). These mice were maintained on a C57BL/6 background. From 9 weeks of age, the mice received intraperitoneal injections of saline or streptozotocin (100 mg/kg). After 2 weeks of injection, development of diabetes in mice was determined by measuring blood glucose level (>200 mg/dL). Then mice were treated orally with empagliflozin (5 mg/kg/day) (n = 8) or vehicle alone (water) as a control (n = 8). After 8 weeks of treatment, the mice were sacrificed and atherosclerotic lesions of aortic sinus and en-face of whole aorta were prepared for immunohistochemistry. The whole aorta or 6-μm-thick frozen sections of the aortic sinus were obtained from ApoE–/– mice and were stained with Oil red O. Lesion size was measured on digital microphotographs of the aortic sinus by measuring the stained surface area using ImageJ software. Plasma total cholesterol, triglyceride, and HDL cholesterol concentrations were measured at Skylight Biotech Inc., (Akita, Japan).
Results: Although there were no significant differences on dietary intake and body weight between control group and emapgliflozin group, casual blood glucose level was lower in emapgliflozin group. Meal tolerance test demonstrated that glucose levels at all time points were lower in emapgliflozin group than in control group. On lipid profile, there were no differences on total cholesterol level and triglyceride level between control group and emapgliflozin group. However, HDL-cholesterol level was significantly higher in emapgliflozin group than in control group. Oil-Red-O staining of aortic sinus and whole aorta demonstrated that size of atherosclerotic lesions was decreased in emapgliflozin group than in control group.
Conclusion: This study provides the first evidence that empagliflozin suppresses the progression of atherosclerosis in diabetic apoE KO mice. These findings may indicate the beneficial effects of SGLT-2is for the prevention of diabetic macrovascular complications in subjects with T2D.

PD-26

Increased grip strength with SGLT2 inhibitors: Sub-analysis by BMI, a new insight to EMPA-REG OUTCOME Study

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Maximal hand grip strength measurement could be a method for cardiovascular risk stratification among patients with type 2 diabetes.
Materials and methods: We examined the change in maximal hand grip strength before and after sodium-glucose cotransporter 2 inhibitor (SGLT2i) treatment. The study included 92 men and 20 women with type 2 diabetes in Japanese. The patients were treated with ipragliflozin 50 mg, luseogliflozin 2.5 mg, or dapagliflozin 5 mg or 10 mg daily for at least 4 weeks. The results showed that both the men and women had increased grip strength in both hands ($P < 0.01$, paired T test). In the sub-analysis, in men, grip strength (GS) of patients whose BMI over 25 (n = 49) was 32.1 ± 1.1 kg (Mean ± SEM) in right hand and 30.5 ± 1.0 kg in left hand at baseline. After SGLT2i, GS of right hand increased to 34.3 ± 1.1 kg ($p < 0.01$), and GS of left hand increased to 32.0 ± 1.1 kg ($p < 0.01$). GS of patients whose BMI below 25 (n = 43) was 28.6 ± 1.1 kg in right hand and 28.1 ± 1.2 kg in left hand at baseline. After SGLT2i, GS of right hand increased to 29.5 + 1.2 kg(n.s.), but GS of left hand was almost the same as 28.2 ± 1.1 kg (n.s.).
In women, GS of patients whose BMI over 25 (n = 11) was 18.5 ± 1.2 kg in right hand and 17.2 ± 1.0 kg in left hand at baseline. After SGLT2i, GS of right hand increased to 20.6 ± 1.6 kg (n.s), and GS of left hand increased to 18.3 ± 1.2 kg (n.s.). GS of patients whose BMI below 25 (n = 9) was 17.5 ± 1.2 kg in right hand and 17.2 ± 0.9 kg in left hand at baseline. After SGLT2i, GS of right hand increased to 20.0 ± 1.5 kg(n.s.), and GS

of left hand increased to 18.3 ± 1.4 kg (n.s.). Thus, in women, because the number of subjects was small, the difference was non-significant statistically.
Conclusion: The results suggest that, in Japanese, obese men over BMI 25 are likely to have an increased GS than lean men. But, in the EMPA-REG OUTCOME Study, obese subjects whose BMI was over 35 were more unlikely to have the benefit of the heart and vascular complication. This difference will give a new insight to understand the difference of races.

PD-27
Blood glucose self-monitoring and control for diabetes patients before and after receiving basic insulin therapies
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Purpose: According to the Taiwan Ministry of Health and Welfare, diabetes is the 5th leading cause of death in 2012. Meneghini has suggested that early insulin therapy not only can effectively stabilize blood glucose for relieving liver and kidney stress, it can further prevent and alleviate comorbidities. Therefore, the diabetes health education team intervention would reinforce patients in monitoring blood glucose, receiving basic insulin therapy, discussing the changes in glycated hemoglobin (A1C) and fasting plasma glucose (FPG) levels before and after insulin therapy for achieving the goal of optimal diabetes management.
Methods: Outpatients with Type II diabetes who have not received any insulin therapy, with A1C >8% and FPG > 150 mg/dL, were selected by the physician and health educator. Patient consents were collected and a glucose meter was provided for each patient for the measurement of FPG of at least 3 times a week. Telephone interviews were performed once a week for the follow-up analysis of the patient's pre- and post-therapy measurement results.
Results: A total of 31 patients were enrolled in this study, 17 of which had an A1C of <7% at 3 month follow-up, and 55% of the 31 patients had HA1c levels of <7%. According to the SPSS12 analysis, the A1C levels showed a significant improvement after therapy (9.58 1.39% to 7.20 1.08%; P = 0.000); the FPG level was also determined to be significantly improved after therapy (217.03 48.16 mg/dL to 142.00 27.98 mg/dL; P = 0.000).
Conclusion: After intervention through health education, with emphasis on the use of blood glucose meter and self-monitoring, the patients' insulin awareness and acceptance of treatment were increased, which had furthered improved the patient self-care and self-management skills. The result is especially significant in improving glycated hemoglobin levels. Therefore, we suggest that health education should emphasize on patient empowerment, and individualized health education to understand the difficulties for each patient in the implementing insulin therapy. The improvements in patient practical self-management abilities can be further applied to other disease management and health education. Therefore, health education intervention can help patients overcome treatment difficulties and enable patients in starting insulin therapy for achieving the goal of efficient of blood glucose management in patients with Type II diabetes.

PD-28
Comparing the effects between atorvastatin 40 mg and vytorin 10/20 mg on lipoprotein parameters and inflammatory markers among dyslipidemic T2DM
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Background: Our study was aim to evaluate the lipoprotein parameters and inflammation modification effects among two equal cholesterol lowering potency medications, atorvastatin 40 mg and vytorin 10/20 mg (10 mg ezetimibe combined 20 mg simvastatin).
Materials and methods: The study was a randomized, 12-week, open labeled study. The study conducted with about 60 dyslipidemic type 2 diabetic patients, who fulfilled additional criteria of age (20–80 yo), HbA1c≦10%, LDL-C≧130 mg/dL, and TG < 400 mg/dL. Laboratory evaluations include total cholesterol, HDL-C, LDL-C, and triglycerides, analyses of ApoA-1, Apo (a), ox-LDL, IL-6, and hsCRP. All anti-diabetic or anti-hypertensive drugs remained constant 8 weeks before and during the intervention period. Evaluations are performed before and immediately after 12-week intervention. Data are reported as mean ± SEM.
Results: 29 subjects (F/M = 17/12, mean age 60 y/o, DM duration 8.0 years) received atorvastatin 40 mg daily, another 31 subjects (F/M = 18/13, mean age 64 y/o, DM duration 7.8 years) received vytorin (10/20 mg) daily. The results showed that after three months of treatment, both atorvastatin 40 mg and vytorin 10/20 mg lowered significant but similar levels of TC (−93.3 ± 6.4 mg/dL [38%] vs −94.1 ± 2.9 mg/dL [41%]), LDL-C (−74.1 ± 4.6 mg/dL [49%] vs −79.9 ± 2.5 mg/dL [55%]), TG (−39.3 ± 13.5 mg/dL [26%] vs −29.8 ± 7.7 mg/dL [20%]), ox-LDL (29.3 ± 3.7 mg/dL [39%] vs 27.0 ± 1.8 mg/dL [36%]). However, no significant change of ApoA-1, Apo (a), IL-6 and hsCRP were found after either atorvastatin or vytorin management.
Conclusion: The effects between Atorvastatin 40 mg and Vytorin 10/20 mg on lipoprotien parameters were similar. Both medications significantly lower ox-LDL, however, there were no effect on Apo (a) and inflammatory markers among dyslipidemic T2DM.

PD-29
The results of utilizing twice daily premixed insulin and lifestyle therapy for treating Type II diabetes
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Purpose: This study was aimed to investigate the diabetes treatment efficiency by utilizing a twice daily premixed insulin and Steno conversation tool for a series of diabetes education, diet control, exercise encouragement, glucose monitoring, and telephone follow-ups.
Methods: This study enrolled Type II diabetes patients in our hospital that have underwent oral anti-diabetics drug (OAD) and basic insulin therapy for at least 3 month, yet, with glycated hemoglobin (A1c) levels of 7.0%, between Feb. 1st and Aug. 31st, 2015. The patients were switched to a twice daily premixed insulin therapy, and were also give 4 sessions of diet and health education classes for the promotion of exercise, instruction on self-monitoring of blood glucose, and telephone follow-up management. The patients were regularly assessed on their number of diabetic medications, fasting blood glucose, postprandial blood glucose, A1c, and weight changes, the patient's attitudes and compliance towards SMBG, exercise, and blood glucose management targets.
Results: A total of 51 patients were enrolled in this study (average age: 64.9 years). During the study period, the patients' OAD number significantly decreased from 1.8 ± 0.4 to 0.1 ± 0.4 type (0–2 types in reduction; with P < 0.001). The average daily basal insulin dose at enrollment was 20.9 ± 10.5U. At the end of the study, the daily premixed insulin dose was 36.8 ± 16.3U (before breakfast: 20.1 ± 9.4U; before dinner: 16.7 ± 7.6U). The insulin dosage increase during this period increased by 16.0 ± 12.8U (between 6 and 48U; P < 0.001). The patient SMBG rate increased from 50% to 95%. The patients with regular exercise increased from 40% to 85%, and the diabetes A1c target knowledge increased from 45% to 100%. The FBG and PBG decreased by 12 ± 42 mg/dL; P = 0.024 (151 ± 28 mg/dL to 138 ± 26 mg/dL) and 70 ± 82 mg/dL; P < 0.001 (244 ± 73 mg/dL to

174 ± 29 mg/dL), respectively. The A1c level and A1C target rate (A1c < 7.0%) decreased by 2.5 ± 1.7%; P < 0.001 (10.2 ± 1.8% to 7.8 ± 0.9%) and increased from 0% to 27.5%, respectively.
Conclusion: The twice daily premixed insulin therapy, in combination with a series of diet and health education classes, regular exercise, and active blood glucose monitoring can be used to significantly improve the blood glucose levels for Type II diabetes patients with histories of OAD and basic insulin therapy.

PD-30

Combination of liraglutide and sitagliptin therapy improves glycemic control in Japanese patients with type 2 diabetes mellitus

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Aim: Liraglutide is a glucagon-like peptide-1(GLP-1) analogue and a GLP-1 mimetic. Sitagliptin is a highly-selective dipeptidyl peptide-4(DPP-4) inhibitor. GLP-1 mimetics and DPP-4 inhibitors are widely used in combination with various kinds of other oral anti-diabetic drugs (OADs) and insulin in Japan. We evaluated the efficacy of sitagliptin when added to liraglutide.
Methods: Japanese type 2 diabetes mellitus (T2DM) patients with inadequate control of HbA1c (HbA1c>=7.0) who treated with 0.9 mg of liraglutide subcutaneously once daily (maximum dosage in Japan) were enrolled in this study (n = 10). Additional therapy was as follows; OADs (n = 1), insulin and OADs (n = 9, insulin dosage was 18.0 ± 10.0 units/day). Means of age, duration of diabetes, body weight (BW) and body mass index (BMI) were 58.6 ± 12.2 years old, 18.0 ± 7.7 years, 73.4 ± 13.8 kg and 29.3 ± 6.0 kg/m^2, respectively. HbA1c, glycated albumin (GA), fasting plasma glucose (FPG), insulin (IRI), C-peptide (CPR) and glucagon were measured. Index of insulin resistance (HOMA-R) and insulin secretion (SUIT index) were calculated as follows; HOMA-R = IRI*FPG/405, SUIT index = 1485*CPR/ (FPG-61.8). BW and body compositions (body fat mass; BFM, lean body mass; LBM, total body water; TBW, protein and minerals) were analysed using the bioelectrical impedance analyser. 50 mg of sitagliptin was added without altering previous therapy. Each parameter was compared using repeated-measure ANOVA. Differences of each parameters between baseline to those in 12 weeks were calculated. P < 0.05 was defined as statistically significant. Data was mean ± standard deviation (SD).
Result: HbA1c and GA were decreased from 8.64 ± 1.43% to 8.19 ± 1.35% and from 21.8 ± 4.6% to 19.6 ± 4.9% (p = 0.003 and p = 0.005, respectively). FPG was reduced from 181.7 ± 22.8 to 150.5 ± 23.4 mg/dL (p = 0.008). SUIT index was increased from 33.8 ± 25.5 to 40.0 ± 31.0 (p = 0.017); while HOMA-R was not changed significantly from 7.3 ± 5.1 to 6.3 ± 6.8 (p = 0.243). BW was not decreased significantly from 73.4 ± 13.8 to 73.1 ± 13.6 kg (p = 0.795). Simple regression analysis showed that ΔHbA1c was correlated with AST(r = 0.701, p = 0.024), ALT(r = 0.670, p = 0.034), γGTP (r = 0.778, p = 0.008), and with or without diabetic retinopathy(r = 0.555, p = 0.096). ΔGA was also correlated with AST (r = 0.870, p = 0.001), ALT (r = 0.909, p = 0.001), γGTP (r = 0.930, p < 0.001) and Δglucagon (r = 0.652, p = 0.041).
Conclusion: Combination of liraglutide and sitagliptin therapy significantly improved glycemic control and insulin secretion. The present data showed that the improvement of glycemic control was correlated with liver finction and reduction of glucagon concentration. The GLP-1 receptor was expressed vrious organs including the pancreas and GLP-1 mimetic activate the GLP-1 receptors, whereas the predominant mechanism of DPP-4 inhibitor was reported to be the local inhibition of intestinal DPP-4 activity and activation of the neural axis(gut-to-pancreas). Our data showed that combination of liraglutide and sitagliptin therapy can be effective in the treatment of Japanese patients with T2DM.

PD-31

Additional effect of metformin and celecoxib against lipid dysregulation and adipose tissue inflammation in high-fat fed rats with insulin resistance

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Aim: We determined the potential synergistic effect of metformin and celecoxib, a selective COX-2 inhibitor, on obesity-induced adipose tissue (AT) inflammation, insulin resistance (IR), fatty liver, and high blood pressure in high-fat fed rats (HFa).
Material and method: Male Sprague-Dawley rats were fed separately a regular or HF diet for 8 weeks. Then, rats fed the regular diet were further treated with vehicle for 4 weeks. Rats fed the HF diet were further divided into 6 groups co-treated with vehicle, celecoxib (30 mg/kg/day), metformin (300 mg/kg/day), metformin (150 mg/kg/day), metformin (300 mg/kg/day) with celecoxib (30 mg/kg/day), and metformin (150 mg/kg/day) with celecoxib (15 mg/kg/day) for an additional 4 weeks.
Results: The HF diet-induced increase in body weight was significantly suppressed in the metformin alone and metformin combined with celecoxib groups, but not in the celecoxib alone group. The increases in the HOMA-IR value and the area under the curve of glucose following an oral glucose tolerance test, systolic blood pressure, and adipocyte size were significantly diminished in treated rats, especially rats undergoing combined treatment. The augmentation of AT macrophage infiltration, as well as AT TNF-, MCP-1, and leptin levels in HFa, were significantly suppressed in the treated groups, especially in rats treated in combination with celecoxib. Furthermore, the elevated hepatic triglycerides content was significantly decreased in the combined treatment group when compared to celecoxib or metformin alone.
Conclusion: A COX-2 inhibitor exerts a synergistic beneficial effect with metformin on and obesity-associated metabolic and cardiovascular disorders in high-fat fed rats.

PD-32

Assessment of Romanian Type 2 Diabetes patients treated with insulin glargine after failure of non-insulin therapy in daily clinical practice

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Background: Large scale prospective studies showed that tight metabolic control reduces microvascular complications and, if implemented soon after diabetes diagnosis, is associated with long-term reduction in macrovascular disease. In the 2012 EASD/ADA position statement, insulin (usually as basal insulin) can be recommended already from the second stage, immediately after metformin monotherapy failure.
Aim: The aim of our study was to assess in daily clinical practice in Romania the metabolic control of T2D patients

treated with insulin glargine after failure of non-insulin therapy, including the reasons for stopping insulin titration.
Material and methods: We performed an open label, non-randomized, cross-sectional, non-interventional registry study on 4601 adult T2DM patients (46.9% Males/53.1% Females) treated for 5–8 months with insulin glargine after failure of non-insulin treatments. Study involved 220 study sites in Romania. Mean age of patients was 61.25 years while mean duration of diabetes was 7.63 years. A total of 84.1% of patients were overweight or obese, with a mean BMI of 30.12 kg/m^2. Comparison between quantitative variables was made with the Student t test or Fisher exact test using the SPSS v21 software.
Results: Mean HbA1c at initiation of insulin glargine (baseline) was 9.4% while mean fasting plasma glucose (FBG) was 232.16 mg%. At that point 97.6% of patients received oral antidiabetics (OADs), of which 74.6% SUs. Mean dose of insulin glargine at treatment initiation was 16.4 IU (0.25 U/kg/day). The majority of physicians planned to use the LANMET titration protocol (in 72.3% of cases) and targeted a HbA1c between 6.5% and 7% (in 66% of cases). Mean value of HbA1c reported at the final visit was 7.3%, with an absolute HbA1c reduction of 2.1%. FBG decreased to 128.61 mg/dL. At final visit, the mean dosage of insulin glargine was 31.09 IU. The most frequent reasons to stop insulin titration were achieving target HbA1c (1904 patients – 41.4%) and FBG (2863 patients – 62.2%). Only 29 (0.63%) patients had documented symptomatic hypoglycemia (BG < 70 mg/dL).
Conclusions: We found a significant decrease of HbA1c and FBG on a cohort of Romanian T2DM patients treated for 5–8 months with insulin glargine after failure of non-insulin therapy. 41.4% of patients initiated on basal insulin glargine could reach the HbA1c target and 62,2% of patients reached the FPG target in the first 5–8 months with an appropriate titration according with the guidelines recommendations. Overall the risk of hypoglycemia was low.

PD-33
Ipragliflozin, a novel SGLT2 inhibitor, improves blood glucose, as shown by continuous glucose monitoring, and ameliorates metabolic syndrome

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Background and aims: Ipragliflozin (Suglat®) was the first selective SGLT2 inhibitor in Japan and has become widely used since April 2014.
Our aims: To assess the plasma glucose changing and efficacy and safety of Ipragliflozin.
Methods: T2DM patients with poor blood glucose control received 50 mg Ipragliflozin once daily as monotherapy or as additional therapy. Efficacy and safety were evaluated for 24 weeks. CGM was performed for one-week periods at week 0 and week 4.
Results: 14 patients were enrolled (male/female: 8/6; age: 53.6 ± 3.0 y; body weight: 79.6 ± 3.8 kg; BMI: 29.8 ± 1.0; HbA1c: 8.0 ± 0.4).
CGM: The daily blood glucose curve at week 4 was consistently lower than baseline. The average whole-day blood glucose was decreased significantly, and nocturnal blood glucose, FPG, PPG, postprandial AUC 0–3h also tended to decrease. However, indicators of fluctuation, such as MAGE and standard deviation, were not changed significantly.
PD: The 24-h urinary glucose excretion and urinary volume were significantly increased consistently around 90 g/day and 900 mL/day respectively.
Efficacy: The change in HbA1c was −0.8% ($P < 0.01$) from week 4 and continued until week 24. The change in body weight was −2 to −3 kg from week 4 ($P < 0.01$). Waist circumference, blood pressure, HDL, and urinary urea were significantly improved.
Safety: No serious adverse events (AEs), symptomatic hypoglycemia or dehydration occurred during the study. Mild AEs based on PD, such as pollakiuria, polyuria, and hunger, occurred more frequently in most patients.
Conclusion: Daily administration of Ipragliflozin was effective in improving glycemic control, body weight, and metabolic syndrome in Japanese obese T2DM patients with good safty and tolerability. We conclude that Ipragliflozin can be beneficial as monotherapy or in combination with other anti-hyperglycemic regimens in the treatment of T2DM patients.

PD-35
The application of mobile APP for diabetic self-management in adolescent with Type 1 diabetes

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Purpose: Adolescence is an important stage in person's independence. Health educator must notice on adolescent patients for learning independent decision-making and self-care. The goal of this study is to assist a teenager with Type 1 diabetes by using mobile phone APP for blood glucose management.
Methods: This study was conducted in a medical center in central Taiwan from Aug. 7th to Sep. 23rd, 2015. A mobile blood glucose self-management APP was used for assisting patient self-care at home. The APP functions include: using instance messages or reminder to assist the user in monitoring and recording their blood glucose, diet, medication, and exercise regime. The APP response was also provided including synchronized and non-synchronized feedback. The effectiveness of APP was evaluated by self-report diabetes management scale, glycated hemoglobin (A1C), and average of blood glucose levels.
Results: A 14 year-old participant was recruited with pre-intervention, the average of blood glucose level was 147 mg/dL (range: 54–341 mg/dL), and 72 times of abnormal blood glucose measurements (out of 129 measurements). The average of blood glucose was changed to 112 mg/dL (range: 63–181 mg/dL), and 31 times of abnormal blood glucose measurements (out of 120 measurements) after intervention. Also, the A1C level was improved from 14% to 8.1% in this program. By APP assistance, the patient's satisfaction of diabetes self-management was high as 90%. The APP can be used to record patient's daily diet and provide suggestions for carbohydrate replacement. Furthermore, with synchronized feedback in APP, patient had a better and instant discussion with health educators for blood glucose management.
Application: The use of mobile APP can provide promptly consultation and visualization of blood glucose fluctuation. The promptly education is one of valuable strategy in assisting the adolescent patient in performing diabetes self-care, learning self-management, and maintaining stable blood glucose. Therefore, we suggest that the application of mobile APP can be as good strategy in clinical health education.

PD-36
Clinical course after discontinuation of the SGLT2 inhibitor tofogliflozin

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Objectives: Sodium-glucose co-transporter 2 (SGLT2) inhibitors induce glycosuria, reduce glucose toxicity and improve insulin sensitivity and β-cell function. In addition, they have other potential benefits in terms of weight loss and reduction of blood pressure. However, in contrast, increased risk of genital and urinary tract infections and osmotic diuresis-related adverse events are consistently reported with the use

of SGLT2 inhibitors. Thus, it is controversial whether we should continue SGLT2 inhibitor administration in the long term after having obtained the expected beneficial metabolic effects. We therefore examined the 1-year clinical course of patients with type 2 diabetes mellitus after discontinuation of the SGLT2 inhibitor tofogliflozin.
Methods: Twenty-one patients with type 2 diabetes mellitus who were treated with 20 or 40 mg/day tofogliflozin for 52 weeks participated in this study (monotherapy, n = 9; combination therapy with sulfonylureas, n = 12). All the patients were involved in the Phase 3 clinical study of tofogliflozin in Japanese patients with type 2 diabetes mellitus. After discontinuation of tofogliflozin, changes in clinical parameters including body weight, HbA1c, serum lipid concentrations and liver enzymes were observed for the following year.
Results: Patient body weight decreased an average of 3.1 kg after tofogliflozin administration for 52 weeks, but increased 2.1 kg on average in the 3 months following tofogliflozin discontinuation. Furthermore, body weight returned to the level before treatment within one year. HbA1c levels also decreased an average of 1.1% after tofogliflozin administration, but increased 0.4% in the first 3 months after discontinuation of the drug, and interventions with other classes of hypoglycemic agents were performed in 19 of the 21 patients. Similarly, alanine aminotransferase and γ-glutamyltransferase significantly decreased during the tofogliflozin treatment period, but increased again after discontinuation of tofogliflozin.
Conclusion: The pharmacological effect of the SGLT2 inhibitor tofogliflozin disappeared immediately following drug discontinuation, and increases in body weight, HbA1c and the liver enzymes were observed within 3 months in most cases. Therefore, careful assessment of patients, including behavioral changes and their metabolic condition, is necessary for making a decision on continuation/discontinuation of SGLT2 inhibitors.

PD-37
The effect of rice-bran dietary fiber on postprandial blood glucose for Type II diabetic patients

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Dietary fiber has important role in the management of postprandial blood glucose (PBG) control for diabetic patients. The rice bran that is left over from the rice refinement process has a large amount of dietary fiber. Therefore, the effect of rice-bran dietary fiber (RDF) on PBG among Type II diabetic patients was investigated. A total of nine volunteering Type II diabetic patients were enrolled in this study. The patients were given, on two separate days, the same breakfasts (including 60 grams carbohydrates) that were with RDF (10 g) or RDF-free. Fasting and postprandial blood was collected at intervals of 30 min for 180 min to determine whole blood glucose. The results indicated that the use of RDF can significantly reduce the area under the curve (AUCglucose) for the PBG plot (36360 ± 6073 vs. 32560 ± 5546.7 mg/dL × min, $P < 0.05$) as well as shortened the PBG peak values and peak time. In conclusion, rice bran dietary fiber can be used to improve PBG for Type II Diabetic Patients.

PD-38
The effect of SGLT2 inhibitors on drug-naive obese type 2 diabetes mellitus patients

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We administered sodium glucose cotransporter 2 (SGLT2) inhibitors to drug-naive obese type 2 diabetes mellitus (T2D) patients for 3 or 4 months. We report changes in blood sugar control of 3 patients. Case 1: 20 mg tohogliflozin for 4 months was administered to 47 year-old female whose duration of diabetes mellitus (DM) was about 3 years. Body weight (BW) was reduced from 85.9 kg to 71.1 kg. Blood sugar levels before meals (preprandial) were lowered from 166 mg/dL to 97 mg/dL. HbA1c was improved from 8.7% to 5.3%. Imunoreactive insulin (IRI) levels decreased from 7.49 mcIU/mL to 4.89 mcIU/mL. Serum C-peptide reactivity (S-CPR) decreased from 2.54 ng/mL to 1.75 ng/mL. Case 2: 50 mg ipragliflozin for 4 months was administered to 64 year-old male whose duration was about 4 years. BW was reduced from 79.3 kg to 75.8 kg. Preprandial blood sugar was lowered from 202 mg/dL to 162 mg/dL. HbA1c was improved from 10.7% to 7.6%. IRI increased from 3.06 mcIU/mL to 7.39 mcIU/mL. S-CPR increased from 1.73 ng/ml to 2.65 ng/mL. Case 3: 5 mg dapagliflozin for 3 months was administered to 43 year-old male whose duration was about 1 month. BW was reduced from 95.3 kg to 83.5 kg. Preprandial blood sugar was lowered from 134 mg/dL to 96 mg/dL. HbA1c was improved from 7.9% to 5.7%. IRI decreased from 11.86 mcIU/mL to 8.94 mcIU/mL. S-CPR decreased from 2.13 ng/mL to 1.61 ng/mL. The improvements of their clinical condition were much due to the loss of their body weight. Insulin resistance could be reduced by the loss of body weight. Insulin resistance is the essential of T2D. Adiponectin levels were slightly increased in Case 1 and Case 2. Free fatty acid was decreased in Case 3. These phenomena indicated that SGLT 2 inhibitor could increase one of insulin sensitivity enhancers, and decrease one of induction factors of insulin resistance. In Case 1 and in Case 3, the patients took care of their BW, and they stopped snacking. As the patient of Case 2 could not stop snacking, neither IRI nor S-CPR were improved. When SGLT2 inhibitors are administered to drug-naïve obese T2D patients who observe the compliance to dietary, we may expect the improvement of their insulin resistance and SGLT2 inhibitors could cure the essential of T2D.

PD-39
Plasma serpinB1 levels are strongly correlated with circulating ANGPTL8 levels in patients with type 2 diabetes

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Background and aims: SerpinB1, a protease inhibitor secreted by the liver, has recently been described as a potent stimulator that increases beta cell proliferation in mice and humans. While we previously reported that ANGPTL8 correlated with insulin secretion capacity, the pathophysiological role of SerpinB1 in patients with type 2 diabetes mellitus (T2DM) remains poorly understood. The aim of the study was to evaluate the relationship between plasma SerpinB1 levels and other biomarkers including ANGPTL8.
Materials and methods: Overnight fasting plasma samples from 8 healthy subjects and 69 T2DM patients were collected. HbA1c, fasting plasma glucose, total cholesterol, triacylglycerol, and creatinine clearance (CrCl) calculated by 24-hour urine collection were measured in all T2DM patients. Plasma levels of serpinB1 (Cusabio, Catalogue No. CSB-EL021065HU) and ANGPTL8 (Eiaab, Catalogue No. E11644h) were determined by enzyme-linked immunosorbent assay according to the manufacturer's protocol. Correlations were evaluated by Spearman's rank test. P values <0.05 were considered statistically significant.
Results: Plasma serpinB1 levels were significantly higher in T2DM patients (0.53 ± 0.28 ng/mL) than in healthy subjects (0.21 ± 0.16 ng/mL; $p < 0.05$). In T2DM patients, plasma serpinB1 levels showed a significant positive association with ANGPTL8 ($r = 0.47$ $p < 0.001$). Both serpinB1 and ANGPTL8 levels

significantly correlated only with age (serpinB1: r = 0.38 p = 0.001; ANGPTL8: r = 0.48 p < 0.001), duration of diabetes (serpinB1: r = 0.36 p = 0.002; ANGPTL8: r = 0.43 p < 0.001), and CrCl (serpinB1: r = –0.32 p = 0.006; ANGPTL8: r = –0.49 p < 0.001). After adjustment for age and CrCl, the correlation of serpinB1 levels with ANGPTL8 levels remained significant (r = 0.38, p = 0.002).
Conclusion: We showed that serpinB1 levels were higher in T2DM patients than in healthy subjects, suggesting that serpinB1 plays a role in regulation of beta cell mass in human. Since both serpinB1 and ANGPTL8 levels correlated with each other and with the same parameters, both proteins could be similarly regulated in T2DM patients.

PD-40
DPP-4 inhibitors treatment in Chinese type 2 diabetes patients: A meta-analysis
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Objective: The aim of this meta-analysis is to assess the comprehensive clinical efficacy of DPP-4 inhibitors in Chinese type 2 diabetes patients and to evaluate whether there is a different response to treatment with different kinds of DPP-4 inhibitors in Chinese.
Methods: Databases were systematically searched and qualifying clinical studies in Chinese type 2 diabetes were included.
Results: A total of 25 studies were included in the meta-analysis. Treatment with saxagliptin resulted in a significantly greater change from baseline in the HbA1c levels (WMD, –1.34%; 95% CI, –1.43 to –1.24%); treatment with sitagliptin led to a significantly greater change from baseline (WMD, –1.20%; 95% CI, –1.52 to –0.88%); treatment with vildagliptin was associated with a significantly greater change from baseline in the HbA1c levels (WMD, –1.21%; 95% CI, –1.54 to –0.87%); treatment with linagliptin led to a significantly greater change from baseline (WMD, –0.73%; 95% CI, –0.86 to –0.60%) and treatment with alogliptin also led to a significantly greater change from baseline (WMD, –0.91%; 95% CI, –1.48 to –0.33%). In terms of body weight, treatment with saxagliptin was associated with no significantly decreases from baseline in Chinese T2DM patients (WMD, –0.17 kg, 95% CI, –4.26 to 3.92 kg). Treatment with sitagliptin and linagliptin were also associated with no significantly changes from baseline in body weight (WMD, 0.03 kg and 0.11 kg respectively, p > 0.05).
Conclusions: In Chinese type 2 diabetes patients, the efficacy of glucose control in all the five kinds of DPP-4 inhibitor treatment is well confirmed and no significant change in body weight is found.

PD-41
Identical hypoglycaemic effect of teneligliptin with linagliptin in type 2 diabetes with chronic kidney disease
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Background: Since the major excretion pathway of both teneligliptin and linagliptin is through the liver, they can be used in regular dose in patients with severe renal dysfunction. However, to date, there have been no studies comparing the hypoglycaemic effect of these two drugs. Therefore, we conducted a study to compare the effectiveness between the two drugs in Japanese patients with chronic renal disease.
Subjects and methods: The outpatients who were administered teneligliptin or linagliptin newly or add-on to existed therapy were retrospectively extracted. Only those who with HbA1c more than 7.0% and eGFR less than 60 mL/min/1.73 m^2 at baseline were selected, and those patients on hemodialysis or discontinued/changed medicine within 6 months were excluded. The HbA1c levels, body weight and serum creatinine levels were investigated before and 3 and 6 months after the drug administration.
Results: A total of 34 patients (male 25; mean age: 70.0 ± 11.6 S. D. years, BMI: 25.5 ± 4.6 kg/m^2, serum creatinine: 1.5 ± 0.9 mg/dL, HbA1c: 8.0 ± 1.0%), with 20 mg of teneligliptin (n = 13; male 10: group A) and 5mg of linagliptin (n = 21; male 15: group B) were enrolled in the study. HbA1c levels were similarly decreased in both groups (3 m: –0.7 ± 0.6% vs. –1.1 ± 0.9% P = 0.09; 6 m: –1.1 ± 1.3% vs. –1.3 ± 1.1% P = 0.52, group A vs. B, respectively). Body weight (3 m: 0.3 ± 2.3 kg vs. 0.0 ± 0.9 kg; 6 m: –0.1 ± 2.7 kg vs. –0.1 ± 1.2 kg) and serum creatinine levels (3 m: –0.1 ± 0.5 mg/dL vs. 0.2 ± 0.4 mg/dL; 6m: –0.1 ± 2.7 mg/dL vs. –0.1 ± 1.2 mg/dL) did not show any significant change in both groups.
Conclusion: The hypoglycaemic effect of teneligliptin was identical to linagliptin in Japanese patients with chronic kidney disease. Either drug did not affect body weight and kidney function during 6 months.

PD-42
The study of anti-diabetic drugs treatment (Monotherapy, Bitherapy, and Tritherapy) among diabetic mellitus patients in Preah Kossamak Hospital, Cambodia
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Objective: To evaluate utilization pattern of anti-diabetic drugs in three different forms: Monotherapy, Bitherapy, Tritherapy on Type II diabetic patients.
Methods: A study was carried out in 250 cases patients for a period of one year in the Department of Diabetology at Preah Kossamak Hospital, from 2014 to 2015. Patients treated with anti-diabetic drugs including Monotherapy, Bitherapy, Tritherapy. The demographic data and utilization of different classes of anti-diabetic drugs as well as individual drugs were analyzed.
Result: The study was shown that the popular treating option for anti-diabetic agent was monotherapy, about 80% overall. And the drug that was used to treat in this type of therapy was Metformin (Biguanides). It was used the most among other hypoglycemic drugs, and there were two kinds of Metformin used: Metformin 500 and Metformin XR. About 75% of the population used Metformin 500, while a smaller amount used Metformin XR. Apart from Monotherapy, Bitherapy of the anti-diabetic agents was popular after that, in which it accounted for 14%. And lastly, Tritherapy was the least popular option among all, 7%.
Conclusion: Metformin 500 was the most commonly used drugs, in both monotherapy and as well as bi- and tritherapy. Overall, those two drugs were used effectively among all patients while the other anti-diabetic drugs' usage percentages were low. Moreover, patient knowledge about their drugs' usage is low. In this study, the cost of drugs per prescription was found to be very high. However, we can reduce the cost per prescription by choosing most economical drugs without changing its quality.

PD-45
The effect of Djulis hull on postprandial plasma glucose of Type II diabetes patients
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Djulis (Chenopodium formosanum Koidz) is a crop that is specific to Taiwan that is rich in dietary fiber, phenols, and betalains. This study was aimed to determine the effect of

Djulis hull supplements on the three hour postprandial plasma glucose (PPG) of Type II diabetes patients. A total of 10 outpatient participants were enrolled in this study. The participants were asked to take or not to take a Djulis hull (5 or 10 g), prior to their standard meal consisting of 75 g of glucose water. The patient PPG levels at 30, 60, 90, 120, and 180 minutes after meal were compared to two measurements of their fasting plasma glucose (FPG) levels. The study results indicated: four of the participants exhibited decrease of area under the PPG curve over 180 mins; four of the participants exhibited delayed glycemic response, yet, with no reduction in the area under the PPG curve; and the other two patients showed no PPG effect with the intake of Djulis hull. It was determined that the dietary fiber rich Djulis hull can have PPG effects that are high individual specific. Therefore, it is suggested that when eating high-fiber diet, Type II diabetes patients should consider their individual glycemic response for adjusting their medication dosage or timing strategies.

PD-46

The effect of transglucosidase for improving postprandial blood glucose of Type II diabetes patients

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Transglucosidase (TGD) can be obtained from the fermentation of Aspergillus Niger. This enzyme can catalyze carbohydrate in the digestive tract into unabsorbable oligosaccharides. Therefore, it is suspected that TGD can be used for lowering postprandial blood glucose (PBG) of diabetes patients. A total of nine Type II diabetes outpatient volunteers were enrolled in this study. Each of the participants were asked to take a TGD capsule or not, prior to eating their standard breakfast that contained 60 g of carbohydrates. The patient fingertip PBG levels at 30, 60, 90, 120, and 180 minutes after meal were compared to two measurements of their fasting blood glucose (FBG) levels. The TGD capsules contain 100mg of TGD that was manufactured by Amano Enzyme Inc. The study results indicated that the intake of pre-meal TGD can decrease the time that it takes for PBG to return to that of a FBG level (from 150 mins without TGD to 120 mins with TGD). The regression analysis also determined that the use of TGD can significantly reduce PBG ($P = 0.028$) and the area under the curve of the PBG plot over the 180 post-meal period ($P = 0.02$). Therefore, the use of pre-meal TGD can be used to lower the PBG for Type II diabetes patient. However, the long term use of TGD and its effect may warrant further investigations.

PD-47

Efficacy and safety of once-weekly GLP-1 RA in patients with type 2 diabetes treated with DPP-4 inhibitor

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Objective: The efficacy and safety of once-weekly glucagon–like peptide-1 (GLP-1) receptor agonist were assessed in Japanese patients with type 2 diabetes who were treated with dipeptidyl peptidase-4 (DPP-4) inhibitor therapy in advance.

Study design and method: We started the treatment of 0.75 mg of dulaglutide or 2 mg of long-acting exenatide once-weekly subcutaneous injection in 36 patients who were already DPP-4 inhibitor therapy at least for 6 months duration with inadequate glycemic control, 32 subjects on dulaglutide and 4 on exenatide respectively. 15 patients were on insulin and 11 out 36 subjects were on Sodium Glucose co Transporters 2 Inhibitor (SGLT2i) together with DPP-4 inhibitor treatment. Insulin was titrated based on glycemic control to avoid hypoglycemia. After 16 weeks, the change in glycated haemoglobin (HbA1c) level, daily dose of insulin, body weight, urinary albumine excretion and the incidence of adverse events were accessed in retrospective way.

Results: The patients were 66.8 ± 14 years of mean age, and 26.0 of BMI with average duration of 11.6 years in Diabetes. The mean level of HbA1c in baseline was 9.0% and decreased to 8.29% at 16 weeks however the mean BMI stayed at 25.9 at 16 weeks later. The mean daily dose of insulin in baseline was 34.2 Units and 18.7 Units daily at 16 weeks. The rates of urinary albumin excretion was decreased, 185 in baseline and 102.4 mg/gCr at 16 weeks. The adverse events were gastrointestinal-related events, 2 out of 36 patients each on dulaglutide and on exenatide were failed to continue within a week after administration.

Conclusions: Once-weekly GLP-1 receptor agonist on insulin-based or oral antidiabetes drugs treatment were effective, for the subjects with inadequate glycemic control on DPP-4 inhibitor treatment, at lowering HbA1c with a remarkable reduction of 45.3% in daily insulin dose and urinary albumin excretion and associated with few adverse event and no weight gain over 16 week.

PD-48

Liraglutide add-on to insulin improved glycaemia but exhibited short durability after cessation in type 1 diabetes with residual insulin secretion

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Background and aims: GLP-1 receptor agonists are expected to be protective against β-cell destruction. Therefore, long-period treatment with liraglutide (Lira) in patients with type 1 diabetes (T1D) who have residual insulin secretion may not only improve glycaemic control but also result in sustained effects through recovery of beta-cell mass. In this study, we investigated the durability of the effect of Lira treatment on glycemic control after its cessation.

Methods: Six T1D patients with residual insulin secretion [fasting C-peptide (CPR) level >0.3 ng/mL] received Lira add-on to insulin therapy for 1–2 years, and changes in HbA1c, body weight and daily insulin doses were investigated during the Lira treatment period and 6 months after its cessation.

Results: The characteristics of the subjects were as follows; male/female 4/2, age 51.3 ± 10.0 yrs (mean ± SD), BMI 21.7 ± 3.2 kg/m^2, fasting C-peptide level 0.18–1.25 ng/mL (median 0.35 ng/mL), anti-GAD antibody 1.5–250 U/mL (median 27 U/mL), and duration of diabetes 1.5–28 yrs (median 7 yrs). HbA1c before Lira was 8.1 ± 1.3%, and was tended to decrease to 7.6 ± 1.0% ($p = 0.11$) at the end of Lira treatment. Total daily insulin dose was reduced from 44.5 ± 20.3 to 40.3 ± 15.5 U/day although it did not reach statistical significance ($p = 0.19$). Immediately after the cessation of Lira, HbA1c level was significantly increased to 7.9 ± 1.2% at 1 month ($p = 0.02$) and finally reached to the similar level to the baseline level before Lira (8.3 ± 1.5%, $p = 0.38$ vs. before Lira). Daily insulin dose was also increased to the identical amount before Lira (44.5 ± 22.1 U/day, $p = 0.50$ vs. before Lira and $p = 0.05$ vs. end of Lira). Body weight showed a slight reduction at the end of Lira treatment, but regained after the stop of Lira (61.9 ± 4.6 kg, 60.4 ± 5.5 kg [$p = 0.04$ vs. before Lira], and 62.2 ± 5.3 kg [$p = 0.07$ vs. before Lira and $p = 0.38$ vs. end of Lira] at baseline, end of Lira and 6 months after Lira cessation, respectively).

Conclusion: In conclusion, adding Lira on insulin therapy in T1D may have a therapeutic potential to improve glycemic control with decreased insulin doses, but the benefit cannot be maintained without continuation of Lira suggesting that the effects were unlikely to be demonstrated though the recovery of beta-cell mass.

PD-49

Effects of teneligliptin in elderly patients with type 2 diabetes mellitus

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Objectives: The aim of this study was to examine the effects of teneligliptin, a dipeptidyl peptidase-4 (DPP-4) inhibitor, in elderly patients with type 2 diabetes.
Methods: One hundred and seventy-five patients with type 2 diabetes treated with 20 mg once daily teneligliptin were studied as the treated set (TS) in order to analyze the safety of teneligliptin. One hundred and thirty-seven subjects whose medications remained unchanged during the observation period were retrospectively investigated as the full analysis set (FAS) to assess the effectiveness of teneligliptin for 6 months. The subjects were divided into two groups: the elderly group (≥70 years of age, n = 66) and the non-elderly group (<70 years of age, n = 71). The parameters were analyzed separately in the subjects receiving monotherapy, additional therapy (i.e. teneligliptin added to the other antidiabetic agents), and switching therapy (i.e. teneligliptin was switched from the other DPP-4 inhibitor).
Results: In the TS, adverse events were recorded in 39 subjects (22%). In the FAS, the HbA1c levels were significantly improved in subjects receiving monotherapy (n = 56) or additional therapy (n = 29) in the elderly group (7.2 ± 0.6% to 6.6 ± 0.4% and 7.5 ± 0.9% to 6.6 ± 0.9%, respectively), similar to the non-elderly group (7.5 ± 1.3% to 6.8 ± 0.8% and 7.4 ± 1.2% to 6.6 ± 1.1%, respectively). The change in the HbA1c levels at 6 months after the initiation of teneligliptin therapy was not significantly different between the elderly and non-elderly groups (−0.6 ± 0.5 and −0.8 ± 1.1, respectively in the subjects receiving monotherapy, and −0.8 ± 0.8 and −0.8 ± 0.5, respectively in those receiving additional therapy). The HbA1c levels were not significantly changed both in the elderly and non-elderly subjects receiving switching therapy (n = 52).
Conclusions: Teneligliptin is equally effective for elderly patients with type 2 diabetes and non-elderly patients.

PD-50

The effectiveness and safety of sulfonylureas in type 2 diabetes with chronic kidney disease in center Taiwan

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Background: The administration of sulfonylureas in Chronic kidney disease (CKD) requires careful attention to dosing and routes of elimination, especially include long-acting sulfonylureas (e.g., glimepiride, glibenclamide). There are not recommended for nondialysis CKD patients with GFR <30 mL/min. But the physicians also prescribe them in some cases in real world. Therefore, we perform a medication evaluation to assess the effectiveness and safety of sulfonylureas.
Objective: The aim of this study was to assess the effectiveness and safety of sulfonylureas in type 2 diabetes with CKD.
Method: We retrospectively review patients with diagnosis of gout (ICD-9 580) concomitant with sulfonylureas (including glimepiride, glimepiride/metformin and glibenclamide) during Jun to Dec 2015 in Changhua Christian Hospital. Patients with prescription of sulfonylureas less than 7 days were excluded. We collect the data of patient age, sex and analyzed the progression of renal function (eGFR, serum creatinine) and preprandial blood sugar. Prescribed Daily Dose (PDD) of sulfonylureas was calculated. Hospital-based spontaneous reporting systems databases were survey for the sulfonylureas adverse reaction reporting.
Results: A total of 131 patients were included with mean age 69 ± 12.3 years. There were 64 female and 67 male. The average duration of prescription was 168.6 ± 128.4 days. Prescribed Daily Dose (PDD) of glimepiride, glimepiride/metformin and glibenclamide was 3.4 mg, 4.3/1065 mg, 5 mg. The serum creatinine was increased from 2.9 ± 2.3 to 3.2 ± 2.6 mg/dL. The eGFR was decreased from 31.8 ± 19.7 to 29.7 ± 19.3 mL/min/1.73 m^2. 48.9% (64) of patients with eGFR < 30 mL/min/1.73 m^2 at the baseline. In subgroup analysis, 79 patients with glimepiride (the duration of prescription average 170.4 ± 134.7 days), 32 patients with glimepiride/metformin (average 172.2 ± 105.5 days), 2 patients with glibenclamide (average 21 ± 14 days), the preprandial blood sugar derement was 16.8 ± 61.2 mg/dL, 2.1 ± 40.9 mg/dL and 0 mg/dL respectively and eGFR derement was 1.2 ± 3.3, 5.6 ± 17.2, 0.6 ± 0.6 mL/min/1.73 m^2. There are no ADR report in three arm, but we found nine cases with glimepiride occurred hypoglycemia. The incidence of hypoglycemia was 6.9% (9/131).
Conclusion: Sulfonylureas is an effective sugar-lowering agent. We found a trend that glimepiride/metformin use, the more eGFR decline. The safety of sulfonylureas was well tolerated from the adverse reaction reported. But the total 9 cases occurred hypoglycemia were glimepiride group. Therefore, we need to closely monitor blood sugar in in type 2 diabetes with CKD patients.

PD-51

Baseline characteristics of patients initiating insulin treatment for type 2 diabetes in the Western Pacific: Evidence from the VISION Study

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Background/objective: The Verifying Insulin Strategy and Initial Health Outcome ANalysis (VISION) is an 18-month, 9-country, prospective observational study of patients with type 2 diabetes initiating insulin therapy as part of routine practice in the Middle East and North Africa and Western Pacific regions. This (ongoing) study is designed to assess treatment approaches and decisions, clinical effectiveness of insulin therapy, cost/resource use, treatment patterns, and the demographic and clinical characteristics of patients. The objective of this analysis was to describe the baseline characteristics, including several patient reported outcomes, of patients from the Western Pacific region enrolled in VISION.
Methods: Patients provided consent to participate in the study after the decision to initiate insulin therapy was made. The Western Pacific region included 1025 patients from Thailand (n = 315), Malaysia (n = 230), Philippines (n = 178), Taiwan (n = 161), and Hong Kong (n = 141). Baseline variables assessed as part of this analysis included glycated hemoglobin (HbA1c), patient questionnaires (satisfaction with diabetes medication and Expectations about Insulin Therapy Questionnaire [EITQ]), and initial insulin regimen prescribed. EITQ total scores range from 0 to 70, with higher scores indicating more positive expectations.
Results: Mean HbA1c at insulin initiation was 9.08% in Hong Kong, 9.87% in Taiwan, 9.93% in Thailand, 10.24% in Malaysia, and 10.57% in Philippines. The proportion of patients dissatisfied with their diabetes medication varied between countries: 7.5% in Thailand; 16.2% in Malaysia; 25.6% in Taiwan; 27.5% in Hong Kong; 43.9% in Philippines. Mean EITQ total

scores were 44.0 in Taiwan, 45.5 in Hong Kong, 48.6 in Philippines, 48.7 in Thailand, and 49.2 in Malaysia. The initial insulin regimen varied considerably between counties; premixed insulin was more commonly prescribed in Malaysia (40%), Philippines (34%), and Thailand (32%), whereas basal insulin was more commonly prescribed in Taiwan (87%) and Hong Kong (99%). No patients were prescribed basal-bolus insulin at initiation and only a small proportion of patients in Malaysia and Philippines were prescribed basal plus prandial insulin at initiation.
Conclusions: There were several differences by country in baseline characteristics among patients from the Western Pacific region enrolled in VISION. These differences may affect subsequent treatment requirements and clinical outcomes.

PD-52

Long-term efficacy and safety of add-on therapy of vildagliptin in type 2 diabetes mellitus with insulin treatment

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Background and aims: Dipeptidyl peptidase (DPP)-4 inhibitors are often used worldwide because they improve glycemic control without increasing the risk of hypoglycemia. Previous studies have shown that intensive treatments with insulin administration increase the risk of hypoglycemia, resulting in the deterioration of quality of life and mortality. Although the usefulness of DPP-4 inhibitors for patients with type 2 diabetes treated with insulin is suggested, the long-term efficacy and safety of add-on therapy of vildagliptin in the patients is still unclear.
Subjects and methods: Patients with type 2 diabetes treated with insulin were enrolled, who had no history of taking DPP-4 inhibitors, if informed consent was obtained after a detailed explanation of the study purpose and methods. The participants in this open labeled trial were divided randomly into two groups as follows, their mean age and HbA1c levels as well as the ratio of men to women were not significantly different between these groups. Vildagliptin was orally administered one or two times after meal (50–100 mg/day) in the vildagliptin group (n = 37), and patients had conventional treatments without any DPP-4 inhibitors in the control group (n = 36). HbA1c levels, dose and times of insulin injection, the number of hypoglycemia episode, as well as liver and renal functions were monitored for 2 years.
Results: The baseline characteristics of the subjects including age, dose of insulin, or HbA1c levels were not different between two groups. In the vildagliptin group, HbA1c levels were significantly decreased, and the significance of HbA1c reduction was maintained for 2 years (form 8.0 ± 1.2% to 7.4 ± 1.0, $p < 0.05$, at the end of observational period). In addition, the dose and times of insulin injection were significantly reduced (−5.6 units, $p < 0.01$, and from −0.9 times, $p < 0.001$). On the other hand, these parameters were not changed in the control group. The number of patients who experienced hypoglycemia three times and more per year was significantly fewer in the vildagliptin group (n = 4) compared to the control group (n = 11) (odds ratio 0.28, 95% CI 0.08–0.97, $p < 0.05$). The serum levels of ALT and estimated glomerular filtration rate were not changed between two groups.
Conclusion: Vildagliptin as add-on to insulin treatment for 2 years was well tolerated and led to sustained reductions in HbA1c, the dose and times of insulin injection, and the risk of hypoglycemia.

PD-53

Comparison of eGFR before and after the administration of ipragliflozin using creatinine and cystatin C as indicators

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Background: Whilst serum creatinine concentration is generally used in the evaluation of kidney function, the production of creatinine is influenced by muscle mass, and thus, it could vary greatly depending on factors, such as gender, age, nutritional condition and muscle mass. Since Cystatin C is not influenced by factors, such as muscle mass, eGFR using Cystatin C is considered to be useful as renal function markers. In this study, comparative assessment was carried out on eGFR before and after the administration of ipragliflozin using cystatin C as an indicator.
Methodology: Subjects of the study were sixteen outpatients with type II diabetes (11 males and 5 females aged 51.7 ± 6.7 and disease duration of 7.5 ± 4.4 years). 50 mg Ipragliflozin/day was administered in combination as pre-treatment. The transition of renal function were compared and examined in eGFR using serum creatinine and cystatin C before the administration and also three, six, nine and twelve months after the commencement of medication. Comparative assessment was also carried out on the transition of HbA1c, body weight and liver function, etc.
Results: Blood glucose level significantly decreased from HbA1c8.4 ± 0.9% before the administration to 7.3 ± 0.9% ($p < 0.05$) after twelve months. Whilst the increase in eGFRcr was marginal from 87.1 ± 16.4 mL/min before the administration to 91.3 ± 18.4 mL/min ($p = 0.16$) after twelve month, eGFRcyc showed significant increase from 94.8 ± 13.7 mL/min to 102.2 ± 15.6 mL/min ($p < 0.05$) during the same period. A significant reduction in body weight was observed which was 81.7 ± 15.8 kg ($p < 0.05$) after twelve months compared to 84.2 ± 16.3 kg before the administration. Liver function also significantly improved from AST: 33.6 ± 16.7 IU/L, ALT: 47.1 ± 26.7 IU/before the administration to AST:26.0 ± 17.7 IU/L ($p < 0.05$), ALT: 32.5 ± 28.1 IU/L ($p < 0.05$) after twelve months.
Conclusion: For Japanese patients with type II diabetes, Ipragliflozin not only had sustained hypoglycemic effects but also showed weight reduction and liver function improving effects. The study also suggested a potential renal protection effect of Ipragliflozin in long-term, and the assessment of eGFR using Cystatin C was considered to be useful in such renal function evaluation.

PD-54

Long-term efficacy of hydrophilic or lipophilic statin therapy in diabetic Taiwanese

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Aim: To evaluate the long-term efficacy of hydrophilic and lipophilic statin therapy for cardiovascular outcomes in diabetic Taiwanese
Method: Newly diagnosed patients with type 2 diabetes were divided into 2 cohorts, namely hydrophilic statin and lipophilic statin cohorts. Cox proportional hazard regression models was used to analyze the risks of cardiovascular outcomes.

Result: In our study, lipophilic statin use was associated with higher risk of cerebrovascular events than hydrophilic statin use.
Conculsion: According to our cohort study, hydrophilic statin use may be an optimal choice to reduce cerebrovascular events in diabetic Taiwanese.

PD-55
Effects of intervention by a nutrition support team on serum albumin level in diabetic patients
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Objective: Both glycemic control and improvement of undernutrition are important in the management of underlying disease in diabetic patients. The effects of intervention by a nutrition support team (NST) on nutritional parameters including serum albumin (Alb) level in diabetic inpatients were investigated and compared with nondiabetic controls.
Methods: This study included 42 diabetic (D group) and 98 nondiabetic (N group) inpatients who received NST intervention during hospitalization. Retrospective investigation was conducted based on the clinical record data. Pre- and postintervention values for clinical parameters (body weight, blood pressure, lipid levels, serum Alb, renal function) were statistically examined. A p value less than 0.05 was considered statistically significant.
Results: Baseline data (D group/N group): age, 73.9/70.5 years; body mass index (BMI), 21.4/19.9 kg/m^2; date of initial NST intervention, day 25/24; duration of NST intervention, 33/36 days; number of NST interventions, 5.5/5.0. The baseline HbA1c in the D group was 7.6%. Underlying diseases included respiratory (36 patients), gastrointestinal (22 patients), orthopedic (20 patients), cerebrovascular (14 patients), and other diseases (48 patients). Nutritional intervention involved enteral (27 patients), intravenous (27 patients), and oral feeding (86 patients). No significant difference in baseline clinical parameters was observed between the two groups. Final results: In the D group, 39 patients were discharged alive and 3 died, while 82 were discharged alive and 16 died in the N group. In both groups, a significant decrease in BMI (D group, 21.2 to 20.1 kg/m^2; N group, 19.7 to 18.8 kg/m^2) and a significant improvement in serum Alb level (D group, 2.6 to 2.8 mg/dL; N group, 2.7 to 2.9 mg/dL) were observed. In the D group, a significant positive correlation was observed between change in serum Alb level and number of NST interventions ($r = 0.32$), while a significant negative correlation was observed between change in serum Alb and baseline serum Alb levels ($r = -0.40$). Multiple regression analysis of factors influencing differences between pre- and postintervention serum Alb levels in the total patient population (dependent variables: sex, age, status of diabetes, BMI, serum Alb, number of NST interventions) identified age and baseline serum Alb level as significant independent factors.
Conclusion: In clinical practice, more frequent NST interventions in diabetic patients resulted in improved nutritional status. Results also suggested that NST intervention in younger patients or for undernutrition might result in improved nutrition regardless of diabetic status.

PD-56
Titration when switching from insulin degludec to insulin glargine U300 among Japanese diabetes patients
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Background: In recent years, there has been a focus on using basal insulin to treat diabetes patients due to its core characteristics regarding stability and persistence. Two of the long-acting and stable types of insulin available in Japan are insulin degludec (IDeg) and insulin glargine U300 (G300). To date, there is no definite evidence regarding how to adjust the dosage of insulin when switching from IDeg to G300 as well as G300 to IDeg in Japanese diabetes patients. Our research compared the efficacy of IDeg and G300 by way of using a continuous glucose monitoring system (CGM) on Japanese diabetes patients in order to evaluate the suitable amount for titration when switching from IDeg to G300.
Method: Four Japanese diabetes patients treated with IDeg under diabetes educational hospitalization between Oct. 2015 and Jan. 2016[type 1 diabetes (T1DM): n = 1, type 2 diabetes (T2DM): n = 3, mean age: 67.5 ± 17.3 years, mean BMI: 28.9 ± 4.6, mean HbA1c: 11.2 ± 1.6%, mean CPR index: 0.95 ± 0.7, mean U-CPR: 28.5 ± 24.4 μg/day] were recruited. The patients were subsequently switched to G300 with the same dosage of IDeg. The patients were under regular examination through the use of CGMs for two days prior to the switch and three days following the switch.
Result: There was no statistical difference between the periods before and after the switch in regards to average blood glucose level and the standard deviation (SD) of the blood glucose level. In T1DM, following the switch, there seemed to be a tendency that the blood glucose level during the early morning (00:00–7:00) was higher compared to the same time period prior to the switch.
Conclusion: In Japanese diabetes patients who have hyposecretion of insulin, there is a possibility that the effect of G300 is shorter than that of IDeg during the titration. According to our results, we think that the dosage of insulin should be the same when titrating from IDeg to G300, so as to avoid hypoglycemia. To further expand and solidify our conclusion, it is necessary to review more cases. By the day of meeting, there will be more cases to present.

PD-57
Study of patients who presented to the emergency outpatient department with the chief complaint of hypoglycemia
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Aim: To investigate the characteristics of patients who presented to the emergency outpatient department of our hospital with the chief complaint of hypoglycemia.
Methods: One hundred twenty patients (68 men, 52 women) with hypoglycemia who were treated at our emergency outpatient department from November 2012 to October 2015 were included in this study.
Results: Among the 120 patients, 32 had type 1 diabetes mellitus, 74 had type 2 diabetes mellitus, and 14 had conditions other than diabetes mellitus. Of the 106 diabetic patients, 61 were men and 45 were women. A high proportion of patients presented to the hospital in March and October (11.7% for both months). The patient characteristics were as follows: mean age, 68 ± 14 years; mean disease duration, 18 ± 10 years; mean body mass index, 21.9 ± 3.9; mean hemoglobin A1c (HbA1c), 7.5% ± 1.6%; mean blood sugar level at presentation, 54 ± 42 mg/dL; mean estimated glomerular filtration rate, 57 ± 37 min-11.73 m^{-2}; and mean C-reactive protein, 0.43 ± 1.00 mg/dL. The most common cause of hypoglycemia, accounting for 42.5% of all causes, was receiving

the usual doses of drugs after consuming less than the normal amount of food (except during sick days). No cases of death were directly caused by hypoglycemia. Hospitalization was necessitated in 52.4% of all cases.
Conclusions: We conclude that avoiding the onset of hypoglycemia and selecting target HbA1c levels and drugs according to the patient's age and disease status should be prioritized.

PD-58

The acute efficacy and safety of dulaglutide in Japanese adults with type 2 Diabetes Mellitus

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Background: Recently, many kinds of GLP-1 receptor agonist are widely used in clinical practices for improving glycemic control in patients with type 2 diabetes mellitus (DM).
Dulaglutide is a novel weekly GLP-1 receptor agonist which came to Japanese market in October 2015 and is expected to have greater glucose and body weight (BW) lowering effect on patients with type 2 DM. In this study, we retrospectively investigated the efficacy and safety of dulaglutide in clinical practice.
Method: Thirty-five patients with type 2 DM in our hospital who were administrated dulaglutide were enrolled from October 2015 to March 2016 consecutively. We observed up to 12 weeks in this study. We collected the clinical data of HbA1c and body weight every month through the study period. Also we investigated adverse side effects, i.e. hypoglycemia. Moreover, we conducted a questionnaire study about dulaglutide and its injection device after its administration.
Results: Baseline characteristics are indicated thus; Male 22 patients (62.9%) Female 13 patients (37.1%). Age: male 64 years old, female 65 years old. HbA1c: 8.0%, BW: 68.9 kg. Before replacement or initiating dulaglutide, the 9 patients used other GLP-1 receptor agonist, the 13 patients used insulin. After 8 weeks, HbA1c in all the patients has decreased –0.45% ($p < 0.05$, vs baseline). In only male after 4 weeks HbA1c has decreased –0.31% ($p < 0.05$, vs baseline) After 8 weeks patients who added dulaglutide on insulin significantly improved HbA1c (–0.35% $p < 0.05$, vs baseline). BW significantly decreased in all patients after 4 weeks treatments (–0.52 kg $p < 0.05$, vs baseline) but not in 8 weeks. There were no reports of any severe hypoglycemia attack during study period. In the questionnaire in this study, 40% of the patients felt that they had better glycemic control and 40% of them felt they had lower frequency of hypoglycemia using dulaglutide than their previous therapy. All patients prefer weekly GLP-1 receptor agonist to daily one.
Conclusion: In this study, dulaglutide improved glycemic control in Japanese type 2 DM patients in clinical practice. Furthermore, continuing to add the diabetes patients and extend the period of observation we are going to report this study.

PD-59

Inhibition of central GSK3 regulates body weight and glucose metabolism

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Overweight and obesity lead to metabolic disorders like insulin resistance and hypertension, which related to development of type 2 diabetes, coronary heart disease and cancer with the increase of body mass index (BMI).
The WHO statistics in 2014 shows that more than 2 billion people are overweight (BMI from 25 to 29.9), and more than half a billion are obese (BMI 30 or greater). This survey indicates that about one-third of the world's population tends to be obese.
GSK3 (glycogen synthase kinase 3) is a ubiquitous kinase and a downstream molecule of insulin signal pathway. Insulin regulates glucose homeostasis with increasing glucose uptake and storage. When it binds to the insulin receptor, glucose uptake is accelerated to promote the glycogen synthesis in the liver and skeletal muscle by GSK3 inactivation. In this mechanism, GSK3 can be a target for the development of treatment for type 2 diabetes, but its central action has not been understood yet.
It has been demonstrated that central administration of insulin causes anorexigenic effect and leads to reduction of body weight. Therefore, we used GSK3 inhibitor to reveal significance of central GSK3 on metabolism and feeding behavior.
All experiments were performed using 8- to 10-week-old male ddY mice. We administered vehicle (PBS) or a GSK3 inhibitor to the mice by ICV injection. The mice were housed individually under 12-hour day and night cycle. In a single dose, ICV administration was performed after 16 hours fast and then we measured the change in body weight, food intake and water consumption. Otherwise, as another experiment, repetitive administration was also performed for 10 days and we conducted ipGTT after 7days treatment.
The single dose of GSK3 inhibitor led to reduction of body weight, food intake and water consumption. The continual administration of GSK3 inhibitor showed more striking effects. An ipGTT revealed that glucose tolerance tended to be improved in the mice administrated with GSK3 inhibitor in comparison to the control mice. The maximum glucose concentration in the GSK3 inhibited mice was lower than the other group.
Recently, GSK3 inhibitors have been developed for medication of Alzheimer's disease. Our results suggested that central GSK3 should be a new target to treat metabolic diseases, and GSK3 inhibitors would be novel anti-obesity agents having antidiabetic effect.

PD-60

Factors related to diabetes' ABC control in a Taipei community hospital – A prospective follow-up study

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Background: The majority of diabetes patients in Taiwan have been cared in either community clinics or local hospitals; however, quality of diabetes control in community settings remains unclear. This study aimed at demonstrating performance of diabetes care and investigating factors that influenced ABC (HbA1c, blood pressure, and low-density lipoprotein cholesterol [LDL-C]) control in a community hospital in Taipei.
Methods: We adopted the current status of ABC control in National Diabetes Health Promotion Centers in Taiwan, which have been regularly supervised and accredited by the Health Promotion Administration, as the performance indicators to evaluate quality of diabetes care in the investigated community hospital. Logistic regressions were used to identify significant factors related to diabetes' ABC control.
Results: Since 2006, the investigated community hospital has implemented a diabetes management program, strengthening dietetic consultation, health education, and case management. The data surveillance center has currently recorded 300 enrollees to this program. The percentage of good ABC control, including HbA1c < 7%, blood pressure <130/80 mmHg, and LDL-C < 100 mg/dL, one year after participating in the program was 40.7%, 33.7%, and 32.8%, respectively. Compared to the corresponding indicators in National

Diabetes Health Promotion Centers, which was 32.5%, 30.6%, and 35.3%, respectively, the blood sugar and blood pressure control in the investigated community hospital were significantly better. Those who had HbA1c < 7% or blood pressure <130/80 mmHg at baseline were more likely to achieve all ABC goals after participating in the program. The significant factors related to ideal blood sugar control (HbA1c < 7%) included male, diabetes duration <5 years, non-smoker, regular exercise, and better glycemic control at baseline.
Conclusion: After implementing a diabetes management program, more than one third of patients enrolled in the program could reach the optimal standard set by the National Diabetes Health promotion centers. Our results indicate more effects needed to promote quality of diabetes care in Taiwan. Our study also implies healthy behaviors such as non-smoking and regular exercise are conducive to better glycemic control. This is empirical evidence supporting health education in diabetes care.

PD-61

Health economic impact of hypoglycemia among 7,289 insulin-treated patients with diabetes: Results from an International survey in 9 countries

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Background and aims: Hypoglycemia is a key consideration in the individualization of treatment in patients with diabetes. However, because observational studies are predominately conducted in Western countries and are limited in number and consistency of design, actual hypoglycemia rates in clinical practice, and their socio-economic impact, remain unclear for many countries.
Materials and methods: The International Operations (IO) Hypoglycemia Assessment Tool (HAT) study is a non-interventional, real-world, observational study of self-reported (using self-assessment questionnaires) hypoglycemic events in Bangladesh, Colombia, Egypt, Indonesia, the Philippines, Singapore, South Africa, Turkey and the UAE among 7,289 patients with insulin-treated type 1 (T1D) and type 2 diabetes (T2D). This abstract reports the health economic (HE) implications, including direct and indirect costs, of hypoglycemic episodes occurring in the 6-month retrospective and 4-week prospective periods of the IO HAT study.
Results: Rates of any hypoglycemia (per patient, per month) were 4.8 and 6.9 in patients with T1D and 1.6 and 2.4 in those with T2D during the retro- and prospective periods, respectively. For both patients with T1D or T2D, reporting of any and severe hypoglycemic events were significantly higher ($p < 0.001$) in the prospective period, whereas that of nocturnal hypoglycemic events was significantly higher ($p < 0.001$) in the retrospective period. The most common direct impact of hypoglycemia was increased blood glucose monitoring which occurred in 43.8% (T1D) and 20.0% (T2D) of patients in the 4-week prospective period. Other impacts included telephone contacts with a health care team member (6.4 and 5.9%, respectively), additional clinic appointments (5.8 and 4.3%) and post-hypoglycemic event hospital admissions (3.0 and 1.7%) in patients with T1D and T2D, respectively.
Indirect impacts of hypoglycemia included reduced work/study punctuality (arriving late or leaving early) in patients with T1D (11.5 and 9.4%) and T2D (3.5 and 3.7%). In addition, some reported absence from their workplace or studies (T1D 6.3%; T2D 3.5%).
Conclusion: Hypoglycemia is a major concern in diabetes treatment and is not just a barrier to reaching appropriate glycemic targets, but also increases HE costs. This study details both direct and indirect HE impacts (to healthcare, employers or patients) of hypoglycemic episodes in patients with T1D or T2D across non-Western countries.

PD-62

Fibrinogen level was correlated with glycemic control, not with lipid profiles in type 2 DM patients

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Background: The worldwide prevalence of type 2 diabetes mellitus (T2DM) has risen dramatically over the last two decades and it indicated that the number of individuals with diabetes will continue to increase near future. Fibrinogen plays a role as a risk factor increasing cardiovascular morbidity and mortality in T2DM. Fibrinogen is determined by several modifiable and non-modifiable factors like BMI, glycemic control and lipid profiles.
Objective: The aim of this study is to analyze the correlation of fibrinogen level, glycemic control and lipid profiles in T2DM patients.
Material and methods: This cross sectional study was conducted at diabetes outpatient clinic Dr. Soetomo teaching hospital Surabaya Indonesia. Inclusion citerias were patiens with T2DM aged over 45 years old and signed informed consent. Patients with severe infection, renal and liver dysfunction, pregnancy, fibrate treatment were excluded in this study. We interviewed and measured body weight and height, BMI, blood pressure and baPWV. Fasting plasma glucose (FPG) and post prandial glucose (PPG), HbA1c, lipid profiles and fibrinogen level were measured as well. Data was statistically analyzed using Pearson correlation test.
Results: We analyzed 40 patients who have been diagnosed with T2DM consisting of 17 males and 23 females. There were 16 T2DM patients with BMI < 25 kg/m^2 (nob-obese) and 24 patients with BMI > 25 kg/m^2 (obese). The overall mean HbA1c was 8.01 ± 1.39%, total cholesterol was 203.57 ± 28.02 mg/dL, LDL-cholesterol was 144.52 ± 36.57 mg/dL, HDL-cholesterol was 47.15 ± 13.02 mg/dL, triglyceride was 179.31 ± 54.42 and fibrinogen 456.75+142.60 mg/dL. One Sample Kolmogorov Smirnov statistical test indicated that the data distribution was normal. There was significant correlation between fibrinogen level and HbA1c (r 0.313; $p < 0.05$). In other hand, there were no significant correlations between fibrinogen level and total cholesterol (r 0.239; p 0.137), LDL cholesterol (r 0.027; p 0.137), HDL cholesterol (r 0.112; p 0.493) and triglyceride (r 0.134; p 0.409). There was significant correlation between fibrinogen level and HbA1c in non-obese patients (r 0.568; $p < 0.05$), but there was not in obese patients (r 0.001; p 0.998).
Conclusion: There was significant correlation between fibrinogen level and glycemic control among T2DM patients, but there was no significant correlation between fibrinogen level and lipid profiles. There was also significant correlation between fibrinogen and glycemic control in non-obese patients, in contrast with the obese patients.

PD-63

Effect of astaxanthin and astaxanthin formula on thrombotic risk factors in type 2 DM patients

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Backgound: Macrovacular complications are the major causes of death among diabetic patients, and hyperglycemia-induced

oxidation with subsequent chronic inflammation play an important role in diabetic macroangiopathy. Astaxanthin (AX) is one of the carotenoids with excellent anti-inflammatory and antioxidative capacity.
Purpose: The purpose of this study was to investigate the effect of astaxanthin and astaxanthin formula (AXF) on metabolic and thrombogenic risks in type 2 diabetic patients.
Material and method: One hundred and three type 2 diabetic patients were recruited from department of metabolism and endocrinology of Cheng Ching Hospital in Taichung city. After exclusion of unqualified patients, all subjects were randomly assigned into three groups including placebo group (P), AXF (AX 6 mg + vitamin E 150 mg + Tocotrienol 45 mg/day) group and AX (AX: 14 mg/day) group, respectively. After two month's supplementation, plasm concentration of AX, fasting blood glucose (FBG), HbA1c, lipid profiles, markers of hepatic and renal function, oxidative and inflammatory markers, coagulation and anti-coagulation factors were measured.
Results: The results showed the plasma levels of AX increased by supplementation in a dose-dependent manner. Plasma concentration of HbA1c, CRP and vWF was significantly decreased in AXF group. Plasma concentration of HbA1c, Triglyceride and Total Cholesterol, GPT, TNF-α, CRP and vWF was significantly decreased in AX group. In addition, plasma concentration of coagulation factor VII and PAI-1 was significantly decreased, and AT-III level was significantly increased in AX group.
Conclusion: In conclusion, AX supplementation for two months may have beneficial effects on type 2 diabetic patients in ameliorating hyperglycemia and hyperlipidemia. AX supplementation also decreases oxidative stress and restrains chronic inflammations, therefore mends endothelial damage and thrombogenic risk in type 2 diabetic patients.

PD-64
The usefulness of newly long acting insulin as Degludec for 2 years in Japanese Type 1 Diabetes

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Objective: We have used the newly long acting insulin as Degludec for 69 Type 1 diabetes outpatients for 2 years. And 29 outpatients of them we performed CGMS (Continuous Glucose Monitering System; Medtronic iProTM2). To assess the usefulness of Degludec (1) for 2 years and (2) for daily profile used CGMS.
Subjects and methods: To analyze (1) the time course of HbA1c, body weight, insulin dose for 2 years in type 1 outpatients, who switch from insulin glargine (n = 36; GroupA) or insulin detemir (n = 28;GroupB) to insulin degludec. n = 69, 53.0 ± 16.8 y/o, BMI 21.6 ± 2.9. C-peptide 0.24 ± 0.41 ng/dL, (2) the time course of blood glucose profile who switch from insulin glargine or insulin detemir to insulin degludec, by CGMS) at the time of switching (n = 19) and 1–3 months after switching (n = 10). We investigated indicators of the dawn phenomenon (DP); ⊿BG (pre-breakfast BG minus minimum BG at 2–6 AM).
Results: (1) The mean HbA1c was significantly improved from 7.94 ± 1.03 to 7.59 ± 1.03 ($p < 0.0001$). Body weight was slightly increased from 56.1 to 57.0 kg ($P < 0.01$). 31 cases were improved >0.5% of HbA1c level without severe hypoglycemia. 28 cases were not changed HbA1c level. Only 7 cases were worsened >0.5%. 3 cases were dropout or changed insulin.
Group A; The mean HbA1c was improved slightly from 8.00 to 7.80 ($p < 0.01$). Body weight was slightly increased. Insulin doses were not changed.
Group B: The mean HbA1c was from 7.86 to 7.58 ($p < 0.01$). Body weight was not changed. Insulin doses was decreased from 16.8 to 11.7
(2) Frequency of nocturnal hypoglycemia was decreased than former insulins ($P < 0.01$). Nighttime and daytime hypoglycemia was correlated with ⊿BG ($P < 0.01$). ⊿BG and CPR were correlated ($P < 0.03$).
Conclusion: (1) For 2 years Degludec is useful to improve HbA1c level switching from Glargine and Detemir in Japanese Type1 diabetes patients.
(2) Frequency of nocturnal hypoglycemia was decreased However, Dawn phenomenon during use is dependent on residual intrinsic insulin secretions, and the patients with more marked Dawn phenomenon tended to experience hypoglycemia during the day or night. Careful titration of the stable insulin degludec is required in response to fasting blood glucose levels in type 1 diabetes.
(3) As a result 45% of patients have continued improvement >0.5% of HbA1c level without severe hypoglycemia for 2 years.

PD-65
Evaluation of the CGMs in type-2 diabetic patients switched from Liraglutide and Insulin Degludec to Liraglutide and Insulin Degludec/Aspart

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Background: The combination of Liraglutide (Lira) and Insulin Degludec (IDeg) is often used. However, there are also some cases therapeutic goals cannot be achieved. Insulin Degludec/Aspart (IDeg/Asp) was newly released. Switching from Lira and IDeg to Lira and IDeg/Asp might possibly improve the glycemic control, without changing the number of injections. However, there are no reports on the effects of the therapy.
Aim: We switched Lira and IDeg to Lira and IDeg/Asp in type-2 diabetic patients, and evaluated CGMs.
Purpose: A patient with type-2 diabetes had been administered Lira and IDeg before breakfast, and we switched the medication to Lira and IDeg/Asp, with same amount of IDeg, during hospitalization. We measured the CGMs over 72 hours, and evaluated average blood glucose levels and the MAGE.
Results: Average blood glucose level for a day decreased from 195 ± 47 mg/dL before the switch to 177 ± 32 mg/dL after the switch. The MAGE decreased from 66 before the switch to 41 after the switch. In the time period from before breakfast to before lunch, the average blood glucose level decreased from 237 ± 49 mg/dL before the switch to 162 ± 22 mg/dL after the switch, and the MAGE decreased from 58 before the switch to 28 after the switch. In the time period from before lunch to before dinner, the average blood glucose level decreased from 230 ± 27 mg/dL before the switch to 180 ± 31 mg/dL after the switch, and the MAGE was 34 before the switch and 37 after the switch. In the time period from before dinner to before sleep, the average blood glucose level was 196 ± 12 mg/dL before the switch and 196 ± 18 mg/dL after the switch, and the MAGE increased from 17 before the switch to 43 after the switch. In the time period from before sleep to before breakfast on the following day, the average blood glucose level was 150 ± 17 mg/dL before the switch and 153 ± 17 mg/dL after the switch, and the MAGE was 26 before the switch and 30 after the switch. Hypoglycemia was not observed during the observation period.
Conclusion: It was shown switching IDeg to IDeg/Asp might make it possible to improve glycemic control during the time after breakfast and before dinner, without increasing the number of injections and burden on the patient. We will investigate more cases and report on them at the conference.

PD-66

Increased body mass index may attenuate the effect of sitagliptin on glucose control

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Background: Few studies have been conducted on predictors of a decrease in glycohemoglobin (HbA1c) level to <7% in Japanese people with type 2 diabetes undergoing long-term treatment with dipeptidyl peptidase-4 inhibitors.
Aim: This study aimed to determine predictors of improvement in HbA1c level in Japanese people with type 2 diabetes treated with sitagliptin.
Methods: We retrospectively evaluated 181 type 2 diabetic patients (mean age: 65.2 years, male-to-female ratio, 125/56) who had been taking sitagliptin 50 mg once daily for inadequate glycemic control for at least 24 weeks, with or without other oral hypoglycemic agents. The outcomes assessed were as follows: (1) changes in Hba1c level from baseline to 8, 16, and 24 weeks of treatment; (2) proportion of patients who achieved an HbA1c level <7% with sitagliptin treatment; (3) differences in predictors (age, sex, body mass index [BMI], diabetes duration, baseline HbA1c level, hypertension, dyslipidemia, and other oral antidiabetic agents) between patients with HbA1c levels <7% and those with HbA1c levels >7%; and (4) independent predictors of achieving HbA1c levels <7% with sitagliptin treatment on multiple logistic regression analysis.
Results: HbA1c level significantly reduced from 7.9% at baseline to 7.4% at 8 weeks, 7.1% at 16 weeks, and 7.1% at 24 weeks. An HbA1c level <7% was achieved in 51.7% of the patients. The BMI and baseline HbA1c level were significantly lower in patients with HbA1c level <7% than in those with HbA1c level >7%. The independent predictors of achieving an HbA1c level <7% were baseline HbA1c level (odds ratio, 1.96, $p \leq 0.001$) and BMI (odds ratio, 1.11; $p = 0.02$).
Conclusion: Our findings showed that HbA1c levels at baseline and BMI are associated with achieving an HbA1c level <7% in patients taking sitagliptin.

PD-67

The efficacy of DPPIV-inhibitor therapy among adult Chinese patients with diabetes mellitus in Singapore

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Objective: To determine the patient and diabetes-specific factors that may modify the efficacy of dipeptidyl peptidase-4 (DPP-IV) inhibitor therapy amongst adult Chinese Singaporeans with diabetes mellitus (DM).
Research design and methods: This is a retrospective study from Jan 2014 to May 2015 of 196 Singaporean Chinese with DM who were prescribed DPP-IV inhibitor as an add-on therapy. We examined the changes in the glycemic control (HbA1c) and body weight over a period of 12 months after initiation of DPPIV-inhibitor using the linear mixed models. HbA1c and body weight were included as dependent variables. Patient factors (gender, age, baseline BMI) and diabetes-specific factors (duration of diabetes, baseline HbA1c [baseline HbA1c <8% vs 8–10% vs >10%], insulin therapy, presence of CKD [defined as presence of kidney damage or eGFR < 60 mL/min/1.73 m^2 for at least 3 months]) were included as independent variables. An interaction term "factor x follow-up time" was introduced as independent variable to examine whether these factors modify the efficacy of DPPIV-inhibitor therapy.
Results: There were 111 (56.6%) males. The mean ± SD age was 59.1 ± 14.7 years and the mean duration of diabetes was 14.0 ± 9.28 years. 83 (42.6%) patients were on insulin therapy. The mean change for HbA1c over the 12 months period was −0.37 ± 1.61% ($p = 0.006$) with the greatest decline seen in the first 3 months (ΔHbA1c = −0.61 ± 1.42%, $p < 0.001$). There was no significant change in the body weight over 12 months (Δbody weight = −0.82 ± 6.21 kg, $p = 0.110$). Using the linear mixed model, the interaction term for "factor x follow-up time" was significant for baseline HbA1c, basal-bolus insulin regimen, and presence of CKD. Those with baseline HbA1c > 10% had a more significant decrease in HbA1c levels as compared to those with baseline HbA1c 8–10% and HbA1c < 8% (P interaction <0.001). Patients on basal-bolus insulin therapy had significantly greater reduction in body weight (P interaction = 0.034) as compared to those who were either on other insulin regimes or were not on insulin therapy. Patients without CKD had a significantly greater reduction in body weight (P interaction = 0.039) but similar reduction in HbA1c as compared to those with CKD. Age, gender, baseline BMI and duration of diabetes did not modify the efficacy of DPP-IV inhibitors in this population.
Conclusions: As an add-on therapy, DPP-IV inhibitors are effective in improving glycemia and body weight in the adult Chinese population in Singapore, particularly in patients with baseline HbA1c>10%, those who are on basal-bolus insulin therapy and patients without CKD.

PD-68

Fenretinide decreases insulin resistance and blood pressure, and inhibits macrophage inflammatory mediators via the peroxisome proliferator activated receptor pathway

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Fenretinide [N-(4-hydroxyphenyl) retinamide] is a synthetic retinoid derivative that has been widely used as a chemopreventive and chemotherapeutic agent in cancer treatment. Recent research also demonstrated that fenretinide prevents obesity and fatty liver in high fat diet-induced obese mice. Furthermore, fenretinide ameliorates insulin resistance through the reduction of retinol binding protein 4 (RBP4) in spontaneously hypertensive rats.
Peroxisome proliferator-activated receptor γ (PPARγ) is a ligand-activated transcription factor belonging to the nuclear receptor superfamily that undergoing transactivation or transrepression by distinct mechanisms, and thus leading to induction or repression of target genes expression. PPARγ plays an important role in many physiological functions, especially those involved in the regulation of vascular tone, inflammation, and energy homeostasis. Therefore, PPARγ may represent an important target for treatment of hypertension, obesity, obesity-induced inflammation, and metabolic syndrome. PPARγ may influence the inflammatory response by direct transcriptional downregulation of pro-inflammatory genes.
Although it is known that fenretinide is a ligand for PPARγ, the role of PPARγ in fenretinide-induced anti-inflammatory activity remains unknown. Despite the role of fenretinide in the improvement of insulin resistance has been known, however, the effects of fenretinide on blood pressure are still obscure.
In this study, we show that treatment with lipopolysaccharide (LPS) decreased the expression of PPARγ in raw264.7 macrophages, and pretreatment with fenretinide reversed the effect of LPS on PPARγ expression. In addition, LPS-induced proinflammatory cytokine productions, including tumor

necrosis factor-α, interleukin-6, and monocyte chemoattractant protein-1, were dose-dependently reversed by fenretinide, and the effects of fenretinide on LPS-induced proinflammatory cytokine productions were blocked by the treatment of PPARγ antagonist. Moreover, fenretinide decreased LPS-induced expression of inducible nitric oxide synthase and nitrogen oxide production. These effects were blocked by the pretreatment of PPARγ antagonist in a dose-dependent manner, indicating fenretinide activated PPARγ to exert an anti-inflammation activity. Furthermore, in view of the role of inflammation in hypertension, and the anti-inflammation action of fenretinide, we found that administration of fenretinide in spontaneously hypertensive rats significantly decreased the blood pressure. Taken together, fenretinide might be a potent anti-hypertensive agent that works by suppressing inflammation via activating PPARγ.

PD-69

Self-reported hypoglycemic rates and insulin regimen among 7289 insulin-treated adult patients with diabetes: An International survey in 9 countries

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Background and aims: Real-world data on hypoglycemia rates are sparse and comparisons among insulin regimens rely heavily on data from randomized clinical trials, particularly in non-Western countries. The aim of the non-interventional International Operations Hypoglycemia Assessment Tool (IO HAT) study conducted in Bangladesh, Colombia, Egypt, Indonesia, the Philippines, Singapore, South Africa, Turkey and the UAE was to assess the incidence of hypoglycemia among patients with insulin-treated (premix, short-acting and long-acting) diabetes.
Materials and methods: Hypoglycemic events were recorded via 2 self-assessment questionnaires and in patient diaries, in 7289 patients with insulin-treated diabetes.
Results: There were 1016 participants with type 1 (T1D) and 6273 with type 2 diabetes (T2D), with a higher percentage of female than male participants (T1D, 57.0% female; T2D, 55.7% female). The mean age (years [SD]) was higher among participants with T2D than T1D (57.7 [10.9] vs. 35.0 [13.0]) while the duration of diabetes was higher among participants with T1D (14.5 [9.8] vs. 13.2 [7.7]). "Any" and "nocturnal" hypoglycemia rates, per patient, per month (PPPM), were highest in patients with T1D on short-acting regimens during retrospective and prospective periods (Any, 6.8 and 10.3; Nocturnal, 3.0 and 1.9 PPPM). Rates of any and nocturnal hypoglycemia were lowest in patients with T2D on long-acting regimens (Any, 1.2 and 2.0; Nocturnal, 0.4 and 0.2 PPPM). In the pooled population of patients with T1D and T2D, there was a significantly lower ($p < 0.001$) rate ratio (RR, [95%CI]) for any hypoglycemic event in patients using premix (RR 0.57 [0.50:0.64]), long-acting (RR 0.39 [0.34:0.45]) or short- and long-acting insulin (RR 0.70 [0.62:0.79]) compared with those using short-acting insulin.
Conclusion: Rates of hypoglycemia varied among treatment regimens in both T1D and T2D; rates of any and nocturnal hypoglycemia were lowest in patients with T2D on long-acting insulin regimens.

PD-71

Self-reported hypoglycemia in insulin-treated patients with diabetes: Results from an international survey of 7289 patients from 9 countries

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Background and aims: The non-interventional International Operations Hypoglycemia Assessment Tool (IO HAT) study assessed the incidence of hypoglycemia in patients with insulin-treated diabetes in Bangladesh, Colombia, Egypt, Indonesia, the Philippines, Singapore, South Africa, Turkey and the UAE.
Materials and methods: The incidence of hypoglycemia was reported in self-assessment questionnaires completed at baseline and after the 28-day prospective period, and in patient diaries.
Results: Of 7289 patients (type 1 diabetes [T1D], n = 1016; type 2 diabetes [T2D], n = 6273), approximately 90% completed their diaries in the prospective period (28 days from baseline). At least 1 case of confirmed hypoglycemia (capillary glucose <56 mg/dL) was recorded in patient diaries by 48.0% of patients with T1D and 12.6% of those with T2D. Based on patient recall, "severe" hypoglycemia was reported for the prior 6 months, and "any" hypoglycemia the 4 weeks before baseline. "Any" hypoglycemia was retrospectively reported by patients (TID, 72.7%; T2D, 48.1%). Nearly all patients reported events during the prospective period (T1D, 97.4%; T2D, 95.3%). Rates of "any" and "severe" hypoglycemia were higher in the prospective period ($p < 0.001$) compared with those in the retrospective period for T1D ("any" 82.3 vs. 57.7 events per patient year (PPY); "severe" 14.5 vs. 7.0 events PPY) and T2D ("any" 28.5 vs. 19.1 events PPY; "severe" 11.1 vs. 3.0 PPY). In contrast, lower rates of nocturnal hypoglycemia were reported prospectively vs. retrospectively (T1D, 14.4 vs. 22.0 events PPY; T2D, 3.4 vs. 5.5 events PPY; $p < 0.001$).
Conclusion: These results are the first patient-reported dataset on hypoglycemia in the participating countries and indicate that hypoglycemia is under-reported and thus underestimated.

PD-72

The effects of lobeglitazone, a novel thiazolidinedione (TZD), on bone mineral density in mice

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Thiazolidinediones (TZDs), a class of anti-diabetic agents, promote insulin sensitivity through the activation of the peroxisome proliferator activated receptor gamma (PPAR- γ). However, it has been hypothesized that activation of PPARγ by thiazolidinedione drugs can increase adipogenesis at the expense of osteogenesis, leading to bone loss. The aim of this study was to examine the effects of lobeglitazone, a novel TZD, on bone mineral density (BMD) in mice compared to other TZDs. Non-diabetic male C57BL/6 mice were used and the mice were randomized into 4 groups with 6 per group: placebo group, pioglitazone (19 ug/g), rosiglitazone group (5 ug/kg), lobeglitazone group (0.6 ug/g) and high dose lobeglitazone groups (1.2 ug/g). The mice were treated each dosing drug daily

by gavage for 12 weeks. BMD was determined using the Piximus instrument and software version 1.46 (GE Lunar, Madison, WI). Mice were anesthetized and scanned prior to the onset of treatment and at sarcrifice. Total body BMD (g/cm^2) excluding the head region and femur BMD was obtained from each scan, and the percent change in BMD was calculated. Rosiglitazone-treated group showed significant greater BMD decrease compared to control group at the end of study at both total body and femur BMD (−4.2% ± 2.75 in Rosiglitazone group vs. −1.9% ± 2.7 in Placebo group in total body BMD, −7.7% ± 3.5 in Rosiglitazone group vs. −1.6% ± 2.1 in Placebo group in femur BMD, $p < 0.05$, respectively). However, pioglitazone- and lobeglitazone-treated groups showed similar decrease in both total body and femur BMD at the end of study compared to the control group. In conclusion, lobeglitzaone, a new PPARγ agonist, exerts neutral effects on bone in mice compared to the effects from rosiglitazone.

PD-73

Risk stratification of diabetic foot disease among new patients in a community based Haemodialysis Programme

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Introduction: Diabetic foot complications are common in diabetic patients undergoing chronic dialysis. Among patients newly admitted In National Kidney Foundation (NKF) Haemodialysis (HD) Programme annually, more than 70% were diabetic (DM). Early identification of risk of developing foot problems may be useful in preventing such complications from arising and/or deteriorating. We therefore explored the risk stratification for foot problems of DM patients upon admission to the NKF HD programme.

Patients and methods:

- All new patients starting on chronic HD in NKF HD program from1 Jan 2012 to 31 Dec 2013 and who were diabetic were included in the study.
- Patients' data captured included demographics (age, gender, ethnicity and marital status), admission date to NKF, and risk category for DM foot disease.
- A total of 366 patients were included in the study
- Patient characteristics were as follows: Median age 58 years (range 24–91), 4.6% was aged 20–40 years, 14.2% was aged 41–50 years, 40.2% aged 51–60 years, 29.5% was aged 61–70 years: and 11.5% aged above 70 years. 58.7% were males and 41.3% were female. 67.5% were married, 11.8% were single, 10.9% were divorced and 9.8% were widowed. Ethnic distribution showed 55.2% Chinese, 36.9% Malay, 7.7% Indian, and 0.3% Others.
- A risk assessment for diabetic foot disease was carried out upon entry to the program. Information was then entered into a structured checklist form. These were collated, transcribed and retrospectively analysed at the end of the study period.
- The risk assessment for diabetic foot problems was carried out using a DM foot screen tool adopted from NICE guideline (NICE, 2004) with exclusion of renal replacement therapy as a risk factor.
- Correlations between the risk assessment and demographics factors were carried out using X^2 analysis

Results: Among the 366 newly joined DM patients, 59.8% were classified as having low risk for DM foot problems, 14.5% had moderate risk, 22.4% had high risk and 3.3% had active foot ulcers. There was no significant relationship between demographic factors and the risk category for DM foot disease.
Conclusions: Over 40% of DM patients starting HD have a significant risk (moderate risk and above) of developing significant diabetic foot disease. 3.3% already have active ulcers. Knowing the risk category may enable a more focused approach for foot care in DM patients.

PD-74

The effect of risk stratification on 1st year lower limb amputation in diabetic patient starting haemodialysis in community setting

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Introduction: Diabetic (DM) foot complications are common in diabetic patients undergoing chronic dialysis. The rate of lower limb amputation among DM patients with ESRD was10 times as great as among the diabetic population at large (PAUL W. Eggers, et al 1999).
In National Kidney Foundation (NKF) Singapore, more than 70% of newly admitted ESRD patients were diabetic. We therefore explored the first year risk of lower limb amputation among NKF diabetic patients based on their risk stratification for foot problem. It aimed to strengthen clinical pathway on DM foot care to achieve reduction in lower limb amputation rate among NKF DM patients.

Patients and Methods:

- All new patients starting on chronic HD in NKF HD program from1 Jan 2012 to 31 Dec 2013 and who were diabetic were included in the study.
- Patients' data captured included demographics (age, gender, ethnicity and marital status), admission date to NKF, and initial risk category for DM foot disease, subsequent follow up for amputation event until 31 Dec 2014. The amputation rate was calculated for the first year after assessment.
- A total of 366 patients were included in the study.
- Patient characteristics were as follows: Median age 58 years (range 24–91), majority were in the 50th-70th. 58.7% were males and 41.3% were female. 55.2% were Chinese and 44.8% were Malay and other races.
- Initial risk assessment for diabetic foot disease was carried out upon entry to the program. Information was then entered into a structured checklist form. These were collated, transcribed and retrospectively analysed at the end of the study period.
- The risk assessment for diabetic foot problems was carried out using a DM foot screen tool adopted from NICE guideline (NICE, 2004) with exclusion of renal replacement therapy as a risk factor.

Results: Among the 366 newly joined DM patients, first year lower limb amputation rate was strongly correlated with initial foot disease risk ($p < 0.05$). The rates were 1.4% (Low risk), 7.6% (Moderate), 9.8% (High) and 33.4% (Active foot ulcer).
Conclusions: Results of this study suggest that active foot ulcers are significantly associated with first year lower limb amputation. Prompt foot screen and intervention to prevent ulcer formation is paramount. Adopting a multidisciplinary approach in the management of DM foot starts from patient admission would largely improve patient outcome on amputation.

PD-75

Comparison of glycemic control in Asian and non-Asian T2D patients initiating insulin glargine 100 U/mL as add-on therapy to OADs

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T2D is an epidemic disease in Asia, with younger age and lower BMI at diagnosis in Asian vs non-Asian patients. This subject-level analysis compared clinical outcomes in Asian and non-Asian patients with T2D from 16 RCTs (target FPG ≤100 mg/dL, ≥24-week duration) adding insulin glargine 100 U/mL (Gla-100) to OADs. Data were compared overall and by concomitant OAD therapy at baseline and Week 24. Of 3,586 participants, 235 were Asian. Patients received either metformin (MET) (n = 76), MET plus sulfonylurea (SU) (n = 111), SU (n = 16) or other OADs (n = 32).

At baseline, compared with non-Asian patients, Asians were younger (53.7 vs 57.9 years; P < 0.001), had lower BMI (27.1 vs 30.8 kg/m^2; P < 0.001) and FPG (169 vs 194 mg/dL; P < 0.001), but had similar diabetes duration (8.9 years) and HbA1c (8.6% vs 8.7%; P = 0.08). Mean baseline fasting C-peptide was available for 104 (44%) Asian and 2,082 (62%) non-Asian patients and was lower for Asian patients (0.95 vs 1.18 nmol/L; P < 0.001). Pearson correlation indicated a clear association of low C-peptide level with low BMI in both Asian and Non-Asian patients (both P < 0.001); this was most prominent in Asian patients.

After 24 weeks of treatment, Asian patients had a smaller HbA1c reduction (−1.30% vs −1.55%; P < 0.001), a higher overall endpoint HbA1c (7.42% vs 7.16%; P < 0.001), and a lower proportion of Asian patients achieved HbA1c ≤7.0% (40% vs 47%; P = 0.002). FPG reductions were similar in Asian and non-Asian patients (−78 vs −75 mg/dL; P = 0.27) with numerically more Asian patients reaching FPG ≤ 100 mg/dL (48% vs 34%; P = 0.21). Final daily insulin dose (0.47 vs 0.45 U/kg; P = 0.16) and hypoglycemia incidences (45% vs 47%) and event rates (5.3 vs 5.7 episodes/patient-year, PG < 70 mg/dL) were comparable in Asian and non-Asian patients. Asian patients had less weight gain (1.3 vs 1.9 kg; P = 0.01). Parameters of glycemic control and weight change were consistently more favorable in the Gla-100 + MET vs Gla-100 + MET + SU treated group, with similar estimated treatment differences between Asian vs non-Asian patients, as observed in the overall treatment groups. However, final insulin doses were higher in the Gla-100 + MET group for Asians (0.57 U/kg) and non-Asians (0.50 U/kg; P = 0.040 between groups) compared with corresponding MET + SU subgroups (Asian: 0.36 U/kg vs non-Asian: 0.41 U/kg; P = 0.045).

At similar Gla-100 doses and hypoglycemia risk, overall glycemic control was worse in Asian than in non-Asian patients, suggesting higher daily insulin doses or additional antidiabetes drugs are needed for adequate glycemic control.

PD-76

A reduced risk of hypoglycaemia with insulin degludec vs. insulin glargine U100 in Asian insulin-naïve patients with T2D

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Background and aims: Insulin degludec (IDeg) is a basal insulin with a long and stable glucose-lowering effect with low within-patient variability. A previous, global, pre-planned patient-level meta-analysis of phase 3a trials showed IDeg was associated with significantly lower rates of overall confirmed, nocturnal confirmed, and severe hypoglycaemia vs. insulin glargine U100 (IGlar U100) in insulin-naïve patients with type 2 diabetes (T2D). This pan-Asian post-hoc meta-analysis compared the rates of hypoglycaemia with IDeg and IGlar U100 in Asian insulin-naïve patients with T2D.

Methods: This Asian patient-level meta-analysis included two 26-week open-label, phase 3a, randomised, treat-to-target trials; BEGIN ONCE ASIA, and the China cohort of BEGIN ONCE representing all insulin-naïve Asian participants of the IDeg phase 3a clinical trial programme with T2D (excluding the BEGIN Flex trials). Both compared once-daily (OD) IDeg (n = 662 [BEGIN ONCE ASIA, n = 289; BEGIN ONCE-China cohort, n = 373]) and OD IGlar U100 (n = 333 [BEGIN ONCE ASIA, n = 146; BEGIN ONCE-China cohort, n = 187]). Trial maintenance period was defined as after 16 weeks of treatment. Confirmed hypoglycaemia was defined as severe episodes (requiring assistance), or plasma glucose confirmed <3.1 mmol/L. Nocturnal confirmed hypoglycaemia included confirmed episodes with onset between 00.01 and 05.59, both inclusive.

Results: Similar glycaemic control was achieved at end-of-trial; IDeg was non-inferior to IGlar in terms of HbA1c reduction in the individual trial populations, with end-of-trial means of 7.2% and 7.1% respectively (BEGIN ONCE ASIA) and 6.9% and 7.0% respectively (BEGIN ONCE-China cohort). Compared with IGlar U100, treatment with IDeg resulted in a significant 24% lower rate of confirmed hypoglycaemic episodes during the total trial period (rate ratio (RR) 0.76 [0.59; 0.97]95% CI), increasing to a 30% lower rate during the maintenance period (RR 0.70 [0.50; 0.99] 95% CI). Furthermore, there was a significant 43% lower rate of nocturnal confirmed hypoglycaemic episodes with IDeg during the total trial period (RR 0.57 [0.37; 0.87] 95% CI) and a numerically 41% lower rate during the maintenance period (RR 0.59 [0.32; 1.08] 95% CI) compared with IGlar. Only two episodes of severe hypoglycaemia occurred (both with IGlar U100), hence no statistical analysis was performed.

Conclusion: In Asian insulin-naïve patients with T2D, IDeg OD had significant hypoglycaemia benefits compared with IGlar U100, consistent with the findings of the global pre-planned meta-analysis. Clinically relevant reductions in both overall confirmed and nocturnal confirmed hypoglycaemia could lead to further improvement in the treatment of T2D.

PD-77

Sequential changes in clinical findings of diabetic patients by replacing insulin glargine with degludec

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Background: Insulin degludec (Deg) has the different characteristics from those of insulin glargine (Gla). However, the changes in clinical findings of patients by replacing Gla with Deg has been rarely investigated by using continuous glucose monitoring (CGM).

Purpose: This study was aimed at investigating how the replacement of Gla with Deg affects the clinical findings of diabetic patients by CGM.

Methods: A total of 26 diabetic outpatients enrolled in this study comprised 17 type 1 diabetic patients (male/female: 4/13, age: 53.9 ± 14.2 years, HbA1c: 7.7 ± 0.9%) and 9 type 2 diabetic patients (male/female: 6/3, age: 64.9 ± 7.4 years, HbA1c: 7.3 ± 0.6%). In 17 type 1 diabetic patients, Gla was given twice a day in 14 patients and once a day in 3 patients. In 9 type 2 diabetic patients, 7 received intensive insulin therapy and 2 were given basal insulin therapy. After replacing Gla with Deg administered once a day, the mean and standard deviation (SD) of blood glucose levels (BG), frequency of hypoglycemia (<70 mg/dL) for a day and at night (0–6 a.m.) were sequentially measured by CGM.

Results: In type 1 diabetic patients, the mean values of BG before and 1–6 days after replacing Gla with Deg were 151.2 ± 29.1, 162.5 ± 51.5, 182.4 ± 53.3, 166.2 ± 39.5, 173.3 ± 55.9, 157.4 ± 45.1, and 156.2 ± 44.3 mg/dl, respectively; and those of BG at night were 132.0 ± 44.4, 147.2 ± 63.2, 180.0 ± 81.7, 166.8 ± 83.1, 167.4 ± 76.7, 162.2 ± 58.6, and 152.4 ± 89.0 mg/dL, respectively. Thus, the mean values of BG both for a day and at night were temporarily elevated significantly 2 days after the drug replacement but thereafter improved. The SD values and frequencies of hypoglycemia both for a day and at night did not significantly change by the drug replacement. In addition, there was no significant difference in the insulin dose between before and after the drug replacement.
In type 2 diabetic patients, the mean and SD values of BG, and frequencies of hyperglycemic both for a day and at night did not significantly change by the drug replacement. There was no significant difference in the insulin dose between before and after the drug replacement.
Conclusion: In both type 1 and type 2 diabetic patients, replacement of Gla with Deg could be accomplished by using nearly the same units of the drugs. Sequential changes in BG by the drug replacement both for a day and at night in type1 and type 2 diabetic patients differed from each other.

PD-78

Efficacy and safety of mitiglinide versus acarbose for treatment of Chinese patients with type 2 diabetes: Open, multi-center, randomized study

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Background: Acarbose was a kind of commonly used oral anti-diabetic drug special for post-prandial blood glucose and had been widely used in China, but its common gastrointestinal adverse reactions could not be tolerated in some patients. Mitiglinide was a rapid- and short-acting insulinotropic sulfonylurea receptor ligand that was known to improve postprandial hyperglycemia in patients with type 2 diabetes mellitus. The aim of this study was to evaluate the efficacy and safety of mitiglinide versus acarbose in patients with type 2 diabetes mellitus.
Methods: In this open, multi-center, randomized controlled trial, patients with type 2 diabetes mellitus within 5 years were divided randomly into mitiglinide or acarbose treatment group, treated with mitiglinide 10 mg or acarbose 50 mg three times a day for 12 weeks, respectively. The primary outcome measure was change from baseline in glycosylated hemoglobin (HbA1c) at 12 week, secondary outcome measure included change from baseline to the end of treatment in fasting blood glucose (FBG), postprandial blood glucose(PBG) and safety. This study was registered with Clinical Trial.gov, Clinical Trials.gov Identifier was NCT02143765.
Results: A total of 248 patients were enrolled and 237 patients could be incorporate to the evaluation analysis (118 in the mitiglinide group and 119 in the acarbose group). After treatment, HbA1c, FBG, PBG were all decreased significantly in the two groups (all, $P < 0.0001$). HbA1c reduction at week 12 was – (0.95 ± 1.11) % in the mitiglinide group and –(0.80 ± 1.27)% in the acarbose group with difference (0.15 ± 1.19) %, but there was no significant difference between two groups ($P > 0.05$). At week 8, the FBG reduction was –(1.31 ± 1.29) mmol/L (mitiglinide) and –(0.86 ± 1.68) mmol/L (acarbose) with difference (0.45 ± 1.51) mmol/L, there was significant difference between two groups ($P < 0.05$). At week 12, the differences in reduction of FBG and PBG from baseline between the two groups were no statistic significance ($P > 0.05$). The incidence of adverse event was14.66% in the mitiglinide group and 6.54% in the acarbose group ($P = 0.0508$). The incidence of abdominal distension in acarbose group was significantly higher than in mitiglinide group ($P = 0.0055$).
Conclusion: HbA1c, FBG and PBG could all be decreased significantly by either mitiglinide or acarbose, and both groups showed similar efficacy. Mitiglinide group had fewer gastrointestinal reaction and better safety

PD-79

Mechanisms of postprandial suppression of hepatic AMPK activity through insulin-PI 3-kinase pathway

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The number of diabetic and prediabetic patients has been increasing all over the world. Diabetes increases the risk of cardiovascular diseases such as arteriosclerosis, myocardial infarction and stroke, which gives ill effects on the quality of life by concurrent complications like retinopathy, nephropathy and neuropathy.
AMPK is known as a serine/threonine kinase protein complex with three subunits. The subunit has a catalytic function while and subunit have a modulating effect. AMPK is considered to be one of the desirable therapeutic targets in the treatment of obesity and diabetes, because activated AMPK inhibits anabolism whereas promotes catabolism.
We have recently revealed that leptin activates hepatic AMPK predominantly through central action via hypothalamus although direct action suppresses the activity, meanwhile, both direct and indirect action of leptin can increase AMPK activity in skeletal muscles. However, the detailed mechanism has not been clarified. Therefore, we searched for another post-translational modulation of AMPK to further reveal the mechanism regulating hepatic AMPK activity in vitro and in vivo.
When mice (ddY, 7 wks, male) were divided into control and 12 h fasted groups, we found a meal-sensitive phosphorylation site of liver AMPK, and the phosphorylation was reduced in the fasting group. Furthermore, insulin injection increased the liver AMPK phosphorylation and lowered the activity of it. Because insulin varies its concentration with meal, this had led us to hypothesize that AMPK phosphorylation is controlled by insulin.
Thus we further studied the possible mechanisms of insulin for AMPK phosphorylation using cultured hepatic cells (FaO). Insulin stimulation increased the phosphorylation of AMPK, and it was unaffected by pretreatment with rapamycin, whereas wortmannin, a PI 3-kinase inhibitor, reduced the phosphorylation by insulin.
In conclusion, our findings may suggest that food intake controls AMPK activity through insulin-PI3K pathway, which enhance development of insulin resistance. Because impaired glucose tolerance will develop diabetes with insulin resistance at a high frequency, this mechanism might be a novel therapeutic target for metabolic diseases including diabetes.

PD-80

The effect of vitamin D-rich diet on advanced glycation end products in overweight and obese women: VINTAGE trial

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Background: High advanced glycation end products (AGEs) diets promote inflammation and oxidative stress and insulin resistance; AGEs levels increase during cooking because of the processing or heat treatment used.
In our previous study reported that the changes in vitamin D were negatively correlated with those of blood AGEs, independent of the changes of weight loss, during a weight loss period among obese women. However, the effect of a vitamin D-rich diet on AGEs is still unclear.
Objective: The primary objective is to determine whether intake of a vitamin D-rich diet on AGEs diet can lower blood AGEs levels of overweight adult women. The secondary objective is to compare changes in inflammation and oxidative stress markers with vitamin D concentration and other health indicators.
Vitamin D-rich diet on Advanced Glycation End products trial (VINTAGE trial).
Methods: Overweight non-diabetic Japanese women (n = 20) will be included. A randomized crossover intervention design alternating normal and Vitamin D-rich diet (4-week duration) with a 4-week washout period will be used. The inclusion criteria will be as follows: female; age, 20–50 years; overweight and obese. The exclusion criteria will include the following: smoking; high alcohol consumption; known allergies; medication use; diseases/disorders (cancer; cardiovascular, hematological, respiratory, gastrointestinal, endocrine, central nervous system, or psychiatric disorders); menopause or pregnancy and/or lactation; judged unsuitable for the study by the medical doctor.
We will measure the following parameters at baseline, after 4-week intervention (first intervention period), and before and after the second intervention period: Height, body weight, body fat content, circumference, and blood pressure will be measured, and urine analysis will be conducted. Skin AGEs will be evaluated by skin autofluorescence. Serum AGEs levels, vitamin levels, and chronic disease risk markers will be evaluated using blood samples. Participants will complete the International Physical Activity Questionnaire for assessment of habitual physical activity. Dietary habits will be evaluated by food recording for 1 week. After baseline measurements, subjects will be divided into two groups based on AGE and diet habit data. During the intervention period, participants will record self-checked data (body weight, blood pressure, and number of steps) and will receive a weekly telephone phone call to ensuring compliance of dietary intake.
Result: The study will be completed in early 2017.

PD-81
Effects of resistance exercise training in type 2 diabetes

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Objective: According to the Standards of Medical Care in Diabetes 2016, adults with diabetes should be advised to perform aerobic physical activity and resistance training. Compare to aerobic exercise, the benefit of resistance training is less emphasized. According to the results of our questionnaires in T2DM patients, the top two problems about resistance training are 1. Have no equipments (44%) 2. Don't know how to do the exercise (12%). Clinical Trials has shown the benefit of resistance training including improve blood glucose control, reduce cardiovascular risk factors and reduce insulin resistance. To promote the clinical use of resistance training, we start the program.
Methods: This program was executed between Jan. 2015 and Dec. 2015 at Fengyuan Hospital. We use the Balanced Score Card concept. The three major strategic perspectives include (1) customer, (2) internal process, (3) learning & innovation. In the aspect of learning &Innovation: Lectures to the diabetes association and community to educate the benefit of resistance training in diabetes. We also trained our case manager and volunteer to promote the program. In the aspect of internal processes: the Endocrinology and Metabolism department cooperate with the Rehabilitation department to design the teaching video for resistance bands. Application of the exercise plans to the diabetes association, out-patient department, Ward, and community. We also put the video on the famous online broadcasting platform-YouTube for sharing and hope to facilitate the use of the video. We incorporate the program to the self-management education in the Diabetes Shared Care Network in Taiwan. In the aspect of Customer: we use the colorful rubber bands-rainbow loom, for hand-made resistance bands-cost about 0.3 dollars. It made the resistance training became easy, interesting and cheap.
Results: After the resistance training program, 89% patients in our diabetes association could perform resistance training constantly and incorporate the program into their regular exercise plan. 34% patients achieved the recommended target of ADA: perform resistance training at least twice per week. The number of patients involved in the training program over 200 persons till the end of 2015.
Conclusion: Resistance training as an adjunct to standard of diabetes care is simple and effective in improving glycemic control. Through interdisciplinary team works and the Diabetes Shared Care Network in Taiwan, resistance band training is potentially less expensive and more accessible.

PD-82
Real-World (RW) treatment patterns in patients with T2DM newly initiated with antihyperglycemic (AHA) medications in the US

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Objectives: Randomized controlled trials have established the efficacy of canagliflozin (CANA) in T2DM; whereas RW studies measuring effectiveness are limited. This retrospective study evaluated treatment patterns with CANA, dapagliflozin (DAPA), GLP-1 agonists (GLP-1s) and DPP-4 inhibitors (DPP-4s) among patients with T2DM over a 12-month follow up from a US managed care perspective.
Methods: Patients newly initiating CANA, DAPA, GLP-1s, or DPP-4s from 2/1/2014–6/30/2014 were identified from the IMS PharMetrics Plus Database (empagliflozin, approved in 8/2014, was excluded). The first fill defined the index date/drug. Patients were required to have a T2DM diagnosis (ICD-9-CM 250.x [0,2]) and ≥360 days of continuous enrollment pre-(baseline) and post-index (follow-up). Up-titration of CANA and DAPA, adherence (proportion of days covered, PDC; medication possession ratio, MPR) and persistence on index therapy were assessed. A gap ≥90 days between two prescriptions defined discontinuation.
Results: The final sample was 23,702 patients (6,546 CANA, 3,087 DAPA, 6,273 GLP-1s and 7,796 DPP-4s; 56% male and mean [SD] age 55 (9.1) years). More than half of CANA patients (57%) initiated 100 mg and 20% up-titrated to 300 mg in a mean (SD) of 138 (93) days, while the majority of DAPA patients (66%) initiated 5 mg and 21% up-titrated to 10 mg in 157 (90) days. The mean PDC for CANA was 0.71 compared to 0.64 for DAPA, 0.56 for GLP-1s, and 0.62 for DPP-4s, respectively; MPR results were similar. More CANA patients were persistent (68%) compared to DAPA (57%), GLP-1s (52%) or DPP-4s (54%) patients, with mean (SD) persistence days of 279 (126), 260 (128), 236 (139) and 242 (138) respectively.
Conclusions: Adherence and persistence were better with CANA compared to DAPA, GLP-1s and DPP-4s. These findings may reflect CANA's better effectiveness and/or tolerability, which may lead to improved diabetes management in the RW setting.

PD-83

Efficacy of canagliflozin (CANA) in combination with metformin (MET) in patients with T2DM: Results from 3 studies

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Objective: In the AACE clinical practice guidelines, SGLT2 inhibitors, such as CANA, are the first oral medication recommended for patients inadequately controlled on MET. This analysis assessed the efficacy of CANA in patients with T2DM in combination with MET in 3 studies.

Methods: Changes in A1C, body weight (BW), and systolic blood pressure (SBP) were assessed in 3 randomized, double-blind, Phase 3 studies of CANA in combination with MET. CANA 100 and 300 mg were assessed vs placebo (PBO) at Week 26 and sitagliptin 100 mg (SITA) at Week 52 in Study 1 (N = 1,284), and vs glimepiride (GLIM) at Weeks 52 and 104 in Study 2 (N = 1,450). In Study 3, drug-naïve T2DM patients (N = 1,186) received initial combination therapy with MET + CANA 100 mg (CANA100/MET) or MET + CANA 300 mg (CANA300/MET) vs MET alone for 26 weeks.

Results: In Study 1, CANA 100 and 300 mg significantly lowered A1C vs PBO at Week 26; CANA 100 mg demonstrated non-inferiority and CANA 300 mg demonstrated superiority vs SITA at Week 52 (–0.73%, –0.88%, –0.73%). In Study 2, CANA 100 mg demonstrated noninferiority and CANA 300 mg demonstrated superiority in A1C lowering vs GLIM at Week 52; reductions were –0.65%, –0.74%, and –0.55% at Week 104. In Study 3, CANA100/MET and CANA300/MET significantly lowered A1C vs MET at Week 26 (–1.77%, –1.78%, –1.30%; P = 0.001). Significant BW reductions were seen in Study 1 with CANA 100 and 300 mg vs PBO at Week 26 and vs SITA at Week 52 (–3.8%, –4.2%, –1.3%; P < 0.001). In Study 2, CANA 100 and 300 mg significantly lowered BW vs GLIM at Week 52 (–4.2%, –4.7%, 1.0%; P < 0.001); BW changes were sustained at Week 104. In Study 3, significantly greater weight loss was seen with CANA100/MET and CANA300/MET vs MET at Week 26 (–3.5%, –4.2%, –2.1%; P = 0.001). CANA 100 and 300 mg were associated with reductions in SBP vs PBO at Week 26 and SITA at Week 52 in Study 1, and vs GLIM at Week 52 and Week 104 in Study 2. In Study 3, SBP reductions were –2.2, –1.7, and –0.3 mmHg with CANA100/MET, CANA300/MET, and MET at Week 26. CANA was generally well tolerated in each study, with increased incidence of adverse events related to SGLT2 inhibition (e.g., genital mycotic infections) and low rates of hypoglycemia.

Conclusion: In 3 studies, CANA in combination with MET improved A1C, BW, and SBP, suggesting that a fixed-dose combination of CANA + MET may be beneficial in patients with T2DM.

PD-84

Real-world 12-month outcomes of patients with type 2 diabetes mellitus (T2DM) treated with canagliflozin in a US managed care setting

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Canagliflozin (CANA), the first approved agent that inhibits sodium glucose co-transporter 2, improves glycemic control through an insulin-independent mechanism. This study evaluates glycemic control pre- and post-CANA over a 12 month period. This retrospective cohort study used data from a large US health plan for adult commercial and Medicare Advantage enrollees with T2DM filling CANA between April 2013 and August 2014 who had A1C results pre and post the first observed CANA prescription and a pre-CANA A1C ≥7.0%. Of identified patients (n = 2,269), 61% had CANA 100 mg on the first observed fill, 41% were female, and mean age was 56 years. Pre-CANA mean A1C was 8.93% ± 1.56%. Patients, on average, used 2.4 ± 1.1 unique antihyperglycemic agents (AHAs) in the pre-CANA period, inclusive of injectables. Based on the last A1C result ≥30 days following the first observed CANA claim in the 12-month post-CANA period, patients had a mean reduction of 0.96% ± 1.56%, with an average time to post-CANA A1C of 262 days. At baseline about 31% patients had mean A1C between 7% and 8%. The proportion of patients achieving A1C <7.0% and <8.0% were approximately 25% and 59% post-CANA. The proportion of patients with mean A1C more than 8% reduced to 41% in post-CANA period from 69% at baseline. CANA was prescribed to patients with T2DM who were often uncontrolled (mean pre-CANA A1C of 8.93%) despite prior treatment with multiple AHAs. Improvements in A1C consistent to those found in clinical trials were observed in the 12 months following the first CANA prescription.

PD-85

Efficacy of canagliflozin (CANA) versus dipeptidyl peptidase-4 inhibitors (DPP-4i) in patients with T2DM: Results from RCTs and Real-World (RW) study

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In RCTs, CANA was shown to be more effective than the DPP-4i sitagliptin (SITA) in lowering glucose. RCT and RW results tend to differ as RW studies may include a broader set of patients with more advanced conditions; thus it is important to assess the effects of agents in clinical practice. We compared the A1C-lowering efficacy of CANA 100 and 300 mg versus SITA 100 mg in 3 RCTs of patients with T2DM, and the effectiveness of CANA (pooled data for all doses) in a retrospective RW matched control-cohort study using US integrated claims and laboratory data from a large population of insured patients with T2DM (65% and 34% of patients received CANA 100 or 300 mg, respectively [1% other]). Three RCTs included in the analysis were 12 week follow up study as add-on to metformin (n = 184), 52 week follow up study as add-on to metformin (n = 1079) and 52 week follow up study as add-on to metformin + suphonylurea (n = 739). Patients in the CANA cohort were matched 1:1 to patients in the DPP-4i cohort using propensity score matching that incorporated demographics and baseline characteristics. In the RW study mean (median) duration of follow up was 182.3 (191.0) days for DPP-4i and 184.2 (197.0) days for CANA respectively. In RCTs with baseline A1C ~8.0%, CANA 100 mg provided similar and CANA 300 mg provided greater A1C reductions versus SITA 100 mg. In the RW study with baseline A1C ~9.0%, greater A1C reductions were seen with CANA (–1.07%) versus DPP-4i (–0.79%). In summary, the relative magnitude of A1C reduction with CANA and SITA was similar in the RCT and RW studies; CANA consistently lowered A1C versus DPP-4i in patients with T2DM.

PD-87

Real-world evaluation of weight loss in patients with T2DM treated with canagliflozin (CANA) – An electronic health-record (EHR)-based study

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Objectives: Weight management remains a challenging goal for most patients with T2DM. However, CANA has been shown

to improve glycemic control and body weight (BW) in T2DM patients. This study leveraged EHR data to evaluate BW over time among patients with T2DM receiving CANA in a real-world setting.

Methods: Adult patients with ≥1 T2DM diagnosis and ≥12 months of clinical activity (baseline) before first CANA prescription (index) were identified in the Cegedim Strategic Data US EHR dataset. Paired t-tests were used to compare baseline BW to BWat 3 and 12 months post-index. Proportions of patients with a weight loss ≥5% from baseline were reported overall and in patients with baseline BMI ≥ 30 kg/m^2.

Results: A total of 16,163 CANA users were identified (35% CANA 300 mg users, 48% female, mean age: 59 years, 76% white, mean Charlson Comorbidity Index: 1.4, mean Diabetes Complications Severity Index: 0.7). At baseline, 90% of patients used ≥1 antihyperglycemic agent and 35% used insulin. Mean exposure to CANA was 155.6 days. Among patients evaluated at 3 months (N = 6,811; mean baseline BW = 102.9 kg), BW decreased from baseline by 1.8 kg (P < 0.001) and 13.3% of patients had a weight loss ≥5%. At 12 months (N = 1,288; mean baseline BW = 103.8 kg), BW decreased from baseline by 2.6 kg (P < 0.001) and 25.8% of patients had a weight loss ≥5%. Among patients with a baseline BMI ≥ 30 kg/m^2, at 3 months (N = 5,155; mean baseline BW = 110.3 kg) BW decreased by 2.1 kg (P < 0.001) and 13.6% of patients had a weight loss ≥5%; at 12 months (N = 995; mean baseline BW = 110.8 kg), BW decreased by 3.0 kg (P < 0.001) and 27.5% of patients had a weight loss ≥5%.

Conclusions: Patients with T2DM treated with CANA in a real-world setting experienced statistically significant weight loss over time, in both the overall population and in patients with BMI ≥ 30 kg/m^2.

PD-88

Semaglutide reduces appetite and energy intake, improves control of eating and provides weight loss in subjects with obesity

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Glucagon-like peptide-1 (GLP-1) therapy has the potential to decrease body weight. Semaglutide is a human GLP-1 analog in development for the treatment of type 2 diabetes. This study examined the mechanisms of body weight loss compared with placebo.

This double-blind, crossover study compared once-weekly subcutaneous semaglutide (dose-escalated to 1.0 mg) with placebo, in 30 subjects with obesity and without type 2 diabetes. The primary endpoint was ad libitum energy intake during lunch (5 h after standardized breakfast) after 12 weeks of treatment.

Ad libitum energy intake with semaglutide vs placebo was 35% lower at lunch (estimated treatment difference vs placebo [ETD] −1255 kJ; 95% confidence interval [CI] −1707; −804), 18% lower at evening meal (ETD −753 kJ; 95% CI −1469; −37) and 22% lower after snack boxes (ETD −1028; 95% CI −1684; −372). Total energy intake during ad libitum meals was significantly lower (24%) with semaglutide vs placebo (ETD −3036 kJ; 95% CI −4209; −1864). Resting metabolic rate also decreased 7% with semaglutide vs placebo (ETD −602 kJ/24 h [−959; −245]). Fasting overall appetite score (visual analog scale) indicated reduced appetite with semaglutide vs placebo (p = 0.0023), while nausea ratings were similar. For semaglutide vs placebo, the Control Of Eating Questionnaire indicated less hunger and food cravings and better control of eating; the Leeds Food Preference Task indicated a relatively lower preference for high-fat vs low-fat foods. Mean body weight (overall mean at baseline 101.3 kg; mean BMI 33.8 kg/m^2) was reduced by 5.0 ± 2.4 (SD) kg with semaglutide treatment compared with a body weight increase of 1.0 ± 2.4 kg with placebo, with proportionally more fat than lean body mass lost.

In conclusion, semaglutide-induced body weight loss was confirmed. Possible mechanisms are: reduced energy intake, appetite and food cravings; better control of eating; and lower relative preference for fatty, energy-dense foods.

PD-89

Semaglutide improves postprandial glucose and lipid metabolism and delays first-hour gastric emptying in subjects with obesity

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Glucagon-like peptide-1 (GLP-1) therapies may delay gastric emptying and thus influence postprandial glucose and lipid responses. Semaglutide is a human GLP-1 analog in development for the treatment of type 2 diabetes. This study investigated the effect of semaglutide on postprandial glucose and lipid responses compared with placebo.

This double-blind, crossover study compared once-weekly subcutaneous semaglutide (dose escalated to 1.0 mg) with placebo in 30 subjects with obesity and without type 2 diabetes (mean BMI 33.8 kg/m^2). After each 12-week treatment period, subjects were given a standardised breakfast or a standardised fat-rich breakfast. Fasting glucose metabolism was assessed prior to standardised breakfast, and postprandial glucose metabolism and gastric emptying were assessed after. Fasting lipid metabolism was assessed prior to standardised fat-rich breakfast, and postprandial lipid metabolism after.

After 12 weeks of treatment, fasting concentrations of insulin were higher with semaglutide vs placebo (estimated treatment ratio [ETR] 1.45; 95% confidence interval [CI] 1.20; 1.75), as was C-peptide (ETR 1.35; 95% CI 1.20; 1.52). Fasting concentrations of glucose were lower with semaglutide vs placebo (ETR 0.95; 95% CI 0.91; 0.98), as were glucagon (ETR 0.86; 95% CI 0.75; 0.98), triglycerides (ETR 0.88; 95% CI 0.80; 0.98) and very low density lipoprotein (ETR 0.79; 95% CI 0.66; 0.95). After a standardized breakfast, postprandial glucose levels were lower with semaglutide vs placebo (estimated treatment difference [ETD]; −1.34 mm*h/L 95% CI −2.42; −0.27), as were insulin (ETD −921 pmol*h/L; 95% CI −1461; −381) and C-peptide levels (ETD −1.42 nmol*h/L; 95% CI −2.33; −0.51). After a standardized fat-rich breakfast, triglycerides were lower for semaglutide vs placebo (ETD −4.51 mmol*h/L; 95% CI −6.15; −2.87); as were very low density lipoprotein (ETD −1.17 mmol*h/L; 95% CI −2.03; −0.32) and apolipoprotein B48 (which facilitates lipid absorption in the intestine) levels (ETD −0.0455 g*h/L; 95% CI −0.0690; −0.0220). No statistical difference between treatments was shown for the overall rate of postprandial gastric emptying (AUC0-5h); however, for semaglutide vs placebo, gastric emptying was delayed during the first hour.

In conclusion, semaglutide improves fasting and postprandial glucose levels, as well as fasting and postprandial lipid metabolism, vs placebo, and delays gastric emptying during the first hour.

PD-90

Renal effects of canagliflozin in patients with Type 2 diabetes

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Background: Canagliflozin, a sodium glucose co-transporter-2 (SGLT2) inhibitor, reduces blood glucose level in Type 2 diabetes (T2DM) patients by lowering the renal threshold for glucose, thereby increasing urinary glucose excretion. With the recent introduction of canagliflozin into the formulary,

we conducted a new-user, active-comparator, retrospective observational study in the diabetes centre of our hospital, between 1 May and 31 Dec 2014, to evaluate the effectiveness and safety of canagliflozin in a real-world setting when compared to Sitaglitin. This study had shown that there was significant reduction in estimated glomerular filtration rate (eGFR), up to 24 weeks of follow-up for the canagliflozin group.
Objective: The aim of this study was to extend our observations in patients on canagliflozin up to 52 weeks to further evaluate the changes in eGFR.
Method: The renal profile of the patients aged 18–69 years with type 2 diabetes and eGFR ≥ 60 mL/min/1.73 m^2 who were initiated on once daily canagliflozin 300 mg in the earlier study were follow-up subsequently up to 52 weeks. The changes in eGFR were measured and compared between the baseline and up to 26 weeks of follow up.
Results: Data from a total of 22 patients who were initiated on canagliflozin 300 mg with follow-up till 52 weeks were included. When compared to baseline eGFR, we observed a significant reduction in eGFR (−9.00 ± 10.04 mL/min/1.73 m^2, p = 0.002) up to 26 weeks of follow up. However, the reduction in eGFR was not sustained up to 52 weeks of follow up (−2.08 ± 5.33 mL/min/1.73 m^2, P = 0.185)
Conclusion: The observations suggest that there is short term reduction in eGFR with patients newly initiated on canagliflozin and these changes stabilized or attenuated over time in patients with T2DM with initial function.

PD-91

Self-monitoring of blood glucose with smart-phone based data sharing improved glycemic control in patients with diabetes

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Background: The advance in mobile technology enables new care models for patients with chronic diseases. We investigated the effects of self-monitoring of blood glucose (SMBG) with smart-phone based data sharing on glycemic control in patients with diabetes.
Materials and methods: Adult patients with diabetes who had inadequate glycemic control, defined as having a glycosylated hemoglobin (HbA1c) >7%, were eligible. Patients were instructed how to do SMBG and upload data with smart phone using Health2Sync Mobile App. Patients were encouraged to have food diary using the established items in the App. The diabetes educators reviewed the massages from patients and replied as needed. The glucose values patients uploaded were analyzed to investigate the changes in glycemic control every two weeks up to week 18. The patients who uploaded less than four glucose values every 2 weeks were excluded from the analysis.
Results: From Sep 2014 to Feb 2016, a total of 186 patients with diabetes were recruited from five hospitals. The number of patients who uploaded at least four glucose values at week 0–2, 3–4, 5–6, 7–8, 9–10, 11–12, 13–14, 15–16, and 17–18 was 186, 159, 146, 132, 112, 100, 90, 82, and 78, respectively. The median number of glucose values uploaded every 2 weeks was 25–29 (i.e. around 2 tests per day). Overall, the mean glucose value improved significantly from 177 ± 53 mg/dL at week 0–2 to 164 ± 52 mg/dL at week 3–4, and thereafter (all p values <0.05 compared with week 0–2). The percentage of glucose value >180 mg/dL significantly decreased from 36.9 ± 26.0% at week 0–2 to 30.4 ± 25.4% at week 3–4, and thereafter (all p values <0.05 compared with week 0–2). The percentage of glucose value <70 mg/dL did not change significantly (5.2 ± 8.3% at week 0–2 and 7.9 ± 11.5% at week 17–18). We further analyzed the glucose values in different daytime periods. We found that the improvement in mean glucose was accompanied with an improvement in postprandial glucose after breakfast and lunch, but not after dinner.
Conclusions: Results from this study suggested that SMBG combined with smart-phone based data sharing improved glycemic control in patients with diabetes. Our results need to be confirmed in future studies with an appropriate control group.

PD-92

The impact of CGMS in subjects of inadequately controlled type 2 diabetes under intensive glycemic control

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Background: The study is to evaluate the effect of continuous glucose monitoring system (CGMS) intervention among patients of poorly controlled type 2 diabetes (T2D) with intensive insulin therapy.
Materials and methods: This is case-control study with enrollment of a total of 40 subjects divided to 2 groups with inadequately controlled T2D. The subjects with ongoing twice daily pre-mixed insulin therapy with glycated hemoglobin (A1C) greater than 8% were enrolled and all switched to pre-mixed insulin therapy three times per day for three months. The case group applied CGMS before and after intensive insulin therapy. The difference of A1C was compared between 2 groups to explore the benefit of intervention of CGMS. The change of index of glucose variability in the case group before and after intensive insulin therapy was also evaluated.
Results: The mean age of the subjects was 47 y/o with mean duration of 9.4 years. Both groups show significant reduction of A1C (9.4% to 8.3%, and 9.3% to 8.6%, both with p < 0.001). Moreover, the case group with CGMS intervention showed greater A1C reduction than that of control group (−1.1% vs −0.7%, p < 0.001). The index of glucose variability demonstrated improvement of mean amplitude of glucose excursions (124 mg/dL to 92 mg/dL, p < 0.001), and standard deviation (63 mg/dL to 44 mg/dL, p < 0.001) by introduction of CGMS with receiving intensive insulin therapy.
Conclusion: The present study confirmed the benefit of CGMS intervention in improvement of glucose variability and glycemic control in subjects of inadequately controlled type 2 diabetes.

PD-93

Dietary patterns influence blood sugar and lipid control among type 2 diabetic patients in Taiwan – A pilot study

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The prevalence of Diabetes Mellitus has increased from 4.8% to 7.1% within five years since 2007. Research showed that changing eating habits may be one of the most effective therapies to treat diabetes. However, dietary patterns among Taiwanese diabetic patients are rarely studied. The objectives of present study were to explore what dietary patterns among diabetic patients and their odds ratios of blood sugar and lipids

control in Taiwan. One hundred and sixty type 2 diabetic patients were recruited from China Medical University Hospital in Taichung, Taiwan. Biochemical data, such as plasma fasting sugar, HbA1c, total cholesterol, triglyceride, HDL-C, and LDL-C, were collected from medical records. Diet was assessed by a validated food frequency questionnaire which composed of 118 food items, and categorized to 23 food groups. Diabetic patient's dietary pattern was analyzed by principle component analysis. Confounders related to both diet and biochemical indices including age, gender, BMI, energy intakes, and physical activity were assessed. Multiple logistic regression analyses were used to predict odds ratios of poor blood biochemical control after adjustment of confounders. Mean age of the study subjects was 57.46 ± 10.67 year-old and had 2.8 year of diabetes history. Four dietary patterns were identified, pattern I (high meat, fish, vegetable, nut and oil), pattern 2 (high refined rice, starchy root, and fish), pattern 3 (high refined rice, meat product, sugar drink, low whole grain, vegetable, nut), and pattern 4 (high vegetable, non-sugar drink, low starchy root, dairy product, and snack). Mean age, energy intake, BMI, and sex proportion were significantly different among different patterns. Compared to pattern 4, the odds ratio of high HbA1c (≥7%) was 3.66 (95% CI 1.21–11.05) for pattern 1 and 2.52 (95% CI 1.00–6.39) for pattern 3 after gender, age, energy intake, and BMI adjustment. Odds ratio of high plasma fasting sugar (>130 mg/dL) was 2.67 (95% CI 1.08–6.65) for pattern 3 compared to pattern 4. For female patients, odds ratio of low HDL-C (<50 mg/dL) was 0.11 (95% CI 0.02–0.80) for pattern 1 compared to pattern 4. In the present study, clusters of food groups might not be representative for Taiwanese diabetic patients; however, different dietary patterns were possible to influence blood sugar and lipid control among diabetic patients. More consumption of vegetables, fish and nuts, less sugar drinks and snacks are beneficial for diabetic treatment.

PD-94

Relationship between indices of daily glycemic variability and long-term glucose fluctuations

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Purpose: We investigated the relationship between indices of daily glycemic variability and long-term glucose fluctuations.
Methods: A total of 123 patients with diabetes (22 patients with type 1 diabetes; 9 males, age 53 ± 16, HbA1c 7.9 ± 1.4%, GA 25.0 ± 6.0%, and 101 patients with type 2 diabetes; 80 males, age 69 ± 10, HbA1c 6.8 ± 0.8%, GA 18.8 ± 3.9%) who underwent continuous glucose monitoring (CGM) in outpatient settings were enrolled in this study. We evaluated the daily glycemic variability from the CGM data as follows; mean glucose level, standard deviation (SD), time of hyper- and hypoglycemia, area under the curve (AUC) of hyper- and hypoglycemia, J-index, hyperglycemic index, hypoglycemic index, index of glycemic control (ICG), continuous overlapping net glycemic action (CONGA), mean amplitude of glycemic excursion (MAGE), M-value, mean of the daily differences (MODD). In addition, Coefficient of variation (CV) of HbA1c and GA were calculated from HbA1c and GA measured before and after 3 years from CGM measurement.
Result: Both CV-HbA1c and CV-GA were correlated with mean glucose level, SD, time of hyperglycemia, AUC of hyperglycemia, J-index, hyperglycemic index, ICG, MODD, MAGE and M-value but were not correlated with time of hypoglycemia, AUC of hypoglycemia, hypoglycemic index, and CONGA-1. Especially, CV-HbA1c was strongly correlated with mean glucose level, time of hyperglycemia, AUC of hyperglycemia, J-index and M-value (r = 0.4), and so was CV-GA. Serum C-peptide level was negatively correlated with the indices of daily glycemic variability, CV-HbA1c and CV-GA, and was also correlated with GA/HbA1c. GA/HbA1c was correlated with the indices of daily glycemic variability, but not correlated with CV-HbA1c or CV-GA. These results were not changed when only the patients with type 2 diabetes were included in the analysis.
Conclusion: The indices of daily glycemic variability were correlated with long-term glucose fluctuations, but were not correlated with the indices of hypoglycemia. These findings suggest that CV-HbA1c and CV-GA may not reflect the risk of hypoglycemia. And β-cell function was correlated with both daily glycemic variability and long-term glucose fluctuations. Clarifying the features of various indices of glycemic variability and the relationship among them could make these indices more useful in clinical practice.

PD-95

Efficacy and safety of once-weekly semaglutide monotherapy versus placebo in subjects with type 2 diabetes (SUSTAIN 1)

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Semaglutide is a glucagon-like peptide 1 (GLP-1) analog in development for the treatment of type 2 diabetes (T2D). This study evaluated the efficacy, safety and tolerability of subcutaneous (s.c.) semaglutide monotherapy versus placebo in drug-naïve subjects with T2D.
In this phase 3, double-blind study, 388 adults with T2D (HbA1c 7–10%) were randomized to s.c. semaglutide 0.5 mg or 1.0 mg once weekly or placebo for 30 weeks, including 4–8 weeks of dose escalation. Primary endpoint was change in HbA1c from baseline to Week 30.
Mean HbA1c (baseline 8.1%) was reduced with semaglutide 0.5 mg and 1.0 mg by 1.5% and 1.6%, respectively, versus <0.1% in the placebo group (estimated treatment difference versus placebo [ETD] −1.4% and −1.5%; p < 0.0001 for both). HbA1c <7% was achieved by 74% and 72% of 0.5 mg and 1.0 mg semaglutide-treated subjects, versus 25% in the placebo group. The corresponding proportions of subjects achieving HbA1c ≤6.5% were 59%, 60% and 13%. Mean fasting plasma glucose (baseline 9.8 mmol/L) was reduced with semaglutide 0.5 mg and 1.0 mg by 2.5 mmol/L and 2.3 mmol/L, respectively, versus 0.6 mmol/L with placebo (ETD −2.0 mmol/L and −1.8 mmol/L; p < 0.0001 for both).
Mean body weight (BW; baseline 91.9 kg) was significantly decreased with semaglutide 0.5 mg and 1.0 mg by 3.7 kg and 4.5 kg, respectively, versus 1.0 kg in the placebo group (ETD −2.8 kg and −3.6 kg; p < 0.0001 for both). Changes in blood pressure (baseline 128.8/79.3 mmHg) were comparable between the semaglutide 0.5 mg, 1.0 mg and placebo groups.
Adverse event (AE) and serious AE (SAE) rates were comparable between groups: 64.1%, 56.2% and 53.5% of patients reported AEs with semaglutide 0.5 mg, 1.0 mg and placebo, respectively, and 5.5%, 5.4% and 3.9% reported SAEs. Proportions of patients discontinuing due to AEs were 6.3%, 5.4% and 2.3% for semaglutide 0.5 mg, 1.0 mg and placebo. Proportions of subjects reporting gastrointestinal AEs in the 0.5 mg, 1.0 mg and placebo groups were 20.3%, 23.8% and 7.8% for nausea; 3.9%, 6.9% and 1.6% for vomiting; and 12.5%, 10.8% and 2.3% for diarrhea. Nausea rate diminished over time.
In conclusion, semaglutide monotherapy, s.c. once-weekly doses of 0.5 mg and 1.0 mg, significantly improved glycemic control and reduced BW versus placebo in patients with T2D. Semaglutide was well tolerated, with a safety profile similar to that of other GLP-1 receptor agonists.

PD-96

Efficacy and safety of once-weekly semaglutide versus sitagliptin as add-on to metformin and/or thiazolidinediones in subjects with T2D (SUSTAIN 2)

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Semaglutide is a glucagon-like peptide-1 (GLP-1) analog in development for the treatment of type 2 diabetes (T2D). This study evaluated the efficacy, safety and tolerability of once-weekly subcutaneous (s.c.) semaglutide versus sitagliptin in subjects with T2D inadequately controlled on metformin (MET) and/or thiazolidinediones (TZDs).

In this phase 3, double-blind, double-dummy study, 1231 subjects with T2D (HbA1c 7–10.5%) on MET and/or TZDs were randomized 2:2:1:1 to once-weekly semaglutide 0.5 mg or 1.0 mg or once-daily sitagliptin 100 mg (sitagliptin/semaglutide placebo arms were pooled in the analyses) for 56 weeks, including 4–8 weeks of dose escalation. Primary endpoint was change in HbA1c from baseline to Week 56. Secondary efficacy endpoints included body weight (BW), blood pressure and other glycemic parameters.

Mean HbA1c (baseline 8.1%) was reduced by 1.3% and 1.6% with semaglutide 0.5 mg and 1.0 mg, respectively, versus 0.5% with sitagliptin (estimated treatment difference versus sitagliptin [ETD] −0.77% and −1.06%; both $p < 0.0001$). HbA1c <7% was achieved by 69% and 78% of 0.5 and 1.0 mg semaglutide-treated subjects, respectively, versus 36% with sitagliptin; corresponding proportions of subjects achieving HbA1c ≤6.5% were 53%, 66% and 20%. Mean BW (baseline 89.5 kg) was reduced by 4.3 kg and 6.1 kg with semaglutide 0.5 mg and 1.0 mg versus 1.9 kg with sitagliptin (ETD −2.37 kg and −4.22 kg; both $p < 0.0001$). Improvements in other secondary endpoints, including fasting plasma glucose and self-monitored plasma glucose, were also observed with both doses of semaglutide.

Proportions of subjects reporting adverse events (AEs) and serious AEs (SAEs) were comparable between groups: 74.8%, 71.4% and 71.7% of subjects reported AEs and 7.3%, 7.3% and 7.1% reported SAEs with semaglutide 0.5 mg, 1.0 mg and sitagliptin, respectively. Six fatal events occurred (2, 1 and 3 in the semaglutide 0.5 mg, 1.0 mg and sitagliptin study arms, respectively). Proportions of subjects discontinuing due to AEs were 8.1% for semaglutide 0.5 mg, 9.5% for semaglutide 1.0 mg and 2.9% for sitagliptin. The most frequent AEs were gastrointestinal (GI), which were mainly mild or moderate. Proportions of subjects reporting GI AEs in the semaglutide 0.5 mg, 1.0 mg and sitagliptin groups were 43.5%, 39.9% and 23.6%, respectively.

In conclusion, semaglutide (0.5 and 1.0 mg s.c. once weekly) was superior to sitagliptin in improving glycemic control and reducing BW in subjects with inadequately controlled T2D on MET and/or TZDs. Semaglutide was well tolerated with a safety profile similar to other GLP-1 receptor agonists.

PD-98

Efficacy and tolerability of gliclazide MR 60 mg in the management of type 2 diabetes: Analysis of the EasyDia Trial

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Background and aims: Progressive intensification of glucose-lowering with gliclazide modified release (MR) has demonstrated long-term safety and renal protection in individuals with type 2 diabetes (T2D). The aim of these analyses was to examine the efficacy and tolerability of the gliclazide MR 60 mg regimen used in the EasyDia trial.

Materials and methods: EasyDia was a 6-month international, open-label study in which 7170 subjects with T2D were prescribed 30–120 mg of gliclazide MR 60 mg, once daily, as a first line, add-on, or switch from a previous oral glucose-lowering treatment. Dosing uptitration was based on fasting plasma glucose at months 1, 2, and 3. In the current analyses, we examined the efficacy of gliclazide MR 60 mg at lowering HbA1c and tolerability in various patient subgroups based on their initial HbA1c, weight and glucose lowering treatment (defined as newly diagnosed; add-on to metformin; or switch from either another sulfonylurea or a DPP-4i).

Results: After 6 months, the mean HbA1c was significantly reduced across all the HbA1c subgroups (−1.03 ± 0.02% for 7–8% subgroup, −1.55 ± 0.02% for 8–9% subgroup, −2.31 ± 0.04% for 9–10% subgroup, and −3.76 ± 0.06% for >10% subgroup). Regarding treatment groups, the mean changes in HbA1c between baseline and 6 months were: −2.13 ± 0.05% for newly diagnosed, −1.76 ± 0.03% for add-on to metformin, −1.62 ± 0.06% when switched from another sulfonylurea, and −1.99 ± 0.30 when switched from a DPP-4i (all $P < 0.01$ vs baseline). Weight neutrality was observed overall across the cohorts between baseline and month 6, with a mean weight difference of −1.34 ± 0.06 kg. These changes reflected significant weight loss in patients with a BMI in the overweight (25–30) or obese (≥30) range (−0.88 ± 0.07 and −2.24 ± 0.11 kg, respectively; $p < 0.01$), with slight weight gain (+0.54 ± 0.16 kg) in patients with normal BMI (18.5–24.9). Few patients experienced hypoglycemia, with no differences observed between the subgroups.

Conclusion: Progressive titration of gliclazide MR 60 mg was well tolerated and consistently effective in lowering HbA1c across a broad range of patients with T2D. The main determinant of the reduction in HbA1c was the level of HbA1c at entry. Very large reductions were observed in patients with initial HbA1c levels ≥10%, while a smaller adapted change was observed when the initial HbA1c was 7–8%. Additional reductions were observed when switched from another sulfonylurea or DPP4-i. Concomitant weight loss was also associated with baseline weight, with obese patients losing significantly more weight than patients with a normal BMI at baseline.

PD-100

Clinical effectiveness study of SGLT2 inhibitors as added-on therapy for 149 insulin treated type 2 diabetes patients

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Background: Sodium-glucose co-transporter 2 inhibitor (SGLT2i) promotes renal glucose excretion through an insulin independent mechanism. SGLT2i has shown ability to improve A1C, body weight (BW), and blood pressure (BP) control. For type 2 diabetes patients (T2DM) with insulin regimen, the effectiveness of SGLT2i on the metabolic control was evaluated in this study.

Methods: A retrospective case note audit of patients was performed in a diabetes clinic located at Yilan County, Taiwan. SGLT2i was added to those adult T2DM patients with insulin regimens. Datum of clinical parameters, self-monitor blood glucose (SMBG), and adverse events were collected to analyze the efficacy of SGLT2i for 6 months.

Results: 149 T2DM patients were selected in this study. The average A1C, BMI, and BP at baseline were 9.0%, 28.2 kg/m^2, and 127.0/75.6 mmHg, respectively. 65.1% of patients used 10mg daily dapagliflozin and 34.9% of patients used 10 mg daily

empaglifozin at baseline. 53.0% of 149 patients used basal insulin regimen once daily. After adding SGLT2i for 6 months, A1C has been reduced in 122 patients, and reduced by equal and more than 1% in 42.3% of 122 patients. Overall A1C has been significantly reduced by 0.9 ± 1.2%. For different A1C groups (<8%, 8–9%, 9–10%, and ≧10% at baseline), the reduction of A1C was 0.4, 0.4, 1.3, and 1.9%, respectively ($p < 0.001$). BW has been reduced in 121 of patients, and reduced by equal and more than 3 kg in 28.9% of 121 patients. Systolic BP and diastolic BP were both significantly reduced by 5.4, and 3.1 mmHg, respectively. Regarding insulin dose adjustment, basal and bolus insulin dose was reduced by 9.4 (n = 87) and 10.3 (n = 53) units, respectively. Before using SGLT2i, hypoglycemia from SMBG readings has been found in 41 patients (33.9%, N = 121), and the incidence of hypoglycemia was 0.36 per patient per month. After using SGLT2i for 3 months, hypoglycemia has been found in 58 patients (45.7%, N = 127), and the incidence has been increased to 0.67 per patient per month. Meanwhile, vaginitis, micturition, and urinary tract infection (UTI) were self-reported in 9.1, 4.2, and 0.7% of patients, respectively.

Conclusions: Adding SGLT2i into insulin regimen significantly improved T2DM patients' A1C, BW, and BP. For those patients with worse A1C control, the improvement in A1C was more significant. However, adding SGLT2i may result in hypoglycemia. Vaginitis, micturition, and UTI were commonly seen adverse events with SGLT2i therapy.

PD-101

Outcomes of holistic care for patients with type 1 diabetes (T1D) by multidisciplinary teams in Thailand

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Objectives: In Thailand, the optimal treatment and experienced care teams for caring of T1D are not available countrywide. This three-year project aims to improve the care and establish multidisciplinary teams for caring patients with T1D.

Subjects: 85 T1D and 31 multidisciplinary teams from 25 participating hospitals were enrolled. T1D were 54 females and 31 males with mean age of 20 ± 11 years. Insulin injection patterns were twice, three times and ≥4 times daily in 13, 22 and 65%, respectively. For those who received insulin ≥4 times a day, 22% used NPH and 43% used long acting insulin analog as basal insulin.

Methods: All care teams were trained for diabetes self-management education (DSME) and skills before the start. All patients were switched to basal-bolus insulin analog regimen with self-monitoring of blood glucose (SMBG) at least four times a day free of charge. The first year, two 3-day diabetes camps were set up to accommodate all patients, parents and teams for learning all essential tasks of diabetes self-management. In the second and third year four 2-day diabetes camps were organized in the 4 regional areas of Thailand to refresh the knowledge and add essential tasks to live happily with diabetes.

Results: The mean ± SD of A1C of the group at enter, the end of first, second and third year were 9.09 ± 2.98, 8.49 ± 1.69 ($p = 0.001$), 8.72 ± 1.99% and 8.91 ± 2.04%, respectively. In patients aged 5–10 years, A1C at enter, the end of first, second and third year were 8.43%, 8.0%, 8.21% and 8.09% ($p = 0.26$), in patients aged 10–18 years were 9.8%, 8.28%, 9.47% and 9.43% ($p = 0.83$), and in those >18 years were 7.9%, 7.85%, 7.7% and 7.73% ($p = 0.03$), respectively. At the end of program, the proportion of patients who achieved A1C < 7.5% increased from 18.3% to 24.5%, while patients with A1C 7.5–8.5% rose from 23.9% to 30.6%. Episodes of severe hypoglycemia declined, SMBG frequency increased from at entry 2.87–3.48 times/day. The carbohydrate counting problems, eating disorders decreased from 35%, 20% at baseline to 11%, 5%, respectively. The care teams had better self-confidence in giving care and communication with patients and families.

Conclusion: The 3-year process of this program has improved DSME skills of the patients and families. The optimal supply of insulin analogs and glucose strips contributed to improve overall glycemic control, although not sustained. This program encourages ongoing communication and interaction among the patients, families and healthcare professionals facilitating better management outcomes.

PD-102

Effect of dapagliflozin in Japanese type 2 diabetes patients who have inadequate glycemic control

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Objective: To evaluate the efficacy and safety of dapagliflozin in the clinical practice.

Method: Subjects were 35 patients with type 2 diabetes who had been treated at our hospital. Dapagliflozin (5 mg/day) was administered to the patients (study subjects) for 12 months. Blood and urine samples were collected at baseline, 6 and 12 months, and physical examination was performed at each time point. Efficacy was evaluated by measuring HbA1c levels, body composition, blood pressure, and liver and renal function.

Results: At 6 month, dapagliflozin significantly reduced HbA1c and glycoalbumin from baseline, and the changes were maintained over 12 months. (HbA1c 6.95 ± 0.66% (12M) vs 7.49 ± 1.06% (baseline) [$P < 0.0001$]; glycoalbumin; 18.5 ± 4.2% (12M) vs 17.3 ± 2.9% (baseline) [$P = 0.005$]). Compared to the baseline value, BMI and waist circumference (WC) were also significantly reduced at 6 month, which were maintained up to 12 months. (BMI 26.6 ± 3.6 (12M) vs 28.6 ± 3.8% (baseline) [$P < 0.0001$], WC 93.7 ± 9.4%(12M) vs 99.6 ± 8.9% (baseline) [$P < 0.0001$]).

Blood pressure, uric acid, and parameters for hepatic function significantly decreased, while hematocrit value and eGFR significantly increased from baseline. In addition, 12 patients who had dapagliflozin with reduced dose glimepiride showed improved blood glucose levels, BMI, and WC.

Conclusions: Dapagliflozin significantly improved blood glucose levels, BMI, and waist circumference in patients with type 2 diabetes. Similarly, dapagliflozin administered to poorly controlled type 2 diabetes patients with glimepiride improved blood glucose levels, BMI, and waist circumference, accompanied by dose reduction of glimepiride.

These results indicate that dapagliflozin is a useful anti-hyperglycemic agent that possibly improves the obesity in the real clinical practice.

PD-103

To investigate the efficacy of dipeptidyl peptidase-IV (DPP-IV) inhibitor therapy in multiethnic Asian patients with type 2 diabetes mellitus

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Objective: To investigate the efficacy of dipeptidyl peptidase-IV (DPP-IV) inhibitor therapy in multiethnic Asian patients with type 2 diabetes mellitus (T2DM).

Research design and methods: This is a retrospective single-center study of 343 Singaporeans with T2DM from Jan 2014 to May 2015. Inclusion criteria included patients started on DPP-IV inhibitor therapy for at least 12 months. We examined the changes in the glycemic control (HbA1c) and body weight at baseline and at 12 months after initiation of DPP-IV inhibitor

using the paired t-test. We also examined if the changes in the HbA1c and body weight differed between ethnic groups by gender (males vs females), DM duration (<10 years vs ≥10 years) and age (<50 years and ≥50 years) using linear mixed models.

Results: We enrolled 196 (57.1%) Chinese, 70 (20.4%) Malay and 77 (22.4%) Indians. The mean age (SD) of Chinese, Malays and Indians were 59.14 (14.72) years, 56.57 (12.61) years and 56.00 (13.63) years respectively ($p = 0.001$). The mean duration of DM was 14.02 (9.28) years for Chinese, 13.52 (8.51) years for Malays and 11.03 (7.62) years for Indians ($p < 0.001$). HbA1c improved at the end of 12 months of follow-up for all three ethnic groups (Chinese, Δ-0.43%, $p = 0.036$; Malays, Δ0.66%, $p = 0.0867$; Indians, Δ0.54%, $p = 0.088$). The interaction term ethnicity*follow-up was not statistically significant. There were no statistically significant changes in the body weight for all the three ethnic groups at the end of the 12-month follow-up. Patients who were older than 50 years old had more sustained HbA1c response over the 12-month follow-up compared to patients less than 50 years old. The change in the HbA1c was similar for both genders, and for those with duration of diabetes <10 years and 10 years or more.

Conclusions: A 12-month treatment regimen with DPP-IV inhibitor improves HbA1c similarly in all three Asian ethnic groups with T2DM. The improvement in the HbA1c is more sustained for those patients older than 50 years. Ethnicity, gender, and duration of diabetes do not modify the efficacy of DPP-IV inhibitor treatment in this Asian population.

PD-104

Effectiveness of the personalized manager service on postprandial blood glucose management in Taiwanese patients with diabetes

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Optimizing glycemic control is an important homework for people with diabetes (PWD). According to the AADE7 Self-Care Behaviors™ model, fulfilling healthy eating, physical activities, structured monitoring, and taking medications regularly are crucial to achieve and maintain metabolic goals.

The aim of this survey was to assess the effectiveness of personalized care by using the platform integrating self-monitoring, dietary management, exercise, medication records along with the engagement of health care team on-and-off line consultation.

From June 2015 to December 2015, voluntary participants were provided with personalized care service software (Health2Sync), downloading to smartphones, uploading demographics, blood glucose measurements, diet, exercise and medication records by PWD for at least 12 weeks. Participants could undergo consultations through a built-in features with certified diabetes educators (CDEs) during the period.

Eleven patients, 4 T1DM (aged 30.3 ± 8.3 years, duration 21 ± 7.8 years, baseline A1C 8.0 ± 1.3%) and 7 T2DM (aged 50.1 ± 14.5 years, duration 10.3 ± 11.9 years, baseline A1C 7.6 ± 1.3%) were enrolled. They monitored their blood glucose for 165.6 ± 153.2 times, executed food records for 18.4 ± 20.7 times and interacted with health care team for 34.5 ± 64.3 times in 12 weeks. Both their mean fasting and postprandial blood glucose levels showed a decline trend from 123.4 ± 42.1 and 153.9 ± 65.3 mg/dL at baseline to 119.2 ± 34 and 140.1 ± 35.1 mg/dL at 12 weeks, respectively. The rate of goal attainment for given postprandial glucose increased from 65.2% to 76.4% ($p < 0.05$) over the observation period.

The implementation of personalized care platform, and the involvement of on-and-off line CDE consultation, can improve postprandial glycemic control in short-term. We hope in the future the application of this working model could overcome the barriers of patient accessibility of self-management education/support, empower the PWD and enhance their performance in metabolic control.

PD-105

The clinical effect of dapaglifrozin in type 2 diabetics with obesity: Retrospective analysis in a real practice setting

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Background: A limitation with randomized controlled trials is that, while they provide unbiased evidence of the efficacy of interventions, they do so under unreal conditions and in a very limited and highly selected patient population. Our aim was to provide data about the effectiveness of dapaglifrozin treatment in a real-world and clinical practice setting.

Methods: In a retrospective and observational study, data from 210 patients (mean age: 53 ± 9 yr, male 47%) with a minimum 6 months of dapaglifrozin therapy were analyzed, who visited Huh's Diabetes Center from Jan. 2015 to Dec. 2015, who gave complete information on all covariates.

Insulin sensitivity was directly assessed by short insulin tolerance test as a rate constant for plasma glucose disappearance (kitt, %/min) after intravenous injection of regular insulin (0.1 U/kg).

Results: Mean baseline glycated hemoglobin (HbA1c) was 8.4 ± 1.2% and mean body mass index (BMI) was 28.3 ± 3.3 kg/m^2. After 6 months of treatment with dapaglifrozin, we observed a change in HbA1c of −1.2 ± 0.9%, −2.9 ± 2.4 kg in weight and −1.1 ± 0.9 kg/m(2) in BMI ($p < 0.001$ for all). Compared to baseline, there was a significant reduction in systolic blood pressure (−7.4 mmHg, $p < 0.001$), LDL cholesterol (−5.7 mg/dL, $p = 0.005$) and triglycerides (−24.3 mg/dL, $p < 0.001$). In patients treated with dapaglifrozin as an add-on therapy, a decrease of −1.4% in HbA1c ($p < 0.001$) and a weight reduction of −2.8 kg ($p < 0.001$) were observed. In patients switched from other antidiabetic drug, dapaglifrozin induced a decrease of −1.1% in HbA1c ($p < 0.001$) and a reduction in weight (−2.9 kg, $p < 0.001$). The difference of efficacy was not noted according to the baseline characteristics (age, sex, BMI, c-peptide and kitt).

Conclusion: Our study confirms the effectiveness of dapaglifrozin in a real-life and clinical practice setting.

PD-106

Comparison of short-and long-acting glucagon-like peptide 1 receptor agonists on postprandial glucose excursion, insulin and glucagon secretions and gastric emptying

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Background and aims: Glucagon-like peptide-1 receptor agonists (GLP1-RAs) are classified into short- and long-acting agents according to their pharmacokinetic differences. It has been suggested that short-acting and long-acting agents exert different actions on insulin and glucagon secretions as well as on gastric emptying, which results in different outcomes of glycemic control. However, alterations in insulin and glucagon secretions and gastric emptying and their contributions to glycaemia in response to short- and long-acting agents have not been fully evaluated.

Materials and methods: We performed meal tolerance test before and 12 weeks after initiation of the long-acting GLP-1RA

liraglutide (Lira) or the short-acting GLP-1RA lixisenatide (Lixi) in Japanese patients with type 2 diabetes. Plasma glucose, insulin, and glucagon were measured using blood sampling and gastric emptying was measured using 13C breath test for 4hours after solid test meal (280 kcal carbohydrate, 100 kcal protein, 100 kcal fat and 13C-sodium acetate 200 mg). Areas under the curve (AUC) of plasma glucose, insulin and glucagon were calculated using trapezoidal rule. Gastric emptying rate (T1/2) was analyzed based on the time-plot of pulmonary 13CO2 excretion rate (% dose/h) according to the Wagner-Nelson method. Data (mean ± SEM) were evaluated using student's t-tests or paired t-test. $p < 0.05$ was considered significant.

Results: Before initiation of the GLP-1RA agents, there were no significant differences in HbA1c, BMI or duration between Lira and Lixi groups (Lira, n = 10; age 55.2 ± 3.0 year old; duration 9.2 ± 2.7 years/ Lixi, n = 5; age 52.4 ± 3.9 year old; duration 10.2 ± 4.2 years). After 12 wks administration of maximum dose agents (Lira 0.9 mg/Lixi 20 ug in Japan), HbA1c and bodyweight were significantly improved in both Lira and Lixi groups (HbA1c(%): Lira, 8.7 ± 0.3 to 6.8 ± 0.3; Lixi, 9.2 ± 0.8 to 7.4 ± 0.8/BMI(kg/m^2): Lira, 28.4 ± 1.2 to 27.1 ± 1.1; Lixi, 30.0 ± 2.2 to 28.8 ± 2.0). Gastric emptying was delayed in Lixi but not in Lira group (T1/2 (min): Lira, 31.3 ± 4.6 to 26.9 ± 2.9 min; Lixi, 23.3 ± 0.9 to 53.8 ± 12.1). Postprandial insulin secretion was significantly enhanced in Lira but not in Lixi group (IRI-AUC0-240 (uIU/dL·min): Lira, 7886 ± 1568 to 10883 ± 2101; Lixi, 5971 ± 1677 to 5653 ± 1255). Postprandial glucagon secretion was not significantly changed in Lira or Lixi group (IRI-AUC0-240 (uIU/dL·min): Lira, 22861.4 ± 2153.8 to 22340.7 ± 4222.3; Lixi, 24260.0 ± 4563.6 to 23911.3 ± 6762.8).

Conclusion: These results partially support the notion that long-acting agents improve glycemic control through enhanced insulin secretion and that short-acting agents do so through delayed gastric emptying.

PD-107

The efficacy of liraglutide for treatment of type 2 diabetes

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Background: Besides control of hyperglycemia, treatment of type 2 diabetes with liraglutide is advantageous for its weight-reducing effect and lack of hypoglycemic risk. As liraglutide has been introduced in Asia only in recent years, treatment experience has been relatively lacking in Asian countries.

Purpose: To investigate the efficacy of liraglutide in the treatment of type 2 diabetic patients in Taiwan.

Methods: This is an observational study conducted in a medical center in central Taiwan. Subjects were randomly selected from type 2 diabetic patients who visited the metabolism clinics of the medical center between 1 March, 2013 and 31 March, 2016.

Result: A total of 184 subjects, including 86 men (46.75%) and 98 women (53.3%) were included. Mean age was 52.97 ± 12.26 years and mean duration of diabetes 12.20 ± 9.25 years. Subjects were treated with liraglutide for a mean duration of 16.13 ± 11.95 months, predominantly with a dosage of 1.2 mg/day. At one year after treatment, there were significant reductions in weight, body mass index, waist circumference, glycated hemoglobin level, and fasting blood glucose ($p < 0.001$). However, at two years none of these parameters had significant change.

Conclusion: Liraglutide had significant efficacy within one year of treatment. After one year, additional therapeutic measures may be required to achieve further metabloic improvement.

PD-108

Beneficial effect on postprandial glucose excursion by ingestion of boiled barley rice and Japanese side dishes

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Suppression of postprandial excursion in plasma glucose level might be important for the prevention and treatment of type 2 diabetes. In Japan, white rice is an indispensable staple food but it leads relatively high postprandial glucose excursion by its high glycemic index (GI). Avoiding hard texture of barley and taking advantage of its lower GI, white rice cooked by mixing 30% with barley, boiled barley rice, would be easier to ingest and could lower postprandial glucose level. In this study, we aimed to investigate the effect of combined ingestion of boiled barley rice with Japanese side dish containing mainly protein on postprandial glucose level.

The study was conducted in a randomized crossover design for six kinds of test meals on 19 Japanese healthy volunteers (M:F, 10:9; mean age ± SD at the baseline, 38.0 ± 7.3 years; BMI, 21.5 ± 1.9 kg/m^2). Each test meal contained 50 g of available glucide. The test meal combination were as follows; white rice (Koshihikari, R) alone, boiled barley rice (B) alone, R or B with side dish of protein source containing each of grilled fish (mackerel, Fi), chicken hamburg steak (Ch), boiled egg (Eg) or fermented soybeans (Natto, Na). Plasma glucose levels were examined at fasting (0), 30, 45, 60, 90 and 120 min after the start of meal load to calculate the area under the curve. Statistical analysis was performed with Friedman multiple comparison test.

Although peak plasma glucose level of B was tend to be lower than that of R, no significant difference was observed between AUC of white rice alone (AUC_R, 4,904 ± 1,549 mg/dL*min) and AUC_B (3,722 ± 1,214 mg/dL*min), $p = 0.170$. In the analysis of AUCs after the meal load combined with side dishes, AUC_RCh (2,492 ± 942 mg/dL*min), AUC_REg (2,910 ± 1,439 mg/dL*min) and AUC_RFi (2,345 ± 1,258 mg/dL*min) were significantly lower than AUC_R ($p < 0.01$, $p = 0.01$ and $p = 0.02$, respectively). AUC_BCh (2,241.0 ± 765 mg/dL*min), AUC_BEg (2,489 ± 834 mg/dL*min) and AUC_BFi (2,023 ± 1,167 mg/dL*min) were all even lower than AUC_R significantly ($p < 0.01$). When compared to AUC_B, on the other hand, AUC_BCh and AUC_BFi were significantly low ($p < 0.01$). AUC_RCh and AUC_RFi were still lower than AUC_B significantly ($p < 0.01$). No significant difference, however, were observed between AUC_R and AUC_RNa (2,881 ± 977 mg/dL*min). Conclusively, combined ingestion of boiled barley rice and Japanese food side dish might improve postprandial excursion in plasma glucose level.

PD-109

Efficacy and safety of gemigliptin as add-on therapy in patients with type 2 diabetes inadequately controlled on metformin and glimepiride

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Gemigliptin is a potent, selective, competitive, and long-acting dipeptidyl peptidase (DPP) -4 inhibitor. This study evaluated the efficacy and safety of gemigliptin as add-on therapy to metformin and glimepiride for 24 weeks compared with placebo in patients with type 2 diabetes mellitus (T2DM) inadequate glycemic control.

In this multicenter, randomized, double-blind, Phase III study, eligible patients with inadequate glycemic control (7% HbA1c ≤ 11%) were randomized to gemigliptin 50 mg q.d (n = 109) or placebo (n = 110). The primary endpoint was change from baseline in HbA1c after 24 weeks. Baseline demographics were similar between groups (age 60.9 years; BMI 24.9 kg/m^2, duration of T2DM 12.9 years), with mean ±SD baseline HbA1c of 8.12 ± 0.82% in the gemigliptin group and 8.15 ± 0.89% in the placebo group. At Week 24, adjusted mean ±SE change HbA1c with gemigliptin was −0.88 ± 0.17% (change with placebo −0.01 ± 0.18%; difference −0.87 ± 0.12%, 95% CI −1.09 to −0.64; p < 0.0001). The differences in proportions achieving an HbA1c < 7 or < 6.5% were also statistically significant (p < 0.0001) between groups. Gemigliptin was generally well tolerated, although there was a higher incidence of overall adverse events (AEs) in the gemigliptin group than in the placebo group (56.1% and 36.0%, respectively). Drug-related AEs were reported for 3.7% and 2.7% of gemigliptin and placebo, respectively. Hypoglycemia occurred in 9.4 and 2.7% of the gemigliptin and placebo groups, respectively.

In conclusion, triple therapy with gemigliptin 50 mg q.d in patients with T2DM inadequately controlled on metformin and glimepiride improved glycemic control and was generally well tolerated over 24weeks.

PD-110

Efficacy and safety of gemigliptin in type 2 diabetes patients with moderate to severe renal impairment

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Renal impairment in type 2 diabetes mellitus (T2DM) limits the available glucose-lowering medication and requires frequent monitoring of renal function. Gemigliptin has balanced elimination between urinary/fecal excretion and hepatic metabolism. Thus, it needs no dose adjustment in patient with moderate to severe renal impairment. This study evaluated the efficacy and safety of gemigliptin in type 2 diabetic patients with moderate to severe renal impairment.

This randomized, double blind, parallel group Phase 3b study comprised a 12-week, placebo-controlled phase followed by a 40-week, double blind active-controlled extension phase. Patients (mean HbA1c 8.4%; age 62.0 years; BMI 26.2 kg/m^2, duration of T2DM 16.3 years; eGFR 33.3 mL/min/1.73 m^2) treated with gemigliptin (n = 66) or placebo (n = 66) for 12 weeks, then placebo group was switched to linagliptin 5 mg q.d and treatment continued to Week 52. Primary endpoint was HbA1c change from baseline at Week 12.

At Week 12, adjusted mean ±SE change HbA1c with gemigliptin was −0.83 ± 0.14% (change with placebo 0.38 ± 0.14%; difference −1.21, 95% CI −1.54 to −0.89; p < 0.0001). After 52 weeks, adjusted mean ± SE change from baseline in HbA1c was −1.00 ± 0.21% and −0.65 ± 0.22% in the gemigliptin and linagliptin groups, respectively. Urinary albumin creatinine ratio (UACR) at week 12 was reduced by 28.0% (95%CI −40.2 to −13.3) with gemigliptin compared with 4.3% (95%CI −19.7 to 14.2) with placebo, with a between-group difference of 24.8% (95%CI −41.8 to −2.9; p = 0.0294). During the 40-week extension, adverse events (AEs) were reported in 68.0% and 73.1% of subjects on gemigliptin and linagliptin, respectively. The incidence of hypoglycemia was similar among treatment groups (gemigliptin, 20.0%; linagliptin, 28.8%). There was no meaningful change from baseline in body weight (gemigliptin, 0.28 kg; linagliptin 0.33 kg).

In conclusion, gemigliptin was efficacious and well tolerated in T2DM patients with moderate to severe renal impairment.

PD-112

Current status of metformin or acabose in addition to insulin therapy in adult patients with T1DM in Guangdong, China

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It was shown in some previous studies that metformin or α-glucosidase inhibitors in combination with insulin contributed to improving the glycemic control in patients with type 1 diabetes (T1D), but the benefits of these agents for T1D were still suspensive. We use data from the Guangdong T1DM Translational Medicine Study to describe the current use and efficacy of additional metformin or acabose therapy in T1D.

Patients aged ≥18 years with T1D were included from the Guangdong T1DM Translational Medicine Study, which was a multicenter registry study of T1D in Guangdong, China. Patients treated with additional metformin (Metformin group, n = 90) or additional acabose (Acabose group, n = 63) added to insulin therapy were compared against those with insulin therapy only (Insulin group, n = 897).

Patients took 1000 mg of metformin or 120 mg of acabose per day on average. At baseline, the body mass index (BMI) of patients in the Metformin group (22.5 ± 3.9 kg/m^2) was higher than that of Acabose group (20.7 ± 2.8 kg/m^2) or Insulin group (20.3 ± 2.8 kg/m^2) (p < 0.001), while patients in Acabose group (38.9 ± 12.7 years old) were older than those in Metformin group (31.4 ± 12.8 years old) or Insulin group (33.2 ± 11.8 years old) (p < 0.001). But gender distribution, duration of diabetes, HbA1c, daily insulin dosage and waist-hip ratio (WHR) had no statistical difference between groups. After 1-year's follow-up, HbA1c improved in all groups, but the changes of it were not significantly different between groups (Metformin group, −0.7 (−1.7, 0.2) % vs. Acabose group, −0.4 (−2.1, 0.4) % vs. Insulin group, −0.4 (−1.6, 0.4) %, p = 0.513). While the daily insulin dosage, WHR and the frequency of hypoglycemia episodes did not change in all groups. Addition of metformin resulted in an unchanged BMI, while patients experienced weight gain with BMI increasing by 0.5 ± 1.3 kg/m^2 in Acabose group (p = 0.038) and 0.6 ± 2.2 kg/m^2 in Insulin group (p < 0.001).

The results suggested that metformin is initiated more in type 1 diabetic patients with higher BMI while acabose is initiated more in older patients with T1D in current practice in China. Additional metformin or acabose therapy does not improve the glycemic control for patients with T1D but additional metformin may contributes to keeping weight. Further study is necessary to explore their efficacy and safety in type 1 diabetic patients.

PD-113

Patient responses following hypoglycemia in the IO-HAT study: A population-based study of insulin-treated patients with diabetes in 9 countries

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Background and aims: Hypoglycemia is a key consideration in the individualization of treatment in patients with diabetes and has broad sociological and economic impacts on patients, their families, healthcare providers and businesses. As observational studies are mainly limited to Western countries, and by number and consistency of design, actual hypoglycemia rates and their impact on patients' lives, remain unclear for many countries in the clinical practice setting.
Materials and methods: The International Operations (IO) Hypoglycemia Assessment Tool (HAT) is a real-world, observational study of self-reported (using self-assessment questionnaires) hypoglycemic events in Bangladesh, Colombia, Egypt, Indonesia, the Philippines, Singapore, South Africa, Turkey and the UAE among 7,289 patients with insulin-treated type 1 (T1D; n = 1016) and type 2 diabetes (T2D; n = 6273). This abstract describes patient responses to hypoglycemic episodes pre-baseline and 4 weeks post-baseline among patients with insulin-treated diabetes in the IO-HAT study. Data are reported as mean (SD).
Results: Rates of any hypoglycemia (per patient, per month) were 4.8 and 6.9 in patients with T1D and 1.6 and 2.4 in those with T2D during the retro- and prospective periods, respectively. For patients with T1D or T2D, reporting of any and severe hypoglycemic events was significantly higher ($p < 0.001$) in the prospective period, while nocturnal hypoglycemic events were significantly higher ($p < 0.001$) in the retrospective period. At baseline, patients reported fear of hypoglycemia on a scale of 0–10 (not afraid–absolutely terrified). Mean (SD) score of 5.5 (3.3) and 4.5 (3.3) was reported by patients with T1D and T2D, respectively. While 17.1, 13.2 and 12.7% of patients with T1D rated their fear as 10, 5 and 0, respectively, this pattern was reversed in those with T2D with 10.8, 13.4 and 19.2% choosing these ratings. A greater proportion of patients with T1D, compared with T2D, reported taking action following hypoglycemia. The most common responses during the retro/prospective periods were increased blood glucose monitoring (T1D 51.6/43.8%; T2D 28.0/20.0%), requiring any form of medical assistance (T1D 56.0/34.9%; T2D 41.0/24.8%) and consulting a doctor/nurse (T1D 54.6/34.3%; T2D 39.6/24.5%).
Conclusion: These results suggest that symptomatic hypoglycemia occurs frequently and the fear it generates has a significant impact on the daily lives of patients with diabetes. Further, as patients may compromise their general health and glycemic control to avoid hypoglycemia, improved education and treatment management strategies are needed.

PD-114

Once-weekly DPP-4 inhibitors: The clinical efficacy and treatment satisfaction in 51 Japanese patients with type 2 diabetes mellitus

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DPP-4 inhibitors (DPP-4i) play an important role in treating patients with type 2 diabetes mellitus in Japan. Once-weekly DPP-4i have recently become available with their usefulness anticipated. We have investigated the clinical efficacy and Treatment Satisfaction of weekly DPP-4i, trelagliptin or omarigliptin, in 51 out-patients with type 2 diabetes mellitus. 20 patients previously treated with other daily DPP-4i were switched to weekly DPP-4i with the rest of anti-diabetics unchanged. 31 patients naive to DPP-4i were treated with weekly DPP-4i as add-on to previous treatment. Random capillary blood glucose (RCBG) test, HbA1c, glycoalbumin (GA), body weight, and Diabetes Treatment Satisfaction Questionnaire (DTSQs) were evaluated. Patients who have been switched from other daily DPP-4i had no significant change in HbA1c and GA at 3 months. HbA1c and GA of patients who had been naive to DPP-4i significantly improved from 9.46 ± 2.59% to 67.11 ± 1.28% ($p < 0.001$) and 26.6 ± 12.1% to 17.6 ± 5.6% ($p < 0.001$) respectively. Nausea and diarrhea were observed as side effects in 2 cases. In DTSQs, total score of the first factor consisted of the six treatment satisfaction items significantly improved from 24.3 ± 8.2 to 28.9 ± 6.6 ($p < 0.05$) in patients switched to weekly DPP-4i and from 19.6 ± 8.2 to 27.9 ± 5.7 ($p < 0.001$) in patients who had been naive to DPP-4i. Scores of 6 items including overall satisfaction, convenience, flexibility, level of understanding, recommendation, and satisfaction to continue treatment significantly improved in patients who had been naive to DPP-4i and the trend was similar and significant in 42 patients who were taking other daily medication. Weekly DPP-4i are effective and well-tolerated treatment which improves patients' treatment satisfaction.

PD-115

Deteriorating glycemic control after fixed-dose anti-diabetic combinations were equally shifted to free-drugs regimens

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Aims: Fixed-dose combination anti-diabetic drugs have well glycemic control and can further lower glycated hemoglobin (HbA1c) by 0.5–1.0%. This study aimed to investigate the glycemic effects when fixed-dose combinations were shifted to free-drugs regimens on outpatients with type 2 diabetes mellitus.
Methods: Between March and April 2015, a total 57 patients (mean age, 63.2 years), who used fixed-dose combination anti-diabetic drugs (Sitagliptin/Metformin 50 mg/500 mg, Vildagliptin/Metformin 50 mg/500 mg and Glimepiride/Metformin 2 mg/500 mg), and were equally shifted to free-drugs agents were enrolled. Those free-drugs agents were maintained for at least 3 months. The fasting blood glucose (FBG) levels and HbA1c were collected and analyzed by paired sample t test.
Results: The FBG levels elevated from 125 ± 29 mg/dL to 139 ± 41 mg/dL (the difference was 13.8 ± 38.3 mg/dL, $p = 0.009$) and the HbA1c increased from 6.7% to 7.0% (the difference was 0.3 ± 0.8, $p < 0.001$) after changing to free-drugs therapy 3 months later. Both FBG levels and HbA1c increased 14 mg/dL and 0.3%, respectively. In addition, the ratio of HbA1c <7% decreased from 67.9% to 58.9% ($p = 0.007$).
Conclusions: Changing Fixed-dose combination anti-diabetic drugs to free-drugs regimen could deteriorate glycemic control 3 months later. Patients with type 2 diabetes with optimal glycemic control (HbA1c <7%) should not change fixed-dose combinations to free-drugs regimens.

PD-116

The effects of once-weekly semaglutide on beta-cell function in subjects with type 2 diabetes

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Background: Semaglutide is a glucagon-like peptide (GLP)-1 analog with an extended half-life in phase 3 development for type 2 diabetes (T2D). This study evaluated the effect of once-weekly subcutaneous (s.c.) semaglutide in steady state versus placebo on beta-cell responsiveness in subjects with T2D.
Methods: In this double-blind, parallel-group trial, 75 adults with T2D (mean HbA1c 7.3%, duration of T2D 8.5 years, body mass index (BMI) 29.6 kg/m^2, age 56 years, 68% male) were randomised 1:1 to once-weekly s.c. semaglutide (escalated to 1.0 mg) or placebo for 12 weeks. Intravenous glucose tolerance tests (IVGTT; 25 g glucose bolus), arginine stimulation tests (5 g arginine 2 hours after glucose infusion) and graded glucose infusion (GGI) tests (target glucose levels: 5, 6, 7, 8, 9, 10, 11 and 12 mmol/L over 180 min) were performed at baseline and at week 12. A control group of 12 untreated healthy subjects (mean BMI 26.8 kg/m^2, age 43 years, 67% male) also underwent a GGI test. Insulin response was measured as the semaglutide: placebo ratio for changes from baseline to end-of-treatment in the area under the curve. The primary endpoint was first- (0–10 min) and second- (10–120 min) phase insulin secretion in the IVGTT.
Results: Following IVGTT, change from baseline for both first- and second-phase insulin responses in subjects receiving semaglutide was significantly greater than in those receiving placebo (estimated treatment ratio [ETR] 3.02 [95% CI: 2.53–3.60] and 2.10 [95%CI: 1.86–2.37], respectively). In the arginine stimulation test, increases from baseline for both insulin concentrations and insulin secretion rate in subjects receiving semaglutide were significantly greater than for those receiving placebo during 0–10 min (ETR 2.82 [95%CI: 2.39; 3.32] and 1.69 [95%CI: 1.49; 1.92], respectively) and 0–30 min (ETR 4.42 [95%CI: 3.74; 5.22] and 2.69 [95%CI: 2.38; 3.05], respectively).
In the GGI test, the insulin secretion rate and slope at end of treatment were significantly greater for semaglutide than placebo. In the semaglutide group, both parameters were comparable to those of untreated healthy subjects.
No new safety or tolerability issues were identified for semaglutide.
Conclusion: Semaglutide (1.0 mg s.c. once weekly) signicantly improved first- and second-phase insulin secretion compared with placebo after 12 weeks of treatment. Beta-cell responsiveness at the end of the study in the semaglutide group was comparable to that of untreated healthy individuals. Semaglutide was well tolerated, with a safety profile similar to that of other GLP-1 receptor agonists.

PD-117

Comparison of the efficacy and safety of insulin degludec between type 1 and type 2 diabetes

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Background: Novel insulin degludec (IDeg), a long-acting basal insulin analog extending more than 24 hours, improves glycemic control without an increasing risk of hypoglycemia in both type 1 (T1DM) and type 2 diabetes mellitus (T2DM). The aim of this study is to evaluate the efficacy and safety of between T1DM and T2DM in daily practice.
Methods: Between March 2013 and March 2016, consecutive 283 DM patients who have received IDeg once a day were enrolled in this study. Of them, patients who were being treated with IDeg for more than 52 weeks after switching their basal insulin to IDeg were examined. Insulin dose and other medications were adjusted at their discretions in routine clinical practice. In order to evaluate the efficacy of IDeg, transition of glycated hemoglobin (HbA1c) level, BMI were evaluated in both groups. Daily total insulin dose, and basal insulin dose, and the frequency of hypoglycemic attack were examined in T1DM group who have been received intensive insulin therapy and SMBG to evaluate the safety of IDeg. These data was evaluated before and after 4, 8, 12, 24 and 52 weeks starting IDeg. Furthermore, frequent hypoglycemia was defined as hypoglycemic attack more than once a week.
Results: Data was available in a total of 148 patients (T1DM; 97 patients and T2DM; 51 patients). HbA1c level (%) was significantly improved at 52 weeks in patients with T1DM (8.4 ± 1.5 vs. 7.8 ± 1.3, $p = 0.048$) and in those with T2DM (7.8 ± 1.1 vs. 7.2 ± 0.8, $p < 0.001$). There is no difference in BMI between at baseline and at 52 week in the 2 groups. In the T1DM group, daily total insulin dose and basal dose (unit/kg/day) were significantly decreased [0.63 ± 0.20 vs. 0.60 ± 0.22 ($p = 0.0012$) and 0.24 ± 0.10 vs. 0.22 ± 0.10 ($p = 0.0057$), respectively]. In the T1DM group, the frequency of hypoglycemic attack more than once a week was improved after switching their basal insulin to IDeg.
Conclusion: IDeg could improve glycemic control for patients with both T1DM and T2DM without an increasing risk of hypoglycemia.

PD-118

Long-term glucose lowering effects of sitagliptin monotherapy and dietary contents in Japanese individuals with type 2 diabetes

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Aims: This study was designed to assess possible relationship of long-term glucose-lowering effects of dipeptidyl-peptidase 4 inhibitor sitagliptin with intake of macro-nutrients in Japanese individuals with type 2 diabetes.
Materials and methods: Changes in bodyweight (BW) and hemoglobin A1c (HbA1c) as well as estimated intake of macro-nutrients were retrospectively obtained for 54 Japanese individuals with type 2 diabetes who initiated and continued sitagliptin monotherapy without any prescription change for 48 week (wk). Patients were categorized into two groups: Group A, ΔHbA1c (48 wk – 24 wk) ≥0.4% and Group B, ΔHbA1c (48 wk – 24 wk) <0.4%. Self-administered 3-day food records were analyzed for estimated intake of macro-nutrients using Healthy Maker Pro (Mushroomsoft Co., Ltd., Japan)
Results: Group A (n = 8; age 61.3 ± 9.3 years) showed increase in BW (kg; 70.6 ± 6.2 to 71.7 ± 6.1) and HbA1c (%; 6.6 ± 0.3 to 7.3 ± 0.4) between 24 and 48 wks. In contrast, Group B (n = 44; age 62.7 ± 8.5 years) showed little change in BW (kg; 62.5 ± 4.8 to 62.1 ± 5.2) and HbA1c (%; 6.5 ± 0.5 to 6.5 ± 0.5). Changes in BW differ significantly between the two groups. Total energy intake was significantly greater in Group A (32.8 ± 4.9 kcal/kg IBW/day) than that of Group B (28.5 ± 5.9 kcal/kg IBW/day). Interestingly, fat intake was significantly greater in Group A (1.08 ± 0.15 g/kg IBW/day) than that of Group B (0.86 ± 0.26 g/kg IBW/day) while carbohydrate intake (Group A, 3.87 ± 0.88 g/kg IBW/day; Group B, 3.66 ± 0.81 g/IBW) and protein intake (Group A, 1.32 ± 0.23 g/kg IBW/day; Group B, 1.16 ± 0.26 g/IBW) did not differ between the two groups.
Conclusion: Among patients receiving sitagliptin monotherapy for 48 wk, those who consumed more fats resulted in deterioration of HbA1c-lowering effects, suggesting that dairy diets play a critical role in maintaining long-term glucose-lowering effects of dipeptidyl-peptidase-4 inhibitors.

PD-119

Eating habits of 84 diabetic out-patients with increased HbA1c level or body weight in SGLT2 inhibitors treatment

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Objective: We investigated eating habits of diabetic patients with SGLT2 inhibitors treatment. And we studied about correlations between eating habits and changes in HbA1c level or body weight.
Subjects: 132 type 2 diabetic out-patients with 6-month with SGLT2 inhibitors treatment.
Method: We conducted a questionnaire to 84 cases. We ask some questions in a field interview survey about that how many times they had meals, how much staple food (e.g. bread, rice) or vegetables they had, if they had some snacks or not (e.g. Western-style confectioneries, Japanese confectioneries, vegetable juice, beverages including high-fructose corn syrup), if they eat at regular times, and if they had a meal after 9 p.m. We investigated relations among these questionnaire results, HbA1c level, body weight and visceral fat mass area.
Result: Both HbA1c and body weight did not improve in 12% of entire cases with SGLT2 inhibitors treatment. In a group with HbA1c level elevation, the patients tended to eat at irregular times. In a group with weight increase, the patients tended to drink a beverage including high-fructose corn syrup, eat at irregular times, and have a meal after 9 p.m. Also, the number of the times they had a meal was less than 3, or they didn't have much amount of staple food or vegetables. On the other hand, some patients whose body weight decreased said that they always had chewed gum or drunk some water when they had felt hungry. And they also said that they had stopped eating before they had felt full, and had had dinner earlier than usual.
Conclusion: We considered that eating habits might be associated with effectiveness of SGLT2 inhibitors. It might be important for medical staffs to ask patients about their eating habits frequently and give advice suited for individual patients on them.

PD-120

Linagliptin reduces the diabetic nephropathy score, DN_Score, in patients with T2DM and microalbuminuria: A predefined substudy from the MARLINA-T2D™ trial

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Background and aims: In the MARLINA-T2D™ study, we applied a novel urinary biomarker panel, DNlite, to investigate the renal effects of Linagliptin in patients with type 2 diabetes.
Materials and methods: The diabetic nephropathy score (DN_Score) is a composite score built from fitting several urinary biomarkers in DNlite to a statistical model, that correlates highly with the stage of diabetic nephropathy. It has been validated in previous studies. MARLINA-T2D™ is a Phase IIIb, multicenter, multinational, randomized, double-blind, placebo controlled, parallel group study to evaluate the glycemic and renal efficacy of once daily administration of linagliptin 5 mg for 24 weeks in type 2 diabetes patients, with micro- or macroalbuminuria (30–3000 mg/g creatinine) on top of current treatment with Angiotensin Converting Enzyme inhibitor or Angiotensin Receptor Blocker. The percent change from baseline in DN_Score at week 24 was analyzed by an analysis of covariance (ANCOVA) based on the full analysis set, with baseline DN_Score as the prespecified covarite. Several other covariates were also explored.
Results: Out of 360 patients in MARLINA-T2D™, urine samples for this substudy were available for 139 and 148 individuals for PBO and linagliptin, respectively. Linagliptin significantly reduced DN_Score from Week 0 to Week 24 vs PBO in patients with type 2 diabetes and UACR < 300 mg/g creatinine at baseline, $p < 0.05$. No effect was seen in patients with UACR ≥300 mg/g creatinine at baseline.
Conclusion: In patients with type 2 diabetes and microalbuminuria linagliptin significantly improved a diabetic nephropathy panel, as assessed by DN_Score. The renal effects of linagliptin in early stages of glomerular damage warrant further research.

PD-121

Incretin-based therapy has better glycemic sustainability and less variability in patients with diabetes on stable anti-diabetic medications

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Aims: Incretin-based therapy was ever proved more effective in lowering glycated hemoglobin (HbA1c) in Asian group. This study aimed to investigate the glycemic sustainability and variability effects of incretin-based therapy in type 2 diabetic patients in real-world practice.
Methods: A total 623 outpatients with type 2 diabetes mellitus (mean age, 64.7 years), received stable fixed-dose combinations oral anti-diabetic agents (OADs) without any adjustment for at least 6 months were enrolled during January to April 2015 after patients who used insulin were excluded.
Those patients were divided into two groups: those who treated with incretin-based therapy (n = 391) and others (n = 232). The medical records were reviewed and laboratory tests were collected and analyzed. The Analyses of Covariance with adjustment of age, gender, years of diabetes diagnosis, renal function, baseline HbA1c and numbers of OAD's categories was using to compare glycemic control between two groups.
Results: The baseline HbA1c (mean ± standard deviation) of incretin-based group and comparison group were 7.1 ± 0.9% and 7.2 ± 1.0%, respectively ($p = 0.211$). The group of incretin-based therapy revealed better glycemic control in the following 6 –month periods. The average HbA1c (marginal mean ± standard error) between groups was 6.9 ± 0.4% and 7.3 ± 0.5% ($p < 0.001$) in 3 months and 7.0 ± 0.4% and 7.2 ± 0.5% ($p = 0.024$) in 6 month. In addition, the statistic variances of HbA1c in the following period in two groups were 0.28 ± 0.49 and 0.367 ± 0.90, respectively ($p = 0.007$).
Conclusion: In this study, incretin-based therapy was shown the effects of better glycemic sustainability and less variability in diabetic patients on stable anti-diabetic medications in real-world practice.

PD-122

A real world experience of long-acting GLP-1 receptor agonists in a medical center in southern of Taiwan

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Objective: To determine whether treatment with long acting agonists of glucagon-like peptide-1 receptor (GLP-1R)-Liraglutide result in weight loss and glycemic control in real world practice. We presented our experience of Long-acting GLP-1 receptor agnists (Liraglutide) in treating of overweight and obese T2DM patients

Method and materials: We collect adult participants in our OPD with a body mass index of 25 or higher; with type 2 diabetes mellitus; and who received liraglutide once daily at clinically relevant doses for at least 24 weeks. We assess the effect of weight loss and assessed markers of glycaemic control: fasting plasma glucose, glycated haemoglobin (percentage of HbA1c.).
Results: During Jun 2015 to April 2016, we collect 128 diabetic patients (M:F = 65:63, age around 20–60 years old, BMI = 27 + 10), who had already received two or three kinds of oral hypoglycemic agents and long-acting GLP-1 receptor agonist (Liraglutide) for more than 24 weeks. In the overall analysis, GLP-1R agonists had beneficial effects on body weight loss. But did not have a significant effect on glycemic control (HbA1c). GLP-1R agonists were associated with nausea, diarrhoea, and vomiting.
Conclusions: The real world experience in our hospital showed that although treatment with GLP-1R agonists deed leads to weight loss in overweight or obese patients with type 2 diabetes mellitus, but no improvement of A1c during 24 weeks treatment in most of the patients.

PD-123

The short-term glycemic effects of a smartphone-based communication application management

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Aims: Web-based telemedicine is proved to improve glycemic control in patients with diabetes. However, around the clock care for diabetes has rarely studied. This study aimed to investigate the impact of a smartphone-based communication technology (Health2Sync) on glycemic control.
Methods: From October 2015 to January 2016, a total 174 type 2 diabetic patients (mean age 51.7 years) with glycohemoglobin (HbA1c) >7% was introduced to participate with a smartphone-based diabetes health care application. Those patients were divided into a novel glycemic management group (n = 24) and a traditional group (n = 150). The novel diabetic management included 2 or 3 nearly full-dose oral antidiabetics drugs initially. Then the regimens were adjusted aggressively to prevent glucose levels less than 100 mg/dL. The medical history and following laboratory tests including glucose levels were collected and analyzed. The Analysis of Variance with adjustment of age, gender, diabetes duration, renal function and baseline HbA1c were used to test the difference of glycemic control.
Results: Overall, HbA1c improved from 8.8 ± 1.6% to 8.0 ± 1.3% ($p < 0.001$) after patients participated with this smartphone-based diabetes health care application. The baseline HbA1c between the novel glycemic management group (n = 24) and the traditional group are 9.9 ± 1.2% and 8.6 ± 1.5% (mean ± SD), and the HbA1c level improved to 7.2 ± 0.3% and 8.1 ± 0.1% (marginal mean ± SE) in 3months later, respectively ($p = 0.003$). There is no episode of severe hypoglycemia during this period.
Conclusions: The application of around the clock smartphone-based diabetic management can successfully improve the glycemic control of type 2 diabetic patients. In addition, a novel diabetic management with aggressive medication adjustment significantly improves patient's glycemic control without further increase in risk of severe hypoglycemia.

PD-124

Influence of digestible carbohydrate in glycaemic index of healthy individuals and diabetes

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South East Asia is second highest number of deaths attributable to diabetes of any of the seven IDF regions, after the Western Pacific Region. More than half (53.2%) of these deaths occurred in people under 60 years of age. In South East Asia, one quarter of all births are affected by high blood glucose in pregnancy. Management of diabetes at the initial stage and prevention of future onset could be easily achieved by dietary management. There is currently much scientific and popular interest in the role of low glycaemic index (GI) food and digestible carbohydrate in the management of diabetes. The digestible carbohydrate content in a food is an important factor in determining Glycaemic index of the food. The objective of the study was to determine the digestible carbohydrates of white, brown rice flour and white wheat flour (white flour/plain flour) made food and glycaemic index (GI) for same flour made food in healthy and diabetic patients. Available carbohydrate of each food was determined in duplicates using 6 replicates by Megazyme essay kit.
The mean age and body mass index of healthy individuals and controlled diabetes were 36 (± 8.89) years, 22.7 (± 1.46) kgm^{-2}, 46 ± 9.5 years and 27.6 ± 4.7 kgm^{-2} respectively. The available carbohydrate in white, brown rice flour and white wheat flour made food were 24.2 ± 2.5%, 23.1 ± 0.9 and 25.4 ± 2.1 respectively. The GI of white, brown rice flour and white wheat flour made food in healthy individuals, controlled and uncontrolled diabetes were 75.1 ± 3.3, 72 ± 2.74 and 84.7 ± 3.7; 89 ± 2.6, 84 ± 1.4 and 98.3 ± 3.5; 97 ± 1.1, 95 ± 1.3 and 103.4 ± 1.2 respectively. Digestible carbohydrate is low in brown rice flour compared to white rice & white wheat flour. Healthy individual shows low GI compared to both controlled and uncontrolled diabetes for the same amount of digestible carbohydrates contained food. From this study it is obvious that whole grain flour made food contained less digestible carbohydrate and refined grain made out of flour contained high digestible carbohydrate. Same digestible carbohydrate contained foods showed different GI in healthy individuals and diabetes. Digestible carbohydrate of a food is important to determine the GI and when it comes to healthy individuals and diabetes even though low digestible carbohydrate foods showed high GI.

PD-125

Efficacy and safety comparison of sitagliptin and glimepiride in elderly Japanese patients with type 2 diabetes: START-J

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Objective: DPP-IV inhibitors which rarely cause hypoglycemia are possible to be anti-diabetic agent as the first line therapy for elderly patients with type 2 diabetes (T2DM) who could not manage hypoglycemia sufficiently. The purpose of this study was to compare the efficacy and the safety of sitagliptin and glimepiride in drug naïve elderly Japanese patients with T2DM.
Subjects: Patients with T2DM who were OHA naïve or on α-GI/biguanide monotherapy (to be washed out 4 weeks prior to randomization). Age ≧60 y.o., HbA1c ≦6.9%, >8.9%.

Methods: A randomized, controlled, open-labeled, multicenter study was performed for 52 weeks. Starting dose for sitagliptin was 50 mg per day, could be increased up to 100 mg (25–50 mg; 30≦GFR < 50). Starting dose for glimepiride was 0.5 mg per day, could be increased up to 6.0 mg. After that, each investigator titrated dose to aim at FPG <130 mg/dL, with concerning about hypoglycemia.
Results: Analyzed subjects were 291 patients (148/143: sitagliptin/glimepiride) whose written informed consent were obtained and who started administration of the study drugs. Average age was 70.3 ± 5.6/71.1 ± 5.6 (yr), BMI was 24.1 ± 3.3/24.5 ± 3.9 and HbA1c was 7.5 ± 0.7/7.5 ± 0.7 (%), respectively. Any parameter did not have significant difference between the randomized two groups. HbA1c decreased significantly within 24 weeks in both groups. The changes in HbA1c from baseline to 24 weeks were −0.69 ± 0.62% (sitagliptin) and −0.86 ± 0.65% (glimepiride), respectively. While glimepiride group had significantly larger decrease in HbA1c (p = 0.008) at 24 weeks, there was no significant difference between the two groups at 52 weeks (−0.65 ± 0.59%/−0.78 ± 0.69% p = 0.069). A significant difference was observed in the changes in body weight from baseline to 52 weeks between the two groups (−0.37 ± 2.44 kg/0.31 ± 2.92 kg p = 0.043). The incidences of hypoglycemia were 7 (sitagliptin) and 23 (glimepiride) patients, respectively. Glimepiride group had significantly more frequent occurrence of hypoglycemia (p = 0.002).
Conclusion: Our results showed that sitagliptin had slightly lower efficiency in 24 weeks, but had no significant difference in 52 weeks and higher safety about hypoglycemia. We propose from this trial that Sitagliptin is effective and safe for elderly Japanese type 2 diabetes patients as a first line therapy.

Delay Diabetes Complication: What Can We Do?

PE-01

Factors associated with diabetic retinopathy in patients with early and late diagnosed type 2 diabetes in Bangladeshi population

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Aim: To assess the determinants of severity and progression of DR among early and late diagnosed type 2 diabetic, and to assess the proportion of sight threatening and visual impairment in type 2 diabetes patients attending BIRDEM hospital in Bangladesh.
Background: Early onset type 2 DM may affect the development of diabetic retinopathy (DR) at a relatively younger age. DR is a serious problem that is well characterized by impaired vision; a condition known as sight threatening retinopathy (STR). The prevalence and incidence of STR in developed countries have been noticed and well recognized. However, there was only one national survey that emphasized on causes of visual impairment and blindness among adults in Bangladesh, but it revealed that DR is not the main cause for blindness or visual loss among this population. No other studies have been conducted in Bangladesh that estimate the magnitude of STR, and the impact of prognostic indicators on STR, visual impairment and blindness. Moreover there is no study that identifies the determinants of severity and progression of DR among early and late diagnosed type 2DM.
Method: A cross sectional study was conducted in outpatient ophthalmic clinic at BIRDEM, Dhaka. Dilated color fundus photography was performed in all patients who have type 2 diabetes, and those showing some degree of retinopathy were included. Data on socio-demographic characteristics, anthropometric measures and blood pressure were obtained from patients meeting the eligibility criteria.
Biochemistry blood test was recorded from the patient book file.
Results: Two hundred and fifty seven patients (110 female, 147 men) with type 2 diabetic were included in the study. Diabetic retinopathy was distributed as follows; NPDR (36%), CSME (43%), and PDR (21%). The proportion of patients with STR and visual impairment (moderate and severe) were 64% and 56.4% respectively. Severe visual impairment was observed in 2.7% of the cases. HDL, FBS, and being diagnosed early with diabetes were associated with progression of DR. The risk of SRT increased with age (P < 0.01). The median time to STR onset was estimated at 17 years for females, and 15 years for men. Hypertension and HbA1c were not significantly associated with STR, visual impairment or progression of DR.
Conclusion: Our study showed that the prevalence of visual impairment was much higher than the national estimate of 13.8%. In resource limited countries, regular screening for diabetic complications should be supported fully by government health institutions if the prevalence of STR and visual impairment are to be reduced substantially.

PE-02

Prevalence of retinopathy in population with prediabetes in China: Results from a cross-sectional survey and retrospective analysis

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Background: It has been estimated that 50.1% Chinese adults (about 480 million) have prediabetes in China. Quantifying prevalence of retinopathy among prediabetic adults, especially those continuously remaining prediabetic, could be used to estimate future healthcare costs and justify priority intervention for prediabetes. However, there is limited data in the Chinese population.
Objective: This cross-sectional survey was designed to estimate the prevalence of retinopathy among those with diabetes, prediabetes and population with normal glucose tolerance (NGT) in China in 2014. This study also retrospectively determined the glucose tolerance status of the cohort in 2010, and compared the prevalence of retinopathy among those who remained prediabetic or NGT from 2010 to 2014.
Method: Chinese adults aged above 18 years old with prediabetes and NGT were identified from four counties/districts in 2010, and were followed up to 2014. Fundus photography was implemented at the end of the follow-up. Retinopathy was diagnosed by two trained ophthalmologists independently using modified Airlie House classification. If the diagnoses were different from each other, a third ophthalmologist was to recheck the fundus photography and make a final diagnosis. Three groups, diabetes, prediabetes, and NGT using ADA diabetes diagnosis definition, were compared according to self-reported diabetic status or based on blood testing in 2014. A further analysis between the subgroups who remained prediabetic or NGT in the 4-year's follow-up was also conducted.
Results: Out of 830 subjects who were successfully followed up in 2014, 92, 342 and 396 were found to be diabetic, prediabetic, and NGT, respectively. Retinopathy was diagnosed in 17 (18.5%), 51 (14.9%), and 46 (11.6%) of the diabetic, prediabetic and NGT individuals, respectively. According to their diabetic status in 2014, compared to NGT individuals, the odds ratio of

retinopathy among diabetic and prediabetic individuals were 1.7 (95%CI: 0.9, 3.2) and 1.3 (95%CI: 0.9, 2.1). Retinopathy was observed in 34 (17.0%) of those remaining prediabetic and 18 (9.2%) of whose remaining NGT during the 4-year follow-up. Compared to individuals who remained NGT, those who remained prediabetic for 4 years were 2 (95% CI: 1.1, 3.7) times more likely to have retinopathy; but the risk became lower (OR = 0.9, 95% CI: 0.5, 1.9) after adjusting baseline age, sex, BMI, hypertension.
Conclusions: Although risk of retinopathy seemed higher in prevalent and long-term prediabetic state than NGT, but no significant association were found between them. Other baseline risk factors, such as hypertension, may play more important role in the relationship with retinopathy.

PE-03

Risk factors of arterial stiffness in patients with type 2 diabetes

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Background: Cardiovascular disease (CVD) is the main causes of death in type 2 diabetes mellitus patients (T2DM). Early identifications of those diabetes individuals at high risk for CVD with subsequent interventions are important.
Objective: Brachial-ankle pulse wave velocity (baPWV), a known indicator of arterial stiffness, is an independent predictor of cardiovascular morbidity and mortality. We investigate the determinants of cardiovascular risk factors from measurements of baPWV in patients with T2DM.
Methods: This was a cross-sectional study with 93 T2DM subjects who had no apparent history of CVD were enrolled. After accurate clinical examinations and biochemical evaluations, the enrolled subjects underwent baPWV examinations by using VP-1000 Automatic Arteriosclerosis Measurement System.
Results: The mean age of T2DM subjects was 61.5 ± 7.8 years and the mean duration of diabetes was 11.7 ± 6.9 years. The mean baPWV value was 15.5 ± 2.0 m/s. We found that values of baPWV had statistically significantly correlations with the age ($r = 0.389$, $p = 0.001$), body mass index (BMI) ($r = -0.194$, $p = 0.06$), duration of diabetes ($r = 0.278$, $p = 0.007$), regular exercise ($r = 0.219$, $p = 0.03$), heart rate (HR) ($r = 0.231$, $p = 0.03$), systolic blood pressure (SBP) ($r = 0.571$, $p < 0.001$), diastolic blood pressure (DBP) ($r = 0.405$, $p < 0.001$), pulse pressure (PP) ($r = 0.459$, $p < 0.001$), mean arterial pressure (MAP) ($r = 0.573$, $p < 0.001$), hemoglobin (Hb) ($r = -0.184$, $p = 0.08$), hemoglobin A1c (HbA1c) ($r = 0.455$, $p < 0.001$), creatinine (cre) ($r = 0.361$, $p < 0.001$), albumin ($r = -0.192$, $p = 0.07$), homocysteine (Hcy) ($r = 0.255$, $p = 0.01$), D-dimer ($r = 0.301$, $p = 0.003$), fibrinogen ($r = 0.277$, $p = 0.007$), tissue inhibitor of metallopeptidase inhibitor 1 (TIMP-1) ($r = 0.364$, $p = 0.003$), plasminogen activator inhibitor-1 (PAI-1) ($r = -0.228$, $p = 0.03$), and urine albumin-creatinine ratio (UACR) ($r = 0.508$, $p < 0.001$). In a multiple linear regression analysis, age (95% CI: 0.011–0.106; $p = 0.02$), HR (95% CI: 0.009–0.073; $p = 0.01$), MAP (95% CI: 0.048–0.107; $p < 0.001$), fibrinogen (95% CI: 0.001–0.014; $p = 0.03$), TIMP-1 (95% CI: 0.0001–0.007; $p = 0.04$), and PAI-1 (95% CI: –0236 to –0.202; $p = 0.02$) were independently associated with levels of baPWV in T2DM after adjustment of confounding risk factors.
Conclusions: These results suggest that older age, higher HR, BP, fibrinogen, TIMP-1, and lower PAI-1 are associated with levels of baPWV in T2DM subjects without CVD.

PE-04

Cases of diabetes complicated by sexual dysfunction

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Objectives: There are 371 million patients of diabetes in the world. The overall prevalence of sexual dysfunction among diabettics is 13.3–90%. Sexual dysfunction is the common problem caused by diabetes. Sexual health is part of care for patients. However, it tends to be neglected and it results in low self-esteem and impact on quality of life. The current study aimed to analyze case of diabetes complicated by sexual dysfunction.
Methods: With diabetes for 11 years, the 40-year-old unmarried male in a medical center in southern Taiwan has suffered from erectile dysfunction, resulting in anejaculation even after masturbation. Although the patient experiences an orgasm, has sexual fantasies, and masturbates for two to three times a week (had masturbated two times a day once), he has been suggested taking Viagra while having checkups in the urological department. Data collection included Arizona Sexual Experience Scale (ASEX-CV), previous medical history, medication use, chart review, and in-depth interview.
Results: The evaluation score of ASEX-CV was 26 and the scores of penis erection and ejaculation satisfaction were both six, thus revealing the participant's erectile dysfunction and anejaculation. The participant did not understand the relationship between diabetes and sexual dysfunction, feeling that life would be meaningless without sex.
Conclusions: Diabetes and sexual function are closely related and the prevalence is very high. What matters is not just cure, but the prevention of sexual dysfunction related to diabetes. The results revealed the close relationship between diabetes and sexual functions.

PE-05

To prevent hemo-dialysis therapy due to diabetic nephropathy. High-risk approach or population approach? From doctors' association's point of view

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Concerning about rapid-aging society in Japan, national and local governments are concentrating on how to reduce medical cost. To reduce high cost of starting and sustaining hemodialysis, high-risk approach has been proposed for people found as diabetes kidney disease by annual checkup held by national insurance. Population approach for "metabolic syndrome" has been done for years by local government and private sectors. The target was citizens who did not have "home doctors" to visit regularly. And the purpose was to prevent them from the onset of diabetes and atherosclerotic disease.
However, at this moment, diabetes patients with nephropathy already progressed and already visit their home doctors regularly are the target.
Objective and Methods: To summarize three years of prevention program of deterioration of diabetic nephropathy that has been held by Tama-city and cooperation of doctors association in Tama-city. Analyzing data of pre- and post-program and compared between participants and non-participants.
Results: Body weight and blood pressure improved after the program. HbA1c improved among poor control group. Non-participants who rejected to participate the program tended to have more proteinuria, more female smokers, and less repeaters of annual checkup. However the data themselves were not different between participants and non-participants.
Discussion: As local government and doctors' association, how to efficiently contribute for people's health was the main point of discussion. The local government started to dig up people who never coming to checkups or who do not have "home doctors" even they received recommendation of

visiting doctors. Doctors' association shared the knowledge of taking urinal albumin regularly for early detection of diabetic nephropathy, recommending their patients to visit ophthalmologists and dentists, evaluating patients' effort of lifestyle modification and adjusting their medication appropriately.

PE-06

Frequency of using eye care among persons with diabetes and diabetic retinopathy in DIY: A rural-urban comparison

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Background: Diabetic Retinopathy is a microvascular complication of diabetes and the leading cause of blindness. Having annual eye examination routinely is a key to reduce the risk of blindness among persons with diabetes. However, poor compliance is common in many areas.
Purpose: To compare the use of eye care among diabetic patients in urban and rural area of DIY, Indonesia.
Method: This was a community-based cross sectional study, involving all adults with diabetes type 2. We obtained all socio-demographic characteristics, behavior towards general and eye care, and history of past illnesses through interview. Each patient underwent fundus examination. Chi square was used for statistical analysis.
Results: 1092 participants with DM type II were participated and divided into 2 categories, 488 from urban and 605 from rural. There were 38.4% urban participants and 45.9% rural participants were known having retinopathy diabetic (RD). Of these, only 3.3% of urban patients and 2.6% of rural patients reported to have had regular eye check on monthly basis, 2.2% of urban patients and 2.2% of rural patients were on 3–6 monthly basis. Nearly all participants in urban (83.6%) and rural (86.9%) area had never had an eye examination. There were no significant differences regarding the use of eye care in urban and rural population ($p = 0.707$). Meanwhile, nearly all participants in urban (95.3%) and rural (95.5%) visit physician routinely to control their diabetes ($p = 0.284$)
Conclusion: There are no significant differences between urban and rural person with diabetes regarding the use of eye care. Nearly all of population with diabetes in urban and rural area of DIY, Indonesia has never used eye care. Thus, barrier to eye care services needs to be identified.

PE-07

Campaign held for clinic outpatients to visit an ophthalmologist at least once a year

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Our clinic has six diabetologists, but no ophthalmologists. We seek effective network with local ophthalmologists. We usually use a small "Diabetes Notebook" and attached "Diabetes Notebook for the Eyes" to show their complication data with their present glycemic control status and to share with the patients' ophthalmologists and our clinic. We investigated the adherence of checking eye complications and obstacles against the regular visit. We also made posters, "Let's to the eye doctor", talked to our patients for three months during this campaign.
We administered a questionnaire about checking eye complications. Consent was obtained by writing down the answers from 1175 diabetes patients (715 male and 462 female). The average age was 61.2 (SD 12.6) years old, and duration of illness was 12.3 (9.0) years.
75 (n = 832) % of patients have visited ophthalmologists in a year. The reasons which they chose most were "A: by recommendation (of our clinic)", "B: the complication will silently progress", "C: had symptoms" respectively. The longer their duration of illness, the more they answered B, and less duration, the more they answered A (Chi-squire test; $p < 0.05$). The utility rate of notebooks was 54% (from Ophthalmologist to our clinic) and 59% (from our clinic to ophthalmologist). 56% of the patients chose B used the notebook as a tool, and 64% of patients answered A did so ($p < 0.01$). The most chosen reason of no visit was "not enough time" and those who chose this was younger than those who chose other reasons (51.9 vs. 62.1 y/o; t-test $p < 0.0001$). 44 out of 509 patients who answered that they did not have retinopathy actually had (Simple 39, Pre-Proliferative 2, stopped PDR 3). 97.3% of the patients who visited ophthalmologists answered they will go this year, too. However, 2.7% rejected going because they "do not understand the necessity" and had "already been operated on". More than half of the patients were told when they should come again.
The rate of regular visits to ophthalmologists was relatively high. The longer they have had diabetes, the deeper they have understood about their disease and how it is tied up with the behavior of the regular visit. However not all the patients correctly understood their status of retinopathy. Therefore sharing the "notebook" among patients, diabetologists and ophthalmologists is considered to be efficacious to obtain the facts and deepens education on diabetes from two directions; ophthalmologists and diabetologists.

PE-08

Tissue inhibitor of metalloproteinase-1 is associated with carotid plaque score in patients with type 2 diabetes and hypertension

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Background: Type 2 diabetes mellitus (T2DM) and hypertension (HTN) are associated with an increased risk of premature death from stroke. Early identifications of those T2DM patients with HTN at high risk of stroke with subsequent interventions are important. It is known that carotid artery plaque score (CPS) is an independent predictor of stroke.
Objective: The aim of the present study was to determine whether there is an association between CPS and cardiovascular risk factors in patients with T2DM and HTN.
Methods: This was a cross-sectional study with a total of 82 subjects with T2DM and HTN who had no apparent history of cerebro-cardiovascular disease. After careful clinical examinations and biochemical evaluations, the enrolled subjects underwent ultrasonography of both carotid arteries to detect presence of plaque. The total CPS reflected the total number of sites with plaques and ranged from 0 to 6 (each of the CCAs, bifurcations, and ICAs, bilaterally). We used linear regression models to assess the relationship between cardiovascular risk factors and CPS in studied subjects.
Results: The mean age of subjects with T2DM and HTN was 63.3 ± 7.5 years and the mean duration of diabetes was 12.4 ± 6.8 years. The mean CPS value was 3.5 ± 2.0. We found that values of CPS had statistically significantly correlations with the age ($r = 0.44$, $p < 0.001$), duration of diabetes ($r = 0.300$, $p = 0.006$), body mass index (BMI) ($r = -0.310$, $p = 0.005$), smoking ($r = 0.194$, $p = 0.08$), systolic blood pressure (SBP) ($r = 0.275$, $p = 0.01$), pulse pressure (PP) ($r = 0.302$, $p = 0.006$), mean arterial pressure (MAP) ($r = 0.309$, $p = 0.005$), red blood cell count (RBC) ($r = -0.239$, $p = 0.03$), heamtocrit (Hct) (-0.191, $p = 0.09$), hemoglobin A1c (HbA1c) ($r = 0.203$, $p = 0.07$), log homocysteine (log Hcy) ($r = 0.225$, $p = 0.04$), tissue inhibitor of metallopeptidase inhibitor-1 (TIMP-1) ($r = 0.396$, $p = 0.002$), estimated glomerular filtration rate (eGFR) ($r = -0.237$, $p = 0.03$),

and use of antiplatelet drugs (OR = 0.197, p = 0.08). In a multiple linear regression analysis, TIMP-1 (95% CI: 0.007–0.003; p = 0.01) was independently associated with CPS in patients with T2DM and HTN after adjustment of confounding risk factors.
Conclusions: These results suggest that TIMP-1 is associated with CPS in patients with T2DM and HTN.

PE-10
Influencing factors of intention to receive examination of diabetes complications
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Aims and objectives: To understand the situation of diabetes patients receiving examinations for diabetes complications and to explore the factors influencing diabetes patients' intention to receive examinations for diabetes complications.
Background: Diabetes mellitus is an important health topic worldwide, and receiving examinations for diabetes complications periodically can aid in early detection and early treatment of diabetes complications.
Design and methods: It was a cross-sectional study that included a total of 251 diabetes patients who visited outpatient clinics of metabolism departments in Tainan.
Results: The percentages of participants who received fundus, foot, and kidney examinations were 67.7%, 61.4%, and 73.3%, respectively. Every point increase on the perceived barriers to taking action to receive diabetes complication examinations scale increased the intention to receive foot examination in the following year by 0.911 times (p = 0.002), and every point increase on the perceived susceptibility to diabetes complications scale increased the intention to receive kidney examination in the following year by 1.195 times (p = 0.045).
Conclusion: A higher level of perceived barriers to taking action to receive diabetes complication examinations reduced the intention to receive foot examination in the following year, and a higher level of perceived susceptibility to diabetes complications. Medical personnel should take the responsibility to increase the intention to receive examination of diabetes complications.
Relevance to clinical practice. The results of this study can promote medical personnel" care efficacy in preventing diabetes complications and can provide medical institutions with reference to establish prevention and control policies for diabetes complications.

PE-11
Inflammation associated with intraocular pressure in the subjects with metabolic syndrome
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Intraocular pressure is associated with metabolic syndrome, a cluster of cardiovascular risk factors. CRP was reported, independent of metabolic syndrome, to be associated with cardiovascular disease. In the present study, we examine the effect of CRP on subjects with or without metabolic syndrome. The subjects underwent physical check-up were enrolled for intraocular pressure and serum CRP measurements.
A total of 1041 subjects were enrolled in this present study. The intraocular pressure was significantly higher in the subjects with metabolic syndrome than those without (14.1 ± 3.0 vs. 13.4 ± 3.0 mmHg, P = 0.002). The intraocular pressures were also significantly different among the subjects with different CRP tertiles. The highest intraocular pressure was in the subjects with metabolic syndrome and highest CRP tertile; the lowest intraocular pressure was in the subjects with lowest CRP tilter and without metabolic syndrome (P value for trend <0.001). CRP, independent to metabolic syndrome, was an independent risk factor for high intraocular pressure (95%CI between 0.080 and 1.297, P = 0.027) in multivariate linear regression analysis.
In conclusion, systemic inflammation, present by serum CRP, is associated with high intraocular pressure.

PE-13
Current metabolic status affects urinary liver-type fatty-acid binding protein in patients with type 2 diabetes
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Aims: We aimed to study the association between urinary liver-type fatty acid-binding protein (L-FABP), a biomarker of tubulointerstitial injury, and the clinical characteristics of normoalbuminuric and albuminuric patients with type 2 diabetes in order to detect the factors affecting urinary L-FABP.
Methods: Urinary L-FABP levels were measured in 788 [466 normoalbuminuric (urinary albumin-to-creatinine ratio (ACR) <30 mg/gCr) and 322 albuminuric (urinary ACR ≥ 30 mg/g)] patients with type 2 diabetes, and again in 666 patients who continued to visit our department for a six-month period after the initial measurement. The association between the urinary L-FABP level and the clinical parameters was investigated.
Results: Both the urinary L-FABP concentration and the frequency of high urinary L-FABP (>8.4 μg/gCr) became significantly higher (P < 0.01) with the progression of ACR. The HbA1c (OR: 1.42, 95% CI: 1.11–1.79, P < 0.01), systolic blood pressure (OR: 1.03, 95% CI: 1.01–1.05, P < 0.01) and estimated glomerular filtration rate (OR: 0.98, 95% CI: 0.96–1.00, P = 0.01) levels were significantly associated with the high urinary L-FABP in normoalbuminuric patients after a forward stepwise selection. However, a logistic regression analysis revealed that use of renin-angiotensin system inhibitors (OR: 2.22, 95% CI: 1.16–4.89, P = 0.02), urinary ACR (OR: 1.01, 95% CI: 1.00–1.01, P < 0.01) and serum HDL-cholesterol concentration (OR: 0.33, 95% CI: 0.11–0.89, P = 0.03) were significantly associated in albuminuric patients. Diabetic vascular complications occurred with significantly higher frequency in the high urinary L-FABP group than in the normal urinary L-FABP (≤8.4 μg/gCr) group among the albuminuric patients. In the follow-up observation, the change in urinary L-FABP was found to be significantly (P < 0.01) influenced by the change in the HbA1c level in both the normoalbuminuric (n = 396, r2 = 0.05, P < 0.01) and albuminuric (n = 247, r2 = 0.06, P < 0.01) patients. The change in urinary L-FABP was not significantly associated with the changes in systolic blood pressure (n = 400, r2 = 0.005, P = 0.18) and eGFR (n = 403, r2 = 0.004, P = 0.23) among the normoalbuminuric patients.
Conclusions: Our results suggest that high urinary L-FABP is associated with current metabolic abnormalities, including high levels of HbA1c and systolic blood pressure among normoalbuminuric patients with type 2 diabetes. The study also indicates that diabetic vascular complications are more frequent among albuminuric patients with high urinary L-FABP.

PE-14
Carotid extra-media thickness is associated with intima-media thickness and renal dysfunction in Korean patients with type 2 diabetes
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Chronic kidney disease (CKD) and carotid atherosclerosis are well known to be risk factors for cardiovascular disease (CVD). Recent studies have documented that carotid extra-media thickness (EMT) is increased in patients with visceral obesity, metabolic syndrome, and coronary artery disease (CAD). However the clinical usefulness of EMT in relation to CVD is not determined yet. We investigated associations of EMT with intima-media thickness (IMT), pulse wave velocity (PWV), and other surrogate markers for obesity and CVD in type 2 diabetic patients.

A total of 491 patients with type 2 diabetes were recruited. Mean values of EMT and IMT were measured by using ultrasound. Brachial-ankle PWV was assessed for arterial stiffness. Anthropometric parameters including waist circumference (WC), body fat, and appendicular skeletal muscle mass were checked. Clinical and biochemical parameters for CVD were assessed. Glomerular filtration rate (GFR) based on creatinine (Cr) was estimated by using CKD-EPI equation. All subjects were divided into three groups by GFR: GFR ≥ 90 mL/min per 1.73 m^2 (n = 224), GFR 60–89 (n = 215), and GFR < 60 (n = 52).

Patients with GFR < 60 are more likely to be elderly and hypertensive and have longer diabetic duration compared to those with GFR ≥ 90. EMT, IMT, and PWV were significantly greater in subjects with GFR < 60 than those with GFR ≥ 90. (GFR ≥ 90 vs. GFR < 60: EMT = 726 ± 73 vs. 766 ± 94 μm, $p < 0.01$; IMT = 675 ± 127 vs. 734 ± 160 μm, $p < 0.01$: PWV = 1535 ± 264 vs. 1901 ± 387 cm/sec, $p < 0.001$). EMT was positively correlated with age, WC, Cr, and IMT and showed negative correlations with HDL cholesterol and GFR. In multivariate regression analysis, EMT was significantly associated with IMT, GFR, and WC independent of age, gender, hypertension, documented CAD, and HDL.

Carotid EMT was independently associated with IMT, GFR, and WC in patients with type 2 diabetes. Further studies are needed to explore a causal relationship between EMT and risk factors for CVD.

PE-15

Evaluation of the potential nephroprotective effects of metformin in diabetes – A systematic review

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Purpose: Nephropathy is an important sequelae of diabetes. Current clinical study of the potential nephroprotective effects of metformin in diabetes is small and outcomes of individual studies insufficient to arrive at a firm conclusion. The objective of this study is to evaluate the relationship between metformin treatment and specific renal outcomes in patients with type 2 diabetes mellitus (T2DM).

Methods: As part of a larger epidemiologic study of the effects of metformin on renal outcomes among a diabetes population in a Middle East country, we conducted a systematic review. Two authors independently performed comprehensive searches in relevant health care and conference databases using pre-determined search terms. Included articles described metformin treatment arm compared to control group(s) (active or otherwise) whereby baseline and follow-up renal parameters of one or all of: (1) glomerular filtration rate (GFR); (2) urinary albumin excretion (UAE); (3) albumin to creatinine ratio (ACR); (4) other relevant renal outcome described. Study year, population, design, duration, renal outcome assessment method and outcome were extracted. Authors independently assessed selected relevant articles according to the Dow and Black framework and otherwise as applicable according to the studies' methodology.

Results: The initial search yielded 1,147 articles of which 6 meeting inclusion criteria and reporting sufficient renal outcome data were included in the overall analysis totaling 98,193 subjects exposed to metformin. Most (n = 5) employed prospective methodologies, with the 1 retrospective analysis accounting for 62% of the evaluated patient population (61,104). Comparators included thiazolidinediones (TZDs), sulfonylureas (SUs), insulin, placebo, and lifestyle. Seven different renal parameters were evaluated across the studies over 12 weeks to 4 years. When change from baseline values is compared, metformin demonstrated more pronounced increase in albumin to creatinine ratio (ACR) than SUs (mean difference [MD] 14.8 mg/g [−4.2 to 25] and TZDs (MD 18.8 mg/g [18.5 to 19.1]). No significant difference in glomerular filtration rate (eGFR) was observed between metformin and TZD (MD 0.22 mL/min [−0.24 to 0.68], while data between metformin and SU was conflicting. Studies demonstrated that when compared to SUs, metformin treatment preserved ACR and GFR over time, but not when compared to TZDs.

Conclusion: Our analysis suggests that objective findings of the potential nephroprotective effects of metformin are lacking among well described epidemiological or prospective clinical studies and further research is needed.

PE-16

The frequency of microalbuminuria in patients with newly diagnosed type 2 diabetes mellitus in suburban population of Jakarta, Indonesia

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Background: Diabetic kidney disease (DKD) is the leading cause of end-stage renal disease. It was reported that microalbuminuria has been associated with cardiovascular event, with suboptimal compliance on microalbuminuria monitoring in patients with type 2 diabetes mellitus (T2DM). Yet, the frequency of microalbuminuria in patients with T2DM in suburban population is still unknown.

Method: The study was conducted in Cilincing General Hospital, Jakarta, during Desember 2015 – February 2016. The subjects were the patients who were referred from primary health cares with clinically suspected for T2DM during the study. Type 2 diabetes mellitus was diagnosed according to Indonesian Society of Endocrinology guideline. Albuminuria was assessed semi-quantitively using dipstick test. Albuminuria was defined as any positive (1+, 2+, 3+, or 4+) for dipstick results, and microalbuminuria was ranging from 1+ to 3+.

Result: There were 62 subjects in this study, mean age 59.58 years old (SD 8.77). Most of the subjects were female (75.80%). The frequency of microalbuminuria in this study was 46.80%. The mean initial fasting blood glucose in microalbuminuria group were 262.28 + 98.24 mg/dL, higher than in non-microalbuminuria group (204.76 + 82.51 mg/dL). There were 15 subjects (51.72%) in microalbuminuria group with eGFR (CKD-EPI) <60 mL/min/1.73 m^2, compared to 16 subjects (48.48%) in non-microalbuminuria group. Of microalbuminuria group, 13 subjects (43.33%) were obese, 9 subjects (30.0%) were hypertension, 1 subject (3.33%) was coronary heart disease, and 1 subject (3.33%) was tuberculosis.

Conclusion: The frequency of microalbuminuria in patients with newly diagnosed T2DM in suburban population was 46.80%. Further investigation and monitor in association between microalbuminuria and DKD are needed.

PE-17

Dyslipidemia in children with diabetes

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Background: Data on prevalence and phenotypic distribution of dyslipidemia in children with type 1 diabetes is scarce. Studies have shown that lipid abnormality tracks from childhood to adulthood and contributes to atherosclerotic process, therefore initial assessment and follow-up is essential.
Aims: To study the prevalence and phenotypic distribution of dyslipidemia in children with type 1 diabetes (T1D) and compare with type 2 diabetes (T2D).
Methods: A cross-sectional sample of diabetes patients, age 7–18 years on active follow-up between 1st January to 31st December 2014 were recruited. Fasting blood sample were analysed for glycated haemoglobin (HbA1C), total cholesterol (TC), high density lipoprotein (HDL), triglycerides (TG) and low density lipoprotein (LDL). Baseline demographic data and biochemical data was analysed using SPSS version 16.
Results: Total 165 patients were recruited, (T1D: n = 115; 69.7%, T2D: n = 50; 30.3%). Prevalence of dyslipidemia was 73.3% (n = 121) and almost similar in T1D & T2D (71.3% vs. 78.0%). T1D had lower mean age at recruitment (13.61 y ± 2.58 vs. 15.36 y ± 2.00; $p < 0.001$) and longer mean duration of diabetes (5.85 ± 3.69 vs. 2.82 ± 2.12; $p < 0.001$) compared to T2D. Phenotypic distribution of dyslipidemia in T1D vs. T2D, (LDL ≥ 2.6 mmol/L:66.1% vs. 70.0%; $p = 0.719$), (TG ≥ 1.7 mmol/L:11.3% vs.42.0%; $p < 0.001$), (HDL < 1 mmol/L :4.3% vs. 12.0%; $p = 0.091$). T1D & T2D had similar mean LDL (2.92 ± 0.86 vs. 3.01 ± 1.06; $p = 0.56$). Mean HbA1c was higher in T1D vs T2D (8.98% ± 1.96 vs. 7.9% ± 2.27; $p = 0.095$). There were 31 (18.8%) patients aged ≤10 yrs, mostly T1D (n = 28; 24.3%), of which 67.7% had LDL ≥2.6 mmol/L and 87.1% had no family history of lipid disorder.
Conclusion: Patients with T1D in the present study showed higher LDL-C but not triglyceride. Significant proportion of T1D patients less than 10 years of age have elevated LDL-C levels without a family history of lipid disorder.

PE-18

GLP-1 action attenuates prostate cancer growth and progression

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Incretin therapy has emerged as one of the most popular treatment for type 2 diabetes. GLP-1R agonist, Exendin-4(Ex-4), has received much attention, because of its tissue protective effects beyond glycemic control. We have previously reported that Ex-4 has anti-prostate cancer effect in prostate cancer cells via reduction of extracellular signal–regulated kinase (ERK)-mitogen-activated protein kinase (MAPK) phosphorylation (Diabetes 2014). Further, we reported that additive anti-prostate cancer effect by combined treatment of Ex-4 and metformin using LNCap cells, prostate cancer cell line (POLS ONE 2015). In our previous report, Ex-4 did not attenuate cell proliferation in a prostate cancer cell ALVA-41, which does not express GLP-1R. In the present study, we examined anti-prostate cancer effect of Ex-4 in ALVA-41 forced expressed GLP-1R using lentivirus vector (ALVA-GLP-1R) and association between GLP-1R expression level and prostate cancer progression in human prostate cancer tissues. Firstly, we confirmed abundant GLP-1R expression in ALVA-GLP-1R using immunohistochemistry and RT-PCR. Ex-4 significantly decreased the proliferation of ALVA-GLP-1R in a dose dependent manner, but not in ALVA-41 transfected with control vector (ALVA-control). Further, we transplanted ALVA-GLP-1R and ALVA-control into non diabetic athymic mice and treated them with vehicle or Ex-4 (300 pM/kg/day) for 4 weeks. As a result, tumor size of ALVA-GLP-1R was significantly decreased compared with ALVA-control, with or without Ex-4 treatment. Immunohistochemistry of Ki67 revealed that ALVA-GLP-1R had a reduction of cell proliferation compared with ALVA-control. Although severe necrotic lesion was observed in all tumors, apoptotic cells were not detected by TUNNEL assay. Prostatic acid phosphatase, a marker of prostate cancer, was decreased in serum of mice transplanted with ALVA-GLP-1R compared with ALVA-control. In addition, we next performed immunohistochemistry of GLP1-R and Ki67 of 40 nondiabetic prostate cancer patients. Interestingly, GLP-1R expression level was inversely associated with percentage of Ki67 positive cells and Gleason grading system of prostate cancers, significantly. Gleason score 6, highly differentiated carcinoma, has significantly higher expression of GLP1-R compared with Gleason score 8 over, lower differentiated carcinoma.
These data suggest that GLP-1R expression and GLP-1 action attenuates prostate cancer growth and progression in model mice and patients.

PE-19

Effects of arecoline on insulin signaling in human endothelial cells

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Background: Betel nut is the most widely used addictive substance in the world, and betel quid chewing is a common oral habit in South Asia and Taiwan. Being a major alkaloid in betel nut, arecoline has long been considered a potential carcinogen. Several reports showed that arecoline can increase reactive oxygen species (ROS) to produce cytotoxicity and genotoxicity. Recent reports indicate that betel quid chewing also increase the risk of atherosclerosis and diabetes. However, the detail mechanism remains unknown. Most recently, arecoline have diabetogenic potential on adipocytes that may result in insulin resistance and diabetes at least in part via the obstruction of insulin signaling and the blockage of lipid storage. In this study, we try to investigate the possible mechanisms of arecoline induced insulin resistance and endothelial dysfunction.
Methods: Human dermal microvascular endothelial cell (HMEC-1) were treated in different arecoline concentrations and tested the ROS levels and the expression of adhesion molecules, insulin signaling pathways and cell adhesion function. Then N-acetylcysteine (NAC) and Rosiglitazone were added to exam the effect on arecoline-induced endothelial dysfunction.
Results: Our data showed that the ROS levels and adhesion molecules (ICAM-1, VCAM-1) significantly increased after arecoline treatment and along with increased adhesion ability between HMEC-1 and monocyte. The results also revealed that increased phosphorylation of JNK then down-regulated insulin signaling pathways through IRS-1 and AKT after arecoline treatment. With the use of reducing agent NAC and Rosiglitazone in the arecoline-induced endothelial cell dysfunction, these cell dysfunctions and downstream signaling were found to be diminished and recovered.
Conclusions: Our present study explore the influence of betel nut extract – arecoline on insulin signaling and endothelial dysfunction and partially explain the increased risk of insulin resistance and cardiovascular disease from betel nut chewing . In addition, our data showed Rosiglitazone reduced arecoline-induced endothelial dysfunction and insulin resistance including of reducing ICAM-1 and VCAM-1 expression and monocyte adhesion by modulating the JNK-IRS-1-PI3K/AKT signaling pathway in endothelial cells.

PE-20

The relationship between type 2 diabetes and hearing impairment

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Object: Recently, several studies have investigated the relationship between type 2 diabetes and hearing impairment, but results were inconsistent. The objective of this study was to identify the prevalence of hearing impairment and audiometric state of type 2 diabetes in the single center.
Methods: A prospective survey was performed in 99 diabetic patients who had attended the diabetic clinics in a Eulji hospital between April 2015 and March 2016. The data recorded included diabetic markers and results of pure-tone audiometric tests at baseline and after 6 months of follow-up. Audiometric thresholds for air-conduction stimuli in both ears were established for frequencies at 500, 1,000, 2,000, and 4,000 Hz.
Results: At baseline, 80.8% of patients had normal hearing on both ears. 15.2% were mild hearing impairment, 3% were moderate hearing impairment, and 1% were severe hearing impairment, separately. After 6 months 18.4% were mild hearing impairment and 1% were moderate to severe hearing impairment on the right hearing. On the left hearing, 13.2% were mild hearing impairment, 2% were moderate, and 1% were severe.
Significant hearing improvement was shown on the left hearing with comparing 16.4 dB at the baseline and 15.7 dB after 6 months of follow-up ($p = 0.024$). However there was no significant difference on the right hearing.
But, according to separate frequency, significant improvement was shown on the right hearing at low and mid level frequencies. The decibel was 11.7 dB at the baseline and 10.4 dB after 6 months ($p = 0.005$).
Conclusion: The type 2 diabetes is strongly associated with hearing impairment especially at low and mid level frequencies. The most high risk factor of hearing impairment is age and other several factors are ABI, total cholesterol, LDL cholesterol.

PE-21

The effectiveness of multiplace chamber hyperbaric oxygen therapy in treating refractory critical limb ischemia patients complicated with diabetes mellitus

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Aim: Angioplasty (e.g. peripheral artery bypass surgery and endovascular therapy) plays the most important role in treating refractory critical limb ischemia (CLI) in diabetes patients, however, it still shows poor prognosis for below knee ulcer lesions. We analyzed the effectiveness of multiplace chamber hyperbaric oxygen therapy (HBOT) for angioplasty-inapplicable, refractory CLI patients with diabetes.
Methods: One hundred and nine consecutive angioplasty-inapplicable refractory CLI patients' prognoses were retrospectively analyzed, comparing them for with or without HBOT (53 patients with and 56 patients without). The endpoints were major leg amputation and death. The prognoses relation to the presence or absence of autologous bone marrow cell implantation (BMCI) was also analyzed.
Results: Average follow-up period was 9.1 years, average age was 63.7 y.o., and 55% of patients were complicated with diabetes. Overall survival rate was 74.5%, and limb salvage rate was 72.5%. HBOT did not show effectiveness for improving survival rate ($p = 0.08$, Log-Rank test), whereas it significantly improved limb salvage rate ($p < 0.01$) in BMCI-treated patients. Regarding BMCI-treated diabetic patients, HBOT combination significantly improved limb salvage rate over that without HBOT ($p = 0.01$, Log-Rank Test, $p = 0.02$, Mantel-Haenszel analysis, odds = 0.3). On the other hand, HBOT-treated patients had significantly better limb salvage rate ($p = 0.01$), but it made no difference in survival rate ($p = 0.1$) in BMCI-inapplicable patients. The same result was shown in BMCI-inapplicable diabetic patients with or without HBOT ($p = 0.01$, Log-Rank Test, $p = 0.01$, Mantel-Haenszel analysis, odds = 0.8). Diabetes was one of the significant negative independent factors for limb salvage in univariate analysis, however, a low-level of albumin (cut off 3.15 mg/dL) was the independent factor for poor prognosis in multivariate analysis ($p = 0.04$, odds = 0.04, proportional hazards analysis).
Conclusions: HBOT improved life expectancy in CLI patients with diabetes, and it improved limb salvage rate in patients who underwent combination HBOT and BMCI. HBOT showed a tendency to improve even BMCI-inapplicable patients' (regardless of diabetic or not) survival rate when used as a last resort. It is expected that HBOT together with BMCI can bring better prognoses for angioplasty-inapplicable refractory CLI patients with diabetes.

PE-22

High prevalence of early small fiber dysfunctions in patients with type 2 diabetes detected by thermal thresholds of lower extremities

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Objectives: Patients with type 2 diabetes are prone to developing peripheral neuropathy and peripheral arterial disease (PAD) which might cause foot ulcerations and subsequent amputations. Although toe-brachial index (TBI) is recommended to detect PAD, diagnosis of early peripheral neuropathy, especially small fiber dysfunctions, are largely undetermined.
Research Design and Methods: We enrolled 725 (male/female: 372/353) patients with type 2 diabetes (mean ± SD: age, 67 ± 11 years) who received ankle-brachial index (ABI)/TBI/brachial-ankle pulse wave velocity (ba-PWV) examinations, and the quantitative sensory test for thermal (warm/cold) thresholds, from January 2015 to December 2015. Those with a history of apparent cardiovascular disease, arrhythmia, end-stage renal disease, malignancy, amputation, and any diagnosed neuropathy of the lower limbs were excluded. The 2009 Chronic Kidney Disease Epidemiology Collaboration creatinine equation was used to calculate estimated glomerular filtration rate (eGFR), and albuminuria was measured by the urine albumin-to-creatinine ratio.
Results: A total of 539 (74.3%) study subjects had abnormal thermal thresholds, with characteristics of older age, male sex, higher systolic blood pressure, lower eGFR, proteinuria, lower TBI values, and higher ba-PWV values, compared with patients with normal cold or warm thresholds of the bilateral lower limbs (all $p < 0.05$). Among patients with abnormal thermal thresholds, 98% had a normal ABI, 84% had a normal TBI, 59% had normal albuminuria levels, and 38% had relative optimal glycemic control (hemoglobin A1c < 7%). In addition, all patients with an abnormal ABI (n = 13) and 93% (87/94) of patients with an abnormal TBI experienced abnormal cold or warm thresholds of the lower extremities. After adjusting for several confounding factors, age, male sex, and a low TBI remained significantly associated with impaired thermal thresholds.

Conclusions: The prevalence of impaired thermal thresholds was extremely high in the type 2 diabetic patients. Age, male sex, and a low TBI are major determinants of peripheral small fiber dysfunction, identified as impaired thermal thresholds of the lower extremities in patients with type 2 diabetes without apparent cardiovascular disease. Early detection of high-risk groups is warranted to reduce complications associated with diabetic foot ulcerations.

PE-23

Overexpression of GLP-1 receptor in hepatocellular carcinoma causes anti-cancer effect of Exendin-4

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Incretin therapy has emerged as one of the most popular treatment for type 2 diabetes. GLP-1R agonist, Exendin-4(Ex-4), has received much attention, because of its tissue protective effects beyond glycemic control. We have previously reported vascular protective effect (Diabetes 2010, BBRC 2011) and anti-prostate cancer effect (Diabetes 2014, PLOS ONE 2015) of Ex-4. On the other hand, liver cancer is one of the most popular and critical cancers in patients with type 2 diabetes and fatty liver. Then, we next examined whether GLP-1 action could attenuate liver cancer in the present study.

First of all, we treated HepG2 cells, human hepatocellular carcinoma cell line, with Ex-4. Unfortunately, Ex-4 did not attenuate HepG2 cell proliferation in vivo and in vitro, because GLP-1 receptor expression was almost negligible amount in HepG2 cells. Then, we next demonstrated overexpression of human GLP-1 receptor in HepG2 cells using lentivirus vector. Abundant GLP-1 receptor expression was observed HepG2 cells transfected GLP-1R (HepG2-GLP1R), compared with HepG2 cells transfected with control vector (HepG2-control). Ex-4 increased intracellular cAMP concentration in HepG2-GLP1R significantly, suggesting that overexpressed GLP-1 receptor should be intact. Ex-4 attenuated cell number of HepG2-GLP-1R in a growth curve significantly and dose dependently. As a mechanism by which Ex-4 attenuates HepG2-GLP1R, we investigated reduction of epidermal growth factor receptor in HepG2 cells. We next transplanted HepG2-GLP1R or HepG2-control into athymic nude mice. Surprisingly, tumor size of HepG2-GLP-1R was larger than HepG2-control, however Ex-4 treatment decreased tumor size and Ki67 positive cells of HepG2-GLP-1R compared with non-treated HepG2-GLP1R.

These data suggest that overexpressed GLP-1 receptor causes anti-cancer effect of Ex-4 in hepatocellular carcinoma.

PE-24

Diabetic retinopathy predicts all-cause mortality in type 2 diabetic patients with chronic kidney disease without overt albuminuria

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Diabetic nephropathy (DN) is a complex disease with heterogeneous clinical courses. Chronic kidney disease (CKD) without overt albuminuria represents a distinct phenotype of DN. In this study, we aimed to investigate whether diabetic retinopathy (DR), another chronic microvascular complication, can predict all-cause mortality in these patients.

Methods: In this retrospective cohort, type 2 diabetic patients who had hospitalized with the main diagnosis of poorly glucose control to one medical center in central Taiwan, between August 1996 and August 2007, were consecutively enrolled. We collected data from medical records, including estimated glomerular filtration rate (eGFR), albuminuria, medication history, and linked to mortality information provided from the national registry dataset. Chronic kidney disease (CKD) was defined as eGFR <60 mL/min/1.73 m^2 calculated by using the Modification of Diet in Renal Disease (MDRD) equation. Overt albuminuria was defined as urine albumin creatinine ratio (ACR) ≥ 300 mg/g

Results: A total of 749 type 2 diabetic patients with were included with median follow-up time of 6.7 years (interquartile range 4.1–9.6 years). Among 332 patients with CKD, 60.8% (N = 202) of them without overt albuminuria. DR was detected in 37.1% of patients of CKD without overt albuminuria. In multivariable cox regression, HR of DR for all-cause mortality was 1.96 (95% CI, 1.19–3.26, P = 0.008) compared with those without DR among CKD without overt albuminuria. DR did not significantly predict all-cause mortality in CKD with albuminuria.

Conclusions: DR is a robust predictor for all-cause mortality in the type 2 diabetic patients with CKD but no overt albuminuria.

PE-25

Serum osteocalcin levels are inversely associated with the presence of nonalcoholic fatty liver disease in patients with coronary artery disease

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Objective: Osteocalcin plays roles in energy, glucose, and lipid metabolism. Consequently, the relationship between osteocalcin and nonalcoholic fatty liver disease (NAFLD) is of interest. The present study explored the possible correlation between serum osteocalcin levels and NAFLD in patients with coronary artery disease (CAD).

Methods: The study enrolled 174 inpatients diagnosed with CAD by coronary angiography. The presence of fatty liver disease was confirmed by abdominal ultrasonography. NAFLD was diagnosed using the working definition of the revised guidelines for the management of NAFLD published by the Chinese Liver Disease Association (2010). Serum osteocalcin levels were determined using electrochemiluminescent immunoassays.

Results: Compared with non-NAFLD subjects, those with NAFLD had significantly higher body mass index (BMI), waist circumference, blood pressure, fasting plasma glucose (FPG), 2 hour plasma glucose, glycated hemoglobin A1c (HbA1c), homeostasis model assessment-insulin resistance, totoal cholesterol, triglyceride (TG), c-reactive protein, alanine aminotransferase, and glutamyl endopeptidase levels ($P < 0.05$). These patients also used more anti-hypertensive drugs, but had significantly lower high density lipoprotein- cholesterol levels ($P < 0.05$). Especially the patients with NAFLD had lower serum osteocalcin levels than those without NAFLD [16.2 (14.2–23.8) vs. 20.7 (15.6–26.2) ng/mL, $P < 0.05$]. After adjustment for gender and age, serum osteocalcin levels correlated with the presence of NAFLD ($r = -0.260$, $P = 0.010$), FPG level ($r = -0.230$, $P = 0.023$) and HbA1c level ($r = -0.229$, $P = 0.023$). Osteocalcin ($\beta = -0.097$, $P = 0.025$), BMI ($\beta = 0.345$, $P < 0.001$), HbA1c ($\beta = 0.641$, $P = 0.004$) and TG ($\beta = 1.002$, $P < 0.001$) were the independent factor for the presence of NAFLD.

Conclusions: Serum osteocalcin levels were negatively associated with the presence of NAFLD in patients with CAD.

PE-26

Physical activity and albuminuria were associated with painful diabetic polyneuropathy in type 2 diabetes in an ethnic Chinese population

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Diabetic neuropathy is a common complication in patients with type 2 diabetes. However, prevalence of painful diabetic polyneuropathy (PDPN) and potential influences of physical activity and albuminuria on development of PDPN have been rarely studied. The aim of this study was to examine the prevalence of PDPN as well as the independent and joint effects of physical activity and albuminuria on it.

This retrospective study enrolled 2,359 outpatients with type 2 diabetes with completed survey of Douleur Neuropathique en 4 Questions (DN4) questionnaire from January 2013 to October 2013 in one of medical center in central Taiwan. Painful neuropathy was defined as a total score exceeding 3 points. Independent and joint effects of physical activity and albuminuria on PDPN were assessed by fixed effect with logistic regression.

Overall, 179 (7.6%) patients were diagnosed as having PDPN. Both less physical activity and albuminuria were associated with a higher mean DN4 score (1.07 for no exercise, 0.87 for daily exercise duration ≦30 minutes, and 0.56 for daily exercise duration >30 minutes, p for trend <0.001; 1.51 for macroalbuminuria, 1.10 for microalbuminuria, and 0.78 for normal UACR, p for trend <0.001). Adjusted analysis showed that the risk of painful neuropathy increased in the groups without physical activity (Odds ratio (OR) = 3.38, 95% CI 1.54–9.79) and daily exercise duration ≦30 minutes (OR = 3.33, 95% CI 1.27–8.73), when compared with the group with daily exercise duration >30 minutes (p for trend 0.006). Comparing with normal UACR, the OR for PDPN were 0.96 (95% CI 0.61–1.50) and 2.31 (95% CI 1.44–3.73) for microalbuminuria and macroalbuminuria respectively (p for trend 0.002). In addition, we observed a joint effect of macroalbuminuria and physical inactivity on PDPN risk (OR = 6.68, 95% CI 2.23–20.04).

Less physical activity and albuminuria, respectively, increased the risk of PDPN and had a joint effect.

PE-27

Osteocalcin improves nonalcoholic fatty liver disease in mice through activation of Nrf2 and inhibition of JNK

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Objective: Recent studies have demonstrated a protective effect of osteocalcin against nonalcoholic fatty liver disease (NAFLD), although the specific underlying mechanisms remain unclear. Nuclear factor erythroid 2-related factor 2 (Nrf2) and c-Jun N-terminal kinase (JNK) pathways play important roles in the pathogenesis of NAFLD. The present study aimed to investigate whether osteocalcin protects against NAFLD by regulating these pathways.

Methods: Male C57/BL6J mice were fed a high-fat diet for 12 weeks to induce NAFLD and were treated with recombinant uncarboxylated osteocalcin (30 ng/g) or vehicle by daily intraperitoneal injection during this period. Intraperitoneal glucosetolerance test, insulin tolerance test, measurement of serum lipid profiles, liver enzymes and hepatic triglyceride content were carried out. Hepatic redox state was examined. The role of osteocalcin on Nrf2 and JNK were investigated by Western blot and Real-time PCR.

Results: Daily injections of osteocalcin can significantly improve lipid metabolism, glucose tolerance and insulin sensitivity in mice fed a high-fat diet ($P < 0.05$). Osteocalcin treatment protected mice from diet-induced hepatic triglyceride accumulation and liver injury. Increased levels of malondialdehyde, 8-iso-prostaglandin F2α and a higher ratio of oxidized/reduced glutathione (GSSG/GSH) in the liver of mice fed a high-fat diet were decreased by osteocalcin ($P < 0.05$). Meanwhile, treatment with osteocalcin resulted in increases in hepatic reduced GSH levels in mice fed a high-fat diet ($P < 0.05$). Osteocalcin treatment not only activated Nrf2 nuclear translocation and up-regulated the expression of antioxidant enzyme genes (catalase, superoxide dismutase, and glutathione peroxidase) ($P < 0.05$), but also inhibited the activation of JNK in the liver ($P < 0.05$). G protein coupled receptor family C, group 6, subtype A (GPRC6A), the putative receptor of osteocalcin, was found in the liver.

Conclusions: Osteocalcin improves NAFLD by activating the Nrf2 pathway to alleviate oxidative stress, and inhibiting JNK pathway.

PE-28

Anterior compartment syndrome with type 1 diabetes mellitus

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Compartment syndrome is defined as an elevation of the interstitial pressure in a closed osteofascial compartment causing microvascular compromise. The common causes include trauma, arterial injury, limb compression and burns. Rarely, it can also occur spontaneously in association with type 1 diabetes mellitus. We report a case of a patient with type 1 diabetes mellitus who presented with lower limb pain without any obvious injury and had a subsequent diagnosis of acute compartment syndromes. Non traumatic acute compartment syndrome secondary to diabetic muscle infarction should be considered in any diabetic patient presenting with pain out of proportion to sustained injury.

PE-29

Prevalence of chronic kidney disease among adults with diabetes or prediabetes in China

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Background: Chronic kidney disease (CKD) is recognized as a global public health problem. Diabetes mellitus is the leading cause of CKD, but little is known about the relationship between CKD and prediabetes, especially among those who remained long-term prediabetic state.

Objectives: To compare the prevalence of CKD among Chinese adults with pre-diabetes and diabetes to those with normal glucose tolerance (NGT). To examine whether the prediabetes progression was associated with CKD prevalence.

Methods: 1,149 Chinese adults aged over 18 years old with prediabetes and 997 with NGT were identified from four counties/districts in 2010, and were followed up to 2014. Blood and urine samples were collected to assess the presence of CKD in 2014. CKD was defined as eGFR less than 60 mL/min per 1.73 m^2 or the presence of albuminuria (urinary albumin to creatinine ratio >=30 mg/g), and estimated at the end of follow-up. Pre-diabetes and diabetes were based on the criteria

recommended by American Diabetes Association in 2010. Trends across different progression categories were determined using the Wald chi-square test for trend. Logistic regression was used to assess the association between progression states of pre-diabetes and CKD.
Results: Among 1,293 successfully followed subjects in 2014 (follow-up rate was 60%), 46% were normoglycemic, 42% had prediabetes (impaired fasting glucose or impaired glucose tolerance or both), and 12% had diabetes. The overall prevalence of CKD among adults with diabetes, prediabetes and NGT was 13.6%, 10.9% and 8.1% respectively. Compared with NGT, subjects with dysglycemia (diabetes or prediabetes) were more likely to have CKD (OR = 1.4, 95% CI: 0.9–2.0) after adjusting age, sex, BMI, central obesity, smoking, drinking, hypertension, dyslipidemia, and family history. The CKD proportions were 8.6%, 12.6% and 15.7% among those who had reverted from prediabetes to NGT, remained prediabetic, or progressed to diabetes between 2010 and 2014, respectively. Trend test indicated that the CKD prevalence increased with the progression categories ($p = 0.006$). Logistic results showed the risks of having CKD were 1.2 (95% CI: 0.7, 2.1) and 1.5 times (95% CI: 0.8, 3.0) higher among subjects who remained prediabetic and progressed from prediabetes to diabetes, respectively, than in those who remained NGT (adjusted variables were the same as before).
Conclusions: There was no significant association between CKD and diabetes status in 2014. Although a significant trend was observed suggesting an association between pre-diabetes progression and CKD, casual association cannot be conclusively determined due to lack of baseline CKD status.

PE-30
Utilizing team cooperation for improving retinal screening compliance and follow-up of diabetes patients
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Purpose: Retinopathy is one of the diabetes chronic comorbidities. Therefore, the use of team cooperation and care process improvements can be used to improve diabetes patient health self-management and participation to increase the retinal screen compliance and early detection for diabetes patients.
Methods: In this study, the diabetes medical team established a complete retinal screening examination process and many methods such as telephone reminder, follow-up reminder forms, establish outpatient electronic reminders, and remind outpatient physician and nursing personnel for assistance and follow-up; were established to remind those patients who haven't received retinal screening. After the implementation of the improvements, the compliance of retinal screening were determined and followed.
Results: After implementation, the retinal screening rate in our hospital from Jan to April, 2014 was 23.4%, the screening rate during the sample period in 2013 was 22.4%. Therefore, the implementation of the outpatient reminder forms and electronic reminder was able increase the retinal screening rate by 1%.
Conclusion: The hospital systematically identified those patients who have not received examination and utilized telephone reminder, outpatient reminder forms, and electronic reminders to outpatient physician to remind the patient to receive their retinal screening. However, some patients have refused the examination due to a lack of knowledge regarding the importance of the screening and the unease towards the use of dilating agents. Further improvements such as the physician can actively inform the patient regarding the important of the examination, establishing health consultation education pamphlets for increasing the awareness and motivation for retinal examination can be used to improve examination compliance and follow-up rate.

PE-31
The relationship between mitochondrial dynamics and insulin resistance in diabetes susceptible cybrid cells
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Background: Mitochondrial dynamics has been proposed as a bridge between mitochondrial dysfunction and insulin resistance (IR). In our previous studies, by comparing cybrid cells derived from osteosarcoma cell harboring diabetes susceptible (B4) and protective (D4) mitochondrial haplogroups, we demonstrated the independent role of mitochondria in the pathogenesis of IR in T2DM. However, how the mitochondrial dynamics affect mitochondrial and cellular functions in insulin-resistant cells remain unanswered.
Methods: To dissect the mechanisms between mitochondrial dynamics and IR in diabetes susceptible cybrid B4, silencing of target genes by siRNA or gain function by plasmid transfection was performed. We constructed Mfn-1, Mfn-2, Drp-1, Fis-1-over-expressing vectors and cybrid cell lines. Mitochondrial membrane potential, mitochondrial network and the insulin signal pathway were compared in the B4 cells with over-expression or knock down of the dynamic proteins.
Results: Cybrid B4 cells had impaired mitochondrial dynamics as compared with D4 cells. Cybrid B4 mitochondrial membrane potential (MMP) was not significantly altered by the chemicals (lipo 2000, GFP) used in the experimental procedure, and the transfection rates of fusion and fission-related molecules (Mfn1/Mfn2/Fis1/Drp1) were satisfactory. By over-expression study, fusion-related molecules increase mitochondrial network while fission-related molecules increase fragmented mitochondria in B4 cells. Further, fusion-related molecules increase MMP, while fission-related molecules decrease MMP of B4 cells. Knock-down of fusion-related molecules also showed decreased MMP. Over-expression of fusion-related molecules enhanced the activation of IRS1-Akt for glucose uptake. Knock down fission-related molecules enhanced the activation of IRS1-Akt for glucose uptake. There was also increased translocation of GLUT1/GLUT4 onto the cell membrane upon over-expression of fusion-related molecules.
Conclusion: Fusion-related molecules increased insulin signaling and glucose uptake while fission-related molecules may inhibit insulin signaling and decreased glucose uptake. These data suggest a causal relationship between mitochondrial dynamics and IR.

PE-32
In situ eNOS/NO up-regulation – A simple and effective therapeutic strategy for diabetic skin ulcer
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Nitric oxide (NO) plays a key role in the physiological regulation of vascular functions. High serum concentrations of glucose and advanced glycation end products in people with diabetes results in reduced eNOS activation and NO synthesis and in increased NO consumption. Various diabetes-related complications are associated with the consequently impaired vascular tone and inadequate delivery of oxygen and nutrients to tissues—including refractory skin ulcers. Statins have proved protective effects on endothelial function involving increasing eNOS expression and NO bioavailability, and promotive effect on neovascularization of ischaemic tissue.

In the current study, we attempted to implement in situ eNOS/NO up-regulation in/around skin wounds in a rat model of diabetes by using statin-loaded tissue engineering scaffolds (TESs). Statin-loaded TESs with different drug loading amounts were prepared by a technique of electrospinning. The obtained TESs were composed of uniform and randomly arrayed fibres, with diameters of 527 ± 80, 466 ± 117 and 550 ± 118 nm, and with theoretical statin loading amounts of 1.0%, 5.0% and 10.0%, respectively. During in vitro drug release, all the TESs exhibited fast release phase in the initial 4 days. The in vitro cell culture experiments showed that the statin-loaded TESs could restore the high-glucose induced low cell viability and decreasing NO synthesis capabilities in human umbilical vein endothelial cells. In the rat model of diabetes, statin-loaded TESs with different drug loading amounts were administered on the skin wounds, with blank TES and natural healing wound as control. With the analysis of immunohistochemistry and microdialysis, the statin-loaded TESs exhibited promotive effect on eNOS expression and NO synthesis in regenerated skin tissues during skin wound healing. Furthermore, the regenerated skin tissues in groups with statin-loaded TESs exhibited promoted angiogenesis and higher skin blood flow value in/around skin wounds, and showed faster wound closure.

The present study indicated that the controlled release of statin from TESs may be a promising therapy for diabetic skin wound.

This work was supported by the National Natural Science Foundation of China (81303239) and the Specialized Research Fund for the Traditional Chinese Medicine Clinical Research Center of China (JDZX2015128).

PE-33

Vegetarian diet is associated with higher SBP and fasting serum triacylglycerol than omnivorous diet in Taiwanese type 2 diabetic

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Vegetarian diets are thought to be efficacious for management of type 2 diabetes mellitus (T2DM), and have been shown to be associated with reduction in the prevalence of T2DM in cohort studies, however differences in vegetarian diet composition could result in diverse physiologic outcomes. The current study evaluated the metabolic effects of vegetarian, breakfast vegetarian (animal foods excluded only from the first meal of the day) and omnivorous dietary patterns in Taiwanese T2DM adults.

Vegetarians (n = 69), breakfast vegetarians (n = 132), and omnivorous (n = 207) diabetic adults were recruited through chart review at a clinic in Taiwan.

Individual demographic, anthropometric, and dietary preference data were collected from consenting participants, and blood glucose, hemoglobin A1c, serum creatinine and lipid profile were analyzed from 8-hour overnight fasting blood samples. Differences among groups were determined by Chi-square and Kruskal-Wallis tests (Statistical Package for the Social Sciences, version 12.0, IBM).

Compared to omnivores, vegetarians had 5% higher systolic blood pressure ($p = 0.023$) and 24% higher fasting serum triacylglycerol ($p = 0.003$) (15% higher than the recommended value), and 14% lower high-density lipoprotein cholesterol ($p < 0.001$). A dose-response relationship was observed between extent of vegetarianism and these metabolic parameters among the groups. Additionally, a higher prevalence of anti-hypertensive medication use was observed in the vegetarians compared to omnivores ($p = 0.003$). Age, body mass index, waist to hip circumference ratio, diastolic blood pressure, duration of diabetes, fasting blood glucose, hemoglobin A1C, serum total cholesterol and low-density lipoprotein cholesterol, and serum creatinine did not vart significantly with dietary pattern. When data was analyzed by gender, diet effects were more pronounced for women than men. Female vegetarians had higher systolic blood pressure ($p = 0.017$) and serum triacylglycerol ($p = 0.044$), and lower high-density lipoprotein cholesterol ($p = 0.001$) and hemoglobin A1c ($p = 0.034$), and had higher prevalence of using anti-hypertensive medication ($p = 0.014$) than female omnivores.

Higher systolic blood pressure and fasting serum triacylglycerol, and lower high-density lipoprotein cholesterol were observed in vegetarian compared to omnivorous type 2 diabetic adults. We hypothesize that selection of a contemporary Taiwanese vegetarian diet may result in alterations in macronutrient distribution, with excessive consumption of refined carbohydrates attributed to vegetarian convenience foods, as replacement of dietary protein and fat with refined carbohydrate has been associated with these observed metabolic alterations in other populations. Further investigation is necessary to identify specific dietary components of Taiwanese vegetarian diets that may be implicated in adverse metabolic changes.

PE-34

A successfully treated case of extremely hyperglycemic crisis accompanied with rhabdomyolysis and acute kidney injury

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We reported a 37-year-old man who demonstrated extremely high level of serum glucose (3,355 mg/dL) complicated with diabetic ketoacidosis and hyperosmolar hyperglycemic state after excessive consumption of sweetened beverage within one day. His blood sugar levels were gradually decreased by aggressive fluid resuscitation and insulin infusion. However, the laboratory evaluation revealed elevated levels of creatinine, creatinine kinase and myoglobin on day 2. Simultaneously, a huge renal stone was found on abdominal plain film. The diagnosis of rhabdomyolysis, staghorn stone and acute kidney injury were made based on these laboratory tests. Interesting, his creatinine kinase concentration continued to rise and persisted with high levels for one week even blood glucose, ketoacidosis and renal function were recovered. Finally, this case was successfully survived after aggressive treatments. Rhabdomyolysis is an uncommon but underestimated complication of hyperglycemic crisis. Hence, physicians should be alerted to this under detected complication of hyperglycemic crisis which may lead to acute renal failure yet can be easily diagnosed by a readily available test—the creatinine kinase level.

PE-35

Comparison of clinical characteristics and outcomes of hospitalized patients with pneumonia between diabetic patients and non-diabetic patients in Japan

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Background: Japan has become a super-aging society, and the number of patients with pneumonia has been increasing. Diabetes is associated with an increased susceptibility to infection and infection-related morbidity and mortality. However, current evidence showing the association between diabetes and pneumonia in Asian population is very limited.

Objective: We aimed to elucidate the influence of diabetes on clinical characteristics and outcomes of pneumonia.

Method: Eligible cases were the patients who were hospitalized with infectious pneumonia in the Department of Internal Medicine and Respiratory Medicine between March 2014 and October 2015. We excluded non-infectious pneumonia and pneumonia developed after admission. We retrospectively reviewed medical charts and collected data about the patient backgrounds, clinical and radiologic characteristics and clinical course, and laboratory and microbiological data. We compared Diabetes group with Non-diabetes group by t test and chi-square test.
Result: Among 274 pneumonia cases, 199 were eligible. One-hundred eleven (55.8%) males were included, and mean ± SD of age and BMI were 78 ± 15 years old and 20.9 ± 6.2 kg/m^2, respectively. Sixty-one patients had concomitant underlying diseases. A number of community-acquired pneumonia (CAP) was 91, and the number of nursing and healthcare-associated pneumonia (NHCAP: a Japanese variant of healthcare-associated pneumonia) was 108. Fifteen pneumococcal pneumonia, one Legionella pneumonia and 103 aspiration pneumonia were included. The mortality rate was 7.5%. The number of patients in Diabetes group was 34 (type 1 diabetes, n = 1; type 2 diabetes, n = 33), mean ± SD of duration of diabetes, plasma glucose and HbA1c were 18 ± 12 years, 181 ± 61 mg/dL, and 7.0 ± 0.8%, respectively.
Compared with Non-diabetes group, Diabetes group was significantly younger (73.1 years vs 78.7 years) and had significantly lower BMI (24.5 kg/m^2 vs 19.9 kg/m^2). Aspiration pneumonia tended to be fewer in Diabetes group than Non-diabetes group (38.2% vs 54.5%). Diabetes group tended to have longer period of antibiotics administration (17 days vs 12 days). There were no significant differences in WBC, CRP, development of the multiple infiltration, pleural effusion, and empyema, length of hospital stay, and mortality.
Conclusion: Diabetic patients hospitalized with pneumonia were significantly younger and showed lower rate of aspiration pneumonia than non-diabetic patients. There were no significant differences in the severity and clinical outcomes.

PE-36

Association of leukocyte subtype counts with chronic inflammation and atherosclerosis in type 2 diabetes mellitus

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Background: Previous studies have shown that circulating leukocyte subtype counts, especially monocyte count, are associated with a risk of cardiovascular disease. However, little is known about the association of circulating monocyte count with chronic inflammation, visceral fat accumulation, serum adiponectin level, and atherosclerosis in type 2 diabetes.
Subjects and Methods: This is a cross-sectional study with a total of 276 Japanese patients with type 2 diabetes (mean age, 62.3 years; 63% men). None of them had hepatic or renal dysfunction so far. Intima-media thickness (IMT) of common carotid artery was evaluated by high-resolution B-mode ultrasonography. Fat areas of visceral (V) and subcutaneous (S) were evaluated by performing computed tomography scan at the level of the umbilicus. Serum total adiponectin levels were measured by an ELISA kit.
Results: Multiple regression analyses adjusted for age, duration of diabetes, body mass index (BMI), HbA1c, and estimated glomerular filtration rate (eGFR) showed that V/S ratio and high sensitive CRP (hsCRP) were significantly and positively associated with monocyte count ($\beta = 0.24$, $p < 0.001$ and $\beta = 0.17$, $p = 0.025$, respectively), while serum adiponectin was not ($\beta = -0.12$, $p = 0.107$). Multiple regression analyses adjusted for risk factors of atherosclerosis such as age, duration of diabetes, BMI, HbA1c, fasting C-peptide, eGFR, albuminuria, systolic and diastolic blood pressure, triglyceride, HDL-cholesterol, and LDL-cholesterol (model 1) showed a significant and positive association of monocyte count with maximum IMT, average IMT, and plaque score independently of V/S ratio ($\beta = 0.38$, $p < 0.001$; $\beta = 0.23$, $p = 0.004$; and $\beta = 0.22$, $p = 0.005$, respectively). However, when hsCRP was added as an independent variable (model 1 + hsCRP), the association turned into no significance ($\beta = 0.11$, $p = 0.164$; $\beta = 0.12$, $p = 0.104$; and $\beta = 0.14$, $p = 0.056$, respectively).
Conclusion: These findings suggest that increased circulating monocyte count is involved in chronic inflammation as well as atherosclerosis in patients with type 2 diabetes.

PE-37

Healing process in diabetic patients with foot ulcer

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Introduction: Diabetic foot is one of diabetic chronic complications. Cause of Diabetic Foot Ulcer (DFU) and amputation are long term hyperglycemia, peripheral neuropathy and peripheral artery disease.
Objective: The aim of this study was to evaluate healing progress of DFU.
Methods: Cohort study included type 2 diabetic patients with foot ulcer visited diabetic clinic last two years. Diabetic foot complication was diagnosed by questionnaire and foot examination, laboratory test and statistical analysis was done by SPSS 19.
Results: Mean age of diabetic patients was 59.4 ± 9.56 (37–78) years old and mean diabetes duration was 11.44 ± 6.4 (1–23 year) years and mean HbA1C was 10.09 ± 1.96% (7–15%). By questionnaire 9 (36%) of diabetic patients was with foot pain, loss of pressure sensation were 44%, vibration sensation was 44% and absent achilles reflex was 88%. Diabetic patients with no pulses of a.pedis dorsalis and a.tibialis posterior were 32% and abnormal results of ABI were 32%. History of diabetic foot amputation was 12% (hallux 4%, digits 8%). Mean initial visit days of diabetic patients with foot ulcer were 25.16 ± 31.59 (2–150). Cause of DFU was trauma 88% (physical trauma 36%, thermal trauma 4%, footwear 48%), ischemia and others 12%. Ulcer size was 1–200 mm and ulcer depth was 0.5–40 mm. By PEDIS wound classification I grade 28%, II grade 32%, III grade 24% and IV grade was 16%. By TEXAS wound classification 0 grade 32%, I grade 36%, II grade 20%, III grade 12% and stage A 40%, stage B 24%, stage C 4% and stage D was 32%. 83.5% of DM patients with foot ulcer with foot amputation was 5 patients (AKA 2, BKA 1, digits 2). Ulcer recurrence of DFU was 72% (once 48%, multiple 24%). Bacterial culture was done in 64% of diabetic foot ulcer in first time and 56% of recurrence ulcer in DFU. Staph.Aureus was 56%, Streptococcus epidermitis 25% and others were 19%. Primary healed DFU <1 month was 60%, 1–3 months were 20%, 3–6 months were 12%, non healed more 6 months 4%, and mortality was 4%.
Conclusion:

1. Primary healed DFU <1 month was 60%, 1–3 months were 20%, 3–6 months were 12%, non healed more 6 months 4%, and mortality was 4%. Ulcer recurrence of DFU was 72%.
2. DM patients with foot ulcer were foot amputation was 20%.

PE-38

Analysis of clinical factors influencing bone mineral density in Japanese patients with diabetes

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Aim: Risk of bone fracture is increased in patients with diabetes compared to that in healthy subjects. Bone mineral density (BMD) is closely related to the risk of fracture. Clinical factors affecting BMD in patients with diabetes were explored.

Methods: Thirty-one Japanese patients hospitalized to our hospital with diabetes for education were recruited. BMD of various parts and body composition were measured by DXA and fat mass index [FMI (kg/m^2)], lean mass index [LMI (kg/m^2)], and Z-scores of the lumbar spine (L-Z), the femoral neck (FN-Z), and the radius (R-Z) were evaluated. Z-scores were calculated on the basis of normal reference values of the age- and sex-matched Japanese group. Simple regression analysis using L-Z, FN-Z and R-Z as dependent variables and years from diagnosis, body weight, BMI, FMI, LMI, urine albumin (U-A), HbA1c, serum C-peptide, eGFR, bone turnover markers (serum ucOC, BAP, and TRACP-5b, and urine NTX), systolic blood pressure (SBP), ankle brachial index (ABI), cardio ankle vascular index (CAVI) and HDL-C as independent variables were performed. Stepwise multiple regression analysis using L-Z, FN-Z and R-Z as dependent variables and years from diagnosis, U-A, HbA1c, CPR, eGFR, BAP, TRACP-5b, SBP, FMI, LMI and CAVI as independent variables were performed.
Results: [clinical background (mean ± SD)] Number of subjects: 31 (21 males, 10 females; type 1: 2, type 2: 28, other: 1); therapeutic method: diet only 1, oral hypoglycemic agents (OHA) without insulin 19 (one patient used pioglitazone at admission), insulin 11; age: 57.3 ± 14.3; BMI: 26.4 ± 5.7; Years from diagnosis: 7.3 ± 6.1 [simple regression analysis] L-Z was correlated with FMI (R = 0.463) and HDL-C (R = −0.444). FN-Z was correlated with FMI (R = 0.413) and HDL-C (R = −0.368). R-Z was correlated with BMI (R = 0.458) and FMI (R = 0.590). No other factors were correlated with Z-sores; interestingly, body weight and LMI were not correlated with Z-scores. [stepwise multiple regression analysis] L-Z, FN-Z and R-Z were independently predicted by FMI, accounting for 21.0%, 12.0% and 27.7% of the variability of the dependent variables, respectively.
Conclusion: Indices of bone turnover, glycemic control, renal function, endogenous insulin secretion, nephropathy, atherosclerosis, and other clinical factors were not correlated with BMD in this small study. A positive correlation between bone mineral density and fat mass was found in these Japanese patients with diabetes.

PE-39

Cilostazol effectively attenuates deterioration of albuminuria in patients with type 2 diabetes: a randomized, placebo-controlled trial

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Cilostazol is an antiplatelet, antithrombotic agent with anti-inflammatory properties. To date, no clinical study has specifically evaluated the efficacy of cilostazol in patients with diabetic nephropathy (DN). We hypothesized that cilostazol might delay renal deterioration in DN patients at high risk of progression. Between April 2008 and April 2010, we screened 156 consecutive patients aged 35–80 years who were first diagnosed with type 2 diabetes after the age of 30 years. Of these, 90 patients with DN, as defined by morning spot urine microalbuminuria (MAU) [20 mg/L or an albumin-to-creatinine ratio (ACR)[30 lg/mg on at least two consecutive occasions within the prior 3 months, were enrolled into a 52-week randomized, single-blinded, placebo-controlled trial of oral cilostazol 100 mg twice daily or placebo (45 subjects in each group). Morning spot urine samples were collected to determineMAUand ACR. Fasting plasma levels of metabolic, endothelial variables, and inflammatory markers were examined. Following 52 weeks of treatment, urinary MAU and ACR were significantly reduced in the cilostazol group compared with the placebo group (P = 0.024 and P = 0.02, respectively). In regression analyses, changes in monocyte chemotactic protein-1, E-selectin, and soluble vascular cell adhesion molecule-1 (sVCAM-1) were significantly associated with changes in MAU and ACR. Net changes of E-selectin (P\0.001) and sVCAM-1 (P\0.05) were independent predictors of change in MAU and ACR, respectively. Our results suggest that cilostazol may effectively attenuate deterioration of albuminuria in patients with type 2 diabetes. This effect is likely mediated by an improvement of adhesion molecules.

PE-40

Relationship between serum iron with renal function of subjects with diabetes

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Objective: To explore the value of serum iron in the diagnosis of type 2 diabetes mellitus (T2DM) with the decline of renal function.
Methods: A total of 100 subjects who were diagnosed T2DM were recruited from the second people's hospital of Huai'an from February to March in 2016. We collected the baseline data and measure serum iron, renal artery doppler ultrasound and GFR determination of nuclide renal dynamic imaging.
Results: Serum iron levels were negatively correlated with nuclide GFR (r = 0.214, P < 0.05).
Conclusion: Serum iron is an independent risk factor for the decline of kidney function in patients with T2DM.

PE-41

Potential nephroprotective effects of type 2 diabetes therapy: Epidemiologic study for South East Asian and Arab populations in Qatar

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Purpose: Metformin is considered a first line therapy for patients with type 2 diabetes mellitus (T2DM). Increasingly evidence is emerging to support not only the safe use of metformin in patients with impaired renal function, but epidemiologic study among Caucasian populations have demonstrated a potential nephroprotective effect. The objective of this study is to evaluate the relationship between metformin and renal outcomes in South East Asian and Arab patients with T2DM in Qatar.
Methods: A retrospective cohort study of patients with T2DM enrolled in health care services provided by Qatar Petroleum, the largest private employer in Doha, Qatar, is being conducted. Patients who received care between 1995 and 2015 are considered. Any adult who received an incident oral glucose lowering drug prescription during the study period will be considered for inclusion ("new user"). Incident prescriptions will be defined as the first oral glucose lowering drug prescription filled after at least 365 days of active use of QP medical services without prescriptions filled for any other oral glucose lowering drug ("baseline year"). Patient health data will be followed from "index date" (date of incident prescription) until documented development of a study outcome or a censoring event, such as: leaving the QP medical system; non-persistence on the incident oral glucose lowering drug; switching or adding new oral glucose lowering drug to the original therapy. Exposure categories will be grouped according to different glucose lowering regimens cohorts. The primary outcome will be a composite of: a GFR event, defined as a persistent 25% or greater decline from the baseline eGFR; reaching ESRD, defined as reaching one of the following: an eGFR < 15 mL/min/1.73 m^2 or documented initiation of dialysis or kidney transplant. GFR and ESRD events will be confirmed between 3 and 12 months after the first documented outcome in order to avoid counting episodes of reversible acute kidney injury.

Results: Data for 7,590 adults with type 2 diabetes adults were initially identified. Of these 3,418 (45%) first started metformin therapy during their care at QP and 2,972 (39%) had an associated baseline serum creatinine recorded. South East Asian (1,933, 65%) populations represent almost two-thirds of the evaluated cohort, while Qatari nationals make up 11% (n = 335) and 12% (n = 361), respectively.
Conclusion: The distribution of nationalities in our studied cohort is consistent with national demographic patterns. Our findings will help further quantify the effects of glucose lowering therapies compared with metformin treatment in previously understudied populations.

PE-42
The correlation between fibrinogen level and arterial stiffness in type 2 DM patients
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Background: Cardiovascular disease (CVD) is increased in type 2 Diabetes Mellitus (T2DM) patients due to a complex combination of various traditional and non-traditional risk factors that have important roles in the evolution of atherosclerosis. Fibrinogen level has been described as independent risk factor for CVD. Many studies have indicated that arterial stiffness also plays a critical role in the pathogenesis of atherosclerosis and CVD. Brachial-ankle pulse wave velocity (baPWV) is a method to measure arterial stiffness. It reflects the stiffness of both the aorta and peripheral arteries in an arm and a leg.
Objective: The aim of this study is to analyze the correlation between fibrinogen level and baPWV in T2DM patients.
Material and Methods: This cross sectional study was conducted at diabetes outpatient clinic Dr. Soetomo teaching hospital Surabaya Indonesia. Inclusion citerias were patiens with T2DM aged over 45 years old and signed informed consent. Patients with severe infection, renal and liver dysfunction, pregnancy, fibrate treatment were excluded in this study. We interviewed and measured body weight and height, BMI, blood pressure and baPWV. Plasma glucose (FPG) and post prandial glucose (PPG), HbA1c, lipid profiles, and fibrinogen level were measured as well. Data was statistically analyzed using Pearson correlation test.
Results: We analyzed 40 patients who have been diagnosed with T2DM consisting of 17 males and 23 females. The overall mean of BMI was 25.66 + 2.91 kg/m^2, HbA1c was 8.01 + 1.39%, FPG was 150.2 + 61.97 mg/dL, PPG was 214 + 74.49 mg/dL and fibrinogen 456.75 + 142.60 mg/dL. One-sample Kolmogorov-smirnov test indicated that the data distribution was normal. There was significant correlation between fibrinogen level and baPWV (r 0.336; $p < 0.05$).
Conclusion: There was significant correlation between fibrinogen level and arterial stiffness in T2DM patients.

PE-43
Cilostazol attenuates the severity of peripheral arterial disease in type 2 diabetes: the plasma soluble receptor for advanced glycation end-products
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Recent studies have demonstrated that the plasma soluble receptor for advanced glycation end-products (sRAGE) play a major role in developing macrovascular complications of type 2 diabetes, including peripheral arterial occlusion disease (PAOD). Cilostazol is an antiplatelet, antithrombotic agent, which has been used for the treatment of PAOD. We hypothesized that cilostazol attenuates the severity of PAOD in patients with type 2 diabetes through the augmentation of plasma sRAGE. Ninety type 2 diabetic patients with PAOD defined as intermittent claudication with ankle-brachial index (ABI) ≦0.9 were recruited for an open-labeled, placebo-controlled study for 52 weeks with oral cilostazol 100 mg twice daily (n = 45) or placebo (n = 45). Fasting plasma sRAGE, endothelial variables of E-selectin, soluble vascular cell adhesion molecule-1 (sVCAM-1), and inflammatory markers of high-sensitivity C-reactive protein (hsCRP) and tumor necrosis factor-α (TNF-α) were determined. After completely the 52-week treatment program, the ABI values were elevated in cilostazol group ($P < 0.001$). The plasma sRAGE was significantly increased ($P = 0.007$), and hsCRP, sVCAM, and E-selectin concentrations were significantly decreased ($P = 0.028$, <0.001 and <0.001, respectively) with cilostazol treatment. In a partial correlation analysis with adjustments for sex and age, the net change of sRAGE significantly correlated with the change of ABI in the cilostazol group ($P = 0.043$). In a stepwise multiple regression model, only the change with regards to sRAGE was significantly associated with the change of ABI ($P = 0.046$). Our results suggest that cilostazol may effectively attenuate the severity of PAOD in patients with type 2 diabetes. Plasma sRAGE plays a role as an independent predictor for improving the index of PAOD.

PE-44
Nonalbumin proteinuria as a simple and practical predictor of the progression of early-stage type 2 diabetic nephropathy
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Recent studies have shown multi-biomarker approaches for risk prediction in diabetic nephropathy. The aim of this study was to pursue the simple and practical predictor among nonalbumin proteinuria (NAP) and six urinary biomarkers contributing to the progression of diabetic nephropathy.
In this observational study, the urine levels of albumin-to-creatinine ratio (ACR), nonalbumin protein-to-creatinine ratio (NAPCR) and six biomarkers [kidney injury molecule (KIM)-1, neutrophil gelatinase-assoicated Lipocalin (NGAL), liver-type fatty acid-binding protein (L-FABP), angiotensinogen, interleukin-18 (IL-18) and YKL-40] were measured in 73 patients with type 2 diabetes and estimated glomerular filtration rate (eGFR) ≥ 60 mL/min/1.73 m^2. We found optimal cutpoints for ACR, NAPCR and six biomarkers and used Harrell's concordance index (C-index) to validate Cox model. The renal outcomes were annual eGFR decline and the development of chronic kidney disease (CKD) stage 3 or greater.
The average rate of eGFR decline over the median of 50 months of follow up was −2.48 mL/min/1.73 m^2/year. NAPCR and six urinary biomarkers were negatively correlated with annual eGFR decline. After adjusting for several clinical factors, only NAPCR showed a significant association with annual eGFR decline (Adjusted R2 = 0.141, $P = 0.035$). NAPCR showed a higher predicted probability of having the CKD stage 3 or greater occur than six urinary biomarkers (C-index 82.7). NAPCR also showed a higher predictive value than six urinary biomarkers applying the concept of "Panel score".
The results of this study suggest that NAPCR may be a better predictor of the development and progression of CKD than the other urinary biomarkers in patients with the early-stage type 2 diabetic nephropathy.

PE-45

The role of RBP4 receptor on the pathogenesis of diabetic kidney

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Mitochondrial dysfunction and oxidative stress are shown as an initiating trigger to induce diabetic nephropathy. We recently reported that the suppression of RBP4 receptor cascades involves dyslipidemia-induced arterial and renal damage. We thus investigated whether the suppression of RBP4 receptor signaling could interact with mitochondrial dysfunction to cause apoptosis and fibrosis in diabetes. In the kidneys of streptozotocin(STZ)-induced diabetes and high glucose(HG)-cultured HEK cells, RBP4 receptor(STRA6), MnSOD, caspase 3 and collagen 1 protein as well as apoptotic cells increased, but CRBP1, RARα, ATP synthase, and cytochrome c expression as well as mitochondrial potential decreased. By immunoprecipitation method using STRA6 antibody, we found the binding activity of RBP4 on STRA6 in diabetes and HG-cultured cells were markedly reduced. ROS inhibitor and MnSOD gene transfection reversed above alterations in HG-cultured cells. MnSOD silencing significantly reversed STRA6, CRBP1 and RARα expression but didn't affect caspase3 and collagen 1 in HG-cultured cells. Interestingly, CRBP1 gene transfection reversed the suppression of ATP synthase, cytochrome c, the increase of caspase 3 and collagen 1 protein and mRNA expression, but increased binding activity of RBP4 with STRA6, and expression of RARα in HG-cultured cells. This study indicates that interaction between the suppression of RBP4 Receptor signaling and mitochondrial dysfunction induces kidney apoptosis and fibrosis in diabetes.

PE-47

Temporal pattern of plasma glucose levels during oral glucose tolerance test and the association with cardiovascular risk

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Backgrounds: The pattern of insulin or glucose levels during an oral glucose tolerance test (OGTT) may provide useful information on the prediction of subsequent cardiovascular disease and diabetes mellitus or its related complication. However, the patient's glucose and insulin response pattern during OGTT are rarely explored. Besides, the clinical implication of the temporal difference of glucose during OGTT to major cardiovascular events or risk are unknown. This study will be carried out to determine whether the glucose response temporal patterns during OGTT are associated with cardiovascular disease risk scores.
Methods: Subjects with impaired glucose tolerance or type 2 diabetes were enrolled in this observational study under routine clinical care in outpatient setting from Taipei Veterans General Hospital. Blood samples were obtained at 0, 30, 60, 90 and 120 min during 75 g OGTT after 8 hours fast. Patients were grouped by the time point when highest glucose level measured (group 30 min, group 60 min, group 90 min and group 120 min). The primary outcome is ten-year cardiovascular disease risk which was calculated by Framingham risk score calculator.
Results: A total of 125 patients who underwent OGTT were included. There are 4, 54, 55 and 9 subjects in the group 30 min, group 60 min, group 90 min and group 120 min separately. 87% of them were in the group 60 min and group 90 min. The group 60 min had younger age (56.15 ± 10.12 years vs 60.58 ± 10.02 years, P = 0.023) and lower HbA1c (6.03 ± 0.44% vs 6.30 ± 0.59%, P = 0.009) but higher LDL-C (135.40 ± 44.30 mg/dL vs 116.61 ± 35.68 mg/dL, P = 0.051) than the group 90 min. Framingham 10-year risk score of group 90 min is 1.7 times of that of group 60 min (4.05 ± 4.60% vs 6.98 ± 6.56%, P = 0.023). After multivariate linear regression, group 90 min is still associated with higher risk score (P = 0.042).
Conclusions: Comparing to the later peak glucose group (group 90 min) during an OGTT, the earlier peak glucose group (group 60 min) had characters of younger age, lower HbA1c level but higher LDL-C. The later peak glucose group also had higher Framingham 10-year risk score after adjusting these variables.

PE-48

HbA1C variability is not associated with renal outcomes in diabetic nephropathy with chronic kidney disease stage 3-5

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Background: Higher HbA1C variability had been reported to be associated with increased risk of progression of nephropathy. However, no previous studies had evaluated the association between HbA1C variability and renal outcomes in patients with diabetic nephropathy. Therefore, the aim of this study was to assess whether HbA1C variability is associated with rate of renal function decline and progression to renal replacement therapy (RRT) in diabetic nephropathy with chronic kidney disease (CKD) stage 3–5 patients.
Methods: This longitudinal study enrolled 352 patients. Intra-individual HbA1C variability was defined as coefficient of variation (CV = SD/mean). The renal end point was defined as commencement of RRT. The change in renal function was measured by estimated glomerular filtration rate (eGFR) slope. The study patients were stratified into 3 groups according to tertiles of coefficient of variation (CV) of HbA1C (<8.4, 8.4–14.1, ≧14.1).
Results: One hundred and nine (31%) patients received RRT during the follow-up period. the median follow-up period was 3.6 years. There was no significant difference of eGFR slope in 3 study groups. The patients with CV tertile 3 (vs. CV tertile 1) were associated with a higher risk of commencement of RRT in the unadjusted model (HR, 1.783; 95% CI, 1.129 to 2.814; p = 0.013) and in the multivariate model after adjusting for demographic and clinical factors (HR, 1.964; 95% CI, 1.212 to 3.181; p = 0.006). This relationship became non-significant after further adjusting for biochemical parameters (HR, 1.457; 95% CI, 0.866 to 2.453; p = 0.157).
Conclusions: Our results demonstrated that HbA1C variability is not associated with rate of renal function decline and progression to RRT in diabetic nephropathy with CKD stage 3–5 patients. Therefore, HbA1C variability may not be the major determinant of renal outcomes in diabetic nephropathy with CKD stage 3–5 patients.

PE-49

Effects of t-PA and PAI-1 on the macro-vascular complications in type 2 diabetes

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Objective: To identify the importance of abnormal fibrinolytic system mainly the content changes of tissue-plasminogen activator (t-PA) and plasminogen activator inhibitor-1 (PAI-1)

in the process of macro-vascular complications in type 2 diabetes mellitus and provide theoretical evidences to suppress or delay the occurrence and development of macro-vascular complications in type 2 diabetes mellitus effectually for clinical research.
Methods: Paired design is applied in this research and 100 cases are selected including 54 men and 46 women. Those two patients are paired with same gender and basically equivalent age, blood sugar, blood pressure and blood-lipid but opposite result of intima media thickness (IMT), so 100 cases are divided into two average groups. Type 2 diabetes mellitus with astherosclerosis (AS-T2DM) group has 50 cases, 27 men and 23 women. So does type 2 diabetes mellitus without astherosclerosis (nonAS-T2DM) group. There are no significant differences in age, blood sugar (GHbA1c), blood pressure (SBP and DBP) and blood-lipid (LDL-C) between the two groups verified by paired samples T test. ($t = -0.334$, 2.832, −5.001, 1.668, 4.502 and $P = 0.796$, 0.215, 0.127, 0.345, 0.138 respectively). The contents of t-PA and PAI-1 in the two groups are measured quantitatively by double-antibody sandwich ELISA at same time. Each sample is measured in three holes to ensure the accuracy of the measurement and the mean is used for statistics. The differences of t-PA and PAI-1 contents between the two groups are compared by paired samples T test.
Result: Compared with nonAS-T2DM group, the content of t-PA reduced significantly ($t = -19.668$, $P = 0.031$) while PAI-1 increased significantly ($t = 20.394$, $P = 0.030$) in AS-T2DM group.
Conclusion: The reduce of t-PA content and increase of PAI-1 content have played some role in the occurrence and development of macro-vascular complications in type 2 diabetes mellitus.

PE-50

To increase smoking cessation rate among diabetic smokers who participate in smoking cessation clinics by means of effective health education

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By implementing the diabetes try-out trial for diabetic smokers and by utilizing clinical smoking cessation treatment techniques: 5A (Ask, Advise, Assess, Assist, Arrange) and 5R (Relevance, Risk, Reward, Roadblock, Repetition), the diabetic smokers' participation and confidence in self health management and attempts in quitting smoking were improved, which resulted in a cessation rate of 34%.
Objectives/methods: The health education center team introduces diabetic smokers to participate in health education counseling at the center. The frontline team records their smoking histories and transfers them to smoking-cessation health education counseling. The medical team applies 5A and 5R to raise diabetic smokers' health awareness and their motivation to quit smoking. Physicians make use of e-message boards at their clinics to effectively persuade smokers to attending smoking-cessation therapies and be away from smoking.
Result: According to statistics in 2014, 51 out of the 178 participants were diabetic and the smoking cessation rate within 6 months was 35.3%. In 2015, 73 out of the 277 participants were diabetic and the smoking cessation rate within 6 months was 35.6%. Comparison between the same period of the two years shows that the number of participants grew from 178 to 277 by 55.6%, and that the number of participating diabetic smokers who quitted smoking grew from 18 to 26 by 69.2%.
Conclusion: According to our experience, through the systematic search for smokers, giving them advice on cessation and later on transferring them to smoking cessation treatments, and education counseling and cessation prescription design, smokers' health awareness can be improved and then so can their motivation for cessation, which motivates them to keep living a healthier lifestyle.

PE-51

Recurrent left hemichoreic movement following to severe hyperglycemia in type 2 diabetes mellitus

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Choreic ballism is a rare neurologic complication of metabolic origin in hyperosmolar hyperglycaemic state (HHS) although the etiologic mechanism is still unclear. Sometimes, it was reported in poorly controlled old female type 2 diabetes mellitus. We experienced a case of recurrent left arm hemichoreic movement following to severe hyperglycemia in type 2 diabetes mellitus patient.
A 68-year-old woman with 11-year history of type 2 diabetes mellitus who was admitted to our hospital for recurred attack of hemichoreic movement in the left upper limb of the body. On admission day, her glycosylated hemoglobin (HbA1c) was 13% (N:4–6%). Her calculated serum osmolarity peaked at 310 mOsm/kg (N: 275–295 mOsm/kg), and the serum glucose level reached 475 mg/dL (N:80–140 mg/dL) with no evidence of diabetic ketoacidosis. The initial serum sodium level was 135 mmol/L (N:135–145 mmol/L), which normalized to 142 mmol/L over 1 day. The physical examination revealed left hemichorea with a ballistic component without focal neurologic finding. Unenhanced computed tomography of the brain was negative. At magnetic resonance imaging, the right putamen showed high signal intensity on T1-weighted images. During the hospitalization, an adequate diet and insulin therapy resulted in progressive normalization of blood glucose values and an improvement of dyskinesia. According to medical records, she was admitted previously due to hemichoreic movement attack 4 times whenever her blood glucose was uncontrolled, HbA1c was over 10%.
HHS, an acute complication of diabetes mellitus, can be associated with neurological involvement ranging from seizures, involuntary movements to reversible focal neurological deficits without any structural lesions. This diabetic choreic ballism is a pathological entity to be considered benign, generally transient and reversible. So we think that early recognition and differentiation from other causes of reversible manifestation in uncontrolled Type 2 diabetes mellitus is important.

PE-52

A nursing experience of implementing interprofessional practice on a diabetic foot ulcer patient

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Neuropathy, occlusive vascular disease, and infection will lead to the formation of diabetic foot ulcers that affect the quality of life of the patient. The diabetic foot ulcer can also lead to foot infections that include cellulitis, osteomyelitis, necrosis and even amputation. Here, we report a 61-year-old man with diabetic foot ulcer. His medical history includes end-stage renal disease under regular hemodialysis, hypertension, type 2 diabetes mellitus, peripheral arterial occlusive disease (PAOD) of the left leg and triple-vessel coronary artery disease. Percutaneous transluminal angioplasty has been performed for PAOD of left lower limb. This time, he was sent to our Emergency Department due to pain and swelling of left 4th toe, without fever or chills. In ER, the wound of left 4th toe presented with wet gangrene and dorsal foot swelling, redness and tenderness were found. The plastic surgeon was consulted, and amputation of left 4th toe was undertaken. After the operation, he was admitted to our ward for care. During his hospitalizations, the left foot wound got worse and worse at the beginning. Then, we carried out wound care and several times of debridement, and we consulted Orthopedics for Hyperbaric Oxygen Therapy, Cardiovascular Surgeon for left leg bypass surgery, and Endocrinologist for glycemic control

and nutrition supply. We altogether treated this patient, and the diabetic foot ulcer was healed eventually.

PE-53

Periodontitis prevention program effectively reduced the incidence of periodontitis in diabetic patients

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A five-year follow up conducted by Firatli found that, clinically, the number of cases of periodontal attachment loss and teeth loss among diabetic patients is significantly bigger compared to people without diabetes. To address the situation, establish a periodic periodontitis screening and care system for diabetic patients and have set up a designated screening site. Diabetes educators help patients learn information about periodontitis and oral care and provides prompt and proper individual medical interventions to reduce the possibility of teeth loss or chewing disorders caused by periodontitis and to enhance diabetic patients' overall health condition. The rate of dental abnormalities among diabetic patients found in screening had gone down from 51.9% to 29.9%. This improvement shows that promulgating oral care allows diabetic patients to take this issue seriously and care more about their oral condition.
Executing Approach:

1. Establish a cross departmental diabetic periodontitis screening team comprise of Dentistry and Health Education Center; members include dentists, physicians of Diabetes Shared Care Network, diabetes educators, oral health educators and administrative assistants to jointly carry out "Diabetic Periodontitis Prevention Program".
2. To prevent patients from withdrawing from screening due to lengthy waits, a designated periodontal screening site besides the education center is set up.
3. Professional oral health educators will later on provide education and relevant instructions and arrange patients with abnormal screening results to receive treatment at Dentistry outpatient clinics.
4. On patients' clinic visits, attending physicians that have written the request sheet to their patients can look up the screening results and give instructions to them while informing them of the importance of oral health or of the prevention of periodontal diseases.

Program Achievement: 12 oral healthcare promulgation events attracted 344 community members to participate in. The number of diabetic patients receiving screening between August 2012 and June 2015 was 4,012. Comparing the screening achievement in 2014 with that in 2013, the rate of dental abnormalities among diabetic patients found in screening had gone down from 51.9% to 29.9%.
Conclusion: The execution of Diabetic Periodontitis Prevention Program has not only raised the awareness of oral care and knowledge and skills about self-care among periodontitis high-risk group: diabetic patients, its promulgation of screening has also helped identify periodontitis patients and helped them seek medical attention. The care provided by Diabetes Case Management annually tracks and reminds patients to receive screening and treatment.

PE-54

Associations of glycated hemoglobin A1c and glycated albumin with subclinical atherosclerosis in the Chinese population with impaired glucose regulation

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Objective: Glycated hemoglobin A1c (HbA1c), which can reflect the mean blood glucose levels over the previous 2 to 3 months, attaches great importance to the glucose monitoring system. Some new indicators, such as glycated albumin (GA) with ability to reflect the blood glucose levels during the previous 2 to 3 weeks, have been gradually put into clinical application and provided HbA1c with complementary information in recent years. The aim of this study was to investigate the associations of HbA1c and GA with subclinical atherosclerosis in middle-aged and elderly Chinese subjects with impaired glucose regulation.
Methods: A total of 640 subjects with impaired glucose regulation and without history of cardiovascular disease or carotid artery plaque in Shanghai community were recruited for this study (256 men and 384 women; age range, 40 to 70 years old). Carotid ultrasonography was used to measure the carotid intima-media thickness (C-IMT), which was an indicator of subclinical atherosclerosis. Increased C-IMT was defined as ≥0.70 mm (the upper quartile). HbA1c was determined by high-performance liquid chromatography. Serum GA was assayed using the enzymatic method.
Results: The HbA1c and GA levels were higher in subjects with increased C-IMT than those with normal C-IMT (both $P < 0.01$). Correlation analysis revealed that both HbA1c and GA were positively associated with C-IMT ($r = 0.135$ and 0.112, respectively; both $P < 0.01$). Logistic regression analysis showed that both HbA1c (odds ratio = 2.630, 95% confidence interval: 1.401–4.935; $P = 0.003$) and GA (odds ratio = 1.215, 95% confidence interval: 1.008–1.466; $P = 0.041$) were independent factors associated with increased C-IMT.
Conclusions: In middle-aged and elderly Chinese subjects with impaired glucose regulation, both elevated levels of HbA1c and GA were associated with increased C-IMT, suggesting that HbA1c and GA could reflect the risk of subclinical atherosclerosis.

PE-55

Asymmetric Dimethylarginine correlates significantly with tumour necrosis alfa but not with brachial ankle pulse wave velocity in the T2DM-METS

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Background: Endothelial dysfunction is an important phenomenon in the pathogenesis of atherosclerosis and is related to the derangements of nitric oxide (NO) synthase in the vessel wall. Asymmetric Dimethylarginine (ADMA) is an endogenous, competitive inhibitor of nitric oxide synthase and is induced by inflammatory cytokines of tumour necrosis factor (TNF)-a in vitro. Increased ADMA levels are associated with reduced NO synthesis as assessed by impaired endothelium-dependent vasodilatation. There is cause and effect relationship between endothelial dysfunction and vascular stiffening. Measurement of brachial ankle pulse wave velocity (baPWV) is simple and applicable for cardiovascular risk screening and as a marker for the severity of atherosclerotic vascular damage.
Aim: To investigate the correlation between ADMA level with TNF-a and baPWV in the type-2 diabetes mellitus (T2DM)-Metabolic Syndrome (Mets) patients.
Method: This is a cross sectional study with T2DM-Mets patients who came to the outpatient clinic of Soetomo Hospital Surabaya during January 2010 to December 2012. Subjects met the inclusion and exclusion criteria were measured their ADMA, TNF-a, and blood glucose levels in plasma. Brachial ankle pulse wave velocity (ba-PWV) was determined by using the V Serra-1000. The study was approved

by the local Research Ethics Committee and subjects gave written informed consent.
Results: Thirty-seven T2DM-Mets patients consisted of 15 (40.5%) males and 22 (59.5%) females who met inclusion and exclusion criteria were enrolled in this study. Their mean of age was 51 ± 5.2 years old, duration of illness was 16.49 ± 23.4 months, A1C level was 8.5 ± 0.9%, BMI was 26.7 ± 4.5 kg/m^2, ADMA level was 0.572 ± 0.2 μmol/L, TNF-a level was 10.0 ± 16.5 pg/mL, and ba-PWV was 1,624.5 ± 295.5 cm/s. Spearman's correlation analysis showed that ADMA level was significantly correlated with TNF-a level ($p = 0.026$; $r = 0.366$). However, no significant correlation found with ba-PWV ($p = 0.134$; $r = 0.251$).
Conclusion: ADMA level is correlated with TNF-a level in this T2DM-MetS population.

PE-56
Limb preservation affects survival for diabetic patients with infectious foot gangrenes
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Objective: Infectious gangrene of foot is a medical emergency for diabetic patients. Lower-extremity amputation (LEA) is usually inevitable for in such circumstance. Nevertheless, the survival and factors associated mortality of these patients has not been understood.
Method: A total of 157 type 2 diabetic patients treated for infectious foot gangrenes at a major diabetic foot center in Taiwan from 2002 to 2009 were enrolled. Prompt major LEA (above the ankle) for life saving was found in 59 patients (major LEA one-stage group). Among 98 patients received initial minor LEA (below the ankle) to remove gangrene tissue, 67 subjects successfully healed (minor LEA group) while 31 subjects needed further major LEA (major LEA two-stage group). After treatment, their survival was followed as of December 2012. Clinical information at admission was used for survival analysis.
Result: One hundred and nine patients died, with a median survival time of 3.12 years. Age [hazard ratio 1.037 (95% CI 1.010–1.066)], dialysis state [2.173 (1.029–4.585)] and major LEA [1.957 (1.113–3.443)] were independent factors associated with mortality.
Patients in minor LEA group had better median survival time (5.5 years) when compared with major LEA one-stage and two-stage groups (1.8 and 2.7 years, respectively). The survival curves of major LEA one-stage and two-stage groups revealed no difference (Log rank P: 0.368).
Abnormal ankle-brachial index (ABI, >1.4 or ≦0.9) was the independent risk for healing failure that lead to two-stage major LEA (multi-variable regression analysis by adjusted with age, smoker, hypertension, major adverse cardiac event, and renal function).
Conclusion: In diabetic patients with infectious foot gangrenes, major LEA and dialysis state were the factors affect survival. Limb preservation to keep amputation level below the ankle has better survival. The abnormal ABI is the independent factor leading to two-stage major LEA.

PE-57
TG/HDL-C ratio predicts development of albuminuria in type 2 diabetes with ACR <10 mg/gm. A prospective cohort study
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Low normoalbuminuria (ACR < 10 mg/gm) is currently recognized as near normal renal function in type 2 diabetes. We hypothesized that TG/HDL-C ratio is the early biomarker to predict the development of DKD for type 2 diabetes. We enrolled 809 type 2 diabetic subjects with ACR < 30 mg/gm between 2003 and 2005 and followed them through the end of 2012. Among them, 518 subjects had ACR < 10 mg/gm. The average follow-up time was 6.2 years. The incidence rate ratio and Cox proportional hazards model were used to evaluate the association between baseline demographics and biochemical variables and development of albuminuria in 518 subjects with ACR < 10 mg/gm and 809 subjects with ACR < 30 mg/gm, respectively. Among 809 subjects with ACR < 30 mg/gm, 390 entered in albuminuric stage while 205 subjects developed albuminuria in 518 diabetes with ACR < 10 mg/gm. By using Cox proportional hazards model, we found that education, basal ACR and HOMA-IR in subjects with ACR < 30 mg/gm are independent predictors for development of albuminuria, whereas and education, basal ACR, and TG/HDL-C ratio are in subjects with ACR < 10 mg/gm. Compared with those in the lowest quartile of TG/HDH-C ratio, the multivariate HR for those in the 2nd, 3rd, and highest quartiles were 1.08 (95% CI 0.66–1.79), 1.38 (0.85–2.24), and 1.71 (1.03–2.82), respectively (trend test: $P < 0.015$) in diabetes p with ACR < 10 mg/gm. According to the dose-response effects of TG/HDL-C ratio shown in this prospective study, we conclude that TG/HDL-C ratio could be an early predictor for development of albuminuria in type 2 diabetes.

PE-58
Specific responsibility team for vascular interventions in diabetic foot decreases major lower limb amputation rate
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Objective: In Kaohsiung Chang Gung Memorial Hospital (KCGMH), patient with diabetic foot received treatment by an intensive team care in internal medicine ward. The intensive team was established by metabolic, plastic surgery, cardiovascular surgery and orthopedic specialist in 2005. And another specific responsibility team for percutaneous transluminal angioplasty (PTA) was also established by cardiologist in 2011. This study aimed to assess the quality of diabetic foot care provided in KCGMH before and after establishment of the PTA team.
Method: This was a retrospective review of data from 2013 to 2015 and in 2009 at Kaohsiung Chang Gung Memorial Hospital. Patient who had been diagnosed with diabetic foot ulcer during the study period were included. We collected the comorbidities, chronic complications and interventions to compare the differences of the major lower limb amputation rate before and after establishment of the specific responsibility PTA team.
Result: In total, 428 patients with T2DM underwent diabetic foot treatment at the KCGMH during the study period. When comparing to the patients distribution in 2009, the rate of comorbidities, including cerebral vascular accident, coronary artery disease, end stage renal disease, hypertension, dyslipidemia are significantly higher in 2013 to 2015. The rate of peripheral artery occlusive disease and people received percutaneous transluminal angioplasty (PTA) in 2013 to 2015 are also significantly higher (29.0% vs. 7.6%, $p < 0.001$). Furthermore, the rates of major lower limb amputation are lower after the intervention of specific responsibility PTA team (15.8% vs. 19.8%) and patients receiving PTA had significantly lower amputation rates during this period (10.1% vs. 19.8%, $p = 0.026$).
Conclusion: This study suggests that the specific team of PTA by cardiologist improves the major lower limb amputation rate in patients with diabetic foot, even with more comorbidities and chronic complications.

PE-59

Outcome analysis of diabetic patients with or without albuminuria

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Objective: This study retrospectively compared the clinical character and outcome of type 2 diabetic patients with normo- (below 30 mg/L), micro- (30–299 mg/L) and macro- (above 300 mg/L) albuminuria

Research design and methods: 79 type 2 diabetic nephropathic (DN) patients were retrospectively reviewed from 2013/01 to 2016/01. All patients were treated with oral anti-diabetes drugs and/or insulin; either angiotensin receptor blockers (ARB) or angiotensin-converting enzyme inhibitors (ACEI) were given in the albuminuria groups. Clinical data including urine albumin creatinine ratio (UACR), glycosylated hemoglobin (HbA1c), systolic blood pressure (SBP) and estimated glomerular filtration rate (eGFR) were analyzed. Patients were divided into normo-, micro- and macro-albuminuria groups according to their latest amount of spot urine albumin. All data were analyzed with Generalized Estimating Equation (GEE) to evaluate the changes in SBP, HbA1c, UACR and eGFR.

Results: Our study includes 33 (41.8%) normal, 13 (16.5%) micro- and 33 (41.8%) macro-albuminuria patients aged 62.1 ± 10.6, 57.8 ± 11.9 and 65.6 ± 11.4 year-old, respectively. After adjusting age, sex and duration of diabetes, both albuminuric groups showed statistical significance of higher UACR (micro-: B = 103.66, SE = 40.24, p = 0.01, macro-: B = 1169, SE = 164.5, p < 0.0001) during the 3-year follow-up period. Macro-albuminuria group showed significantly higher level of HbA1c (B = 1.067, SE = 0.48, p = 0.027) and SBP (B = 11.89, SE = 4.25, p = 0.005) when compared to normal albuminuria group. Both normo- (B = –2.03/year, SE = 0.98, p = 0.038) and macro- (B = 200.76/year, SE = 86.31, p = 0.02) albuminuria groups showed significant annual UACR increment. Deterioration of renal function was found statistically significance in both normo- (B = –4.08/year, SE = 0.71, P < .0001) and macro- (B = 2.8/year, SE = 0.87, P = 0.001) albuminuria groups by reducing annual eGFR without significant difference in their decreasing slope in all 3 groups. Finally, the rate of major adverse cardiac events (MACE) was similar in all 3 groups.

Conclusions: Renin-angiotensin system blockers may protect DN patients from renal function exacerbation by reducing eGFR but not by preventing urinary protein loss in the abnormal albuminuria groups regardless of their degree of severity.

PE-60

A study of increasing access to diabetic retinopathy screening and referral if indicated

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Objective: The World Health Organization (WHO) statistics show that the possibility of suffering from blindness among diabetic patients is 10 to 20 times higher than that among people without diabetes. One researcher's study also shows that the prevalence of diabetic retinopathy ranges from 15% to 45%. As such, a simplified ophthalmoscopy, ease of screening and referral will hopefully increase the access to diabetic retinopathy screening and referral if indicated, and more importantly, the knowledge of and prevention against diabetic eye disorders in diabetic patients.

Method: Our Health Care Center has been equipped with ophthalmoscopy instruments for screening. Healthcare education and retinal photography may be performed at the same venue, improving the accessibility to screening in patients. The environmental features are designed to facilitate health promotion, and moreover, referral if indicated to our ophthalmologists is available for further follow-up and treatment.

Result: Through this program, 3,278 patients successfully joined our hospital's Diabetes Shared Care Network. During the period when the program was active (May 25, 2015 to October 23, 2015, for 5 months), 1,772 diabetic patients received screening. Compared with the same period in 2014, the number grew by 616 with a growth rate of 53.3%. Out of the 24 patients receiving ophthalmoscopy and indicated for referral, 14 were successfully referred to Ophthalmology, with a success rate of 58.3%. According to the analysis of the other 10 patients, 30% indicated that they did not feel ill while the 20% reported that they were under follow-up by Ophthalmology.

Conclusion: Education on preventing diabetic eye complications and simple access may substantially improve the screening of diabetic eye disorders. The referral if indicated, however, is paramount. Over 40% of diabetic patients still refuse to be referred to Ophthalmology; the referral rate is only 58.3%. The reason for most cases is that patients do not have eye discomfort. The pre-program ophthalmoscopy focused on the number of screened patients (quantity) rather than further ophthalmology care for patients (quality). In the light of this program, it is hopeful that diabetic patients may be accessible to more comprehensive care for their eyes as a result of increased referral rate in screened patients if indicated, as well as widespread concept of early screening and early treatment among healthcare professionals and patients.

PE-61

Correlation of glycemic control and arterial stiffness in patients with type 2 diabetes mellitus

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The PWV has been identified as an independent predictor for cardiovascular related mortality. The uncontroled T2DM induced hyperglycemic condition and caused depletion of endothelial nitric oxide (NO) which further leading to endothelial dysfunction.

In this study we showed that poor glycemic control in patients with T2DM is associated with abnormal arterial stiffness.

Methods: This is a cross sectional study. We recruited 50 patients with T2DM from out patient clinic. We excluded patient undergo Dialysis treatment, haemoglobin level <10 gr/dL, and all of the sample were performed baseline data including the blood pressure, HbA1c levels and all patient were measured the arterial stiffness using ba-PWV. We evaluate the relationship of HbA1c levels and the result of ba-PWV test.

Results: The mean of age was 58,98 ± 12,28 years, and the mean of HbA1c level: 7,69 ± 0,98%. The mean of PWV: 16,41 ± 2,43 m/second. Test results showed the correlation between HbA1c level and PWV and shows strong and significant result (r = 0,403; P < 0,05).

Conclusion: There was a significant correlation between Glycaemic control and arterial stiffnes in T2DM.

PE-62

DESMOND…Does it deliver for Aboriginal and Torres Strait Islander people

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Background: Traditional methods of health promotion and education such as the distribution of materials and didactic program delivery has had limited success in reducing the burden of chronic diseases, especially in rural and remote Aboriginal communities. Evidence behind using a patient empowerment approach is mounting, with many

organisations adopting client-centred approaches that empower individuals to build confidence and take responsibility of their health.
Despite high rates of type 2 diabetes and diabetes-related complications in Aboriginal communities, there is a lack of evidence based diabetes self-management programs designed for Aboriginal people. The DESMOND program is an evidence-based, quality diabetes self-management program where participants are supported to discover/share knowledge of their personal journey with diabetes.
The Diabetes Education and Self-Management Ongoing and Newly Diagnosed (DESMOND) program is one example of this. DESMOND is a client-centred diabetes education program that uses innovative adult learning theories and philosophies to build confidence, skills and promote diabetes self-management. Diabetes WA is trialling the effectiveness of the program, and this approach, in Australian Aboriginal communities.
Aim: This project aims to explore the cultural fit, effectiveness and sustainability of delivering DESMOND in Aboriginal communities.
Method: Diabetes WA developed and strengthened partnerships with a number of health services across the state of Western Australia to enable DESMOND trained diabetes educators to deliver the program to Aboriginal communities in Perth and regional Western Australia. Following completion of the program, attendees were invited to share their experience of DESMOND, its cultural fit and what changes they would recommend to improve the program.
Results: Qualitative data was collected and preliminary results show that Aboriginal participants felt respected by educators and open discussions, storytelling and hands-on activities were enjoyable. A number of minor adjustments have been made to the program, with the length of the program, access to biomedical results, and appropriateness of foods used presenting challenges. Evaluation measures are currently in place to assess participant's HbA1c, cholesterol and blood pressure three to six months post program.
Discussion: Adapting the DESMOND program to meet the needs of Aboriginal and Torres Strait Islander people has the potential to slow the progression of diabetes, impact biomedical results, and lead to a reduction in diabetes-related complications. Additionally the results of this trial will contribute to best practice evidence on effective, sustainable chronic disease education for Aboriginal communities.

PE-63

A novel scoring system for the early detection of diabetic kidney disease in patients with type 2 diabetes

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Background: Diabetic kidney disease (DKD) is one of the most common diabetic complications, as well as the leading cause of end-stage renal disease (ESRD) worldwide. At present, urinary albumin-to-creatinine ratio (UACR) and estimated glomerular filtration rate (eGFR) are the standard diagnostic methods for DKD. However, their accuracies are limited due to the heterogeneous disease nature, especially in type 2 diabetes (T2DM). DN_Score is a scoring system generated from the profiles of DNlite, a urinary biomarker panel composed of alpha2-HS-glycoprotein precursor (AHSG), alpha-1-antitrypsin (A1AT) and acid-1-glycoprotein (AGP). In this cross-sectional study, we investigated the correlation between DN_Score and clinical profiles of patients with T2DM, in order to evaluate its potential for diagnosis of DKD.
Methods: 308 patients with T2DM and UACR <300 mg/g were enrolled in this study. Phenotypic and biochemistry profiles were recorded. DN_Score was calculated according to the urinary DNlite profile. UACR and the composite Kidney Disease Improving Global Outcomes (KDIGO) classification system were used for assessing the severity and risk of DKD.
Results: There were 174 male and 134 female participants. The mean age was 60.64 ± 9.84 years. The mean DN_Score was 10.69 ± 0.9. The DN_Score in participants with UACR <30 and ≥30 mg/g was 10.42 ± 0.72 and 11.89 ± 0.63, respectively ($P < 0.01$). While classified by the KDIGO system, the DN_Score in participants with low, moderate-increased, high and very-high risk was 10.41 ± 0.72, 11.74 ± 0.7, 12.56 ± 0.29, 12.19 ± 0.03, respectively ($P < 0.01$). Intercorrelations of DN_Score were found with BMI, ACR, eGFR, blood pressure, fasting plasma glucose, HbA1c and plasma triglyceride level. After adjustment for significant covariates, DN_Score was significantly associated with UACR ($P < 0.01$)
Conclusions: DN_Score is correlated significantly with the traditional indicators of DKD in the early stage of the disease. Long-term outcome study will be necessary to validate the predictive role of DN_Score on the progression of DKD.

PE-64

The relationship between CVR-R and 2-year glycemic control in type 2 diabetic patients

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Background: Diabetic autonomic neuropathy (DAN) is a manifestation of diabetic neuropathy. DAN is frequently observed in patients with a long duration of diabetes and causes various symptoms once it advanced.
Autonomic nerve dysfunction can be expressed quantitatively by a coefficient of variation in R-R intervals (CVR-R).
Objective: The aim of the study was assess the relationship between the autonomic nerve disturbance and glycemic control in type 2 diabetic patients.
Material and Methods: Fifteen patients (male 7, female 8) with uncontrolled type 2 diabetes were enrolled.
All patients firstly were received with intensive insulin therapy.
HbA1c were measured every 2 month. ECGs were recorded in the resting position and 100 consecutive R-R intervals were processed computer. CVR-R were measured at baseline and 2-year later.
Results: At baseline, age, duration, BMI and HbA1c were 63.9 years old, 9.9 year, 24.2 kg/m^2 and 10.3%.
The mean HbA1c was significantly lower in 1-year's (6.9%) and 2-year's (6.9%) than the baseline's.
CVR-R was significantly higer in 2-year's (3.00%) than the baseline's (2.02%).
Conclusion: These results suggest that long-term glycemic control may ameliorate diabetic autonomic neuropathy.

PE-65

The effect of nutrition counseling on glycemic control and cognitive function in type 2 diabetic patients

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Objective: It's known that blood glucose was associated with cognitive function in animal studies. In addition, poor glycemic control has emerged as a possible risk factor for cognitive decline among elderly adults with diabetes mellitus (DM). Medical nutrition therapy is important in managing DM. The aim of this study was to evaluate the effects of the

nutrition counseling on glycemic control and cognitive function in type 2 diabetic patients.
Methods: This was a cross-sectional study. The participants were recruited from a systematic sampling of Keelung Hospital, Ministry of Health and Welfare, R.O.C. Patients who have history of type 2 DM for more than 10 years, aged between 50 and 70 years, and treated and followed by an endocrinologist were enrolled in the study. The patients who had received nutritional counseling were allocated into the intervention group (N = 26), and those hadn't received nutritional counseling were allocated into the control group (N = 13). The questionnaires of diet were collected to estimate the effectiveness of nutrition intervention by registered dietitian. The Mini-Mental State Examination (MMSE) was used as a tool to quantify cognitive capacity by psychiatrists. The body mass index (BMI) and metabolic profiles including glycated hemoglobin A1c (HbA1c), blood glucose, total cholesterol and triglyceride.
Result: All thirty-nine patients had completed the study measures and all of the data had been corrected for statistical analysis. The questionnaires score was significantly higher in the intervention group than the control group ($p < 0.02$). Although HbA1c in the intervention group was lower than the control group, there was no significant difference. There were also no significant differences in total cholesterol, triglyceride, BMI and MMSE score between the two groups.
Conclusion: Nutrition counseling can improve understanding of diet therapy in patients with type 2 DM. Long term follow-up is mandatory to clarify the effect of nutrition counseling on BMI and metabolic profiles.

PE-66
The effects of different Korean red ginseng fractions on diabetic progression and diabetic complication markers in obese diabetic NSY/Hos mice
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Object: Although Korean red ginseng (KRG) has been shown positive effects on glycemic control by improving insulin sensitivity and insulin secretory functions, the distinct roles of its specific fractions (saponin, SFR; or non-saponin, NSFR) is unclear. Moreover, the protective roles of KRG and its fractions on the transition from pre-diabetes to diabetes have been merely investigated. This study examined the effects of KRG, SFR and NSFR on various metabolic parameters in obese diabetic NSY/Hos mice
Methods: 12-wk-old NSY/Hos mice were fed 200 mg/kg/day or 400 mg/kg/day of KRG extract (KRG200, KRG400), SFR (SFR 200, SFR 400) or NSFR (NSFR 200, NSFR 400) in their diets for 24 weeks. The parameters for glucose homeostasis, diabetic complications, obesity, inflammation and oxidative stress were measured.
Results: KRG200 showed significantly lower fasting blood glucose; KRG200 and KRG400 showed significantly attenuated glucose intolerance in response to intraperitoneal glucose loading; SFR 200 and SFR400 showed significantly increased insulin secretory response to glucose as measured by insulinogenic index (IGI); KRG400, SFR 200, SFR400, NSFR 200, and NSFR 400 showed significantly attenuated oxidative stress parameter as measured by oxidized LDL-C; KRG400, SFR 200, and SFR400 showed attenuated diabetic blood-vessel complication marker as measured by advanced glycation end products (AGEs). (*all p compared to the non-treated control)
Conclusion: Although KRG, NSFR, NSFR 400 were not able to prevent transition from prediabetes to diabetes, KRG appeared to be more effective in glycemic control. However, each fraction may attenuate hyperglycemia-related complications to the different extent.

Psychosocial Status of Diabetes: What Have We Learned? Psychosocial Perspectives on Diabetes Caring and Health Behavior

PF-01
HbA1c is not a biomarker for depression in the era of DPP-4 inhibitors
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Patients who have both depression and diabetes mellitus (i.e. diapression) have the characteristics of poor glycemic control, high psychological stress and poor adherence to anti-diabetic medicine. Since 2009, DPP-4 inhibitors have become available for prescription in Japan. We did a cross-sectional study on 151 diabetic patients with regard to diapression at the Department of Psychosomatic Medicine, Fukuoka Tokushukai Medical Center in July 2013. Among the 151 diabetic patients, 22 non-type 2 diabetic patients were excluded, and the remaining 129 type 2 diabetic patients who met the inclusion criteria were asked to fill out 2 questionnaire surveys, the Beck Depression Inventory (BDI) and Fisher's Diabetes Distress Score (DDS). We conveniently categorized BDI ≥ 16 as depression group and BDI < 16 as non-depression group, we then compared the clinical features of the two groups. We retrospectively examined the HbA1c data of the 129 patients for 2 years from the day of survey of each patient. Despite the fact that the prevalence of diapression in 2013 was almost the same as previous study, we did not find a statistical difference in HbA1c between the depression and non-depression group. However, when we retrospectively examined the HbA1c data for 2 years since 2013 we found HbA1c from the depression group was higher than that from the non-depression group. We speculate that after DPP-4 inhibitors were made available for prescription in Japan, the HbA1c readings in the depression-group has improved. Thus, it might be difficult to detect diapression by looking at HbA1c alone. In order to look for patients with diapression, we need to use questionnaire survey tools such as BDI and DDS.

PF-02
Finding patients who do not have a sense of urgency to improve hyperglycemia
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Objectives: Achieving an optimal blood glucose levels is essential for diabetes treatment. Although most patients make efforts to control blood glucose levels, there are some who do not take actions against hyperglycemia, which could eventually lead to the development of diabetic complications. Finding such patients as early as possible and encouraging them to modify their behaviours might be important in diabetes practice. In this study, we described the prevalence of patients who do not have a sense of urgency to improve their blood glucose levels and investigated their characteristics.
Methods: A total of 1,262 diabetic patients who regularly visited Saiseikai Central Hospital and completed the Diabetes Treatment Satisfaction Questionnaire were included. In the questionnaire, the following question was asked; how often have you felt that your blood sugars have been

unacceptably high recently? Patients rated the perception of hyperglycemia from "0 (none)" to "6 (most of the time)." We defined patients whose answers were "0" despite their HbA1c of 7.0%≤ as patients who did not have a sense of urgency to improve their blood glucose levels. Clinical characteristics related to such patients were investigated using a logistic regression model which included age, sex, body mass index, use of insulin injection and the number of oral medications for diabetes.
Results: Of the 1,262 patients (mean age, 66; men, 75%; type 1 diabetes, 10%), 184 (15%) gave "0" as the answer in the question. The proportions of the patients who answered as such were 26% and 9% in those with HbA1c of ≤6.9% and 7.0%≤, respectively. All the patients who did not have a sense of urgency to improve their blood glucose levels were those with type 2 diabetes. Patients with older age were more likely to be such patients. The odds ratios were 2.76 and 4.06 in those aged 60–69 years and 70≤ years as compare to those aged ≤59 years. Patients with insulin therapy were less likely to be such patients. The odds ratio was 0.51 in relation to those without insulin therapy. On the other hand, sex, body mass index, or the number of oral medications for diabetes were not significantly related.
Conclusion: In the patients who did not achieve an optimal glycemic control (HbA1c ≥7%), 9% did not have a sense of urgency to improve their blood glucose levels. In order to detect such patients, patients with type 2 diabetes, older age and not using insulin injections were carefully examined in diabetes practice.

PF-03

Effect of memory training on cognitive function in diabetes patients

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Background: Diabetes greatly increases the risk of stroke. The incidence and disability rate of stroke is increasing, with a reported 75% of stroke survivors having some cognitive dysfunction.
Objective: To observe the effect of memory training on cognitive function in diabetes patients.
Methods: This was Quasi-Experimental Design sign. A total of 60 diabetes survivors enrolled in this study. They were randomly assigned to the experimental group (n = 30) and control group (n = 30). Participants in the experimental group under took 14 sections of memory training including stories, cards of daily items, association and so on. Each section lasted for 45–60 minutes. The control group received standard care only. Both groups were evaluated with the cognitive function (Mini-Mental State Examination, MMSE) before and after the intervention.
Results: After the intervention of diabetes patients through memory training, cognitive function of the experimental group ($t = -10.290$, $p < 0.001$) had significantly improved, compared with the control group and the cognitive function ($t = -3.936$, $p < 0.001$) have significant. Cognitive function was significantly improved in the experimental group. There were significant differences between the 2 groups in MMSE.
Conclusion: Memory training provided for the diabetes survivors is supported as effective strategies in promoting their cognitive function. Health care personnel should raise the awareness of assessing cognitive function for diabetes patients to enhance their quality of life for patients.

PF-04

Shift in parenting style in parents of children with type1 diabetes

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In rearing school-aged children with type 1 diabetes, one of major goals of parenting is to help their children maintain a normal level of blood sugar. However, with the growth of children and change in the course of diabetes, parents constantly experience new conflicts and challenges and need to adjust their original parenting style whenever necessary. However, there are limited studies focusing on understanding the experience of compelling parents to change their parenting style.
This study used qualitative in-depth interviews, and adopted purposive sampling to interview a total of 10 mothers of preschool children with type 1 diabetes. Age range of the parents was 33–49, and the average of disease period of their children was 4.1 years. The children aged 7–12 were a total of 4 males and 6 females. This study used content analysis for data processing and analysis. The results showed that when parents perceive the following 6 types of needs of their child, they adjust their parenting style afterwards: children need age-appropriate normal life; children need to be able to take care of themselves; children need to be treated fairly; children need happiness; children need their parents to be their friends; and lastly children need strict discipline.
It is suggested that the results can be employed to assist healthcare professionals and parents in understanding the contexts and factors faced by parents of school-aged children with type 1 diabetes during child-rearing, as well as be used as reference for future interventions in order to improve the quality of life of children with type 1 diabetes.

PF-05

The effect of healthcare word-of-mouth and behavioral status on improving patient self-management: 1-on-1 interviews with volunteers regarding their own experiences

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Background: Patient engagement and self-efficacy are complicated issues in chronic disease management. This qualitative research investigates key factors to improve the efficacy of patient self-management and find suitable word-of-mouth (WOM) engagement scenario based on the personality, psychological status, and behavioral maturity of the patient.
Method: Semi-structured one-on-one interviews were conducted with 10 volunteers who had been diagnosed with Diabetes Mellitus (DM). Each patient was interviewed for 50–60 min. The interviews included eight communication threads, and the interviewees were previously notified of the main topic in advance to ensure a relaxed interview. The interview would be terminated in case that any discomfort occurred during the process.
Result: The research results indicate that there is some relevant connection between the patient's characteristics and whether they like it or not by the positive or negative WOM. The medical WOM will affect the patient's self-monitoring, self-management, disease cognitive level, and

their behavior and expectation. It is easier to be accepted by patients and execute the plan when the volunteers spread out their self-experience through WOM than through professional health educator. The disease age and patient self-management maturity level of the theoretical model (TTM) are irrelevant to the clinical results.
Conclusion: It is possible to have the different effects and results when the patient's characteristics and medical WOM in different ways and social media. This dedication is reflected through patient's personal interesting topics, WOM inference model, and personalized on-line to off-line (O2O) interactive engagement. Not only does the patients' mental status affect their behavioral maturity when they are consulting with the diabetes volunteers, but the volunteers' training, the difficulty of the public health education, and the scale of the institution will affect the depth and coverage in the future research.

PF-06

Effects of community-based self-weighing campaign over holiday seasons: Effects on weight loss, rates of diabetes and prediabetes, and medical costs

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Objectives: The prevalence of diabetes is increasing with the westernized lifestyle and aging in Japan. Diabetes prevention is an urgent issue in Japan. Weight loss of overweight and obese people is a key to preventing diabetes. However, the body weight tends to increase in holiday seasons (Christmas through New Year). Long-term weight management programs are needed over such holiday seasons. The standardized mortality ratio (SMR) for diabetes is high in Kato City, Hyogo Prefecture, Japan. The aim of the present study was to evaluate the effect of a community-based self-weighing campaign on weight changes, rates of diabetes and prediabetes, and medical costs.
Methods: This study was a public health campaign using self-weighing twice a day held in Kato City from 2008 to 2015. Inclusion criteria included an age of 20–74 and BMI ≥ 23 kg/m^2. The goal of this campaign was to lose 3 kg of body weight over 3 months from November to February, every year. During this period, 47 shops in Kato City supported the campaign in various ways, for example, some fitness gyms reduced the joining fee, several restaurants offered special low-calorie menus, and a number of electronics stores sold weight scales at a bargain price. The city homepage delivered the effective and safe weight reduction program using a weight chart. Cable TV also delivered programs including diabetes prevention with a doctor, healthy eating with a dietician, and increased activity with an exercise trainer. Propensity score matching was performed to reduce the effects of confounding factors. Data were collected from annual health checkups and medical costs.
Results: Of 9,996 community dwelling people, 429 subjects (male: 38.9%, mean age: 60 ± 10 years, mean BMI: 25.9 ± 2.3 kg/m^2) participated in the program and reported weight changes. A total of 429 subjects in the intervention group were compared with a propensity score matched-control group of 429 subjects. After 1-year intervention, body weight and serum triglyceride levels in the intervention group were significantly decreased compared with the control group (−1.75 kg vs. −0.76 kg, respectively; $P < 0.001$). In females, HDL-cholesterol and HbA1c levels were improved compared with the control group. After 8-year intervention, rates of diabetes and prediabetes in Kato City were gradually decreased. Medical costs per person in Kato City was lower than in surrounding areas.
Conclusions: The findings suggest that this program had beneficial effects on weight changes, serum lipids, rates of diabetes and prediabetes, and medical costs.

PF-07

A follow-up study of treatment beliefs to insulin of patients with failure to oral hypoglycemic agents

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Aim: To learn about the difference in treatment beliefs of type 2 diabetes individuals before and after initiation of insulin treatment.
Methods: The follow-up survey was conducted on 101 outpatients in a medical center, who were recruited in a previous study for the Illness Perceptions, Treatment Beliefs to Insulin, and Intention to Insulin Therapy of Patients with Failure to Oral Drugs in 2013. About two years after the former study, 70 cases can be recalled in the outpatient department of the same hospital and agreed to participate this follow-up study by using a same questionnaire survey for measuring Insulin Treatment Appraisal Scale (ITAS) that had been collected in 2013. We compared the changes of treatment beliefs to insulin in patients who initiated insulin during this period vs. those who hesitated to start insulinization.
Results: Of the recalled 70 subjects, 27 subjects successively initiated insulin treatment (acceptance group), while 43 subjects had not initiate insulin treatment (resistance group). We found that when compared with the resistance group, the acceptance group showed significantly lower negative beliefs. In the resistance group, there were no significant changes of negative beliefs. The positive beliefs were significantly larger than the negative beliefs in acceptance group after they initiated insulin treatment. Cross-group comparison of the difference in positive and negative beliefs found that with the positive and negative beliefs offset mutually, the rest of positive beliefs in the acceptance group were significantly larger than those in the resistance group.
Conclusion: We found that for type 2 diabetes patients who failed on oral hypoglycemic agents, the acceptance group with insulin initiation had lower negative beliefs to insulin treatment, and higher positive beliefs. Higher positive beliefs of insulin treatment will help patients to initiate the insulin treatment.

PF-08

The correlation between health behavior and self-efficacy of obese diabetic patients

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Purpose: Due to the ever increasing global obesity population, the prevalence of obesity related diabetes is also gradually increasing. Obese diabetes patients are faced with higher risks of cardiovascular and other chronic comorbidities. Therefore, other than blood glucose management, weight related health management is also an indispensable treatment for these patients. Although health self-management is an important topic for diabetes patients, the lack of weight control is a difficulty that is faced by many obese patients. This research is to investigate the weight management behavior, self- efficacy, and social support for obese diabetes patients who have failed in managing their weights.
Methods: The primary data collection method utilized in this study was of questionnaire surveys. A total of 152

patients, who have started by have fail weight-loss trials, were conveniently sampled. The survey tools include "weight management knowledge scale", "weight management attitude scale", "weight management behavior scale", "weight behavior scale", " objective exercise management self-efficacy scale", " objective diet management self-efficacy scale", "self-esteem scale", and "social support scale". The descriptive and inferential statistical analysis of the data was performed with SPSS 20.0.

Results: The results in this study indicated that 62.5% of the obese diabetes patients have actually gained weight after undergoing weight management. These patients also reported low social support scores in their surveys. The number of weight-loss failures and weight management knowledge is positively and significantly correlated with each other ($r = .647$, $p < .004$). Furthermore, the number of weight-loss failures and self-esteem scores are correlated negatively, with statistical significance ($r = -0.327$, $p < .003$).

Discussion: The results from this study suggested that other than health education for weight management knowledges, the self-esteem and social support for diabetes patients undergoing weight-loss is also very important. The physiological support for weight-loss and the timely instruction on weight management strategies can be used for aiding obese diabetes patients in achieving sustained weight-loss for the goal of health self-management.

PF-09

Effects of nutritional care to diabetic elderly in the long-term care settings

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Diabetes mellitus is highly prevalent and increased in person aged 65 and older. Higher body mass index (BMI) value is at increased risk of hypertension, dyslipidemia and hypertension, also has greater relative risk of mortality than normal-weight diabetes elderly. Despite it is reasonable to set relaxed glycemic goals for some diabetes elderly, acute complications may occur in poorly controlled diabetes. This study evaluated the effect of different BMI value and fasting plasma glucose (FBG) on nutritional status and glucose-lowering medication use in diabetes elderly. Diabetes elderly who had stayed in a long-term care settings for over 6-months and ≥65 years of age were enrolled (n = 71). Exclusion criteria included with poor kidney function and edema. The mean age is 81.6 ± 7.8 years old. They were recorded weight and annually health-checked data. The results showed that after at least 6-months nutritional care, diabetes elderly had higher albumin and total protein concentrations in blood, moreover, FBG and triglyceride (TG) concentrations were significantly improved. FBG, cholesterol and triglyceride concentrations were all elevated when the BMI ≥27 Kg/m^2. Those with higher FBG concentration also had higher TG and cholesterol. In the comparison of different glucose-lowering medication use, treated with insulin had higher BMI value, FBG and triglyceride concentrations. Furthermore, after a period of at least 6-months nutritional care, originally FBG < 90 gm/dL subjects, the average FBG concentration significantly increased from 79.1 ± 7.1 to 92.0 ± 14.5 gm/dL. On the other hand, FBG concentration between 90–150 gm/dL and >150 gm/dL subjects, FBG concentration significantly decreased and located within normal range. In conclusion, although BMI values correlated with FBG concentration and further increasing the risk of dyslipidemia, but after professional nutrition care in long-term care settings, it could significantly enhance the nutritional status in diabetes elderly and effectively control FBG concentration, also helped to reduce the risk of hypoglycemia and hyperglycemia.

PF-10

The effectiveness of the Steno Balance Cards on complementary health management of poorly controlled diabetes patients

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Purpose: In this study, poorly controlled type 2 diabetes (T2DM) patients were investigated. The patients were divided into two groups based on the modality of psychosocial education, as follows: traditional Peer Education group (PE group) and the "Psychological Balance Dialogue" group (PBD group). To enhance the effectiveness of mental health self-management.

Methods: T2DM patients with HbA1c > 8% were recruited during September to October, 2015. Ninety-two patients were randomly assigned to the PBD group (n = 46) and the PE group (n = 46). The PBD group received instruction about diabetes knowledge using the "I feel" themed Steno dialogue picture cards to elicit group dialogue. The Steno dialogue picture cards were developed by the Danish Steno Diabetes Center. An illustrated Taiwan version was employed in the present study with five sub-themes. In the PE group generally receive instruction using an interactive peer education approach.

Results: In the PBD group, A1c decreased by 1.9% from 8.8 ± 1.7 to 6.9 ± 1.2%, whereas it was decreased by 0.7% in the PE group from 8.7 ± 1.2 to 8.0 ± 1.33%, with all $p < 0.05$. The issues raised in the PBD group were glycemic control factors, mainly with respect to the themes of challenging relationship and bodily infirmities. The Challenging Relations topics raised included that self-monitoring of blood glucose cannot be easily performed at regular times and is difficult to accomplish with demands of family life, and so on. The aforementioned action plan may help to reduce friction with family members. The Bodily Infirmities topics included in the conversation sessions were physical discomfort (malaise, frequent urination, bad temper) complications and psychological concerns which lead to poor sleep quality. The Action Plan was to meet the target to control blood sugar, reduce complications, and improve family relationships.

Discussion and conclusions: Three months after performing the psychosocial balance of dialogue sessions, the PBD group and the PE group completed a health-related quality of life questionnaire (SF-12). In the PBD group, the difference before and after showed that the psychological balance physiological score increased by 27.6, the mental component score increased by 28.6; in the PE group, the physiological score increased by 10.9, while the mental component score increased by 11.1. There was a statistically significant difference between the two groups ($P < 0.001$). The study concluded that psychological balance dialogue using Steno Balance Cards is beneficial for T2DM patients in glycemic control and quality of life.

PF-11

Diabetes related distress among patients with type 2 diabetes in Taiwan

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Purpose: To understand the quality of life and distress of patients with type 2 diabetes in Taiwan

Methods: The study was part of a nationwide survey conducted by Taiwanese Association of Diabetes Educators for examining the quality of diabetes care among Diabetes Health Promotion Institutes from year 2011 to year 2012. A subgroup of 981 adult diabetic patients were selected by randomized sampling from the nationwide survey sample and invited to complete questionnaires including the Diabetes Related Distress Questionnaire (DRDQ). DRDQ is composed of 15 items with 4-point Likert scale (1 = completely disagree, 4 = completely agree) and higher score indicate more distress. This study excluded patients with type 1 diabetes, leaving 947 patients with type 2 diabetes, of whom 486 (51.3%) was male. We analyzed the data of DRDQ, medical history from chart reviews and biomedical data (HbA1C) measured in the nationwide survey.
Results: The mean age of participants was 61.5(±11.9) (mean ± SD) years, with an average duration of 9.9 years of diabetes. The mean A1C was 7.6% (±1.5), with 27.9% being treated with insulin, 71.1% being treated with oral hypoglycemic medication, and 1.0% being controlled by diet only. The mean sum score of DRDQ was 30.5 (±8.91) with 70% of patients felt their diabetes was well regulated. The top four higher scoring items of DRDQ were "…afraid of my disease getting worse", "… feel stressed because of my disease", "…afraid of burdening my family/child", and "… diet control causes a lots of troubles to my life". DRDQ scores were significantly higher among insulin treated patients than oral medication treated or diet treated patients (32.9 vs. 29.7, $p < .001$). Patients with lower A1C also had lower DRDQ score ($r = .206$, $p < .001$). Age negatively correlated with DRDQ score ($r = -0.176$, $p < .001$). Female patients had significantly higher score in 8 items of DRDQ than male, but lower score in one item about reduced sexual life.
Conclusion: Patients with type 2 diabetes in Taiwan faced some degree of diabetes related distress. Most of patients concerned about their disease getting worse. Patients with insulin treatment, with worse glycemic control, or younger age had more distress than their counterparts. The results will be useful for health care providers to understand and improve quality of life in patients with diabetes.

PF-12
Utilizing transtheoretical model for transforming a uncooperative diabetes nephropathy patient into a cooperative patient undergoing hemodialysis

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Objectives: The most difficult aspect in diabetes education is behavioral corrections. Often the patients will not accept changes to their diet. However, inappropriate diet can lead to high blood glucose levels and that can result in other comorbidities. During the care period, the behavioral changes that resulted from the patients' prognosis were compared with the 5 transformative behaviors outlined in the "Transtheoretical Model". The case was transformed from pre-and contemplation phase, where they were undecided about diet changes, to the action phase, where they have started a healthy diet. It is with hope that the investigation can give us insights on the effects of behavior based education for nutrition therapy.
Methods: A 61-year-old male patient in a medical center in southern Taiwan was studies. The patient was emitted to the hospital due to peritonitis and septic shock that have resulted from ulcer perforation. The patient had histories of diabetes, hypertension, and a brain aneurysm surgery that was performed 20 years ago. The patient assessment included height, weight, body mass index, blood and urine biomarker levels, current medication, SGA, and other physiological examination and treatment. Furthermore, by using 24 hr regression questioning. The patient was given appropriate nutrition education and proper diet that is in accordance to his conditions as well as behavior phase. The patient was follow-up for the determination of the effect of the interventions.
Results: After underwent hospitalization interview, assessment, and educations, the patient, followed-up for 2 years after discharge, had improved his diet nutrition. His behavior changed from pre-contemplation (pre-hospitalization), to contemplation (during the first interview), and to become action and maintenance phase (after discharge). The nutrition diagnosis and education for the patient throughout the care process are: lack of diet and nutrition related knowledge in the beginning; familiarized with the six major food groups after persisting education; and the patient was finally about to distinguish and select a proper diet. However, patient's nephropathy also required a low protein diet; the miss selection caused his condition to worsen and required hemodialysis therapy. Therefore, the patient was educated further on protein adjustment and identifying food with sodium, sulfur, potassium, iron, and purine. Finally, the patient has started the habit of daily exercises.
Conclusions: The transtheoretical model emphasized the complexity of behavioral changes. This case study demonstrated a patient that was able to change his 20 year habits is a prime example for nutritionist. Therefore, the actual care experiences and results from this study are shared for future references.

PF-13
The co-occurrence of depressive symptoms and cognitive impairment and its relationship with diabetes self-care behaviors

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Background: Depressive symptoms or cognitive impairment is prevalent in older adults with diabetes. To date the epidemiology of the coexisting diabetes, depressive symptoms, and cognitive impairment among older persons has yet to be adequately characterized. Little is known about how depressive symptoms in combination with cognitive impairment associated with diabetes self-management.
Aim: The main aim of the present study was to investigate the co-occurrence of depressive symptoms and cognitive impairment in community dwelling older adults with diabetes and its relationship with specific diabetes self-care behaviors.
Methods: We analyzed data from two national sample of older adults (65 years or older) with self-reported physician-diagnosed diabetes (N = 1,034), who participated in the 2005 or 2009 National Health Interview Survey in Taiwan. The Mini-Mental State Examination (MMSE) was used to assess cognitive function. The Center for Epidemiologic Studies Depression Scale (CESD) was used to assess depressive symptoms. The study assessed self-care behaviors including adherence medication, exercise, healthy diet, and self-monitoring of blood glucose. We excluded 77 persons who had diagnosed dementia or depression and 86 persons who had incomplete data for MMSE or CESD. This resulted in 871 eligible participants for analysis. We conducted logistic regression on the effects of cognitive impairment and depressive symptoms on respondents' self-care behaviors after controlling for demographics, comorbidities, diabetics-related attributes, and health care utilization.
Results: We found that among participants with diabetes, 13.4% had depressive symptoms only, 16.4% had cognitive impairment only, and 8.8% had both depressive symptoms and cognitive impairment. After adjusted for other factors,

participants with depressive symptoms alone were less likely to adhere to exercise (Adjusted Odds Ratio [AOR] = 0.63; 95% CI = [0.39–0.99]). Participants combined with cognitive impairment and depressive symptoms were less likely to adhere to exercise (AOR = 0.39; 95% CI = [0.21–0.71]), to healthy diet (AOR = 0.30; 95% CI = [0.15–0.61]), and to self-monitoring of blood glucose (AOR = 0.46; 95% CI = [0.21–0.99]).
Conclusion: Our results highlight the combined presence of depressive symptoms and cognitive impairment was prevalent in older adults with diabetes. Furthermore, this combination was associated with worse self-care behaviors, especially exercising, healthy diet, and self-monitoring of blood glucose for older adults with diabetes. These findings highlight the importance of improving depressed mood and cognitive function in older to performing self-care behaviors for older adults with diabetes.

PF-15

Psychological benefits of peer support: Implications for peer support programs and diabetes self management and support in China

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Peer support is an effective strategy to initiate and sustain healthy behaviors and improve diabetes management. Peer support may also enhance psychological and emotional well being. With the huge need for basic diabetes education, however, thinking about peer support may overlook how it may benefit psychosocial status and how this may contribute to behavior change and improved health. Peers for Progress (PfP), developed to promote peer support worldwide, has been facilitating the adaptation of peer support programs for people with diabetes in China since 2009. Collaborative workshops with the Chinese Diabetes Society and Zhongda Hospital in Nanjing have trained over 500 physicians and nurses who have established more than 30 programs. Drawing from this experience and specific programs of the Beijing Diabetes Prevention and Treatment Association, Zhongda Hospital, and the Second People's Hospital of Guilin, three themes have emerged that highlight the psychosocial impact of peer support. First, peer support helps participants reduce negative emotions such as fear, distress, and feeling hopeless about their conditions. . Some participants particularly shared that because of the program they were no longer afraid of having diabetes. Second, by connecting with others "like them", participants often find a sense of belonging. They feel they are not alone anymore. In a group setting, some even referred to their groups as "families". Third, people gain happiness from finding others with whom they can share the journey of managing diabetes. Notably, participants reported that the happiness and feeling of acceptance were important motivators for them to engage in healthy behaviors and continue participation in the programs. Quantitative data reported by the programs support these qualitative findings. For example, despite being in a low-resource setting, the program in Guilin maintained an average of 90% participant attendance over a 2 year period. The programs in Beijing and Nanjing found improvements on measures of depressed mood as well as metabolic status. What program participants revealed not only illustrates the psychosocial benefits of peer support but also has important implications for peer support programs. Although peer support programs frequently is to emphasize building diabetes knowledge and self management skills, it also important to address rapport building among participants and other features that lead to psychological benefits. More generally, these observations from peer support underscore that relationships with others and quality of life are important features of diabetes management and key health-behaviors.

PF-16

The effect of mental disorders on glycemic control of patients with type 2 diabetes

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Objective: The relationship between mental illness and glycemic control in diabetic patients is largely unknown. We aimed to compare the characteristics and glycemic control in diabetic patients with and without mental illness, and to clarify the factors to achieve good glycemic control (HbA1c < 7.0%) 1 year after the first visit.
Methods: We retrospectively reviewed the patients with type 2 diabetes who visited outpatient department of internal medicine for the first time between December 2011 and April 2013. We investigated the patient background, history of diabetes and mental illness, and laboratory data at the time of the first visit, and the glycemic control after 1 year. We compared patients with mental illness and patients without mental illness, and also compared patients who achieved good glycemic control with patients who could not achieve by chi square test and t test. We analyzed the factors associated with the achievement of good glycemic control by logistic regression model.
Result: Among 186 eligible cases, 58% were male. Mean age was 62.5 years old, mean HbA1c was 8.4%, and mean duration of diabetes was 5.6 years. Of the 69 cases with mental illness, 27 had schizophrenia, 21 had mood disorder, and 8 had dementia. Patients with mental illness had significantly younger age (58 vs 65), higher BMI (28 vs 25) and shorter duration of diabetes (3.8 vs 6.6 year) than those without mental illness. There was no significant difference in mean HbA1c. The patients who could not achieve HbA1c < 7% after 1 year had significantly higher insulin usage rate before first visit (24 vs 7%) and longer duration of diabetes (9.4 vs 3.6 years). The patients with mental illness tended to have better glycemic control 1 year after the first visit. Logistic regression analysis showed longer duration of diabetes was significantly associated with lower rate of good glycemic control 1 year after the first visit (odds ratio 0.92 per annum, 95% confidence interval 0.88, 0.96, $p < 0.01$).
Conclusion: Our study showed the existence of significant differences in clinical characteristics of diabetic patients with and without mental illness, and also indicated patients with mental illness could achieve good glycemic control by appropriate treatment.

PF-17

Characteristics of type 2 diabetes patients with low aerobic exercise capacity

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Introduction: Indicators of aerobic fitness such as oxygen uptake (VO2) at anaerobic threshold (AT) are often used for functional evaluation of various populations. In patients with type 2 diabetes mellitus (T2DM), VO2 at AT (ATVO2) is decreased in comparison with that of a healthy population. Decrease in aerobic fitness reduces the effect of exercise

therapy. Clinically, there are patients with T2DM whose aerobic capacity is preserved and those whose aerobic capacity is not preserved. However, no studies have assessed the factor of aerobic fitness.

Purpose: The purpose of this study was to examine the characteristic differences between patients with T2DM whose ATVO2 was normal and those whose ATVO2 was low.

Method: Forty-six patients with T2DM (mean age: 43.9 ± 6.2 years, mean HbA1c: 10.3 ± 2.4%) underwent expiratory gas analysis while performing incremental exercise test on a cycle ergometer 3 h after eating. The ramp protocol (20 W/min) was used. VO2, carbon dioxide output (VCO2), and maximum lipid oxidation were measured during the exercise test. The amount of lipid oxidation (g/min) during exercise was calculated using the Bruzstein formula. AT was evaluated as ventilation threshold using the V-slope method. ATVO2 was compared with the standard value of the Japanese Circulation Association. The subjects were divided into two groups based on normal or low ATVO2. Normal and low AT groups were defined as ATVO2 higher than 90% and lower than 90% of the standard value, respectively. We compared the body mass index (BMI), HbA1c, fasting plasma glucose, skeletal muscle and fat amount, visceral fat sectional area, maximum lipid oxidation amount, and respiratory quotient at rest between normal and low AT groups using t-test or Mann–Whitney U test. A software package (IBM SPSS Statistics Version 22) was used with a significance level at <5% for statistical analysis.

Result: The normal and low AT groups had 15 and 31 patients, respectively. The following characteristics were observed in patients in the normal AT group as compared with those in the low AT group with statistically significant difference: lower BMI ($p < 0.01$), lower skeletal muscle amount ($p = 0.02$), higher fat amount ($p < 0.01$), lower visceral fat sectional area ($p = 0.04$), and higher maximum amount of lipid oxidation ($p < 0.01$).

Conclusion: In patients with T2DM, high BMI, high fat amount, and low lipid oxidation at exercise decreased aerobic fitness. It is suggested that aerobic fitness in patients with T2DM is determined by lipid metabolism.

PF-18

The association between self-reported sleep quality and arterial stiffness

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Sleep has a major role in maintaining health, and is involved in the regulation of metabolism, vascular and autonomic nervous functions. Short and long sleep duration, and poor sleep quality are associated with an increased risk of cardiovascular disease (CVD). In addition, epidemiologic studies show that poor sleep quality is associated with cardiovascular risk factors, such as diabetes, obesity, and metabolic syndrome. Furthermore, poor sleep quality without change in total sleep time lead to insulin resistance and increased sympathoadrenal activity.

Arterial stiffness, a decrease in the compliance of the central arterial system, is recognized a surrogate marker for cardiovascular disease. Apart from ageing, many pathophysiological conditions are associated with increased arterial stiffness, such as hypertension, diabetes, obesity, hyperlipidemia, smoking, and metabolic syndrome. In addition, previous studies suggest that insulin resistance is associated with arterial stiffness. Although sleep quality and arterial stiffness are both associated with insulin resistance, their interactions have not been clarified. Therefore, the aim of this study is to investigate the association between sleep quality and arterial stiffness.

Cross-sectional data were collected from a decoded database of the National Cheng Kung University. Subjects with history of hypertension, diabetes, coronary heart disease, old stroke, peripheral atherosclerosis with an ankle-brachial index less than 0.95, amputation of either lower limb, alcohol consumption of greater than 30 g/wk, and those taking medications influencing blood pressure, plasma glucose, and lipid profile were excluded. Hospital. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI). Arterial stiffness was measured by brachial-ankle pulse wave velocity (baPWV).

Of the total 400 participants enrolled, 200 were poor sleepers (PSQI > 5) and 200 were good sleepers (PSQI ≤ 5). Poor sleepers had significantly higher baPWV, systolic blood pressure (SBP), diastolic blood pressure (DBP), and prevalence of hypertension than those of good sleepers. The multivariate logistic regression analysis showed that age, baPWV, and snoring were independent determinants of being poor sleepers after adjusting for gender, body mass index (BMI), SBP, fasting plasma glucose, creatinine, lipid profile, alcohol drinking, tea and coffee consumption, smoking habit, and habitual exercise.

Poor sleepers had a significantly higher baPWV value than those of good sleepers. Furthermore, age and baPWV were associated with being poor sleepers independently of cardiometaolic risk factors. In clinical practice, subjects who complain sleep disturbance should be evaluated for the presence of cardiometabolic risk factors, including baPWV.

PF-19

The applicability research of portion-controlled tableware developed by Taiwanese Association of Diabetes Educators in common Chinese food

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Background and aims: In 2013, Taiwanese Association of Diabetes Educators (TADE) developed a set of portion-controlled tableware for diabetes who need diet control to achieve their goals. In this research, we investigated the applicability of this tableware for common Chinese food.

Method: We chose common Chinese food in different categories including staples, meat and vegetables from the menu which provided for hospitalized patients in Chen-Hsin Hospital and served them with the TADE portion-controlled tableware according to its instructions. We investigated the quantitative rules of dish arrangements by elaborating the quantitative functions and visual impression.

Results: The scales labeled on the bowl are accurate for staples, such as rice, gruel and noodles. Food cut into small cubes or grounded meat was easy to fill the oval-shaped sections and facilitating for portion estimation. We modified the quantitative instructions of TADE plate when we encountered mix-meat-vegetable dishes and ingredients with loose composition which often seen in Chinese food services, such us fired egg with meat, steamed egg and dried fish floss, and re-defined a portion filling one small section of the TADE plate as 0.5 instead of 1 exchange of soybeans, meat and eggs. When meat served with larger portion such as chicken leg or pork chops, we suggest to place them in another container and defined as 2 exhange of meat.

Conclusion: By demonstrating more ways to arrange dishes and providing quantitative rules will enhance the practicality of applying TADE tableware. Furthermore, this TADE tableware is appropriate not only for diabetic portion teaching but also for personal use at home.

PF-20

Predictors of polypharmacy among diabetes in Japan

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Objectives: According to published works, polypharmacy can be simply defined as the use of multiple medications by a patient. It is clearly highlighted that the use of greater number of prescriptions has been independently associated with increased health care cost and risk for adverse drug events. Polypharmacy has been shown to be associated with many risk factors, such as renal function and age. However, whether diabetes is a risk factor of polypharmacy is not well established. The present study aimed to determine the predictors of polypharmacy among diabetic patients in Japan.

Subjects and methods: We recruited 6,706 in-patients (with diabetes n = 2,766, without diabetes n = 3,940) between January 2014 and January 2016. We defined polypharmacy as the concurrent use of six or more prescriptions. To assess the odds ratio (OR) of polypharmacy, we constructed a logistic regression analysis, having adjusting for age, gender, BMI, eGFR, number of prescriptions and with or without diabetes.

Results: At baseline, age, BMI, eGFR and number of prescriptions were significantly different between patients with and without diabetes (age; 69.6 vs.55.8 years, BMI; 24.1 vs.22.4 kg/m^2, eGFR; 57.3 vs. 67.5 mL/min/1.73 m^2, number of prescriptions; 7.4 vs. 4.9, respectively). In multivariate logistic regression analysis, diabetes (OR: 2.8, 95% CI; 2.5–3.1), age (65–<75 y: 1.6, 95% CI; 1.4–18, 75 y≦: 3.0, 95% CI; 2.7–3.5) and CKD (G3: 2.0, 95% CI; 1.6–2.5, G4: 3.3, 95% CI; 2.3–4.7, G5: 8.1, 95% CI; 5.4–12.2) were associated with the presence of polypharmacy.

Conclusion: This study shows that diabetes, as well as the elderly and CKDG4-5, was associated with the presence of polypharmacy. In diabetic patients, prescribing and managing multiple regimens need regular reviews and evaluations to ensure that medications are appropriately and effectively continued. Patients and providers need to regularly discuss the goals of therapy, and address concerns about adherence, unnecessary healthcare cost, avoidance of adverse health outcomes, and other matters of significance in achieving an individualized and realistic therapeutic plan.

PF-21

Using models of group therapy in diabetes patients with enhancing the effectiveness of self-health care

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Objective: Patients with psychosomatic disorders and diabetes, often because of lack of diabetes knowledge and strong oral, lazy, lack of regular exercise and diet control concepts, nor received conventional drug therapy, so the concept of group therapy in patients with diabetes amounted to 5 to help promote self-health care of patients with diabetes efficacy and self-control, adjustment capabilities.

Method: 1. Notwithstanding the time 60 minutes per week, a total of 3 groups to teach diabetes knowledge. 2. the integration of professional communication and assessment: the note nutritionist, and diabetic diets and dietary education and designed by occupational therapists easy sport, in 2 times a week, 1 hour per day group therapy time. 3. implementation of the plan of care: encouraging the daily 20-minute morning exercises, and movement of every 10 minute walk after meals, and by assessing the degree of implementation of the active evaluation.

Results: (A) enhancing medical compliance and trust: through the curriculum, from passive to active acceptance of oral medications and insulin regular treatment of the concept. (B) to promote positive learning and motivation for change, health habits: understanding the concept of diet and exercise to control blood sugar and learn healthy lifestyle. (C) restore confidence: through the power of group therapy affect learning and change motivation, and the capacity of maintaining healthy behaviors.

Application: Using the power of group therapy to strengthen efficiency of self-health care, mining groups implement treatment activities, strengthen compliance and sustainability, this programme guide nursing staff to provide quality care, for health promotion purposes.

PF-22

Associations between insomnia and glycemic control in Hong Kong Chinese patients with type 2 diabetes

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Increasing evidence suggest insomnia may play a role in increasing insulin resistance and worsening glycemic control in patients with type 2 diabetes. Around 10% of Hong Kong Chinese adults suffered from insomnia while the rate of insomnia in diabetic population is under-explored. We aimed to explore the rate of insomnia in Hong Kong Chinese patients with type 2 diabetes and its associations with glycemic control. This was a cross-sectional study including a consecutive cohort of patients with type 2 diabetes recruited from the Hong Kong Diabetes Registry between July 2010 and June 2015. Shift workers and patients with obstructive sleep apnea (OSA) were excluded. Indices of glycemic control including fasting plasma glucose (FPG) and glycated hemoglobin (HbA1c) were measured and sleep parameters were assessed by validated questionnaires including Insomnia Severity Index (ISI). Insomnia was defined as ISI score >14 whereas HbA1c ≤ 7.0% was considered as reaching glycemic goal.

A total of 4,786 patients with type 2 diabetes were enrolled during the study period. After excluded shift workers and patients with OSA (11.8%), 4,221 eligible patients were included in this analysis. Mean age was 54.0 ± 8.6 (standard deviation, SD) years and 57.9% were men. Median disease duration of diabetes was 7.0(3.0–11.0) (inter-quartile range, IQR) years. Mean score of ISI was 6.5 ± 5.6. Among the cohort, 9.7% had insomnia. Compared to non-insomniac subjects, type 2 diabetic patients with insomnia had higher FPG (7.9 ± 3.1 mmol/L versus 7.5 ± 2.4 mmol/L, P = 0.022) and higher HbA1c (7.7 ± 1.7% versus 7.5 ± 1.4%, P = 0.005), as well as longer disease duration of diabetes [8.0 years (IQR: 3.0–14.8) versus 7.0 years (IQR: 3.0–13.0), P = 0.026]. After adjustment for age, gender, BMI and disease duration of diabetes, insomniac state was positively associated with FPG and HbA1c (P = 0.030 and P = 0.012 respectively). Higher percentage of type 2 diabetic patients with insomnia did not reach glycemic goal compared to their non-insomniac counterparts (59.4% versus 52.9%, P = 0.02).

Insomnia is prevalent in Hong Kong Chinese patients with type 2 diabetes. Type 2 diabetic patients with insomnia were associated with poorer glycemic control compared to type 2 diabetes without insomnia.

PF-23

The validation of the community pharmacists' motivation to lifestyle support for diabetics: the effect of "3 star pharmacists training program"

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Background: Type 2 diabetes mellitus (T2DM) is rapidly becoming one of the major health issues of the 21st century. Approximately 7.2 million people have diabetes in Japan. Though most of Japanese T2DM patients who is cared by primary care settings, the shortage of medical resources has become a serious problem. Pharmacists are well placed to develop an expanded role in diabetes care. The community pharmacy offers an excellent opportunity for patients to access education and support. So we started COMPASS project which is a randomized controlled trial (RCT) for T2DM patients in community pharmacies in Japan.
"3 star pharmacist training program"
It was made originally for intervention study: COMPASS project. This study was to evaluate of the community pharmacists' support for T2DM to HbA1c. Community pharmacists in this study were trained in motivational interviewing and coaching skills within 3 minutes in this program. After finishing COMPASS study, we named the program "3 Star Pharmacist program" and made it available to community pharmacists in some city of Japan, Tokyo, Osaka and Fukuoka. This program was structured 3 steps (3 days, 8 hours) and it practiced for 3 months 3 times.
Objective: To evaluate the effect of "3 Star Pharmacist training program" which trained for community pharmacists every 3 months a day.
Methods: To evaluate the effect of "3 Star Pharmacist training program" which trained for community pharmacists every 3 months a day, web survey was carried out in December 2015 for 87 trained and certified pharmacists who attended the program in 2014. Baseline data was collected by the same questionnaire before training on paper. This describes the result of the questionnaire which include knowledge, confidence and job satisfaction of the before and after baseline data over 1 year.
Results: Total 65 community pharmacist reply the web questionnaire for a month (response rate 75%). The score of Diabetes education knowledge (out of 20) was significantly difference 14.6(2.1) to 17.1(1.5) and the score of Diabetes education confidence (out of 6) was also significantly improve 3.5(0.8) to 4.1(0.8) and maintain for 1 year.
Conclusions: We have launched a new training program for community pharmacists named "3 Star Pharmacist Training Program" based on RCT. This program is expected to contribute to the improvement of patients' QOL in real world settings.

PF-24

The relationship between quality of life and health beliefs in diabetes patients

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Background: The purpose of this study was to explore the relationship of quality of life and health belief among diabetic patients.
Methods: The cross-sectional study was conducted on diabetic patients referred to health service center in Taichung city, Taiwan. The data was collected by a questionnaire including Diabetes 39 (D-39) Instrument Evaluation and health-care belief questionnaire and demographic variables. The Diabetes 39 (D-39) Instrument Evaluation, containing five dimensions: energy and mobility (15 items), diabetes control (12), anxiety and worry (4) social overload (5) and sexual behavior (3), was used. Health Belief Questionnaire (18 items), contains dimensions of perceived benefits, barriers, severity, and disease susceptibility.
Results: The range of their ages was 26–75 with mean 55.2 (SD = 10.66) years. Fifty-Three participants were enrolled. About 13.2% are aged 51 or more, 38.5% are between 36–50 years, and 50.9% are between 18–35 years. About 43.3% of them were married. The education level of about 58.5% of participants had a university degree. Fifty-three participants were enrolled. About 13.2% are aged 51 or more, 38.5% are between 36–50 years, and 50.9% are between 18–35 years. About 43.3% of them were married. The education level of about 58.5% of participants had a university degree. The dimension of disease awareness in Health Belief has the highest agree, especially in the item of "worry about their diabetes complications, include heart disease, nephropathy and retinopathy". The dimension of anxiety and worry in Quality of Life demonstrate the highest agree, especially in the item of worry about quality of life after diagnosis of diabetes. There was a correlation between barriers in activity and "vitality and motility", "diabetes control", and "anxiety and worry". Duration of diabetes was correlated with "perceived benefits" dimension of Health Belief. Treatment modality was correlated with the "anxiety and worry" dimension in Quality of Life, in particular, the insulin pump users has the highest score.
Conclusion: Overall, Health Belief was correlated with Diabetes quality of life, duration and treatment modality may affect health belief and quality of life.

Diabetes Education: Focus on Minds

PG-01

The effect on condition control among type 2 diabetic patients using diabetes conversation map tools

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To probe the patients' glycated hemoglobin levels and weight change after their participation in a small group health education session that introduced "diabetes conversation map tools" to them. The sampling object is type 2 diabetic patients who regularly received medical attention at a certain medical center in southern Taiwan and were on medication but still with a glycated hemoglobin level of over 7%. Among them, 29 were willing to take part in this conversation map group health education session, which took place between March 19th and August 18th, 2015. The differences in the patients' glycated hemoglobin levels and weight change before and after the session were analyzed by paired sample T test. The result shows that the improvement in glycated hemoglobin level of those who attended the session is statistically significant (8.3 ± 1.3 vs 7.5 ± 0.9, $p < 0.01$), while their weight change is statistically insignificant (67 ± 15.8 vs 66.5 ± 15.8, $p = 0.112$). After the session, the improvement in percentage of patients achieving the exercise goal of ≧150 minutes per week (34.5% to 62.1%) and of self-monitoring of glucose ≧twice per week (51.7% to 72.4%) has shown that the effect of patients' self-care action has improved. That is to say, diabetes conversation map tools can help diabetic patients with their self-management, and their blood glucose control as well as quality of life can be improved accordingly.

PG-02

The comparison of different health education tools and their effects in glucose management for type II diabetes patients

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Purpose: Experts estimated that in 2035, there will be approximately 5.9 billion diabetes patients worldwide. Studies have indicated that the primary cause of death for diabetes patients were cardio vascular diseases and other comorbidities. Therefore, long term blood glucose management has been the target for diabetes patients worldwide, and many diabetes health education tools have been established for this same purpose. This study was aimed to investigate the blood glucose management efficiencies of each of the different diabetes management conversation tools.
Material and Method: This study was a randomized controlled trial that enrolled type II diabetes patients. The participants were randomly allocated into the "conversation map group" and "steno group", in a 1:1 ratio, with 143 and 150 patients, respectively. A questionnaire was used for data collection at pre- and 1 month post-intervention.
Result: Multivariate linear autoregressive models were used for comparing the corrected pre-intervention values and their related factors for the steno and map group. The results indicated that the steno group had significantly improved post-intervention glycated hemoglobin ($\beta = 0.171$) and post-prandial blood glucose ($\beta = 0.136$) than the map group. Additional, $\chi 2$ test and pair t-test, performed by SPSS 20.0, determined that post-intervention glycated hemoglobin, fasting blood glucose, postprandial blood glucose, diet, and exercise were all improved for both of the groups. Furthermore, the steno and map group demonstrated significant ($p < 0.05$) glycated hemoglobin (HBA1C) reductions of 2.37% and 1.28%, respectively.
Conclusion: The results in this study demonstrated that both diabetes management conversation tools can be used to improve patient blood glucose levels and behavior. Furthermore, the steno group was demonstrated to have has better HBA1C improvement than the map group. Therefore, any of the two health education tools can be used to improve patient blood glucose. However, further investigation is required to determine the effect mechanisms and the specificities of each health education tools.

PG-03

Fruit-eating habit in Hong Kong people with diabetes

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Introduction: Fruits are rich in carbohydrate, fibre, antioxidants, and phytochemicals. Observational studies shown that high levels of fruit and vegetable intake are associated with increased psychological well being, reduced risk of CVD and type 2 diabetes. As a result, many national and international guidelines recommend at least five portions of fruit and/or vegetables a day (a portion equates to 80 g). In Hong Kong, Department of Health has recommended at least 2 servings of fruits and 3 servings of vegetables daily as part of a balanced diet. However, such guidelines are not always followed, especially in patients with diabetes.
Objectives: This study is to examine the fruit-eating habit in Hong Kong people with diabetes.
Methods: An interview based questionnaire was distributed to consecutive patients attending the diabetic centre of Tung Wah Eastern Hospital in the first week of January 2016. The questionnaire included demographic data, fruit-eating habit, and some basic knowledge about the beneficial effect of fruit.
Results: Of 374 questionnaires received for evaluation, 52.6% (197) were male, 47.3% (177) were female, mean age were 63.2 and 64.3 years old respectively.
Less than half (44%) reported eating fruit every day and only 24% (90 patients) knew the correct serving of fruit intake. Patients had different reasons for not eating fruit daily, 56 patients thought that eating fruit everyday is not necessary, 26 of them said that "diabetic patient should not eat fruit". On the other hand, 28.3% (106 patients) thought that excess fruit intake would not cause weight gain. Furthermore, many of them had misconception about the choice of fruit, esp. durian and water melon.
Conclusion: As part of healthy diet, 2 servings of fruits daily are recommended. This study showed that Hong Kong diabetic patients have some misconception about the choice and amount of fruit intake. To promote health in patients with diabetes, the benefit of fruit-eating can be introduced during consultation, and also through poster, information leaflets and health talk.

PG-04

Improvement of blood glucose in type II diabetes mellitus after health education

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Objective: According to the guidelines of diabetes mellitus healthcare 2015, medical professionals should do the immediate and right intervention to prevent the complications in patients with diabetes mellitus. Our study aimed to evaluate the improvement of blood glucose after intervention of diabetes mellitus educator.
Methods: We divided participants with glycated hemoglobin over 7% to experiment and control groups. The experiment group received health education by diabetes mellitus educator face to face every month and health education by telephone every two weeks. The content of health education included diet, exercise, self-monitor of blood glucose, symptoms and managements of hypoglycemia or hyperglycemia. After three months, we analyzed the effect between the two groups.
Results: In experiment group, there are 7.8 ± 2.5 times by telephone and face to face each participant. The times of blood sugar test were 56.7 ± 42.5. There were fifteen participants (50%) with hypoglycemia. Nine (60%) of them can do the immediate managements and others can speak the managements of hypoglycemia after reeducation by diabetes mellitus educator. There were six participants (20%) with the diet record, fourteen (46.7%) participants took the 24-hour recall record to improve diet and medication adjustment in seven (23.3%) participants. There was significant improvement in glycated hemoglobin from $9.7 \pm 2.0\%$ to $7.4 \pm 1.2\%$ ($P < 0.05$). The fasting blood glucose was significant improvement from 171.0 ± 66.4 to 126.5 ± 46.6/mg/dL ($P < 0.05$). The postprandial blood glucose was significant improvement from 262.0 ± 141.7 mg/dL to 179.9 ± 70.6 mg/dL ($P < 0.05$). The glycated hemoglobin showed significance between experiment ($7.3 \pm 1.2\%$) and control group ($8.8 \pm 1.5\%$) in post-test. The fasting blood glucose showed significance between experiment (126.5 ± 46.6 mg/dL) and control (182.5 ± 94.3 mg/dL) group.
Conclusions: There was improvement in glycated hemoglobin and fasting blood glucose by using face to face and telephone health education. However, the rate of diet record was low, there was difficult to manage the abnormality of blood glucose after 24-hour recall record of diet. Besides, the blood glucose test strips were consumables, the participants cannot immediate check the blood glucose after the intervention. In the future, we can calculate the blood glucose test strips by

evaluating the blood glucose level and enhance the management of postprandial blood glucose.

PG-05

Metformin for patients under iodine-based contrast medium

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Background & Aim: Metformin is the first choice for diabetes having no contraindication. Metformin is metabolized by kidney. Studies indicate that the risk of contrast media-induced nephropathy is higher for diabetes with renal impairment than those with normal renal function. Considering the risk of contrast-induced nephropathy, patients who take metformin should use iodine-based contrast medium carefully. According to ESUR Guidelines on Contrast Media (2011), "patients receiving intravenous contrast medium with an eGFR between 30 and 44 mL/min/1.73 m^2 should stop metformin 48 h before contrast medium and should only restart metformin 48 h after contrast medium if renal function has not deteriorated. For patients with eGFR less than 30 mL/min/1.73 m^2 (CKD 4 and 5)…, metformin is contraindicated and iodine-based contrast media should be avoided." The aim of this study is to investigate the compliance with ESUR Guidelines in our hospital.
Methods: A retrospective study was conducted. We started a chart review among patients who used both metformin and intravenous iodine-based contrast medium from June to November 2015. The information collected includes: date of examination on iodine-based contrast medium, eGFR level, date of eGFR measurement, and nephropathy events if any.
Results: 148 results were analyzed, in which 6 patients had eGFR within 30–45 mL/min/1.73 m^2 and 1 patient had eGFR below 30 mL/min/1.73 m^2, and the 7 patients used both metformin and iodine-based contrast medium. 3 of the 7 patents were examined urgently. Therefore, they did not discontinue taking metformin. There were other 5 patients who did not measure their renal functions within the 6 months before examination and still took the examination using iodine-based contrast medium. No contrast media-induced nephropathy was found.
Conclusion: Education for doctors and patients is important for preventing contrast media-induced nephropathy. For doctors, it is needed to measure patients' renal function before and after the examination using iodine-based contrast medium for patients who take metformin. A reminder toolbar may be established via computer system to automatically remind doctors to measure patient's renal function when the patient attends an examination. Additionally, it is required to provide enough information to patients before and after examination. Education handouts should include (1) the risk of contrast media-induced nephropathy; (2) the timing of stopping and restarting metformin; (3) the importance of drinking sufficient water; and (4) contact information for consultation when adverse reactions happen. Providing information through APPs of smartphones can also be considered. Providing education case by case can also improve safe use of medication.

PG-06

Analysis of correlation between eating speed and blood glucose control among diabetic patients from a medical center in southern Taiwan

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Objective: This study is to probe patients' eating speed's effect on their blood glucose and weight control, as well as the factors for the effect.
Method: Between December 21st and 31st, 2015, during the nutritionist health education session, diabetic patients of Metabolism Department of our hospital were randomly selected. Using questionnaire, nutritionists assessed data of the patients' dietary carbohydrate consumption collected based on their recollection of their diet for the past 24 hours. Eventually 200 patients' data were collected. With patients doing exercises, using insulin or not sticking to one diet portion regularly excluded, 69 patients regularly having three portions of carbohydrate for dinner were selected. They were grouped up into five by their eating speeds. The data were analyzed by ANOVA.
Result:

1. The questionnaire shows male patients' eating speed is faster than female patients'. The speed difference is statistically significant and correlated with gender.
2. Groups 1 and 2 have the fastest eating speeds, where their patients' average glycated hemoglobin levels and BMI levels are higher than those of three other groups. Possible factors are as follows:
    1. Groups 1 and 2 have the highest average age and proportions of patients with full dentures, which is statistically significant and correlated with their eating speed.
    2. Groups 1 and 2 have relatively lower education levels, which is statistically significant and correlated with their eating speed.
    3. Groups 1 and 2 have the largest in-work population, which is statistically significant and correlated with their eating speed.

Conclusion: Diabetic patients' eating speed has an effect on their blood glucose level and weight control. The factors for the effect are correlated with gender, age, education level, employment status and the presence of denture.

PG-07

Analysis of the effectiveness of patients' self-management of exercise and control of blood glucose

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Purpose: To investigate the effectiveness of exercise on blood glucose and weight control in patients.
Method: 1,170 patients in the TQIP were randomly recruited from the outpatient Division of Metabolism & Endocrinology at the hospital from January 2015 to March 2015. Retrospective chart review was conducted to screen patients' drugs and diets and only stable patients with no changes within one year were included. 281 patients met the criteria and were screened into 230 with regular exercise and 51 without regular exercise.
Results: 1. Glycated hemoglobin fell from 7.21% to 6.78% ($P < 0.001$) in the continued exercise group after 1 year. 2. 79% exercised for ≧150 minutes per week and glycated hemoglobin fell from 7.12% to 6.75% ($P < 0.001$) in this group after 1 year; 10% exercised for ≧90 minutes and <150 minutes ($P < 0.001$) and glycated hemoglobin fell from 7.54% to 6.94% after 1 year; 11% exercised for >90 minutes per week and A1C fell from 7.48% to 6.89% ($P < 0.079$) after 1 year. 3. Average weight of subjects in the no exercise group was 68.73 kg and decreased by 0.52 kg ($P < 0.33$) after 1 year; average weight of subjects in the exercise group was 67.71 kg and decreased by 0.91 kg after 1 year ($P < 0.25$).
Conclusion: As a healthcare educator, improving patients' willingness to exercise is a major challenge. Without any other influencing factors, if subjects exercise for over 90 minutes per week in frequency, it will be significant for controlling blood glucose and glycated hemoglobin and body weight will also remain stable.

PG-08

A probe into the improvement in HbA1c among diabetic patients on multiple insulin injections along with carbohydrate substitute diet

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Many factors for a good control of diabetic conditions are in the hands of the patients themselves, including diet content and portion, approaches to regular monitoring of blood glucose level, patients' physical activity levels, and the consistency in medication dose taken. Sticking to a fixed diet portion regularly and taking medication in line with doctor's advice can substantially improve blood glucose level control and reduce the occurrence of diabetes-related complications, such as coronary artery diseases, kidney diseases and the risk of nerve injury.

Accurate carbohydrate calculation and more frequent blood glucose monitoring are associated with reduction in type 1 diabetic patients' glycated hemoglobin levels. This study is to probe the improvement in glycated hemoglobin levels among type 1 diabetic patients on multiple insulin injections along with carbohydrate substitute diet.

Method: Type 1 diabetic patients receiving more than 4 insulin injections were lodged and boarded for 1 to 2 weeks in the hospital. During their stay, they followed a fixed portion of carbohydrate in each meal and a fixed amount of exercise. Their blood glucose levels were checked before the 3 meals, 2 hours after the 3 meals and before sleep, for a total of 7 times daily. Pre-prandial and postprandial targets for blood glucose level were set. Nutritionists and health educators engaged in teaching the patients how to keep their own dietary diaries and educating them about carbohydrate substitute diet, for them to find out about their own carb-to-insulin ratio based on the carbohydrate intake/activity level and the flexible titration of insulin. Eventually, 25 cases were included in this study, whose HbA1c and total insulin changes were tracked in month 0, 3, 6, 9 and 12. The average HbA1c before the session was 11.81%; in month 3 8.63%; in month 6, 8.26%; in month 9, 8.8% and in month 12, 8.3%. The average total insulin before the session was 42.89u; in month 3, 41.39u; in month 6, 42.21u; in month 9, 43.36u and in month 12, 43.5u. This study shows that accurate carbohydrate substitute and a flexible titration of insulin can significantly improve patients' glycated hemoglobin levels. Despite an increase in total insulin by 0.61u, with a more flexible diet, patients' glycated hemoglobin levels were still improved. Diabetic patients on multiple insulin injections should execute carbohydrate substitute in their diet for a better control of their blood glucose levels and a better quality of life.

PG-09

Analysis of food order's effect on postprandial glycated hemoglobin level among diabetic patients from a medical center in southern Taiwan

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Objective: Diabetes is a chronic disease; its patients' diet is predominant in their blood glucose control. The article: Food Order Has a Significant Impact on Postprandial Glucose and Insulin Levels published in one of Diabetes Care journals in 2015, pointed out that adjusting patients' food order can help control their postprandial blood glucose levels. For this, we have designed a questionnaire in an attempt to find out if Taiwanese nationals' diet may affect their postprandial blood glucose control in a similar manner.

Method: By means of questionnaire, this study took place between December 14th and 31st, 2015, in a diabetes health education room at the Metabolism Department of a medical center, where a nutritionist entrusted by a diabetes educator inquired the patients about their food order, and made a comparison between three different food orders' effects upon the patients' glycated hemoglobin level control.

Result: According to ANOVA, which analyzed the differences in glycated hemoglobin levels among the three groups of patients, food order's effect on postprandial glycated hemoglobin level is not statistically significant. Neither is significant in the effects of work patterns and sex on the food order amd the glycated hemoglobin levels.

Conclusion: Sub-factors that affect blood glucose level such as exercise, medication, diet portion can also trigger the variance in blood glucose level, which leaves the assumption that food order affects postprandial glycated hemoglobin level still in question

PG-10

A probe into the analysis of cause of hypoglycemia among patients joining diabetes health improvement program

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Objective: To foresee the risk factors that cause severe hypoglycemia to provide references for diabetes clinical healthcare.

Method: This is a questionnaire-based study, whose object must be patients that have received diabetes healthcare for over a year, and also meet one of the three criteria as follows: 1. over 70 years old; 2. receiving insulin injection for over a year; 3. GFR < 60. A total of 200 patients meet these requirements.

Result:

1. Length of healthcare received: The highest occurrence rate of hypoglycemia is 55.6%, among patients receiving healthcare for more than 10 years; the lowest occurrence rate is 38.4% ($P < 0.001$), among patients on healthcare between 3 and 6 years.
2. Age: In groups aged 31–40 and 41–50, the occurrence rate of hypoglycemia is 100% ($P < 0.43$); the lowest occurrence rate of 36% ($n = 100$; $P < 0.001$) is in group aged >70.
3. HA1C: Group HA1C 8.1–9% has the highest occurrence rate of 51.5%; Group HA1C≦6% has the lowest occurrence rate of 23.1% ($P < 0.001$).
4. GFR: Group GFR < 15 has an occurrence rate of 60%; Group GFR≧90 has the lowest occurrence rate of 34.6% ($P < 0.001$).
5. Use of Insulin: patients on solely oral medication have an occurrence rate of 30.7%; patients on insulin injection have an occurrence rate of 90.9% ($P < 0.001$).

Conclusion: According to the data analysis in this study, a more advanced CKD stage and insulin injection treatment are the main factors for a high occurrence rate of hypoglycemia. The factors such as receiving long-term healthcare, old ages, a strict control of HA1C are statistically significant and correlated with the occurrence of hypoglycemia. These factors are not the same as those hypoglycemia risk factors mentioned in previous literatures. They are likely attributable to the smaller sample size, a single-center study, etc.

PG-11

The investigation of mobile communication software "Line" intervention for diabetes nutrition and health education

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Purpose: With the ever increasing prevalence of diabetes, self-health management for diabetes patient has become an important health care topic. Also, with the progressive improvement of communication technologies, more and more people have started using the internet or mobile devices as their primary communication tool. Therefore, this study was aimed to utilize health care instant messages for aiding

diabetes patients in their self-management. The mobile communication tool used in this study is "Line". It was used for the fast and efficient tool for diabetes health education communication and reminder. The quality and success of diabetes health education of Line, the mobile communication software, intervention was further investigated.
Methods: This study consisted of 12 months of research and follow-up. A total of 86 diabetes patients have participated in this study. The participants' pre and post-intervention biological markers and satisfactions were determined and analyzed. Statistical analyses were performed with SPSS 20.0, and the results presented as descriptive statistics and pair-sample T-tests.
Results: Therefore, the use of the mobile communication software Line) was demonstrated to produce significant improvements for A1C, total cholesterol, and LDL. The survey portion of the study indicated that the service acceptance and satisfaction correlated positively with each other. The diet compliance also increased from 34.8% to 76.2%, post intervention; and the regular clinical visit rate also increased from 76.4% to 98.6%.
Discussion: The use of mobile communication software for diabetes health education intervention was demonstrated to significantly improve patient A1C, total cholesterol, and LDL. The patients' acceptance, satisfaction, diet compliance, and regular clinic visit rates were also increased. With the improvement of communication technologies, it is with hopes that in the future, the use of mobile communication software can be used as an important tool for the medical care team in health education communication.

PG-12

Symptom management education program for people with type 2 diabetes

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The purpose of this study is to examine the effects of the Symptom Management Model-based education program for patients living with type 2 diabetes. Purposive sampling obtained from outpatient department of a medical center in southern Taiwan. Sampling criteria included: (1) diagnose of type 2 diabetes, (2) age between 20 and 80 years olds, (3) clear mental status and able to communicate, (4) HbA1C 8% or higher. This was a pilot study. Patients were randomly assigned into experiment or control group. Subjects in control group received the routine clinical care. The subjects of the experimental group received a symptom management- based education program. The program was held 60–90 minute interview. The data were collected by Diabetes Symptom Checklist, Diabetes Self-Care Scale, Diabetes Quality of Life Scale, and blood HbA1C before the education program and 3 months after the intervention program.
The results of this study indicated that patients in the experiment group significantly improved their levels of self-care behaviors, quality of life at 3 months post-intervention; however, their HbA1C levels and symptom experience hadn't difference significantly.
In conclusion, the results of this study provide a reference for health education, practice, and research for diabetes patients. To promote the health and quality of life of patients living with type 2 diabetes, a symptom management based education program could be used.

PG-13

Elucidation of lifestyles that affect the quality of life (QOL) related to the therapy for patients with type 2 diabetes

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High adherence to diabetes therapy is a key to maintain a good glycemic control. To keep patients in high adherence, it is important to increase their diabetes therapy related (DTR)-QOL to higher state. In this study to elevate DTR-QOL by patient education, it was elucidated what kind of lifestyle affected the DTR-QOL. Study subjects were 65 outpatients with type 2 diabetes (male 31, female 34). DTR-QOL was quantified with a questionnaire. This questionnaire consisted of 29 questions relating to 4 factors; "burden on social activities and daily activities", "anxiety and dissatisfaction with treatment", "hypoglycemia", and "satisfaction with treatment". Score of DTR-QOL was shown by the 100-point scale. Lifestyle of patients was asked using a questionnaire consisting of 24 items about lifestyle. It was answered in a 4-point scale (1 = agree to, 4 = not agree to). The subjects were classified as follows; 1 and 2 were the Yes, 3 and 4 were the No. Age of subjects was 71.4 ± 8.7 year-old, BMI was 23.9 ± 4.2, and HbA1c was 6.9 ± 1.5%. Total score of DTR-QOL was compared between the Yes and the No. Significant differences were observed in two items; "Do you try to do physical activity in everyday life for health maintenance? (Yes: 76.1 ± 13.3, No: 57.4 ± 14.5)", and "Do you feel stress or fatigue? (Yes: 68.5 ± 13.5, No: 79.7 ± 14.0)". We next analyzed the score of each DTR-QOL factor. In addition to 2 items described above, 3 items were found to be affected the score of DTR-QOL. Score of "burden on social activities and daily activities" was significantly lower in the Yes as to "Do you have the situation you are hard to sleep? (Yes: 71.0 ± 17.9, N: 82.9 ± 17.6)" and "Do you skip a meal (Yes: 63.6 ± 24.0, No: 80.7 ± 17.0)". In the Yes as to "Do you eat until fullness?", the score of "satisfaction with treatment" was also significantly lower, compared with the No (Yes: 48.1 ± 16.7, No: 63.5 ± 20.8). It was demonstrated that five kinds of lifestyle were associated with DTR-QOL. "To do physical activity in everyday", "not to skip a meal", and "not to eat until fullness" were lifestyles that could be improved through education for patients. Higher DTR-QOL would be achieved if patients were educated, focusing on improvement of these lifestyles.

PG-14

Pilot implementation of a novel post-graduate medical education program: Steno REACH certificate course in clinical diabetes care – Malaysia

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The Steno REACH Certificate Course in Clinical Diabetes Care (SRCC) is a comprehensive, competency-based educational program that blends eLearning and classroom-based group work with the aim to improve the capacity of primary care doctors and nurses to deliver high-quality diabetes care. Using the pedagogical model of the flipped classroom, 100 hours of foundational material is delivered in a self-paced, online platform while another 50 hours of classroom time is devoted to reinforcing core concepts through interactive learning activities, mini-lectures, and case discussions. Classroom learnings are facilitated by a team of Malaysian Endocrinologists, Family Medicine Specialists, Diabetes Nurses, and dieticians who completed a train-the-trainer program hosted by Steno Diabetes Center. Completing the learning circle are clinic-based learning activities. Unlike most long-format, post-graduate medical training programs, participants are able to work full-time – thereby overcoming a common barrier to participation in extensive continuing medical education.
Through an agreement between the Ministry of Health Malaysia and Steno Diabetes Center Malaysia, 12 doctors and 24 nurses working in ten public health clinics in two states in Malaysia were enrolled in the pilot class of SRCC on 10 October 2015. This pioneering batch of participants will complete the training on 10 April 2016. The aim of the pilot

is to identify early indicators of success, discuss opportunities to strengthen the learning experience and apply lessons learned before a national scale-up of the SRCC. Diabetes-related knowledge and clinical reasoning skills will be measured before and after course participation and change will be measured at the individual and cohort level. Changes in diabetes attitudes will also be measured before and after participation. Pre-participation test data suggests that knowledge of clinical diabetes care is low to moderate, particularly among participating primary care nurses where the average score on the pre-test was 42% of all questions answered correctly. Post-course testing will be completed in April 2016.
Visits to all participating clinics have been completed. The major learning points from these visits highlight the importance of teamwork in approaching the learning materials and motivating and supporting each other through the clinic-based learning process. The Family Medicine Specialists were also found to play a major role in providing the necessary enabling environment to maximize the learning experience. These invaluable learning points will provide input to further refine the implementation of future SRCC classes.

PG-15

Combining community resources and utilizing creative health education for improving diabetes support group functions

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Purpose: Diabetes is the number four leading cause of death in Taiwan, in 2014. Thus we can see the impact of diabetes can have on the health of an individual. In 2015, there were 3,336 diabetes patients in our hospital, where 53.7% of the patients had HbA1C >7%, indicating further improvement is needed in blood glucose management for the patients. In 2011, "Fongshan medical diabetes workshop", a diabetes support group was established by our hospital. The establishment of this support group enabled the patients to understand more about sugar management and to improve daily living self-management for achieving blood glucose level targets and reducing diabetes complication and mortality.
Methods: The "Fongshan medical diabetes workshop" diabetes support group is an extra-institutional group that combined the efforts of the neighboring basic clinic, Fonshan community center, farmers union home economics classes, and other community care facilities for organizing many innovative diabetics related classes to encourage high risk individuals and diabetes patients in joining the support group. A social network website was also established for the "Fongshan medical diabetes workshop" support group.
Results: The support group members increased from 43 to 79. The patients who performed weekly blood glucose monitoring, at least once a week, increased from 20 to 56. The patients who exercised for at least 150 mins (weekly) increased from 18 to 43. Significant differences were observed in the average glycated hemoglobin levels (8.28% to 7.12%; $P < .05$) and average patient weight (65.7 kg to 63.1 kg). The support group and the patients were awarded National Health Department model diabetes support group, diabetes patient improvement award, and diabetes support group weight loss champion in 2015.
Conclusions: Interventions through the diabetes support group, with brainstorming efforts of the medical team, and with entertaining interactive activities, the members shared encouragement and support for each other, in changing their self-management behavior for achieving the improved results of blood glucose monitoring, regular exercise, reduce glycated hemoglobin, and weight loss.

PG-16

Using healthy diabetes plate for inadequate glycemic control among patients with type 2 diabetes

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Purpose: The aim of the present study was to examine the effects of consumption of foods using a healthy diabetes plate in patients with type 2 diabetes mellitus (T2DM).
Method: A total of 43 patients with T2DM were randomly assigned to the intervention of healthy diabetes plate diet group (n = 20), or to control group (n = 23). Both groups followed the same instructions of diet provided by a registered dietitian (RD). However, for the health y diabetes plate group, we used the plate format to teach participants about the type and amount of foods they should consume at each meal, the education emphasized on the concept of substituting carbohydrate quantity with the usage of quantitative plate; and for control group, we used a standard pamphlet nutrition education to teach the participants about the diabetes nutrition management. The parameters were obtained at the third month. The treatment was unchanged during this 3 months period.
Results: Participants' mean age was 49.64 (±12.06) years, hemoglobin glycated A1c (A1c) 9.84 (±1.86)%, diabetes duration of 4.3 (±0.2) years. After 3 months of intervention, The A1c reduction was greater in healthy diabetes plate than control group, from 9.95 ± 2.25 to 7.01 ± 0.67% in healthy diabetes plate group; from 9.73 ± 1.81 to 7.80 ± 1.55% in control group ($p < 0.05$). Both group a significant reduction in A1c after nutrition intervention, but with a greater magnitude in healthy diabetes plate.
Conclusions: From our study results, the benefit in pursuing a healthy diabetes plate in these patients showed greater improvement in their glycemic control. Using healthy diabetes plate control carbohydrate amount may be is a strategy for diabetes self-management.

PG-17

A pilot study on a diabetes link-nurse program to enhance nurse confidence and competence in diabetes care

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Background: Diabetes is a common chronic disease. About 30–50% of hospitalized patients have diabetes, and with a higher percentage in Medical Wards. To enhance quality diabetes care to these patients, nurses with update diabetes nursing knowledge and skills are crucial. Diabetes specialist nurses should therefore influence diabetes care in a larger group of nurses in order to improve the quality of diabetes care as a whole. Therefore, we designed and implemented a Diabetes Link-nurse Program.
Objectives: The program was aimed to train nursing staff to become Diabetes link-nurses, and enhance their i) professional knowledge and skills in diabetes care, ii) confidence in providing diabetes care and education, iii) communication with the diabetes specialty nurse team, and iv) effective use of the diabetes education kit provided.
The overall effectiveness of the program was evaluated based on the change in Diabetes link-nurses' self-confidence in diabetes education and their participation in educating patients and staff on diabetes.
Methods: The program was conducted from November 2014 to December 2015 in an acute hospital. The program provided: i) 8 structured educational seminars; ii) scenarios management discussion; and iii) joint-consultation to assist link-nurses to discuss actual clinical problems with the diabetes

team; iv) resources support to facilitate link-nurses to provide patient teaching.
Purposive sampling was employed. The Diabetes Link-nurse Perceived Role Competency Questionnaire was administered to the nurses before and after the program. Participation in diabetes education was counted by the number of staff and patient education reported.
Results: Twenty nurses completed the program. Sixty percent of the link-nurses had delivered more than one episode of diabetes education to patients, and 44% of them had shared their knowledge and information with their colleagues.
Link-nurses had shown significant improvement in perceived role competency ($p < 0.01$), especially in the areas of teaching patients on common oral anti-diabetic drugs and identifying diabetic issues or problems for discussion. However, the improved perceived competency did not correlate with link nurses' years of nursing experience, educational level, previous specialty training nor academic level.
Conclusion: The results concluded that the Diabetes Link-nurse Program is effective in enhancing link-nurses' participation in educating patients and colleagues on diabetes. The education, support and resources provided also increased link-nurses' confidence in performing their roles in communication and patient care.

PG-18
Clinical implication of diabetes education program declaring a goal in life for patients with diabetes mellitus

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Objectives: For patients with diabetes mellitus, individualized diabetes education program (DEP) is created and used to facilitate the knowledge, skills, and ability necessary for diabetes self-care management in many Japanese hospitals. We have newly developed "My Goals Sheet" (MG Sheet), which is a self-evaluation tool for declaring a patient's goals to achieve within shorter, intermediate and longer period and self-directed goal setting in healthy eating, physical activity, medication and reducing risks for micro- and macro-vascular complications. The aim of this study is to investigate whether declaration of individual goals for patient's life affect the subsequent glycemic control.
Methods: Retrospective, observational study was conducted with 138 patients who participated in DEP and completed their own MG Sheet (male/female = 76/62, mean ± SD age: 60.2 ± 14.2 years; BMI: 25.9 ± 5.6 kg/m^2; HbA1c: 9.4 ± 2.0%). The participants were categorized into four groups according to their goals of life: "to live a long life/die in peace (group A)", "to improve their health (group B)", "to enjoy their job or hobby (group C)" and "to dedicate to others (group D)". HbA1c level in each group was followed-up until 6 months after the admission with DEP.
Results: Among the participants, 4 patients were excluded from the study because they did not complete their MG Sheet correctly. Fifty-eight (43.6%) patients were categorized into group B. In male, group A was predominant to group C (group A, B, C, D = 34.7%, 41.7%, 15.3%, 8.3%), whereas group C was predominant to group A in female (group A, B, C, D = 21.3%, 45.9%, 31.1%, 1.6%) (P = 0.0334). There was no difference with category distribution: patients lower than 70 years of age (group A, B, C, D = 25.5%, 47.9%, 21.3%, 5.3%), patients in 70 years and higher (group A, B, C, D = 35.9%, 33.3%, 25.6%, 5.1%). With respect to glycemic control, changes in HbA1c at baseline and at 6 month were as follows: group A; 9.2% and 7.1%, group B; 9.4% and 7.5%, group C; 9.6% and 7.1%, group D; 10.0% and 7.1%, respectively. Achievement rate of HbA1c <7.0% within 6 months in the 4 categories were as follows: group A, B, C, D = 51.4%, 46.3%, 41.4%, 42.9%, respectively.
Conclusions: Patients who participated in DEP achieved good glycemic control irrespective of any category of individual goal in life.

PG-19
Efforts to improve the enrollment of education and quality of care in type 2 diabetes: experience of a community hospital

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Background: Although an educational program may be helpful for disease management and quality of care for type 2 diabetes mellitus, the enrollment rate of our patients into such a program was less satisfactory.
Purpose: To determine whether a multi-discipline approach could improve the enrollment rate of education and quality of care for patients with type 2 diabetes mellitus in a community hospital.
Methods: After H2 of 2014, we initiated several strategies focusing on patients and health care providers to increase enrollment. Eligible but not enrolled diabetic patients were informed for our education program through visual teaching materials and direct telephone contact. Lists of potentially eligible patients were also pre-notified to the nurses and physicians before the start of outpatient clinic. We chose four process indicators including the completeness of urine albumin/creatinine ratio (UACR), fundoscopy, blood LDL-c and HbA1c tests, and three outcome indicators including rate of HbA1c < 7%, BP < 140/90 mmHg, and LDL-c < 100 mg/dL, before and after the implementation of our quality improvement strategies (H1 of 2015 vs. H1 of 2014).
Results: The enrollment rate was higher in the H1 of 2015 than in the H1 of 2013 (42.3% vs. 35.4%, $p < 0.001$). The process indicators also improved for the completeness of UACR (45.8% vs. 41.5%, $p < 0.001$), fundoscopy (30.4% vs. 28.4, $p = 0.025$), LDL-c (67.6% vs. 64.6%, $p = 0.001$), and HbA1c (86.9% vs. 82.6%, $p < 0.001$). Quality indicators of diabetes care also improved for the rate of HbA1c < 7% (48.4% vs. 43.1%, $p < 0.001$), BP < 140/90 mmHg (11.9% vs. 10.9%, $p = 0.048$), and LDL-c < 100 mg/dL (67.2% vs. 61.8%, $p < 0.001$).
Conclusion: Our multi-discipline strategies improved both the enrollment rate and quality of care for patients with type 2 diabetes. Further study is needed to determine whether such improvement could maintain thereafter.

PG-20
Effectiveness of the food craving management tool in Korean adolescents

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Food cravings defined as an intense desire or urge to eat a specific food could lead to a failure of weight control in connection with overeating or binge in obese subjects. Our research team developed the food craving management tool to treat and manage of obesity in adolescent using mobile application. It supports the subjects endure the desire to eat about 5 minutes through calling the subject's attention to various contents of application when cravings occur. We aim to assess the effectiveness of the food craving management tool by applying to Korean adolescents. This study was performed over 3-weeks as a randomized clinical trial in Chung-ju city. A total of 60 female middle-school students were included and randomly assigned to intervention or control groups. The subjects belonged in intervention group used the mobile application when they experienced food cravings during study period. To assess food craving status at entrance and 3-weeks later, general-food cravings questionnaire (G-FCQ-T) were investigated. A 2(group: intervention, control) by 2(time: baseline, after intervention) mixed model ANOVA was done to compare the change of the G-FCQ-T score. The mean (S.D.) age and BMI percentile of subjects were 13.4 (0.5), 71.8 (18.8) respectively. At entrance, there was no significant difference of G-FCQ-T score (intervention: 73.6, control: 79.2) between two groups. The subjects in intervention group reported using the application for 60% of food craving episode, and decrease of craving degree they felt subjectively after using. There was a significant interaction between group and time (F: 4.96, p: 0.029). In intervention group, G-FCQ-T score significantly decreased from 73.6 ± 19.6 to 61.6 ± 18.6 (p: <.001) whereas that of the control group did not show significant difference (p: 0.096). These findings show that effective management of food cravings will be available by using food craving management tool and furthermore, it is expected to help weight control for obese adolescents through intake reduction specific food occurs cravings.

PG-21

Association relationship between periodontal disease severity of periodontal bone loss and clinical features in type 2 diabetic patients

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Introduction: Diabetes mellitus is currently considered as an established risk factor for periodontitis and contributes to increased prevalence, severity and progression of periodontitis. In According to some previous reports in diabetic patients, in addition to glucose control, the age and diabetic duration are correlation to the risk factor of periodontitis severity. the risk factors of periodontitis severity are not only glucose control but also age and diabetes duration in diabetic patients. But there are some different results in the young type 1 diabetes research. In this our study, we try to know the association between the determine whether severity of periodontitis are associated with and the correction factors (glucose control, clinical features, biochemical variables and pro-inflammatory markers) in our type 2 diabetic patients.

Methods: We recruited A total of 66 adult type 2 diabetic patients were recruited from our outpatient clinics and all collected general and biochemical data (Age, Sex, Diabetes history, BMI, WHR, BP, lipid profiles, creatinine), blood glucose (Fasting glucose, HbA1c) and oral X-ray. (for C/A, missing tooth evaluation)

Results: Our data showed that there is no significant associations between glucose control (fasting glucose and HbA1c) and periodontal bone loss (C/A value). But the results revealed significantly positive correlation between periodontal bone loss, and age, hsCRP and missing teethes. The multiple logistic regression analysis also demonstrated age, hsCRP and missing teethes were associated with periodontal bone loss. Finally, the stepwise regression analysis showed age and hsCRP were the major risk factors of the severity of periodontal bone loss in our type 2 diabetic patients.

Conclusions: Previous reports are indeed associated with poor blood glucose control and periodontitis of high severity in diabetic patients. Our study find age and systemic inflammatory condition might have play more significant important roles than glucose control in periodontitis severity in our type 2 diabetic patients.

PG-22

Diversified creative diabetes education in Mackay Memorial Hospital, Taiwan

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Traditional health education is mostly conveyed in a setting that resembled classrooms. However, this setting can bore the patients and hinder their learning interests. Therefore, a diversified creative education model was used in the planning of diabetes education for increasing the patient's interest as well learning results. The Mackay Memorial Hospital in Taiwan has adopted the following creative education models in 2015: (1) live action videos that teaches about the correct insulin injection procedures, hypoglycemia education, and proper feet hygiene for the clarification of patient care process; (2) establish specific education topics that can be utilize in a small group setting that encourages interactions among the participants; (3) a vibrant point based reward system was establish to make the quizzes feel like games and encouragement; and (4) establish special group education that targets the needs of the elderly and young patients. This type pf education activity can satisfy the health education requirements of the current aging and birthrate declined society.

It is with hope that the aforementioned four types of creative education model can represent our goals of Innovation, resilient, outreach, distinction, and effectiveness. This diversified education model is current being developed among many medical centers and diabetes promotion institutions in Taiwan. The goal of the education model development is to utilize limited human resources, with mutual collaborations and learning, for creating more interesting ideas for improving diabetes health education.

PG-23

Application of intensive diabetes management program by conversation maps on poor controlled insulin naïve type 2 receiving insulin injection

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The effect of glycemic control by utilizing diabetes educational tools – Conversation Maps in diabetic patients.

"Conversation Maps" are diabetes educational tools by interacting with diabetic patients, peer effectiveness, and achieving the goals of applying the related knowledge to life. There are seven topics in Conversion Maps, include Living with Diabetes, How Diabetes Works, Healthy Eating and Keeping Active, Starting Insulin Treatment, Diabetes and Caring for Your Feet, Understanding the Many Factors of Managing Diabetes, Living in a Family with Type 1 Diabetes. In this study, we will focus on the two topics – Healthy Eating and Keeping Active, and Starting Insulin Treatment. According to our clinical experiences, it is hard to accept insulin therapy for diabetic patients. As long as diabetic patients would like to try insulin treatment, most of them will face the body weight gain problem. That is why we would like to focus on these two topics to resolve

the biggest issues within diabetic patients. There are 2 to 3 activities of Conversation Maps per month, and 60 to 80 minutes each time. 3 to 10 diabetic patients would join for each activity. Diabetes educators will give guidance in the activity, and made patients discuss or shared experiences and found the best answer by themselves based on the different topics.
The objective of this study is to improve the effectiveness of glycemic control by Conversation Maps. Including criteria for subjects are newly diagnosed and poorly control diabetic patients (HbA1C >7%). This study has started since Feburary to July in 2014, and there were total 55 participants in the end. We collected subjects' glycemic and blood lipid data before and after activity to assess the outcome.
The results showed the average HbA1C from 9.8% to 7.8% ($p < 0.001$), fasting blood sugar from 193 mg/dL to 135 mg/dL ($p < 0.001$), total cholesterol from 189 mg/dL to 159 mg/dL ($p < 0.01$); however, there is no significant difference between low-density lipoprotein cholesterol and triglyceride.
Under the leading from diabetes educators, the Conversation Maps are effective diabetes educational tools to help diabetic patients to know more diabetes and behavior change by triggering their motivation. Eventually, diabetic patients have better glycemic control by arranging health eating habits and lifestyle. We still more similar studies to identify our results.

PG-24

The results of nutrition education for diabetes patients in a community in Changhua County, Taiwan

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There are many remote village and towns in Changhua County, Taiwan, that consisted of mostly elderly patients, where the access to medical care is limited. Due to the insufficient diabetes nutrition education, the Changhua Health Department has contracted Lukang Christian Hospital to perform diabetes nutrition educations at 45 basic clinics in Changhua County. In order to assess the effect of the education, 264 diabetes patients were sampled from the 45 basic clinics, between 2013 and 2015. The patients were assessed according to their dietary changes at 3 to 6 months after the education intervention. The results indicated that most patients have increased their intake of food belonging to the five major food groups. The percent of patients with adequate intake of low-fat dairy, wholegrain and starchy, protein, vegetable and fruit increased from 47.3 to 52.7%, 68.4 to 79.5%, 71.6 to 78%, 67 to 79.2% and 58.3 to 73.5%, respectively. Furthermore, the intake of inappropriate diets such as desserts, surgery drinks, and foods that are high in fat or sodium were reduced. Therefore, it was determined that diabetes nutrition education intervention in a community setting can be utilized to change patient diet behaviors for the goal of diabetes management.

PG-25

Patients' opinions regarding the continuous glucose monitoring system (CGMS) for self-control in adult patients with type 2 diabetes mellitus

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The aim of this study was to verify the effectiveness of a continuous glucose monitoring system (CGMS) for self-management of type 2 diabetics. Six adult patients with type 2 diabetes used a CGMS (iPro2) for 1 week. Semi-structured interviews were conducted, and the interview data were analyzed using a grounded theory approach. The following two core categories were identified: awareness of unbalanced diets and anxiety over diabetic complications. Graphical presentation of continuous glucose levels led patients to realize that their diets were unbalanced, which motivated them to improve their eating habits. As for the second core category, anxiety over diabetic complications, patients expressed regret for not knowing more about diabetic complications. They requested diabetic education that uses plain language instead of technical terms. CGMS is extremely effective in treating patients unaware of hypoglycemia and in controlling daily variations in blood glucose; however, implementation of continuous monitoring in the standard clinical nursing care setting has not yet been established. This research suggests that this new equipment is effective in motivating patients to become aware of an unbalanced diet and to improve their eating habits in self-management among adult patients with type 2 diabetes mellitus.

PG-26

The impacts and care trends of type 1 diabetes during the transition phase on patients aged between 16 to 25

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Type 1 diabetes occurs mostly in children and adolescents. For type 1 diabetes patients in the "transition phase" between late adolescence and early adulthood, they are exposed to the four transitional impacts caused by development, changes in interpersonal roles, illness-health and the organizational transition from the child-oriented nursing system to the adult-oriented health care system. Moreover, they witness a transformation in their disease management and different disease control results. Literature review suggests that type 1 diabetes at an age between 16 and 25 tends to worsen during the transition phase, thus making the nursing care of this disease even more important. This paper summarizes the key issues concerning type 1 diabetes during the transition phase, which include the impacts of type 1 diabetes during the transition phase, detectable changes during the transition phase and the current situation concerning the care of type 1 diabetes during the transition phase. The findings can contribute to the improvement of nursing care of type 1 diabetes during the transition phase and lay the foundation for future interventions, thus generating better disease control results and enhancing the quality of patients' lives.

PG-27

Effects and predictors of the diabetes conversation map education tools for maintaining glycemic control in patients with type 2 diabetes

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Purpose: To investigate the effects and predictors of the Diabetes Conversation Map educational tools on glycemic control in patients with type 2 diabetes attending a diabetes self-management education program.
Methods: Outpatients with type 2 diabetes and a glycated hemoglobin (A1c) level of 7% or above were recruited from the division of metabolism and endocrinology in a regional hospital in southern Taiwan to enroll in a diabetes self-management education program based on the Diabetes Conversation Map educational tools. Data on A1c and fasting blood glucose (FBG) were collected at baseline, post-

intervention, and three months post-intervention. Logistic regression analyses were used to assess baseline factors associated with achieving A1c < 7% three months post-intervention.

Results: A total of 79 patients (54% males) with a mean age (± standard deviation) of 63.9 ± 9.8 years completed the intervention and 72 patients completed the three months post-intervention follow-up. The mean baseline and post-intervention A1c levels were 9.2 ± 2.1 and 7.8 ± 1.3, respectively, with a significant difference of 1.4 ± 2.0 ($p < 0.001$). The mean baseline and post-intervention FBG levels were 187.3 ± 70.6 mg/dL and 157.8 ± 62.6 mg/dL, respectively, with a significant difference of 29.5 ± 69.7 mg/dL ($p < 0.001$). The mean differences between three months and baseline levels of A1c (1.3 ± 2.4, $p < 0.001$) and FBG (30.4 ± 84.0 mg/dL, $p = 0.003$) were also significant. Results of the logistic regression analyses showed that exercise regularly (>5 days a week, with >30 minutes each time) at baseline compared with no exercise were significantly associated with an A1c level of <7% post-intervention (odds ratio [OR] = 4.43, 95% CI = 1.22–16.17, $p = 0.024$). Regarding the results three months post-intervention, patients who had changed from oral antidiabetic therapy to insulin therapy after the intervention showed a trend of association with an A1c level of <7% three months post-intervention (OR = 3.03, 95% CI = 0.87–10.61, $p = 0.082$), compared with those who had not changed. Conversely, a body mass index of >27 versus <24 at baseline (OR = 0.29, 95% CI = 0.08–1.11, $p = 0.07$) were less likely to be associated with an A1c level of <7% three months post-intervention.

Conclusions: Completion of an education program based on the Diabetes Conversation Map educational tools was able to significantly improve both A1c and FBG levels at least three months after the intervention. Patients who had a body mass index >27 at baseline and had not change to insulin therapy after the intervention were less likely to achieve the desirable A1c goal of <7 three months post-intervention. Additional efforts should be focused on these patients in future interventions.

PG-29

Investigating the results of utilizing diabetes conversation map for patient blood glucose management

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Purpose: Investigate the effectiveness of utilizing diabetes conversation map for blood glucose management.

Methods: The study subjects consisted of patients in community hospitals in the southern Changhua County in Taiwan, between March 1st and Oct. 31st, 2015. This study was of a quasi-experimental design that consisted of pre- and post-intervention testing of the same group of patients. The patients were purposely sample, and consisted of 30 type II diabetes patients who have received basic insulin treatment (once a day, long or medium-long acting) for at least three month; with fasting plasma glucose (FPG) of <150 mg/dL and HbA1Cof >7%. The study tool "what is diabetes" and "living with insulin" is a diabetes educational conversation map and a total of 10 educational seminars were organized. The participants were also required to participate in all seminars (at least once) such as "healthy diet and exercise", "feet nursing care", "comorbidity and risk factors". A total of 18 seminars were organized, with 6–15 participants per session. The results of the diabetes educational conversation map intervention was assessed at 6 month after intervention, with self-established surveys that included "insulin knowledge and attitudes", "diet knowledge and attitudes", and "simple exercise".

Results: A total of 30 participants were enrolled in this study (male N = 16, 53%; female N = 14, 47%). The average age of the participants were 64.7 years, and the average education level of the participants was elementary school or lower (43%). The participants had an average diabetes diagnosis for 7.00 ± 5.64 years, and their pre-intervention average HbA1C was at 0.4 ± 2.45%.

1. At six months follow-up, the patients' average HbA1C was significantly reduced from 10.4% to 7.1% (average reduction of 3.3%; $P < 0.05$).
2. The fasting and postprandial blood glucose exhibited reductions of 4.9% (254.5 ± 99.60 mg/dL to 127.7 ± 22.53 mg/dL) and 2.7% (314.4 ± 98.68 mg/dL to 229.4 ± 51.88 mg/dL) after the educational intervention, respectively.
3. In terms of diet behavior improvements, all scores were significantly improved post-intervention ($P < 0.001$); the scores for glycemic food increased from 2.5 ± 1.39 to 4.4 ± 0.50; the ability to discern food groups increased from 1.80 ± 1.00 to 4.4 ± 0.50; the understanding of simple diet replacement increased from 2.16 ± 1.17 to 4.28 ± 0.58; portion control increased from 1.93 ± 1.01 to 4.47 ± 0.51; and avoiding sugary drinks increased from 4.47 ± 0.51 to 5 ± 0.

Discussion: The "Diabetes Conversation Map" exercise can be utilized in small groups for proving a visual learning experience. The patients will be also motivated in taking responsibility for their conditions in achieving the optimal blood glucose management goals.

PG-30

Utilizing simplified nutrition screening short form for investigating the nutrition and blood glucose management of elder patients

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Malnutrition is a common problem for the elderly in institutions and communities. Therefore, an efficient and easy to use nutrition assessment tool is required for the regular nutrition asse this study, a simplified nutrition assessment short form and diet log were used for understanding nutrition and blood glucose management among elderly patients with diabetes. The study was performed from June to Dec, 2014. The participants were purposely sampled from elderly outpatients that have participated in the "Diabetes medical care benefits improvement program". A total of 70 patients were enrolled. The study data include demographic information, physical measurements, nutritional assessment-short form (MNA-SF), blood biochemistry, urine test, daily dietary record, and diet health education. The results from this study indicated the followings. In terms of nutrition screening, there were 18 patients (25.71%) who had MNA-SF total of ≦11, which could indicate possible malnutrition. The patient MNA-SF scores were determined to be significantly related to patient waist size, calf circumference, hemoglobin, and serum albumin levels ($p < 0.001$). In terms of diet, the daily intake of calories and protein (1,683.4 ± 234.6 kcal/day and 59.9 ± 13.5 g/day) were higher than those suggested by the nutritionists. The male patients' diet exhibited the lack of dairy and vegetable intake, while having too much protein and fat. The female patients were determined with insufficient dairy, vegetable, and fruits, while having too much fat intake. In terms of elderly diabetes management markers, there were 49 patients (70%) with glycated hemoglobin (HbA1c) of <7.5; 38 patients (54.29%) were determined with blood pressure (BP) of <140/80 mmHg; and 31 (44.29) patients were shown with low density lipoprotein (LDL) -C of <100 mg/dL. Furthermore, there were 41 (58.57%) patients that were diagnosed with nephropathy during the renal screening. Due to the regular care and

nutritional education received from the medical care team, most of the elderly diabetes patients exhibited good blood glucose, BP, and blood lipid management. Further improvement in the nutritional intake of dairy, vegetable, and fat still required for patients with nephropathy. However, there is a 25.71% of patient that were determined by MNA-SF to be malnutrition. Therefore, it was demonstrated that MNA-SF can be included in the outpatient screening for elderly diabetes patients to identify malnutrition.

PG-31

Improvement of glycemic control in Taiwanese patients using modified Diabetes Conversation Map® tools

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The landmark studies demonstrated the importance of good glycemic control in the prevention of diabetes-related complications while self-management of diabetes is essential for achieving and consolidating the metabolic goals.

The trick to maintain proper lifestyle and optimal glycemic control lies in the development of patients' literacy and the availability of on-going education and support.

Conventional methods for diabetes education include lectures and one-to-one interaction between the patient and the diabetes educators.

However, there has been an increase in execution of group education programs, such as Diabetes Conversation Map®, to yield the social support and reinforce the peer communication. Due to the busy life of some patients, it is difficult for them to participate in the diabetes classes. To overcome these barriers, IT and e-tools are used to recruit group instead of individual patient for shared education.

Here in, we reported our experience in the practice of traditional Chinese character version of Diabetes Conversation Map® at Cheng Hsin General Hospital. From February to December 2015, a total of 31 type 2 diabetes patients were randomized to two groups, i.e. line group diabetes education (LG) and conventional group education (CG) approaches. The demographics and the changes in metabolic outcomes over a mean of ten months were as follows. Patients' mean age in the LG group and in the CG group was 46.8 ± 7.7, and 67.4 ± 13.4 respectively. The duration of patients with T2DM was 6.8 ± 5.2 years in the LG group, and 7.1 ± 5.1 years in the CG group. 1% of HbA1C reduction ($P < 0.05$), 17.3 mg/dL of FPG reduction ($P < 0.01$) and 60.2 mg/dL of PPG reduction ($P < 0.01$) were found in the LG at ten month, which were respectively 0.89% ($P < 0.05$), 25.7 mg/dL ($P = 0.09$) and 20.2 mg/dL ($P < 0.05$) in the CG group. In addition, the reduction of HbA1C and PPG were not significant difference between the LG group and the CG group ($P > 0.05$). Interestingly, the reduction of FPG in the LG group was better than in the CG group ($P < 0.05$).

Our findings confined the useful materials of Diabetes Conversation Map® tools in improving the glycemic control in Taiwanese patients, and it was similarly affected through conventional and Line-platform approaches.

PG-32

Nurse-led training and education program on insulin pump therapy in Japan

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Objective: Insulin pump therapy is a diabetes management tool that can significantly aid children, adolescents and adults with type 1 diabetes mellitus (T1D) in achieving treatment goals. These goals include optimal glycemic control, lifestyle flexibility, quality-of-life improvement, and independent self-care management.

However, the incidence of T1D is low and the percent of use of continuous subcutaneous insulin infusion (CSII) is also low. There are two reasons why insulin pump user is low is that the manufacturer is not allowed to send insulin pump trainers to hospitals. The other is diabetes educators are unfamiliar to insulin pump therapy because diabetologist mainly initiate patients to insulin pump therapy. The aim of this study is to evaluate the effect of nurse-led training and education program of insulin pump therapy on knowledge, skills, and confidence of handling insulin pump in diabetes educators.

Method: Fourteen diabetes educators (7 registered nurses, 2 registered dieticians, 2 pharmacists, and 3 medical doctors) participated in this program. The structured program consisted of 14 sessions (one session is 30–60 min lecture and handling an insulin pump practically). The program included "introduction to the insulin pump", "practical skills in handling an insulin pump", "adjusting insulin dosage according to blood glucose and estimated carbohydrate intake", "let's use bolus calculator".

The analysis on outcome of T1D diabetic patients was performed by evaluating glycemic control (HbA1c) and 6 questions of the Diabetes Treatment Satisfaction Questionnaire (DTSQ).

Results: The percentage of attendance on this program was 86.5%. The knowledge, skills, and confidence of insulin pump in diabetes educators were significantly increased. During 3 years after the end of the program, 15 T1D patients were initiated of insulin pump therapy using the team approach in our outpatient clinic. The average number of initial education sessions on insulin pump for patients was 4–6 times. Diabetes educators provide pump technical support and keep educating patients to improve their lifestyle flexibility. The data of HbA1c levels and DTSQ scores were significantly improved after intervention. (HbA1c:8.04 ± 1.03 to 7.06 ± 1.21(%) and DTSQ: 16.25 ± 8.66 to 30.5 ± 5.20).

Conclusion: We developed the nurse-led structured training and education program on insulin pump therapy in diabetes educators. Further research is required to motivate diabetes educators and introduce a new system such as sensor-augmented pump (SAP) therapy.

PG-33

The metabolic effect of diabetic education frequency

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Diabetes self-management education (DSME) and diet education improves glycemic control in adults with diabetes mellitus. However, the benefit declines over time. The purpose of this population-based propensity score-matched longitudinal follow-up study was to evaluate the metabolic effect of diabetic education frequency.

This is a 3-year follow-up study of 413 patients with type 1 and type 2 diabetes, who had received intensified education more than 2 years. A total of 91 diabetic patients was enrolled in the group of non-intensified education, in which the education frequency decreased from 4 times per year to once per year. We used a logistic regression model that includes A1c, and years of DSME and diet education as covariates to compute the propensity score. The group of intensified education consisted

of 322, propensity score-matched subjects. Patients were evaluated at baseline, one-year, 2-year and 3-year follow-up.
At follow-up, A1c significantly increased in both groups. Mean A1c was 6.7 ± 0.6% at baseline. Mean A1c was 6.9 ± 0.8% at 3-year follow-up. A1c was higher in the group of intensified education than non-intensified education at the 1-year and 2-year follow-up. However, the effect of education frequency on A1c was insignificant over 3 years. Total cholesterol decreased in both groups. In the group of non-intensified education, HDL improved at 3-years follow-up.
Decrease of diabetic education frequency did not showed impact on A1c and total cholesterol in patients who had trained for coping with diabetes for more than two years. Although A1c deteriorated, lipid profile improved over time in those patients.

PG-34

Report of Conversation Map sessions held by a nephrologist

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Background: Diabetic patients need to learn methods of controlling themselves. Controlling themselves needs power for collecting their relevant information of improving their health. Diabetic education would be more fruitful when they are empowered with psychological approach. Conversation Map is a one of decisive education tools and the number of facilitators is increasing in Japan.
In the other hand, the number of diabetic nephropathy patients also increasing and nephrologists confront same healthcare problem. Psychological approach can be used with the help of psychologists But not so many nephrologists are interested in Conversation Map Now, we report the cases and experience of a nephrologist facilitator.
Method: After a training of Japan Association of Diabetes Education and Care, the author got licensed for Conversation Map and conducted participant sessions. Sessions were held for admitted patients and their family, participants of educative events for outpatients and lectures open to the public. Patients who were CKD 4 or CKD 5 were excluded because contents of Conversation Map are not partially fit for CKD patients.
Result: For 2 years, 30 sessions were held and approx. 50 persons have participated. At each ice breaking, they complain about negative feelings for their own diabetes. After sessions they asked questions like: "What shall I do to improve my diabetic control?" "Is there any room for changing my daily diet?" They tried to figure out their own relevant problems and find its solutions.
And furthermore, they talked their bad health habit on the condition that we keep it secret from the physician in charge. And the facilitator himself was taught needs of patients who can be candidates of department of nephrology.
Conclusion: Conversation Map is amazing tool for educating diabetic patients and can be used even by a nephrologist. It also might be a good tool for educating healthcare providers like a nephrologist.

PG-35

Effects and predictors of a STENO intensive multifactorial intervention for HbA1c target achievement in Taiwanese patients with type 2 diabetes

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Purpose: To investigate the effects and predictors of a STENO Intensive Multifactorial Intervention on glycemic control in Taiwanese patients with type 2 diabetes.
Methods: Outpatients with type 2 diabetes and a glycated hemoglobin (A1c) level of 7% or above were recruited from the division of metabolism and endocrinology in a regional hospital in southern Taiwan. These patients were invited to enroll in a STENO Intensive Multifactorial Intervention, which consisted of three in-person sessions over a period of 6 to 12 weeks. Data on A1c and fasting blood glucose (FBG) were collected at baseline and post-intervention. Paired t-tests were used to compare the changes in A1c and FBG levels between baseline and post-intervention. Logistic regression analyses were used to assess baseline factors associated with achieving A1c < 7% post-intervention.
Results: A total of 112 patients (52% males) with a mean age (± standard deviation) of 57.9 ± 12.5 years completed the intervention. The mean baseline and post-intervention A1c levels were 8.6 ± 1.3 and 7.9 ± 1.2, respectively, with a significant difference of 0.7 ± 1.0 ($p < 0.001$). The mean baseline and post-intervention FBG levels were 169.1 ± 53.8 mg/dL and 149.3 ± 44.1 mg/dL, respectively, with a significant difference of 19.8 ± 48.3 mg/dL ($p < 0.001$). At the end of the intervention, 25 patients (22.3%) achieved the desirable A1c goal of less than 7%. Results of the logistic regression analyses indicated that patients who were under the age of 65 years at baseline were less likely to achieve an A1c level of <7% post-intervention (odds ratio = 0.37, 95% confidence interval = 0.15–0.92, $p = 0.033$). Sex, duration of diabetes diagnosis, educational levels, and treatment type (oral antidiabetic therapy versus insulin therapy) were not significantly associated with an A1c level of <7% post-intervention.
Conclusions: Completion of a STENO Intensive Multifactorial Intervention was able to significantly improve the mean levels of both A1c and FBG in Taiwanese patients with a baseline A1c level of 7% or above. Nevertheless, less than a quarter of the patients were able to achieve a desirable A1c level below 7% at the end of the intervention. Further studies are needed to identify predictors, in addition to age <65 years, for the inability to achieve the desirable A1c goal.

PG-36

Improvements in the views of insulin therapy among Taiwanese patients with type 2 diabetes participating in a STENO multifactorial intervention

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Purpose: To investigate the effects a STENO Intensive Multifactorial Intervention on the views and perceptions of insulin therapy, based on the Diabetes Attitudes, Wishes and Needs (DAWN) instrument, in Taiwanese patients with type 2 diabetes.
Methods: Outpatients with type 2 diabetes and a glycated hemoglobin (A1c) level of 7% or above were recruited from the division of metabolism and endocrinology in a regional hospital in southern Taiwan to enroll in a 3-session STENO Intensive Multifactorial Intervention. The views and perceptions of insulin therapy of the patients were assessed using the 22-item DAWN instrument at baseline and post-intervention. Six subscales of the DAWN were (A) benefits of insulin therapy, (B) frustration and concerns about insulin therapy, (C) inconvenience of insulin therapy, (D) impaired social relationship, (E) discomfort of insulin therapy, and (F) side effects. A lower score means a more positive view towards insulin therapy. Non-parametric Wilcoxon signed-ranked tests were used to compare the changes in the DAWN scores. Logistic

regression analyses were used to assess baseline factors associated with a decrease (improvement) in DAWN with the intervention.
Results: A total of 112 patients (52% males) with a mean age (± standard deviation) of 57.9 ± 12.5 years completed the intervention. At the baseline, 37 patients (33%) were on oral antidiabetic therapy and 75 patients (67%) were on insulin therapy. After the intervention, 19 patients had changed from oral antidiabetic therapy to insulin therapy and 10 patients had increased their frequency of insulin injections. The overall DAWN score and the scores of all 6 subscales except subscale F were significantly decreased with the intervention, indicating that the patients had a more positive view towards insulin therapy with the intervention. Seventy-nine patients (71%) had a more positive view towards insulin therapy with the intervention. **Results** of the logistic regression analyses of the subscales indicated that patients who were 65 years or above at baseline were significantly more likely to show improvement in subscale A of DAWN post-intervention (odds ratio = 3.03, p = 0.009). Moreover, patients who were on oral antidiabetic therapy at baseline were more likely to show improvement in subscale E of DAWN post-intervention (odds ratio = 2.08, p = 0.073).
Conclusions: Completion of a STENO Intensive Multifactorial Intervention was able to significantly improve the views and perceptions of insulin therapy in Taiwanese patients with type 2 diabetes. Further studies are needed to identify the reasons for patients who did not show improvements.

PG-37

Impact of drama-based educational program, diabetes theater, on healthcare professionals' attitudes toward diabetes care: a mixed method evaluation

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Background: Patient empowerment is considered to be crucial for healthcare professionals (HCPs) in diabetes. However, how to learn this concept is yet unclear. Thus we developed a drama-based educational workshop, Diabetes Theater (DT), to teach HCPs the philosophy of patient empowerment. Participants reflect on their own practice by watching a play based on common misunderstandings between patients and HCPs in a clinical practice, and then discussing by focusing on the good points and areas for practice improvement in the drama.
Aims: The aim of our study was to investigate the effect of DT on participants' attitudes toward diabetes care using a mixed method.
Method: The study design utilized both quantitative and qualitative methods (mixed-method). Participants in DT held at the 57th annual scientific meeting of the Japanese Diabetes Society in 2014 were requested to answer a questionnaire before and after the program. To compare the scores before and after, a paired t-test was performed with a significance level of alpha = 0.05. Attitudes were measured by four items from the Diabetes Attitude Scale, using an eleven-point Likert scale ranging from 10 = strongly agree to 0 = strongly disagree. Free descriptions for the open-ended questions were analyzed qualitatively.
Results: We analyzed data from 131 respondents (male 15, female 116); nurses 54%; dietitians 16%; doctors 11%; pharmacists 11%; and others 8%. HCPs' attitude scores increased significantly in each item. In detail, "HCPs should be trained how to communicate with their patients" (from 8.1 ± 2.0 to 9.1 ± 1.5); "HCPs should learn counseling skills" (from 8.0 ± 1.9 to 9.2 ± 1.4); "HCPs should learn how to set goals with patients" (from 8.5 ± 1.6 to 9.4 ± 1.3); "people with diabetes have the right not to take good care of their diabetes" (from 6.2 ± 2.5 to 7.4 ± 2.5) (from before to after, mean ± SD, all $p < 0.05$). What participants learned from the program were summarized: (1) HCPs should wait till the time is ripe; (2) Two-way communication between patients and HCPs is important.
Discussion: In conclusion, HCPs who participated in DT changed their attitudes toward diabetes care positively. They put more focus on the importance of special training in key elements of patient empowerment, such as communication, counseling, and collaboration with patients. These results suggest that DT could be useful to improve the attitudes of HCPs in diabetes care in terms of patient empowerment.

PG-38

A 6-month nutritional education program for patients with diabetes mellitus is effective to improve HbA1C

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Background: It is important to prevent and treat diabetes mellitus with lifestyle as an important component. However, the best form of education program to control and correct lifestyle measures of people with diabetes is not always performed. Continuous nutrition education was performed individually to support patients with diabetes and the effectiveness of this education was assessed.
Subjects and methods: Thirty four patients took part in the education program for six months from May 2013 to October 2014. The program was performed at four discrete timepoints: baseline, one month, three months, and six months. Also the program was provided four to six times. It was individually targeted based on HbA1c level and duration of treatment. In patients with dementia, the education program was provided mostly to the patient's family. At baseline the personal information of patients was collected and education was provided about diabetes mellitus. At the second timepoint, education was provided about a well-balanced diet. The third timepoint involved education regarding appropriate snacks and drinking alcohol, and at the final 6-month timepoint, a review of all the education components was provided together with education on achieving the target goals for diabetes mellitus. HbA1C, body weight, abdominal circumference, diet, medication and activity level were compared and investigated before and after the nutritional education program.
Results: HbA1C decreased by 0.8%, from 8.1 ± 1.8% to 7.3 ± 1.2% ($p < 0.01$). In patients with HbA1C > 8.0% (n = 13), the value decreased by 1.7% from 10.0 ± 1.4% to 8.3 ± 1.4% ($p < 0.01$). On the other hand, in patients with HbA1C < 7.9% (n = 21), it dropped by 0.1%, from 6.9 ± 0.5% to 6.8 ± 0.6%. Body weight decreased by 0.8 kg, and abdominal circumference decreased by 1.2 cm (not statistically significant). There were thirteen patients whose medication was changed during the six months period. Analysis of activity found that, the step counts changed from 4,249 to 3,891 steps, and activity levels changed from 2.1METs to 2.3METs. These changes are not statistically significant.
Conclusion: The use of a 6-month education program for diabetes was able to significantly reduce HbA1C by 0.8 percentage points. A greater benefit was seen in patients with a higher baseline of HbA1C > 8.0%. However, our education program performed only by dietitians could not improve physical activity levels. A potential team consisting of dietitians, pharmacists, rehabilitation therapists, nurses and doctors should continue to support these patients with diabetes to improve their lifestyles.

PG-39

Performance comparison of average daily risk range obtained by continuous glucose monitoring and self-monitoring of blood glucose in diabetic outpatients

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Background: Recently it has been known that postprandial hyperglycemia and severe hypoglycemia may cause various cardiovascular events and enhance risks for death, and therefore monitoring of blood glucose variability is important. As the indices for evaluating blood glucose variability, the standard deviation of daily blood glucose levels (SD) and the mean amplitude of glucose excursion (MAGE) have so far been widely used, whereas there has been a problem that both of them depend on hyperglycemic ranges but reacts insufficiently to hypoglycemic ranges. In 2006, Kovachev et al. proposed the concept of average daily risk range (ADRR) as the index for evaluating blood glucose variability which sufficiently reacts to both hyper- and hypoglycemic ranges. ADRR is converted to risk values that will be expected as the index for prediction of risks for severe hyper- and hypoglycemia. Continuous glucose monitoring (CGM) is useful in evaluating blood glucose variability. However, CGM can be performed only in facilities which suffice the facility standards, and has problems in the possible period of glucose sensor (the Enlite® sensor) only for 6-day use.
Purpose: Performance comparison was conducted between ADRR obtained by CGM (ADRRc) and ADRR obtained by SMBG (ADRRs) using 7 points. And also, performance comparison was conducted between ADRRc and ADRRs calculated using only 3 points of SMBG before meal or ADRRs calculated using 3 points of SMBG before meal with 1 point of SMBG after meal.
Patients: 13 outpatients with diabetes mellitus (type1/type2: 4/9) (mean age: 59.5 years, mean HbA1c: 7.1%) were enrolled.
Methods: The study patients underwent CGM (iPro2) for 6 days and SMBG was daily recorded 7 times (3 times before meal, 3 times 90 min after meal, and 1 time before going to sleep). In SMBG, One Touch Ultra Vue was used. ADRRc and ADRRs were calculated using CGM and SMBG data obtained for 6 days, respectively.
Results: There is a strong correlation between ADRRc and ADRRs. ADRRs calculated using only 3 points of SMBG before meal were low compared with that calculated using 3 points of SMBG before meal with 1 point of SMBG after meal, and the latter approximated to ADRRc.
Conclusion: ADRRs calculated using 3 points of SMBG before meal with 1 point of SMBG after meal correlated well with ADRRc. Results demonstrated that ADRRs calculated using 3 points of SMBG before meal with 1 point of SMBG after meal was the good index capable of expressing the blood glucose variability.

PG-40

The experience of using "Steno Diabetes Dialogue Card" for small group patient education and its effect on glycemic control

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Aims: To improve the glycemic control of adult diabetic patients, the feasibility of a self- motivated and –oriented glycemic control program assisted by an education tool was assessed.
Patients and methods: From 2015/06 to 2016/02, a total of 35 poorly controlled (mean diabetic duration 9.8 ± 5.61 years and mean HbA1c 8.68 ± 1.79%) adult type 2 diabetic (T2DM) patients (15 male and 20 female, aged 62.06 ± 10.06, ranged from aa to bb y/o) were enrolled. After randomly subgrouped, a patient based, problem-oriented and self-motivated interview model was conducted by using the "Diabetes Dialogue Card corrected from the Steno Tool" under the guidance of an expert diabetic educator.
Results: After a 9 months "intervention, most of the patients obtained better knowledge of diabetic complication and pitfalls of diabetic control. Glycemic control was statistically improved when the following parameters (before and after, p value) were assessed, which include HbA1c (8.68 ± 1.79% to 7.83 ± 1.00%, $p < 0.003$), body weight (64.64 ± 1.8 to 63.96 ± 10.6 kg, $p < 0.025$), drug compliance (4.77 ± 1.59 to 5.74 ± 0.71 days/week, $p < 0.001$), frequency of exercise (2.54 ± 0.45 to 3.89 ± 1.74 days/week, $p < 0.001$) and frequency of self-monitoring of blood glucose (1.66 ± 0.35 to 2.17 ± 2.06 days/week, $p < 0.001$).
Conclusions: Through enhancing the acknowledgement of self-deficit in diabetic control, Diabetes Dialogue Card effectively improved glycemic control of T2DM patients through a problem-oriented, self-motivated group interview under the guidance of expert diabetic educators.

PG-41

Scenario-based training to improve nursing staff knowledge and competence in diabetes care

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Background: Currently patient with diabetes comprise up to 30% of the census of adult medical admissions in our hospital. As there is a turnover of ward nurses each year, a structured and tailor-made training program is essential to ensure a good level of knowledge and competence in diabetes care so that patient safety and quality care could be enhanced.
Method: The training module consisted of two parts, namely scenario-based case conference and post conference newsletter sharing. At the case conference, ward nurse would take turn to present a case of diabetes and raise questions regarding the management. A pre-conference quiz related to the scenario was also given to all participants for knowledge assessment. Interactive case discussion was guided by a Diabetes Nurse Consultant. After the conference, all valid learning and discussion points would be summarized in a newsletter and posted to all related units.
Results: Three interactive case conferences were organized and attended by a total of 49 nurses in 2015. The case-mix selected for presentation was comprehensive, including insulin treated diabetes with advance complications, uncontrolled diabetes, gestational diabetes complicated with bipolar affective disorder, etc. Regarding the knowledge assessment, more than 90% of the participants could recognize the actions and side effects of traditional anti-diabetic drugs, whereas less than 50% of them seemed not familiar with the nature of those novel medications. All the frontline nursing colleagues could point out the proper management for patient develop hypoglycemia but only a few were competent to address the highlights when caring for gestational diabetes. Through the interactive discussion, ward nurses could learn from real cases that they came across and found interesting. All participants welcomed the initiation of this program.
Conclusion: The Scenario-based training is a tailored-made program for the ward nurses to enhance their knowledge and competence in caring in-hospitalized patients with diabetes. From the learning experience gained in this program, the nurses could address patients' need timely and grasp the valuable teaching opportunity during their hospitalization, thus facilitating early discharge and shorten their length of stay. Continuous enhancement of the program would help to fine-tune and optimize the training contents and learning activities in future.

PG-42

Fostering regular exercise behavior to improve metabolic control in patients with diabetes

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Background: Research evidence consistently supports the benefits of exercise on people living with diabetes. In addition, regular exercise is crucial for the prevention of diabetes and other related metabolic disorders. In order to understand the exercise pattern among patients with diabetes, a survey was conducted and a set of exercise in the form of a dance going with a song, was promulgated in our Hospital to facilitate patients to perform safe and appropriate exercise.
Method: The program was conducted in two phases. Phase 1 was a cross-sectional survey to understand exercise behavior and metabolic control in patients with type 2 diabetes. Phase 2 was a feasibility study to test the effectiveness of a Diabetes Dance training program. The Diabetes Dance as a safe and appropriate exercise for people with diabetes had been endorsed by a panel of experts, including physiotherapists and diabetes educators. The diabetes nurses who conduct the exercise program had received specific professional training to do the coaching. In addition, the precautions about performing exercise (e.g., hypoglycaemia, heart conditions) were well explained for alertness at the beginning of the exercise program. A DVD containing the exercise movement and important messages on self-management through the meaningful lyrics and delightful melody was given to patients for take-home practice.
Results: A total of 328 subjects were recruited in the exercise behavioral survey with mean age 64% and 45% were male. The mean hemoglobin A1c level was 7.6% and mean body mass index (BMI) 27. 113 subjects (36%) reported they had less than 150 minutes exercise per week and other 35% even did not have any exercise at all. For Phase 2 study, eighteen patients were recruited (female = 17) with mean age 54 and mean BMI 31.9. Blood glucose level was significantly lower after the 30-min dance ($P < 0.01$). Improvement of exercise knowledge was also noted after the training.
Conclusion: Although the beneficial effect of regular exercise on metabolic control is highly acknowledged, there are still many barriers, such as lack of time and low motivation, for people to initiate exercise habit. The exercise program of this study was established based on the use of dance and music in order to facilitate the enjoyment of exercise and improve exercise habit adherence. It is suggested to develop large-scale and structured study in future to evaluate the effectiveness of exercise activity on long term glycemic and metabolic outcomes.

PG-43

Factors associated with self-care behavior among community-dwelling elderly Taiwanese with diabetes mellitus: findings from the 2009 national health interview survey

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Purpose: To investigate the factors associated with self-care behavior, including both adherence behavior and self-management behavior, among community-dwelling elderly Taiwanese with diabetes mellitus, using data from a nationwide, population-based health survey.
Methods: Individuals aged 65 years and older were identified from the dataset of the 2009 National Health Interview Survey. Seven adherence behavior indicators and seven self-management behavior indicators were evaluated. Three composite scores were calculated to represent better adherence behavior, self-management behavior, and self-care behavior. Separate logistic regression analyses were conducted to investigate independent factors associated with adherence behavior scores, self-management behavior scores, and self-care behavior scores, dichotomized with their respective medians as the cut-off values.
Results: Of the 2,399 respondents (sampling weight-adjusted) aged 65 years and older, 434 (18%) had diabetes. The mean age of these patients was 74.1 years (range 65.0–93.2 years). Of them, 46.2% were males. Multivariate logistic regression analysis revealed that an educational level of senior high school or above (adjusted odds ratio [aOR] = 3.04, $p = 0.001$) and having difficulty with mobility or immobile (aOR = 2.36, $p = 0.005$) were significantly associated with better adherence behavior. Moreover, older age (aOR = 1.54, $p = 0.043$), being married or having a partner (aOR = 2.17, $p = 0.001$), and residing in urban areas (aOR = 2.30, $p < 0.001$) were significantly associated with better self-management behavior. Finally, for the overall self-care behavior, older age (aOR = 1.54, $p = 0.039$), living with someone (aOR = 2.23, $p = 0.029$), and residing in urban areas (aOR = 2.05, $p = 0.001$) were its three significant independent associated factors.
Conclusions: Findings from this secondary data analysis of a population-based heath survey revealed that older age, living with someone, and residing in urban areas were significant factors associated with better self-care behavior in community-dwelling elderly Taiwanese with diabetes.

PG-44

The effect of dietary intervention in T2DM patients who could not succeed in losing body weight after taking Dapagliflozin

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New oral hypoglycemic agents, Dapagliflozin, highly selective inhibitor of sodium-glucose co-transporter 2 (SGLT2), has been reported to reduce body weight, which appears to be attributable to the loss of glucose energy with no effects on appetite. By the way, body weight is also related to dietary intake, which motivated us to observe add-on effects of diet therapy for persons with T2DM whose body weights were not reduced despite taking dapagliflozin.
We enrolled 31 T2DM patients who failed to lose their weights on dapagliflozin for 2 months. A trained clinical dietitian offered individually-tailored dietary advice based on their eating habits and recommended calories, and assessed dietary intake by 24-hr recall. We investigated the changes in weight, BMI, WHR, and FBS before and after dietary intervention. The subjects' undesirable eating habits were categorized into 4 main findings; having large meal, frequent snacking, eating too much fruits, and frequent drinking alcohol.
The mean age and duration of diabetes were 62.3 ± 1.6 years and 13.3 ± 1.5 years. From the first day of taking dapagliflozin to the intervention day, the mean weight and BMI change were 0.30 ± 0.19 kg and 0.12 ± 0.08 kg/m^2. According to the dietary assessment, the subjects had $127.9 \pm 7.4\%$ more excessive calories when compared with the individually recommended level. At the follow-up day, 61.3% of subjects (n = 19) were succeeded in losing weight, and the mean weight and BMI change during 2 months after diet therapy were -1.19 ± 0.38 kg and -0.44 ± 0.13 kg/m^2, which were significantly lower than those before the intervention ($P < 0.01$, respectively). There were no differences in dosing period, FBS and WHR change, and other antidiabetic treatment before and after the intervention. According to gender, men (n = 13) showed significant weight and BMI change (-2.12 ± 0.72 kg and -0.75 ± 0.25 kg/m^2, $P = 0.03$), but women didn't. When compared with the individually recommended level, men had higher ($P < 0.01$) percentage of calorie intake ($152.4 \pm 10.1\%$ in men vs. $115.8 \pm 5.3\%$ in women). Having large meal and frequent drinking alcohol were more common in men than in women ($P = 0.04$, and $P = 0.01$, respectively).

In conclusion, dietary intervention was effective in T2DM patients who could not succeeded in losing weight with dapagliflozin. Having large meal and frequent drinking alcohol were undesirable eating habits which could affect higher intake of calories especially in men, but these might have been corrected after dietary intervention and led to losing weight. Dietary intervention and individually-tailored advice could lead an additive effect on body weight loss of dapagliflozin.

PG-45

The effect of "Diabetic dialogue cards" accompanying peer support for diabetic control

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Purpose: To evaluate the effect of interactive group education of "Diabetic dialogue cards" accompanying peer support on diabetic control and adaptation.
Method: We trained nine patient experts first. The health education activities of "Diabetic dialogue cards" were held twice in a month. Each time we invited about seven diabetic patients who had an HbA1c level higher than 7.5% to participate. All patient experts have to participate these activities for two times to serve as volunteers and telephone interviewers afterwards.
Results: We held group education of "Diabetic dialogue cards" for 18 times during June 2015 to March 2016. Out of 135 registered patients, 97 (72%) patients have participated in our activities. There were 23 patients completing three courses on diet, exercise and medication, respectively. The questionnaires before and after the courses were collected for the 23 patients. The main results are showing as follows:
a. Self-monitoring of blood glucose (SMBG) and exercise behavior: the rate of SMBG, at least 1–2 times per week, increased from 65% to 69%n; the rate of exercise, more than 3 times per week, increased from 70% to 70%. The differences were not statistically significant.
b. Life experience and daily living state: there was improvement in aspects of "subjective health condition comparing present state to half a year ago", "subjective health condition comparing with persons of the same age" and "global living satisfaction as compare to half a year ago". There were also decreased rates of "trouble with taking medication", "trouble with diet control", "nervous and anxious", "tearing for feeling sad", "feeling sad and depressed", "feeling angry", and "feeling worry and fear".
c. Improvement in A1C and fasting plasma glucose (FPG): there were significant improvement in A1C (from 9.7 ± 1.9% to 8.2 ± 1.4% in 3 months, $P < 0.001$) and FPG (from 201 ± 60 mg/dL to 140 ± 42 mg/dL, $P < 0.001$).

Conclusion: The group education program of "Diabetic dialogue cards" accompanying peer support is effective for diabetic control and psychological and social adaptation.

PG-46

Effects of diabetic education on metabolic parameters in type 2 diabetic patients using insulin

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Patients using insulin treatment were hospitalised due to poor glycemic control. Patients were selected from last 6 months in 2015 from Endocrinology inpatient clinic. 46 males (46.6%) 57 females (55.33%) totally 103 patients were recruited in the study. Mean ages were 57.9 ± 12.2 (27–76). All patients were Type 2 diabetic patients and using insulin treatment. Initial mean fasting plasma glucose levels were 248 ± 95.28 mg/dL (82–568). Mean HbA1c percentage was 9.44 ± 2.22 (5.9–14.5). Total cholesterol was 198.06 ± 43.11 mg/dL, LDL cholesterol was 120.65 ± 41.94 mg/dL, triglycerides 181.06 ± 132.77 mg/dL. After hospitalisation no change in insulin medication was done, instead changing daily activities, increasing physical activity, improving dietary adharence and education was done for 5 consecutive days. After 6 months of discharge mean fasting plasma glucose was 168.15 ± 69.53 mg/dL (80–411) $p < 0.001$, HbA1c 7.8 ± 1.74 (4.9–10.9) $p < 0.001$, total cholesterol 193.09 ± 53.92 mg/dL (96–366) $p < 0.05$, LDL cholesterol 111.30 ± 41.82 $p < 0.05$, TG 155.06 ± 53.92.
As a result, in chronic diseases like diabetes ellitus, lifestyle interventions such as increasing physical activity, improving dietary adharence can result in good control on various metabolic parameters so education shuold be repeated and lifelong.

PG-47

Who should give insulin education?

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In patients with Type 2 Diabetes Mellitus using insulin; injection techniques such as rotation, needle insertion angle, using skinfold, waiting for 10 seconds inside the skin are important determinants of glycemic regulation. In the inpatient clinic of Endocrinology and Metabolism of Necmettin Erbakan University, Meram Medical Faculty, patients who took insulin education between August 2015–February 2016 were recruited into the study. Totally 278 patients were educated between these dates. 169 (60.70%) patients were educated by diabetes nurse where as 109 (39.2%) were educated by someone else (doctor, pen educator, pharmacist). Effect of diabetes nurse education was studied retrospectively. Among patients educated by diabetes nurse, 70 (41.4%) patients reported that they use rotation method, 99 (58.6%) patients reported that they did not rotate insulin injection sites. 155 (91.7%) patients reported that they waited for at least 10 seconds after insertion of the needle where as 14 (8.3%) were not aware of it. 27 patients (15.97%) were using 4 or 5 mm needle length, 25 (14.79%) were using 6 mm, 117 (69.23%) were using using 8 mm needle length. Among 27 patients using 4 mm, 20 (74.07%) reported that they insert needle at a 90° angle where as 7 (29.92%) patients were using skinfold tecnique. Among 6 mm users 14 (56%) were using 90° angle method, 11 (44%) were using skinfold technique. Among 8 mm users, 74 (63.24%) were using skinfold where as rest 43 (36.75%) patients were using 90° angle. 109 patients who were educated by someone else other than diabetes nurse, 91 (83.48%) were not rotating injection areas, 18 (16.51%) were rotating. 63 (57.79%) patients were waiting for 10 seconds, 46 (54.54%) were not waiting. Among 11 patients using 4–5 mm needle users, 6 (54.54%) were using 90°angle method, 5 (45.45%) were using skinfold tecnique. Among 24 patients using 6 mm needle length, 13 (54.16%) were using 90° angle method, 11 (48.83%) were using skinfold. Among 74 patients using 8 mm length, 35 (47.29%) were using 90° angle method, 39 (52.70%) were using skinfold tecnique.
According to the data that we presented, one of the reason of poor glycemic control is injection techniques. Patients who

were not educated by diabetes nurse, used wrong techniques that may lead to ineffective insulin absorbtion. Not only education of patients but also education of educators must be repeated regularly.

PG-48

Effectiveness of the Diabetes Conversation Map education tools on diabetes-related parameters of outpatients with diabetes

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Objective: Diabetes Conversation MapTM Tools are interactive instruments for health education invented by International Diabetes Federation. With groups' brainstorming as well as visually learning methods, these tools have better effects on education than the traditional ones. In order to help diabetes patients to have better control of their blood sugar, they need to acquire more knowledge and understanding about their diabetes self-care. In this study, we examined the changes of patients on diabetes-related parameters after receiving the conversation map classes.
Materials and methods: We provided two-hour Conversation Map health education classes 1 to 2 times per month hosted by registered dietitian or diabetes educator and 3–8 participants joined it each time since February 2014. Blood glucose, HbA1c, weight data, knowledge, exercise frequency, scores of Diabetes attitude, wishes and needs (DAWN) and health-related quality of life(HRQL) short-form 8 (SF-8) questionnaires were collected before and after classes.
Results: Eighty-four participants had joined the study which included 15 times of group education. Blood sugar controlling had significantly improvement. The fasting blood sugar had decreased from 151.3 ± 53.4 mg/dL to 132.5 ± 42.9 mg/dL ($p = 0.033$). Postprandial blood sugar had also declined from 187.1 ± 42.7 mg/dL to 167.8 ± 52.8 mg/dL($p = 0.028$), and HbA1C decreased from 8.2 ± 2.1% to 7.2 ± 1.1%($p = 0.001$). Average weight and BMI had slipped from 68.0 ± 12.1 kg to 67.6 ± 12.1 kg ($p = 0.275$) and 25.9 ± 3.7 kg/m^2 to 25.8 ± 3.6 kg/m^2 ($p = 0.232$) respectively. The average percentage of knowledge was improved from 63% to 73%. With regard to the self-management, the portion of people exercising more than 150 minutes per week had increasing 23%. The physical component score (PCS) and the mental component score (MCS) from SF-8 were increased 20% and 22% respectively, which were assumed better performance on their quality of life. Also, noteworthy is a fact that knowledge about the diabetes and insulin was improved.
Conclusion: This study showed that the diabetes small-group education classes effectively improved patients' blood glucose, HbA1c, weight data, self-management behaviors and quality of life through the structural and interactive tools (Diabetes Conversation Map).

PG-49

Study on the effect of three kinds of food in diabetic patients with hypoglycemia

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Objective: To explore the simple and effective methods for treating hypoglycemia in diabetic patients and evaluate the satisfaction of the dietary treats such as sugar, cookies, and yogurt. Method 126 cases of diabetic hypoglycemia were divided into three groups according to the time of admission: group 1 ate three and a half of sugar, group 2 ate a bottle of yogurt (250 mL), group 3 ate four pieces of biscuit, three kinds of foods all contain 15 grams of glucose or carbohydrate. To monitor the blood glucose of each group after they ate the corresponding food and to evaluate the degree of satisfaction with diffence dietary treats.
Result: The mean blood glucose values of the three groups of patients were greater than 3.9 mmol/L after they ate food 15 minutes. The retest blood glucose level had no statistically significant difference between group 1 and group 2 ($P > 0.05$). The retest blood glucose value of group 3 was lower than the other two groups ($P < 0.05$).
Conclusion: Three kinds of food all can correct hypoglycemia, yogurt and sugar have the same effect in correcting hypoglycemia. Biscuit glycemic index is lower than the other two kinds of food, yogurt tastes good, biscuit can bring a sense of fullness, which can also be carried and buied relatively convenient, the patients can accept all the three kinds of food.

PG-50

Knowledge, attitudes and practices and its association with glycemic control among type 2 diabetes mellitus patients in a tertiary hospital

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Introduction: Patient education is the cornerstone of diabetes care. This study was conducted to determine the knowledge, attitudes and practices (KAP) among patients with type 2 diabetes mellitus and find out if these factors are associated with glycemic control.
Objectives: This cross-sectional analytic study aims to identify the demographic profile of the subjects and assess their level of Knowledge, Attitude and Practices (KAP) towards diabetes mellitus (DM). It also aims to determine the association between the patients' KAP and glycemic control of DM among patients in a diabetic clinic.
Methods: Type 2 DM patients were recruited using the convenient sampling method from a diabetes clinic. KAP were assessed using a 54-item structured KAP questionnaire and control of DM was evaluated from the most recent HbA1C levels.
Results: A total of one-hundred sixty-eight patients (168) with type 2 DM participated. In this study, we found out that the level of knowledge, attitude and practices among patients following up in a diabetes center in a tertiary hospital is adequate, achieving 56%, 66% and 91%, Good KAP is found in majority of females, above 60 year old, overweight, high waist-to-hip ratio, at least high school level, unemployed, with family history of DM, less than 10 years diabetic, those who attended DM classes, and without smoking history. However, these results were found not be statistically significant except for educational attainment for knowledge domain, female gender for attitude domain and unemployment status for the practice domain. There was a strong association between knowledge and attitude, but not with knowledge and practice ($P > 0.05$). No significant association was noted between good KAP and glycemic control.
Conclusion and recommendation: This is study showed that good KAP is not associated with good glycemic control. Other plausible factors like socioeconomic constraints and lack of resources to facilitate medication adherence must also be identified and addressed to achieve better disease control. This study also emphasizes that providing patient education through diabetes classes and the presence of an integrated multidisciplinary team is important for enhancing patient KAP.

PG-51

The impact of small interactive group education plus basal insulin on the glycemic response of type 2 diabetes mellitus

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Background: Type 2 diabetes is a progressive disease, and most patients will eventually need insulin to achieve euglycemia. Although it was observe that the rate of insulin injection in Taiwan increased from 18% in 2006 to 21.6% in 2011, less than 10% attained the recommended diabetic "ABC" targets. To improve these suboptimal metabolic control, and reduce the risk of diabetic-related complications, a more intensive glycemic management is warranted. Management and support to enable patients to effectively advocate diabetes self-management.
Aim: To investigate the effect of early basal insulin therapy with or without added intervention by diabetic educator on the glycemic control of type 2 insulin naïve diabetic patients.
Method: A randomized controlled trial was conducted at Wan Fang Hospital from August 25 2014 to November 30, 2014. Basal insulin was initiated to type 2 DM insulin naïve patients with fasting blood glucose(FBS) >150 mg/dL and hemoglobin A1c (HbA1c) > 8%. Patient with previous history of insulin injection or refused insulin were excluded. Patients were randomly divided into "intervention" by diabetic educators or "conventional" group. Basic knowledge about insulin therapy was given to all diabetic patients. The group with "intervention" had regular small class session, weekly telephone communication from diabetic educators, and self-monitoring of blood glucose Breeze 2 glucometer (BAYER) with smart cable Health2 Sync to optimize glucose monitoring.
Results: 52 patients were included in the "intervention" group and 20 patients in the "convention group". 27 male and 25 female with mean age of 64.5 years in "intervention" and 11 male and 9 female with mean age of 65.6 years in "conventional" group. Baseline HbA1c and FBS of "intervention" and "conventional" group were 9.5 ± 0.2% and 9.9 ± 0.3%; and 227 ± 7.9 mg/dL and 234 ± 10.7 mg/dL, respectively. After 3 months of treatment, HbA1c and FBS of "intervention" and "conventional" group were 7.4 ± 0.1% and 8.9 ± 0.2% ($p < 0.001$); 135 ± 3.5 mg/dL and 192 ± 5.6 mg/dL ($p < 0.001$), respectively. A decrement of HbA1c in the "intervention" and "conventional" group were 2.17% and 0.9%, respectively. HbA1c < 7% and FBS < 130 mg/dL attained by "intervention" and "conventional" group were 28.9% and 0%; and 50% and 0%, respectively. On the contrary, HbA1c > 8% and FBS > 200 mg/dL attained by "intervention" and "conventional" group were 9.6 and 85%; and 1.9% and 85%, respectively.
Discussion: This randomized trial demonstrated that aggressive diabetic educator intervention added to early basal insulin lead to a better glycemic control than basal insulin therapy alone.

PG-52

The role of diabetic education added to biphasic insulin on the glycemic control of type 2 diabetes mellitus

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Background: Glycemic control in diabetes mellitus (DM) is a cornerstone in reducing its chronic complication. Although glycated hemoglobin (HbA1c) remains the gold standard for assessment of glycemic control, there is no consensus whether fasting plasma glucose (FPG) or post-prandial plasma glucose (PPG) is a better predictor of glycemic control.
Aim: To investigate the effect of shifting to bi-phasic insulin in patients who fail to achieve HbA1c in after basal insulin therapy had achieved fasting glucose goal.
Method: A randomized controlled trial was conducted at Wan Fang Hospital from April 1, 2015 to August 31, 2015. Type 2 DM patients on basal insulin for more than 3 months but FPG < 150 mg/dL and hemoglobin HbA1c > 7% were included in this study. Patients were randomly divided into "intervention" by diabetic educators or "conventional" group. Basic education on insulin therapy was instructed to all DM patients. The group with "intervention" had regular small class session, weekly telephone communication with diabetic educators, and paired self-monitoring of blood glucose (SMBG) were done to optimize glucose monitoring.
Results: A total of 44 patients (23 male and 21 female) with mean age of 62.5 ± 2.2 years were included in this study. 25 patients (14 male and 11 female) with mean age of 69.4 ± 2.5 years were included in the "intervention" group and 19 patients (9 male and 10 female) with mean age of 53.4 ± 2.9 years were included in the "convention" group. Baseline FPG, PPG, and HbA1c in the "intervention" and "conventional" group were 111.5 mg/dL ± 3.2, 211.0 mg/dL ± 8.2, 8.4% ± 0.2, respectively. While the conventional group had a baseline FPG, PPG, and Hb1Ac of 179.8 mg/dL ± 8.6, 170.9 mg/dL ± 4.7, 8.8% ± 0.24, respectively. After 3 months of treatment, FPG, PPG, and HbA1c of "intervention" and "conventional" group were 130.2 mg/dL ± 3.6 ($p < 0.001$), 176.3 mg/dL ± 4.0 ($p < 0.001$), and 7.7 ± 0.1% ($p < 0.01$); and 154 mg/dL ± 6.2 ($p < 0.05$), 173.4 mg/dL ± 6.4 ($p < 0.8$) and 8.2 ± 0.27% and ($p < 0.08$), respectively. The decrement of HbA1c in the "intervention" and "conventional" group were 0.85 ± 0.2% and 0.65 ± 0.2%, respectively. In the "intervention" group, 7.8% and 40% attained HbA1c of < 7% and 7.1–7.5%, respectively. While in the "conventional" group, 10.5% and 21.2% attained HbA1c of <7% and 7.1–7.5%, respectively. On the contrary, HbA1c of >8%, FPG > 200 mg/dL and PPG > 200 mg/dL attained by the "intervention" and "conventional" group were 16%, 0%, and 12%; and 42%, 0% and 21.1%, respectively.
Conclusion: This randomized control trial demonstrates that aggressive intervention by diabetic educator with SMBG added to bi-phasic insulin therapy attained better glycemic control.

PG-54

The effectiveness of the camp of "Free Sugar, LOHAS" on type 2 diabetes patients, in the regional teaching hospital

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The incidence of type 2 diabetes in the world has been rising year by year, the researchers forecast that to 2025 the world will have 380 million adults suffer from diabetes. Diabetic patients are exposed to a high risk of cardiovascular disease and other chronic complications. The well blood sugar controlled is needed to reduce the risk.
Aim: The aim of this study was to examine the effect of group program (GP) on knowledge, attitude, self-efficacy in the patient with type 2 diabetes under insulin control. This study was pre-posttest design. Samples included in this study were who had diagnosed with type 2 diabetes and A1C was great than 7% of teaching hospital in Yilan County, Taiwan. The intervention period is 3 months. Chart review for A1C and Body weight collecting, structured questionnaires comprised scale for determining the diabetes knowledge, diabetes

attitude, and diabetes self-efficacy in the patient with T2DM under insulin control. Descriptive statistics, independent t-test, $\chi 2$, Mann-Whitney U test and Wilcoxon signed ranks test were used to analyze the data. There were 72 participants in this study, 35 patients in GP group and 37 in usual care (UC) group. After 6 months follow-ups, physical measure such as A1C of patients in the GP group was better improved than those of patients in the UC group. The score of diabetes knowledge, diabetes attitude, and diabetes self-efficacy in GP group were 11.7 ± 2.4 v.s. 16.6 ± 1.6, 47.3 ± 4.1 v.s. 54.2 ± 4.9, 158.9 ± 34.0 v.s. 183.8 ± 16.4. There was a significant difference in the mean scores of patients' knowledge, attitudes and self-efficacy between GP groups ($p < 0.05$). The score of diabetes knowledge, diabetes attitude, and diabetes self-efficacy in UC group were 14.5 ± 3.3 v.s.15.0 ± 2.7, 47.3 ± 4.1 v.s. 52.7 ± 3.9, 158.9 ± 34.0 v.s.183.8 ± 16.4. The study indicates that after 3 monthes group program intervention on the type 2 diabetes patients with insulin controlled, there is significant improvement of the HbA1C, the scores patients' knowledge, patients' attitudes, and patients' self-efficacy were also effectively enhance and improved in GP group than that of UC group.

PG-55

Innovation calendar as an education appliance for self-management at home

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Taiwan is rich in delicacy in traditional festival seasons. The holiday food containing high carbohydrate is likely to affect the glycemic control of people with diabetes (PWD) during and after holidays. To remind PWD diet control in the special occasion such as Chinese new year, lantern festival, tomb sweeping day, dragon boat festival and moon festival, we hosted the group education by using Taiwanese Diabetes Conversation Map® at the beginning and introduced the carbohydrate counting of festival food at the end, expecting PWD could pay attention to the special delicacy to minimize the impect of overloading.

To help PWD carry out self-managememt at home, we designed the 2016 Innovation Calendar containing the information of festival food, physical activities and medication. There are 52 cards of food and exercise, we try to explicit the equivalent of bowls of rice to festival food and the time needed to consume 100 kcal for each physical activity. By the end of 2016, the cards of food and physical activities could be detached and conver to a deck of cards for repeated use. On the other hand, the information of medication could be obtained by scanning QR code on the calendar.

From December 2015 through January 2016 at Cheng-Hsin General Hospital, we distributed 64 calendars, free of charge, to anyone who was intrested. In April 2016, we telephone interviewed 30 PWD for satisfaction. 5 patients didn't use calendar much because "the size was too big", "no place to hang" and "no intention to control diabetes". The other 25 patients were satisfied with the design of the Innovation Calendar and 19 patients are willing to buy the calendar next time. As to the impact of the calendar on the literacy, self-care behavier and glycemic outcome are to be investigated.

PG-56

Original diabetes education program including individual self-care plan "My Goals Sheet" ameliorates long-term glycemic control in patients with diabetes mellitus

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Objectives: Diabetologists and health care professionals usually provide hospitalized Diabetes-educational program (DEP) for patients with diabetes mellitus in Japan. In our hospital, we have created a new DEP including lectures, discussions with patients, diet and exercise instructions, Diabetes Conversation MapTM provided by diabetes specialists, nurses, dietitians, pharmacists, physiotherapists, laboratory technicians and so on. We also developed "My Goals Sheet" (MG Sheet), which is a self-evaluation tool for declaring a patient's goals in his/her life for shorter, intermediate and longer period and self-directed goal setting in healthy eating, physical activity, medication and reducing risks addressed through DEP. The aim of this study is to investigate the efficacy and validity of the new DEP in glycemic control.

Methods: Retrospective, observational study was conducted with 51 patients who participated in the new DEP and completed their own MG Sheet (Group N, male/female = 31/20, mean ± SD age: 60.5 ± 13.9 years; BMI: 26.8 ± 4.3 kg/m^2; HbA1c: 9.2 ± 1.9%). As a control group, patients who participated in previously adopted DEP (mainly video lectures) (Group C, n = 51) were included. Their age, sex, anthropometric factors and glycemic control were matched with Group N. HbA1c levels were evaluated until 12 months after the admission with DEP.

Results: HbA1c levels after both of DEP decreased during follow-up period: Group N vs Group C; HbA1c(%)9.2 ± 1.9 vs 9.1 ± 1.6 at baseline; 7.3 ± 0.9% vs 8.0 ± 1.5% in 12 months. HbA1c in Group N sustained significantly lower level after 12 months (P = 0.0074) compared to Group C. Reduction in HbA1c from baseline to 12 months was significantly greater in Group N (Group N vs Group C: −1.9 ± 2.1 vs −1.2 ± 1.6; P = 0.0490). Furthermore, patients who could set detailed individual goals in their own MG Sheet (6 or 7 items out of 7 goals) in Group N achieved greater HbA1c reduction in 9 and 12 months compared with those in group C (in 9 months, Group N vs Group C: −2.1 ± 2.5 vs −1.1 ± 1.6; P = 0.0182, in 12 months, Group N vs Group C: −2.2 ± 2.4 vs −1.2 ± 1.6; P = 0.0254).

Conclusions: Multidisciplinary and interactive diabetes education program including declaration of individual goal setting may help patients with DM achieve better glycemic control.

PG-57

Dietary survey among type 2 diabetes patients newly enrolling diabetes shared care

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Background: To evaluate baseline dietary pattern and correlate each component of dietary intake with glycemic control in patients with type 2 diabetes.

Methods: Food intakes were surveyed and analyzed in 67 patients (aged 31 to 86 years) with type 2 diabetes from Diabetes Shared Care System in a Medical Center in Northern

Taiwan. At first referral, food frequency questionnaire based on semi-quantitative food groups was used to assess how well for diabetes patients to conform to recommended eating pattern. Biochemical and anthropometrical data were collected and analyzed.
Results: Patient's mean (±SD) age and DM duration were 60.9 ± 11.8 and 10.1 ± 8.9 years, respectively. The mean A1C value was 7.6 ± 1.6% and mean BMI was 26.0 ± 3.9 kg/m^2. Mean proportions of patients who conformed to daily dietary recommendation for vegetable (≥3 Exchanges), fruit (2 Exchanges), grains (Male 12 Exchanges; Female 8 Exchanges), red and white meats/fish/egg (≥4 Exchanges), and soy products/nuts (1 Exchange) were 56.5%, 18.6%, 9.8%, 46.7%, and 40.3%, respectively. More patients did not meet the daily dietary recommendation for fruit and grains than other food groups. Furthermore, compared to group with A1C ≤ 7.5%, more of patients with excessive carbohydrate intake either from fruit group or grain group were found in the group with A1C > 7.5%, (51.8% vs 35.1%).
Conclusion: Most of type 2 diabetes patients before intensive diabetes education program did not follow the dietary recommendation. Inadequate or excessive consumption from carbohydrate-rich food groups is the most common found among these patients. Therefore, nutrition education for type 2 DM patients should focus firstly on carbohydrate knowledge and portions.

PG-58
Effects of peer support activity by using theater for diabetes and CKD Japanese patients

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Objective: In japan, over 20.5 million people have Diabetyes Mellitus and Prediabetes, and over 13.3 million people have CKD (chronic kidney disease). The purpose of this study was to investigate the effects of peer support activity by using original theater by a questionnaire.
Method: On 10th April 2016, original theater (living well with CKD) was done in Nagoya University Hospital. Act1: Salty temptation, new diagnosis CKD patient and his family; Act2: CKD roost talking, Linkages to detection and clinical care, the theater was composed by Act (10-minute) and talking each other session (20-minute) for the participants. The questionnaire was making by ARCS-V (attention, relevance, confidence, satisfaction, volition) model.
Results: 190 participants and the respond of questionnaire was 145(76.3%), male patients; 69, <CKD 52, not CKD 17, CKD with diabetes 23(44.2%)>, female patients; 68, <CKD29, not CKD39, CKD with diabetes 9 (31.0%)>, and health care providers 8<not CKD 8>. Over 70 years participants were 70 members (51%). The ARCS-V model, satisfaction was very high score (strong agree and agree) 117 (85.5%).
Conclusion: These results suggested that the participants were highly advanced age and developing severe complications. The participant talked openhearted his confused feelings, and the interaction, the empathy was happened by the peer support, theater was a strategic oppotunity to express the client's emotion and reflect own self-care behaviors.
This work was supported by JSPS KAKENHI Grant Number 26463302:Grant-in-Aid for Scientific Research (C).

PG-59
Development of the active eating behavior improvement program using the conjoint analysis

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Background and aims: In the therapy for diabetes, nutrition education is indispensable. In Japan, dietitians are the ones who give the personal nutrition education to diabetic patients based on their dietary records and interviews. This conventional instructional method is similar to a teacher-student relation, and it lacks the independence of a patient.
However, the approach of organizational behavior focused on eating behavior is difficult to evaluate its effectiveness, and has yet to be commonly practiced.
The aim of this study is to create a program tool to improve eating behavior based on behavioral medicine approach.
Methods: Essential factors for diabetic patients to improve their behavior and achieve their objectives are goal setting and the PDCA Cycle.
First, specific small goals are set for them between the starting point and their ultimate objectives. Patients then repeat four stages of PLAN → DO → CHECK → ACTION to achieve these small goals and meet the ultimate objectives.
In order for patients to build this habit, it requires five elements including ① S (Specific), ② M (Measurable), ③ A (Agreed upon, uncomplicated), ④ R (Realistic, practical), and ⑤ T (Timely, clear deadlines).
We conducted conjoint analysis to investigate which elements are essential in each of the four stages.
This is an observational study. A survey using self-completed questionnaires was conducted among 70 patients with type 2 diabetes who had been received conventional nutrition education.
Results: The two most essential elements and a program outline for each stage are shown below.
P→ST Set small weekly goals
D→RM Use a check list to help consume nine types of healthy food
C→MA Visualize the progress by summarizing the scores and keeping a diary
A→AS Clarify what to do by quantifying the progress
The characteristics of this program are ① simple and straightforward, ② future-oriented, and ③ diverse.
Conclusion: Visualizing set objectives in this program enabled patients to choose the menu of their next meal by themselves, which helped establish an eating behavior improvement program that can be adopted by anyone, anytime and anywhere.

PG-60
Impact of medication review by pharmacist toward the medication adherence of type 2 diabetes in outpatient setting

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Background: Medication adherence is very important for disease management. In 2003, WHO made calls to remind everyone to take medication to control the disease have a considerable influence. The purpose of this study is to provide diabetes patients with Pharmaceutical services in order to improve medication adherence rates.
Method: We conducted a prospective cohort study including patients with diabetes diagnosis under metabolic department regular OPD follow-up over 1 year, and aged over 45 years. Patients diagnosed with type 1 diabetes are excluded. All participants were divided into two groups according to hemoglobin A1C (A1C): well-controlled group (WC) A1C ≦ 7 and poor-controlled group (PC) A1C > 7. Each group is divided into two subgroups. We intervene the patients in two different ways: one subgroup received regular health education (regular intervention), and the other group received intensive health education (telephone call intervention).

Morisky-4 Questionnaire was completed for every patient during the telephone interview. The end point of this study is to evaluate the clinical biomarker such as A1C, Fasting glucose, Cholesterol, LDL-C to determine the disease control status objectively and the effects of pharmaceutical care. Data was assessed by comparing baseline characteristics using independent sample t-tests for continuous variables and chi-square tests for categorical variables. Outcomes for continuous variables were using paired t-tests to study the effect within each study group. Data was run by the Excel® software.
Result: From Oct. 2013 to May 2015, 76 eligible patients were enrolled and informed consent were obtained. The patients were divided into two groups by their A1C. There were 37 patients in the WC group, and 30 patients in the PC group. Patients' characteristics (gender, age, education et al.) were not statistically different between the two groups, except the duration of disease (WC vs PC, 5.9 y vs 9.4 y $p = 0.002$). The results of questionnaire showed that the patient's recognition of the importance of medication adherence was improved, however, this acknowledgement had not been revealed by the difference of their laboratory data.
Discussion: Although, the results of patient's clinical outcome was not as improved as we expected. We found that their awareness of being actively engaged in glycemic control was much better with intensive caregiver intervention. We expected to establish a communication model for physicians, nurses, pharmacists, and all other health care providers to achieve and implement an individualized holistic patient care.

Beta Cell Replacement Therapy and Imaging

PH-01
Different dose of PSP/reg affect biological behavior of beta-cell through induction of autophagy and apoptosis

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Background and aims: A great deal of evidence indicates that pancreatic stone protein/regenerating protein (PSP/reg) promotes beta-cell proliferation and the administration of PSP/reg may be advantageous to improve diabetes. The aim of this study was to investigate whether PSP/reg provide protective effect only within certain concentration range and the underlying mechanism.
Materials and methods: MIN-6 cells were treated with or without PSP/reg at different dose (0, 30, 100, 200, 300 ng/mL). Cell viability was measured by CCK-8 assay, cell function was determined by measuring insulin secretion, autophagy level was measured by detecting LC3-II, LC3-I and p62 expression, cell apotosis was measured by flow cytometry.
Result: MIN-6 cells viability maintained optimum state when the dose reached to 100 ng/mL and incubated for 24 h ($P < 0.01$). However, high dose of PSP/reg (300 ng/mL) resulted in a significant decrease in cells viability. No significant difference in insulin secretion was observed at the dose of 30 and 0 ng/mL. But insulin secretion significantly increased at 100 ng/mL and decreased at 300 ng/mL. Autophagy level significantly elevated as determined by the increased ratio of LC3-II to LC3-I and decreased p62 expression, a dose-dependent manner in this effect was observed. There was no significant difference in the rate of apoptosis between treatment with PSP/reg (100 ng/mL) and the control group.
Conclusion: In the present study, low concentrations of PSP/reg is able to preserve the viability and function of MIN-6 cells, but high concentrations of PSP/reg can exert cellular toxicity. These evidence leads us to conclude that treatment with PSP/reg at an appropriate concentration is necessary to induce protective effect, the mechanism may be related to autophagy and apoptosis.

PH-02
Involvement of glycosphingolipids in the insulin secretion pathway

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Background and aims: Glycosphingolipids (GSLs) are amphipathic molecules consisting of a hydrophilic sugar chain head and a hydrophobic ceramide tail. They are mostly located in the outer leaflet of the plasma membrane, in which they are anchored by the ceramide moiety. Their sugar chain moieties have enormous structural diversity, and the variety of glycan structures in GSLs contributes to determine specific cell functions. As for involvement of GSLs in the field of diabetes study, roles of GSLs in diabetic insulin resistance are well known. However, the contribution of GSLs to insulin secretion β-cell function is still unclear. The aim of this study is to investigate whether the GSLs in β-cells affects insulin secretion.
Materials and methods: MIN6 cells, mouse pancreatic beta-cell line, have been reported to show functional heterogeneity with increasing passage number. Therefore, for analysis of the relationship of the GSLs and ß-cell function, selection of a single optimal cell line was required. Subcloning of MIN6 cells was performed by the limiting dilution method. The cells were then screened and selected by an index of glucose- and potassium-stimulated insulin secretion (GSIS and KSIS). The glycosphingolipids in MIN6 and its isolated subclone cells were analysed by thin-layer chromatography. Insulin content, GSIS and KSIS were examined in MIN6 subclones after inhibition of the first enzyme for GSLs biosynthesis by D-PDMP (a competitive inhibitor of glucosylceramide synthase). Quantitative RT-PCR was used for analyzing mRNA expression of components of insulin secretion pathway.
Results: MIN6 and GSIS and/or KSIS responsible subclone cells commonly expressed GM3 and GD1a gangliosides. Subcloned MIN6 cells treated with D-PDMP showed about 82.8%, 81.1% and 56.6% decrease in insulin content, GSIS and KSIS compared to the controls ($p < 0.01$), respectively. In addition, the mRNA level of Insulin1, Glut2, Sur1 and Snap25 were decreased in D-PDMP-treated subcloned MIN6 cells when compared with the control cells ($p < 0.01$). Therefore, the decreased mRNA expression of these genes may have reduced the insulin content and secretory response in the D-PDMP-treated cells.
Conclusion: These results indicate that GSLs, especially GM3 and/or GD1a, play important role(s) in insulin secretion mechanisms by influencing not only the insulin biosynthesis but also the insulin secretion pathway. The reduction of KSIS, which stimulates insulin secretion by directly depolarizing the plasma membrane, was decreased than that of GSIS, suggesting that GSLs play a role in insulin secretion by affecting the pathway downstream of ATP production.

PH-03
Cytomegalovirus transmission after islet transplant in comparison to other solid organ transplant

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Background: Cytomegalovirus (CMV) is readily transmitted from seropositive solid organ donors to CMV seronegative recipients (CMV-mismatch) despite the use of antiviral prophylaxis and can cause highly morbid and even fatal illness. Type 1 diabetic patients are known to have reduced odds of CMV seropositivity when compared with potential donors. Therefore, the proportion of transplant recipient who has CMV-mismatch in islet cases is significantly higher than that in solid organ transplant (SOT). Our previous study has shown that there is a lower rate of CMV transmission in islet transplant recipients. It is unclear if the recent modification of islet transplant induction protocol has an impact on the rate of transmission.
Methods: Our study was an observational retrospective study comparing the rate of transmission of CMV, in CMV mismatched islet transplant recipients (n = 45) to a control group of CMV mismatched SOT recipients (n = 27) corresponding to the same donor at the University of Alberta Hospital from March 1999 to May 2014.
Results: CMV mismatched islet transplant recipients were less likely to have CMV transmission (8.9%) than CMV mismatched SOT recipients (78%) despite receiving tissues from the same donors. CMV transmission rates in islet transplant had increased due to the recent modification of induction protocol.
Conclusions: Low number of contaminating leukocytes due to stringent retrieval and purification process of islet, the success of immunosuppression protocols in maintaining low rejection rate along with low cytokine response which might promote CMV reactivation and the lack of surgical procedure which might lead to pro-inflammatory state that reactivates CMV in recipients are the postulated reasons for the lower transmission rate in islet transplant cases. The recent intensification of islet transplant induction protocol which renders islet recipients more immunosuppressed than before might have contributed to the higher rate of CMV transmission in this current cohort than the one from our previous study.

PH-04

Identifying a new pathway to regulate AMPK activity under metabolic stress

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Metabolic stress is associated with diabetes and insulin resistance and these patho-physiologies are linked with dysfunctions of nutrient-sensors such as AMP-dependent protein kinase (AMPK). Additionally pro-inflammatory cytokines such as TNFα secreted from adipose tissue contributes to chronic low-grade inflammation and whole body insulin resistance. Previously we reported that Fyn knull mice display increased energy expenditure and fatty acid oxidation due to increased AMPK activity in peripheral tissues. More recently, we demonstrated that Fyn regulates AMPK activity not only indirectly via its action on LKB1, but also by direct modulation of AMPK activity through Y426 phosphorylation of the α subunit. To investigate how Fyn regulates AMPK activity, we made AMPK α-Y426F mutant and examine functional interactions of the α subunit with the β and γ subunits. Although co-immunoprecipitation demonstrated no significant difference in β and γ subunit binding, the α-Y426F mutant displayed increased kinase activity compared to the wild type α subunit. These data suggested that Fyn-dependent tyrosine phosphorylation of AMPK α subunit on Y426 regulates its intra-molecular activity.
To assess this pathway has a critical role under metabolic disease, we further investigated the signaling crosstalk between Fyn and pro-inflammatory cytokines, TNFα on AMPK regulation. Time course analyses revealed that acute treatment with TNFα (10 ng/mL for 12 h) enhanced AICAR (2 mM, 10 min) dependent phosphorylation of the AMPK α subunit on the activation T172 site. In contrast, prolonged incubation with TNFα (24–36 hr) suppressed AICAR stimulated T172 α subunit phosphorylation. In parallel, TNFα increased Fyn tyrosine kinase activity and siRNA knockdown of Fyn prevented the chronic TNFa inhibition of AICAR-stimulated AMPK T172 α subunit phosphorylation. Taken together, these data suggest that prolonged stimulation of TNFα blunts AICAR dependent AMPK activation through Fyn-dependent tyrosine phosphorylation of AMPK α subunit.

PH-05

High molecular weight adiponectin and lipid profile in the type-2 diabetes mellitus-Mets

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Background: Dyslipidemia is a major component of the metabolic syndrome (Mets) and a strong risk factor for the development of cardiovascular disease. High Molecular Weight (HMW) Adiponectin is an adipocyte-derived hormone that enhances insulin sensitivity. It plays an important role in glucose and lipid metabolism. Plasma HMW adiponectin level is decreased in patients with type 2 diabetes. The effects of dyslipidemia on plasma HMW adiponectin levels in human subjects have not yet been studied.
Aim: To investigate the correlation between HMW adiponectin level and lipid profile in the type-2 diabetes mellitus (T2DM)-Mets patients.
Method: This is a cross sectional study with T2DM-Mets patients who came to the outpatient clinic of Soetomo Hospital in Surabaya during January 2010 to December 2012. Subjects met the inclusion and exclusion criteria were measured their HMW adiponectin level in plasma using ELISA method. Index lipid profile measured were serum high-density lipoprotein cholesterol (HDL-C), triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), LDL/HDL ratio and TG/HDL ratio. The study was approved by the local Research Ethics Committee and subjects gave written informed consent.
Results: Forty T2DM-Mets patients consisted of 16 (40%) males and 24 (60%) females who met inclusion and exclusion criteria were enrolled in this study. Their mean of age was 51 ± 5.2 years old, duration of illness was 16.49 ± 23.4 months, HMW adiponectin level was 2,195.6 ± 4.6 ng/mL, A1C level was 8.52 ± 0.9%, BMI was 26.62 ± 4.5 kg/m^2, LDL-C level was 148.35 ± 31.1 mg/dL, triglyceride level was 173.00 ± 100.2 mg/dL, HDL-C level was 48.15 ± 8.93 mg/dL, LDL/HDL ratio was 3.15 ± 0.7, and TG/HDL ratio was 3.78 ± 2.4. Spearman's correlation analysis showed that HMW adiponectin level was significantly correlated with triglyceride level and TG/HDL ratio ($p = 0.009$; $r = -0.407$ and $p = 0.014$; $r = -0.387$, respectively). However, no significant correlation found with HDL-C, LDL-C, and LDL/HDL ratio.
Conclusion: Triglyceride cholesterol and TG/HDL ratio are correlated with HMW adiponectin level in this T2DM-MetS population.

PH-06

Fluoxetine treatment impairs E-cadherin-mediated cell adhesion and altered calcium homeostasis in pancreatic beta cells

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Selective serotonin reuptake inhibitors (SSRIs) are the most common prescribed drugs for anxiety and mood disorders. Long term use of SSRIs is associated with an increased risk of diabetes, but the mechanism(s) underlying this association is not fully elucidated. Evidences showed that E-cadherin-mediated cell adhesion plays an important role on glucose-stimulated insulin secretion (GSIS) in pancreatic β-cells. Calcium signaling is essential for the release of insulin granules. We showed that Fluoxetine significantly reduced GSIS of mouse insulin secreting MIN6 cells. MIN6 cells formed smaller colonies of loosely packed cells with reduced cell-cell contact after fluoxetine treatment. Immunohistochemistry revealed that E-cadherin largely accumulates in cytosol, mainly in Golgi apparatus. Fluoxetine reduces the membrane-localized E-cadherin due to increase of its endocytosis. Fluoxetine inhibits spreading of cells attached to E-cad/Fc as well as disrupts E-cadherin-mediated actin filament. Furthermore, single β-cell calcium measurement indicated that fluoxetine significantly suppresses ER calcium release and the activation of store-operated calcium entry (SOCE) via reduction of ER calcium storage and inhibition of STIM1 trafficking after ER calcium depletion respectively. Our results suggested that exposure to fluoxetine results in impaired β-cell function, occurring in concert with reduction of E-cadherin-dependent cell adhesion and alterations of calcium homeostasis.

PH-08

A comparison of intraportal islet transplantation outcome between intraportal and intravenous injection of bone marrow derived spheroids

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Object: Recently stem cells have emerged as a helper for supporting islet engraftment following islet transplantation. Previously, we showed the enhanced therapeutic efficacy of islet after co-transplantation of bone marrow-derived spheroids (BM-spheroid) formed using 3-dimension culture from BM-derived mononuclear cells (BM-MNCs) in a marginal mass renal subcapsular islet transplantation model. In the present study, we compared the intraportal islet co-transplantation outcome with BM-spheroid between two injection routes via portal vein and peripheral vein (portal-spheroid vs. venous-dissociated spheroid).
Methods: Transplanted BM-spheroids were traced using green fluorescent protein transgenic (GFP-Tg) mice and MRI with nanoparticle labeling. The morphology of intraportally transplanted islet, revascularization of islets and iron-labeled BM-spheroids were examined by immunohistochemistry. The efficacy of co-transplanted BM-spheroids via intraportal or intravenous route was investigated using a syngeneic marginal mass intraportal islet transplantation model. Blood glucose concentration was monitored for 1 month.
Results: Portal-spheroid co-transplantation with islets improved the post-transplant outcomes in terms of glucose tolerance, serum insulin levels, and diabetes reversal rate when compared with islet alone or venous-dissociated spheroid co-transplantation. The area of grafted endocrine tissue and vascularization of individual islets within the graft-bearing liver was significantly higher in the portal-spheroid group compared to the islets alone or the venous-dissociated spheroid group. Also, BM-spheroid cells were found more frequently within the graft-bearing liver in the intraportal administration group compared to the intravenous administration group.
Conclusion: Our results suggest that co-transplantation of BM-spheroids via portal vein presents a promising strategy for improving the efficacy of intraportal islet transplantation.

PH-09

Impaired incretin-induced insulin secretion in enlarged pancreatic islets in a novel animal model of obese type 2 diabetes

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Objective: We recently reported the prediabetic changes in glucose tolerance and insulin resistance in a novel animal model of obese type 2 diabetes (T2D), the Zucker fatty diabetes mellitus (ZFDM) rat (Gheni et al., J Diabetes Res, 2015). Our data suggests that impaired incretin secretion and/or impaired incretin-induced insulin secretion are involved in the pathophysiology of the disease. In fact, the latter was confirmed by insulin secretion experiment using isolated pancreatic islets, but the mechanism is still unclear. In this study, we aimed to elucidate the mechanism of the impaired incretin-induced insulin secretion in prediabetic ZFDM rats.
Methods: The ZFDM rats harboring the fatty mutation (fa) in the leptin receptor gene were used in this study (fa/fa, obese diabetic; fa/+, non-obese control). We measured plasma glucagon-like peptide 1 (GLP-1) and glucose-dependent insulinotropic polypeptide (GIP) concentrations during OGTT in 8- and 12-week-old prediabetic rats. We also measured the diameter of isolated islets, and defined enlarged islets as those with diameter more than 300 μm and normal islets as diameter less than 300 μm. We then evaluated the mRNA expression levels of GLP-1 receptor and GIP receptor as well as incretin-induced insulin secretion from these islets.
Results: Plasma GLP-1 and GIP concentrations during OGTT in fa/fa rats were higher than those in fa/+ rats, indicating no impairment in the incretin secretion in fa/fa rats. The relative number of enlarged islets of fa/fa rats was significantly increased at 12 weeks of age as compared to that at 8 weeks of age. The mRNA expressions of GLP-1 and GIP receptors in fa/fa rats at 12 weeks of age were significantly decreased in both enlarged and normal islets as compared to those at 8 weeks of age. Incretin-induced insulin secretion from enlarged islets of fa/fa rats was significantly decreased than that from normal islets.
Conclusion: Our data suggests that the enlargement in pancreatic islets with age may be associated with impaired incretin-induced insulin secretion in prediabetic state of ZFDM rats.

PH-10

The role of leucine in stimulation of adipocyte lipolysis

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Branched chain amino acids (BCAA), including leucine, have been shown to be linked to the development of insulin resistance under high fat conditions in both human subjects and mouse models (Newgard 2012). While some evidence suggests that activation of mammalian target of rapamycin (mTOR) is important for the effects of BCAA on whole body metabolism, the exact mechanism is unknown. Adipose tissue is a major site of BCAA metabolism and is thus a potential driver of BCAA-related insulin resistance. We conducted studies to determine the effects of the BCAA leucine on adipocyte metabolism and function.
Leucine is taken up and processed by cultured adipocytes with expected changes in the levels of amino acids, organic acids and acyl-carnitines related to BCAA metabolism. A novel finding was that leucine enhances the ability of isoproterenol to stimulate lipolysis in adipocytes. The downstream

metabolite of leucine, alpha-ketoisocaproic acid (KIC) was unable to stimulate lipolytic activation. Leucine exposure results in phosphorylation of mTOR in adipocytes. However, blocking mTOR activation with rapamycin had no effect on leucine-mediated stimulation of lipolysis. Efforts are underway to determine the site of action for leucine-stimulation of lipolysis in cultured adipocytes. The novel finding that leucine can sensitize adipocytes to lipolytic activation provides a possible explanation for the link between elevated circulating leucine levels and the development of insulin resistance.

Reference

Newgard C.B., Interplay between lipids and branched-chain amino acids in development of insulin resistance. *Cell Metab*, 2012. 15(5): 606–14.

PH-12

Impaired RBC deformability is associated with pancreatic beta cell dysfunction and diabetic retinopathy in patients with type 2 diabetes

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Aim: Red blood cell (RBC) deformability is an ability of RBC to change shape under stress, and it has been known to be decreased in diabetes. However, the role of RBC deformability is not determined in type 2 diabetes (T2D) yet. We attempted to clarify whether RBC deformability is related with diabetic complications.

Methods: This was a cross-sectional study, and 452 T2D patients were enrolled. RBC deformability was measured by using a microfluidic ektacytometer and expressed as elongation index at 3 Pa (EI@3P, %).

Results: 388 patients (mean age 60.37 ± 11.98 years, male 233) were finally included. When subjects were categorized into three groups by hemoglobin A1c (HbA1c; <7% vs. 7≤ <9% vs. ≥9%), mean EI@3 Pa was significantly lower in the poorly controlled group (31.23 ± 1.60 vs 31.00 ± 1.82 vs. 30.70 ± 1.64, $p < 0.05$ by ANOVA). HOMA-B and insulinogenic index were positively correlated with EI@3 Pa but not with HOMA-IR in multiple regression analysis. EI@3 Pa was significantly lower only in patients with retinopathy than those without retinopathy (30.53 ± 1.95 vs. 31.20 ± 1.53, $p = 0.001$). Of quartiles from lowest EI@3 Pa to highest (reference), the odds ratio (OR) for Q1 was 2.86 (95% confidence interval 1.24, 6.62, $p = 0.014$) after adjustment for age, gender, hypertension, smoking, duration of diabetes, GFR, and triglyceride. If EI@3 Pa increase by 1%, the risk of diabetic retinopathy will decrease by 24.9%.

Conclusions: These results suggest that impaired RBC deformability is related with decreased pancreatic beta cell function and the risk of diabetic retinopathy.

PH-13

Inhibition of RAC1-NOX signaling attenuates high-glucose-induced CD36 expression in pancreatic β-cells

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Objective: Cluster determinant 36 (CD36), a fatty acid transporter, was reported to have a pivotal role in glucotoxicity-induced β-cell dysfunction. However, little is known about how glucotoxicity influences CD36 expression. So, the predominant objective is to reveal the role of RAC1-NOX in CD36 activation and its impact for the β-cell dysfunction during diabetes mellitus.

Methods: To address this question, we subjected INS-cells and primary rat islets to high glucose (30 mM) for 24 hours in the absence or presence of RAC1 inhibitor NSC23766. Apoptosis was measured by TUNEL-Nick End Labeling assay. RAC1 and NOX activity was assessed using the Rac1 Activation Assay kit (Merck Millipore) and by chemiluminescenceassay. Reactive oxygen species and mitochondrial membrane potential were measured by using DCFDA and DIOC6 dye respectively. Moreover, the protein expression level of CD36, MAPK signaling pathways in response to high glucose is assessed by western blot analysis.

Results: Exposure of INS-1 cells to high glucose (30 mM) upregulated RAC1 and NADPHoxidase activation, and induced apoptosis. Interestingly, upregulated RAC1 and NADPH oxidase induced CD36 expression. These effects of high glucose were significantlydecreased in INS-1 cells treated with NSC23766. Moreover, RAC1 inhibition by NSC23766 significantly reduced high glucose-induced mitochondrial dysfunction assessed by measuring the mitochondrial membrane potential and cytochrome c release. Inhibition of RAC1 also attenuated MAPK signaling.

Conclusion: RAC1 regulates NOX activity, thereby increasing the expression of CD36 and its downstream signaling lead to β-cell dysfunction under high glucose conditions.

PH-14

A comparison of sympathetic and parasympathetic nerves density ratio in pancreatic islets in experimental animal model

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Purpose: The change of sympathetic and parasympathetic nerves ratio in pancreatic islets have been unclear during diabetes progression. A connection and an insulin secretion of sympathetic and parasympathetic nerves in pancreatic islet are studied on the area of innervated sympathetic, parasympathetic nerves in normal and diabetes rat.

Method: The pancreas of normal and diabetes induced Sprague–Dawley (SD) rats (n = 4–5/group) were fixed by formalin and were dehydrated by sucrose. After cut by freezing microtome into 40 μm thick sections, the tissues were stained with protein gene product 9.5, tyrosine hydroxylase and choline acetyltransferase for islet cell, sympathetic and parasympathetic nerves. All of the stained sections were imaged by confocal microscopy and the images were analyzed to area of sympathetic and parasympathetic nerves by pixel and calculated the ratio of parasympathetic to sympathetic ratio.

Result: There was no significant difference in the area of parasympathetic nerves between normal and diabetic rat pancreatic islets, but the area of sympathetic nerve of diabetic rat was much higher than normal in pancreatic islet. The parasympathetic to sympathetic nerve density ratio of diabetic rat was smaller than normal control rats (9.84 vs 40.3).

Conclusion: This study is demonstrated that parasympathetic to sympathetic nerve density ratio markedly decreased in diabetic animal model.

PH-15

Sympathetic to parasympathetic nerve density ratio change in adipocytes in diabetic animal models

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Background: White adipose tissue in relation with lipid mobilization is innervated by sympathetic peripheral nerve and lipid metabolism is also important in peripheral nerve regeneration. Autonomic neuropathy involving these sympathetic and parasympathetic nerves is an important and common chronic complication in diabetes and adipocyte is also important for metabolic parameters in diabetes. However, there is no research about the relation between adipose

tissue and autonomic neuropathy in diabetes. Therefore, we investigated the morphologic changes of autonomic nerves in the adipose tissue in diabetic animal model.
Method: Animals were divided into two groups; male db/db mouse and age matched control mouse were used. White adipose tissues were collected from db/db control mouse and were stained with immunohistochemistric method. Tyrosine hydroxylase and choline acetyltransferase were labeled for noradrenergic sympathetic and cholinergic parasympathetic axons of adipose tissue respectively and observed by confocal microscopy and analyzed. And, protein gene product 9.5 used for whole autonomic and sensory nerve staining.
Result: Sympathetic nerve fiber density of adipose tissue was not significantly changed in diabetic and control mouse adipose tissue. However, Parasympathetic nerve fiber density of adipose tissue was significantly increased in diabetic mouse compare to control. The sympathetic to parasympathetic nerve density ratio of adipose tissue is lower in diabetic group compared to control group (0.72 vs 0.55).
Discussion: Both sympathetic and parasympathetic nerve fibers were observed in white adipose tissue. And sympathetic to parasympathetic nerve fiber density of adipose tissue density ration was decrease in diabetic group. Further evaluation for the mechanism of the parasympathetic nerve fiber density change was needed.

PH-16

Patient with latent autoimmune diabetes in adult (LADA) and autoimmune haemolytic anemia (AIHA), a probable case of autoimmune cross reactivity

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Introduction: Incidence of autoimmune diseses are increasing in many part of the world. AIHA and LADA are among the autoimmune diseases that being studied recently. The pathologic correlation between AIHA and LADA in a patient is not yet fully understood.
Case illustration: A 34-years-old female patient came with chief complaint of general weakness since 3 days before admission. She was diagnosed of having ketosis and anemia. She has the same symptom 2 year ago and was diagnosed with anemia and got blood transfusion. About 1 year ago she was diagnosed with diabetes mellitus and got treatment with glibenclamide and metformin. No history of diabetes mellitus and autimmune diseases in the family. From the physical examination in general is within normal limit. Laboratory examination show Coomb's test positive, ANA positive, high LDH level: 321, GAD 65: >30.0 U/mL (<1.1), ICA: >1:8 titer (<1:2), Insulin Autoantibody <0.4 U/mL (<0.4), Random Blood Glucose: 300 mg/dL, blood Ketone: 1,1. She got treatment with methyl prednisolone 3 × 12 mg, folic acid 2 × 5 mg, vitamin B12 3 × 50 mg, basal insulin 1 × 30 U and prandial insulin 3 × 28 U.
Discussion: Prevalence of AIHA and LADA diagnosed in a single patient is not yet known. Autoimmune cross reactivity is one theory that suggest the connection between both diseses. The role of HLA is another possible theory that being studied. Management of patient with LADA and AIHA need special concerned due to steroid used as immunosupression for AIHA that can worsen patient blood glucose profile. Insulin is preferable for blood glucose control in this kind of patient.
Conclusion: Adult patient with diabetes mellitus whom diagnosed of having an autoimmune disease such as AIHA, should be evaluated weather the diabetes it self is due to an autoimmune process. So the patient can have better management and prevent complication.

Obesity/Diabetes & Bariatric Surgery

PI-01

Relation of MPV with serum PON-1 activity and BA-IMT in diabetic patients with respect to obesity and diabetic complications

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Objective: To evaluate the relation of mean platelet volume (MPV) levels with serum PON-1 activity and brachial artery diameter(BAd) and (BA-IMT) in diabetic patients with respect to obesity and diabetic complications.
Methods: A total of 201 diabetic patients grouped with respect to obesity [obese (n = 89) and non-obese (n = 112) and diabetic complications [with (n = 50) or without (n = 150) microvascular complications and with (n = 91) or without (n = 108) macrovascular complications groups were included. Correlation of MPV values to PON-1 activities as well as to(BAd) and (BA-IMT) was evaluated in study groups.
Results: PON-1 activity values were respectively in the overall population, with no significant difference with respect to obesity and macrovascular diabetic complications, where as significantly lower values for PON-1 activity were noted in patients with than without diabetic microvascular complications. MPV values were 9.10 (0.87) fL in the overall population, with no significant difference with respect to obesity and diabetic complications. No significant correlation of MPV values to PON-1 activity and to(BAd) and (BA-IMT) was noted in the overall study population as well as in study groups.
Conclusion: In conclusion, our findings revealed a significant decrease I PON-1 activity in diabetic patients with microvascular rather than macrovascular complications, whereas regardless of obesity and diabetic complications, no increase in thrombogenic activity and no relation of thrombogenic activity with PON-1 activity and(BAd) and (BA-IMT).

PI-03

Effect of bariatric surgery on diabetic complications: the Taiwan diabesity study

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Background: The effect of bariatric surgery on diabetic microvascular complications not certain
Methods: In this prospective multi-center study, we compared renal and retinal complications between 10 obese/overweight (BMI > 25 kg/m^2) diabetic patients receiving bariatric surgery (including gastric bypass and sleeve surgery) versus 75 patients receiving intensive medical control after follow-up for 12 months without or with adjustment for baseline age, gender, oral medications, insulin therapy, glucagon-like peptide analogues therapy, and life style (including smoking, alcohol use, and betel nut chewing).
Results: At baseline, the mean age was 43.6 and 51.6 years (P < 0.001); the mean body mass index (BMI) was 36.03 and 30.1 kg/m^2 (P < 0.001); the mean hemoglobin A1c (HbA1c) was 8.6% and 8.0% (P = 0.2); mean estimated glomerular

filtration rate (eGFR) was 86.3 and 92.7 mL/min/1.73 m^2(P = 0.5); mean urine albumin-creatinine ratio (ACR) was 103 and 132 mg/g (P = 0.5); the percentage of retinopathy was 50% and 16.0% (P = 0.006) for patients receiving bariatric surgery and intensive medical controls respectively. There is no significantly difference in baseline blood pressures, lipid profile, or medications. After 12 months of follow-up, patients receiving bariatric surgery had significantly greater percentage reduction in BMI (–29% vs 0.3%, P < 0.001, adjusted P < 0.001), greater percentage reduction in HbA1c (–32% vs –1%, P < 0.001, adjusted P < 0.001), greater increase in estimated GFR (24% vs –3.5%, P < 0.001, adjusted P = 0.001), greater reduction in urine ACR (–8.3% vs 0.1%, P < 0.001, adjusted P = 0.04), and a trend of greater regression of retinopathy (–20% vs 1.3%, P = 0.2, adjusted P = 0.3) as compared to patients receiving intensive medical control. After further adjustment for HbA1c reduction, the relative improvement in eGFR remained significant (P = 0.004) but the improvement in urine ACR is attenuated (P = 0.11).

Conclusion: Obese/overweight diabetic patients receiving bariatric surgery have significantly reduced nephropathy and possibly reduced retinopathy as compared to intensive medical control.

PI-04

Visceral adiposity index predicts the conversion of metabolically healthy obesity to an unhealthy phenotype

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Background: Some individuals with metabolically healthy obesity (MHO) convert to metabolically unhealthy obesity (MUO) phenotype, and visceral adiposity is one of proposed mechanisms underlying such conversion. Visceral adipose index (VAI) is a novel model which estimates visceral adiposity based on anthropometric and lipid profiles. We aimed to determine the association of VAI-estimated visceral adiposity with the MHO-to-MUO conversion and the predictive value of VAI in estimating such unfavorable outcomes.

Methods: 5,187 Korean subjects with the MHO phenotype were enrolled and stratified by body mass index and metabolic health state according to Wildman criteria at baseline and last follow-up examinations. VAI was calculated at baseline.

Results: Over a median follow-up period of 37.9 months, 27.6% of subjects converted to MUO phenotype. Higher VAI quartiles were associated with a greater proportion of subjects who underwent MHO-to-MUO conversion, and also with increased odds ratios for such conversion even after multivariate analyses. According to ROC analyses, the optimal VAI cut off value was 1.30, with a sensitivity of 56.1% and a specificity of 64.4% (AUC, 0.636; 95% CI, 0.618–0.654, P < 0.001), and the predictive value of VAI was superior to that of WC (differences between areas, 0.072; 95% CI, 0.048–0.096, P < 0.001).

Conclusions: VAI-estimated visceral adiposity is well correlated with the prognosis of MHO subjects, and VAI has a good predictive value in determining the MHO-to-MUO conversion.

PI-05

Association between human adenovirus-36 infection, obesity and glycemia in prospective follow-up of Hong Kong Chinese school children

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Increasing evidence suggest a link between obesity and viral infection. Adenovirus-36 (Ad-36) is the only human adenovirus known to be associated with obesity. We aimed to examine the associations of Ad-36 infection with cardiometabolic risk factors including obesity, glycemia and other obesity associated cardiometabolic risk factors in school children. Stored aliquots of Hong Kong Chinese school children from two territory-wide surveys conducted in 2003 and 2007–08 were examined for Ad-36 infection using serum neutralization test for Ad-36 antibodies. The school children were called back for repeated examinations of their anthropometric indices and cardiometabolic profile including fasting plasma glucose and lipid, as well as serum for their Ad-36 antibodies. A total of 983 school children (41.8% male) were called back for prospective study. Mean follow-up duration was 8.7 years (standard deviation, SD = 2.7 years). Mean age of the participants was 14.0 (SD 3.2) years and 22.7 (SD 4.9) years at baseline and follow-up respectively. The prevalence of Ad-36 infection at baseline was 1.5%, while the prevalence increased to 3.3% at follow-up (p = 0.002). Using mixed-effects model, there was no significant association between Ad-36 infection status and obesity and obesity-associated conventional cardiometabolic risk factors including fasting plasma glucose after adjustment of age and sex. Likewise, there was no significant association between Ad-36 infection status and obesity and obesity associated cardiometabolic risk factors using one-way ANOVA analysis by comparing BMI with the status of Ad-36 infection. To conclude, the prevalence of Ad-36 infection in Hong Kong Chinese school children was low and there was no significant association between Ad-36 infection and obesity, glycemia and obesity associated cardiometabolic risk factors.

PI-06

Ferulic acid stimulates muscle insulin signaling pathway in high-fat diet-induced obese mice

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Ferulic acid (FA) is a plant phenolic acid that has several pharmacological effects including antihyperglycemic activity. Thus, the objective of this study is to investigate the effect of FA on impaired glucose metabolism in high-fat diet-induced obese mice. Five-week-old ICR mice were fed with normal or high-fat (45 kcal% fat) diet for 16 weeks. During the last 8 weeks of induction, mice were divided into 4 groups of 8 mice each: normal control mice, obese control mice, and obese mice treated with FA (25 and 50 mg/kg/day). After 8 weeks of treatments, FA significantly reduced the elevated blood glucose and serum insulin levels, and improved glucose tolerance. Interestingly, FA increased the protein expression of insulin receptor substrate 1 (IRS1), phosphoinositide-3-kinase (PI3K), and protein kinase B (Akt) in skeletal muscle tissue of obese mice. Our findings demonstrate that FA improves glucose metabolism in HFD-induced obesity by stimulating the insulin signaling pathway in skeletal muscle tissue.

PI-07

Young women with severe obesity by gastric sleeve resection of successful weight loss and pregnancy case report

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Obesity is a problem facing the world today, countries in the world rising prevalence of obesity problems arising States

caused considerable health care costs, the case of a 26-year-old female, height 167 cm, BW: 107 kg, BMI: 38.3, no other chronic disease, endoscopy have gastroesophageal reflux, abdominal ultrasound fatty liver, HbA1C: 5.7, working in a convenience store clerk, working hours Intermediate (12:00 Am–20:00 Pm), because of his living and working outside, eating Indefinite meals (mostly convenience store diet food such as bread, Oden, eating dinner time around 21.00 Pm) have a drink and snack eating habits, weight gain readme States every year since graduation, 104 in March to the hospital linked to general surgical want Bariatric surgery seek assistance, a number of checks done after 104 years July 2 to perform sleeve gastrectomy surgery, in stable condition on July 7 to return home, after eating progress through each texture after about 3 weeks after the general progress to diet, weight also successfully after decreasing from 105 in March reduced to 107 by the weight 72.9 Kg (decrease 34.1 kg) BMI: 26 (overweight, especially severe obesity →), while successful pregnancy pregnant five weeks, this young woman by sleeve gastrectomy surgery and diet under control, within eight months succeeded in reducing nearly 30% of body weight, and track the biochemical values were normal and smooth pregnancy in marriage.

PI-09

The effect of metformin therapy on insulin resistance and Ferriman-Gallwey Scores in patients with idiopathic hirsutism

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Introduction: It is well known that hyperandrogenism and insulin resistance are now closely associated. Our aim was to investigate the affect of metformin therapy on insulin resistance and FG scores in overweight presenting with hirsutism.

Material and methods: 40 overweight women were investigated who applied to outpatient clinic with hirsutism complaint, retrospectively. Hirsutism was defined as Ferriman-Gallwey (FG) score >8. The diagnosis of IH was based on the presence of hirsutism, regular ovulatory menstrual cycles, and a normal serum androgen profile including free testosterone (normal: 0.04–3.9 pg/mL) and dehydroepiandrosterone sulfate (normal: 35–430 μg/dL). There was no history of diabetes mellitus in the study group. All participants had not used any medication or oral contraceptives for the last three months. In the study group, blood sampling was done in the early follicular phase of spontaneous or induced (by medroxyprogesterone acetate 10 mg/day for 7 days) menstrual cycles. Insulin resistance was calculated with homeostasis model assessment of insulin resistance (HOMA-IR), using the following formula: fasting serum insulin (μU/mL) × fasting plasma glucose mmol/l)/. All patients were overweight and hyperinsulinemic. They underwent metformin therapy due to hyperinsulinemia. Hormone, metabolic, insulin, FG scores and HOMA-IR scores were investigated at the beginning, 3th, and 6th month of the metformin therapy. SPSS-16 was used for the statistiscs. Wilcoxon test and pearson correlation were used for the statistics.

Results: 40 patients (mean age ± 6,14) were evaluated. The Ferriman-Gallwey score (FG) was significantly differ at the beginning- 3th and 6th month ($p < 0.005$). There was only significant differences between at the beginning and 6th month of HDL level. There were significant differences between total testosterone levels at 0,3th and 6th months. We found significant differences only 0 and 3th monts of 17OH levels in patients. There were statistically significant differences between 0,3th and 6th months glucose, insulin and homa-IR levels ($p < 0.05$).

Conclusions: Insulin resistance should be assessed in all hirsute women. Metformin therapy is the first choice for insulin resistance. The metformin therapy significantly improved insulin resistance, imbalance of endocrine hormones, hirsutism and menstrual cyclicity in women even though idiopathic hirsutism. FG scores and testosterone levels should be improved with metformin therapy in hiruste women. More studies in larger numbers of patients should be performed to investigate the role of insulin resistance in women with IH.

PI-10

Gender difference on the eating styles and the effect of group diet education in adolescents in Taiwan

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Objective: Nowadays, the issue of school children obesity and metabolism syndrome is getting more pressed and continues to draw attention. It is known that Chia Yi has the highest rate of school children obesity in Taiwan. Therefore we focus this issue on the adolescents aged 13–14 in Chia-Yi region and conduct a study on the eating styles of the subjects, with a focus on the food they consumes and the way they eat relate to body weight. We also strive to investigate if diet education according to group characteristics based on the results we obtained could succeed in reducing obesity and maintain body weight control in school children. This might prove useful for establishing guidelines for body weight control.

Method: Group of 89 obese students with a mean BMI of 27.28 were analyzed on the effect of co-ed on body weight reduction.

Results: Of both the girls and boys, the following factors were found to have influence on body weight statistically, including meal frequency, school lunch intake, bed time, water intake, vegetable consumption, fried food consumption, rice intake, snack food intake, how fast they eat, bowel movement.

On the co-ed effect on body weight reduction. There are three classes, one with both girls and boys(co-ed), the other two classes with either girls or boy only. With the same mean BMI of 27.28 and being led by the same teacher on skills of nutrition improvement and physical fitness for one semester, significant difference of BMI reduction was found. The girls only class achieved a lower BMI (1.89 reduction) than boys only class (1.12 reduction), while the co-ed class achieved the least (0.67 of BMI reduction).

Conclusions: The eating styles of school girls and boys were different in chia-Yi region. For the obese students in the context of group diet education, gender conscience has a role in achieving body weight reduction. It is conjectured that competitiveness could be heightened and lead to better result in class of the same sex only, esp in girls. This hints that gender segregation might be useful in achieving better weight reduction.

PI-11

Decreased serum betatrophin levels after Roux-en-Y gastric bypass in obese Chinese patients with type 2 diabetes: a 1-year follow-up

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Background: There is increasing evidence that serum betatrophin levels, a hormone derived from adipose tissue and liver, are elevated in type 2 diabetes mellitus (T2D).

Objective: To investigate the relationships between betatrophin and metabolic control, insulin resistance (IR), and pancreatic β-cell function in obese Chinese patients with T2D who underwent Roux-en-Y gastric bypass (RYGB).

Methods: This 1-year follow-up study included 34 obese T2D individuals (18 males, 16 females) who underwent RYGB in our hospital. Anthropometric results, glucose levels, lipid profiles, and serum betatrophin levels were determined before and 1 year after RYGB.
Results: The serum betatrophin level decreased significantly after RYGB [72.0 (33.4–180.9) vs. 35.7 (14.8–103.3) ng/mL; $P < 0.001$]. The change in betatrophin was significantly positively correlated with the changes in haemoglobin A1c (A1C) and fasting plasma glucose (FPG) and negatively correlated with the changes in the 2-h C-peptide/fasting C-peptide (2hCP/FCP) and HOMA of beta cell function (HOMA-β%) ($P < 0.05$). Multiple stepwise regression analysis showed that the change in the serum betatrophin level was independently and significantly associated with the changes in FPG ($\beta = 0.586$, $P < 0.001$) and 2hCP/FCP ($\beta = -0.309$, $P = 0.021$).
Conclusions: Circulating betatrophin might be involved in the regulation of glucose control and insulin secretion in obese Chinese with T2D soon after RYGB.

PI-12

Relationship between gestational weight gain and pregnancy complications, delivery outcome

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The aim of this study is to analyze the relationship between gestational weight gain and delivery outcomes, pregnancy complications.
This retrospective study included 1,102 pregnant women. Data were extracted from electronic medical records. Baseline weight and weight change during the whole pregnancy were recorded. For the statistical analysis, these participants were divided into four groups based on the weight gain quartiles in different trimester of pregnancy.
Weight gain in the second trimester (9.1 ± 3.0 kg) of pregnancy was positively correlated with macrosomia, and negatively correlated with neonatal death, which is an independent risk factor of postpartum hemorrhage (OR = 1.067, 95% CI 1.002–1.137, P = 0.04) and macrosomia (OR = 1.145, 95% CI 1.027–1.276, P = 0.02). Weight gain in the third trimester (6.1 ± 2.6 kg) was positively correlated with neonate weight and macrosomia, and negatively correlated with neonatal death, preterm birth, gestational diabetes, infant of low-birth weight. It is an independent risk factor of preterm birth (OR = 0.770, 95% CI 0.646–0.916, P < 0.01), infant of low-birth weight (OR = 0.813, 95% CI 0.668–0.990, P = 0.03) and gestational diabetes (OR = 0.828, 95% CI 0.743–0.923, P < 0.01). Total gestational weight gain (15.3 ± 5.2 kg) was positively correlated with neonate weight and the morbidity of macrosomia, and negatively correlated with the neonatal death, gestational diabetes, preterm birth and infant of low-birth weight, which is an independent risk factor for the development of neonatal death (OR = 1.063, 95% CI 1.019–1.109, P < 0.01), postpartum hemorrhage (OR = 1.096, 95% CI 1.020–1.178, P = 0.02), macrosomia (OR = 0.890, 95% CI 0.793–0.998, P = 0.05), infant of low-birth weight and gestational diabetes (OR = 0.922, 95% CI 0.865–0.982, P = 0.01).
According to this analysis, the weight gain during pregnancy was associated with the gestational complications, adverse pregnancy outcomes, status of neonatal abnormality in varying degrees.

PI-15

Assessment of the Dynamic Insulin Secretion and Sensitivity Test (DISST) in morbidly obese subjects pre and post gastric bypass

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Recently a new test for the assessment of insulin resistance, the Dynamic Insulin Sensitivity and Secretion Test (DISST) [1,2], has been developed as a suitable substitute for the current but complex reference method, the euglycaemic hyperinsulinaemic clamp (EIC). The DISST method has been validated against the clamp in a range of stable state situations but not after an intervention which is known to fundamentally change glucose homeostasis and insulin sensitivity. The primary aim of this study is to test preliminary performance of DISST relative to the EIC in a morbidly obese cohort before and after bariatric surgery.
Methods: The DISST test was compared to the EIC in pre surgery morbidly obese patients and at 3 weeks post gastric bypass surgery. Correlation and Bland-Altman analysis was performed.
Results: A total of 11 subjects were recruited with 10 having pre surgery and 8 having post surgery DISST and EIC data. Matched data for all DISST versus EIC showed good correlation between the two (r = 0.76, CI 0.45–0.90, n = 18). Bland-Altman analysis showed DISST underestimated the clamp by 0.96×10^{-2} mg L kg^{-1} min^{-1} $pmol^{-1}$ (95% confidence intervals −2.24 to 0.32). For just the pre surgery group correlation between DISST and EIC was r = 0.81(95% CI 0.37–0.95, n = 10) and with Bland-Altman analysis DISST again under estimates the clamp by 1.16×10^{-2} mg L kg^{-1} $pmol^{-1}$ (95% confidence intervals −2.65 to 0.33). In the post surgery group correlation between DISST and EIC was only r = 0.47 (95% CI 0–0.88, n = 8) and Bland Altman analysis DISST underestimated the clamp by 0.71×10^{-2} mg L kg^{-1} $pmol^{-1}$ (95% confidence intervals −1.61 to 0.19).
Conclusion: The DISST test shows promise for use in morbidly obese individuals compared to the EIC but numbers are small with wide confidence intervals. Further investigations on utility especially in the post surgery setting are needed.
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PI-16

Correlation between uric acid and body fat distribution in type 2 diabetes mellitus

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There has been a renewed interested in hyperuricemia and its association with a number of clinical disorders other than gout, including hypertension, cardiovascular disease, metabolic abnormalities such as obesity and metabolic syndrome. The relationship between the regional distribution of body fat and uric acid in patient with type 2 diabetes mellitus (DM) is not well established. The aim of this study was to investigate the relationship between uric acid and body fat distribution in patient with type 2 DM. A total of 228 subjects with type 2 DM (184 normouricemia and 44 hyperuricemia) were included in this study. Hyperuricemia was defined >5.7 mg/dL. Clinical and anthropometric profile, such as body mass index (BMI), waist and hip circumferences, waist-to-hip ratio, skinfold thickness, and lipid profiles were measured. Abdominal fat amount was measured by single slice abdominal computed tomography scanning. Hyperuricemic group compared with normouricemic group had statistically increased visceral fat (132.06 ± 42.58 vs 111.39 ± 42.58 cm^2, p = 0.004) amount and triglyceride (173.41 ± 73.59 vs 130.53 ± 69.41 cm^2, p < 0.001). Uric acid levels were positively correlated with visceral fat amount

($r = 0.254$, $p < 0.001$), BMI ($r = 0.175$, $p = 0.008$), and triceps skinfold thickness ($r = -0.216$, $p = 0.001$). In addition, uric acid levels were strongly correlated with triglyceride ($r = 0.255$, $p < 0.001$), HDL-cholesterol($r = -0.249$, $p < 0.001$), Apo A($r = -0.143$, $p = 0.033$) in Pearson's correlation. Our data shows that uric acid levels were correlated with body fat compositions of peripheral as well as central lesion, and lipid profiles in patients with type 2 DM. Uric acid may be related to the visceral adiposity and triglyceride, and help to define a risk factor for the complications with type 2 DM.

PI-17

Correlation between Computed Tomography indices of abdominal fat distributions and lipid metabolism in patients with type 2 diabetes

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Central obesity is related to lipid metabolism abnormality in diabetic patients. The aim of this study was to investigate the relationships between Computed Tomography indices of abdominal fat distributions and glucose, lipid metabolism in Patients with type 2 diabetes. Total 642 subjects with type 2 diabetes were enrolled. Abdominal fat amounts were measured by single slice abdominal computed tomography scanning. Clinical and anthropometric profile, such as body mass index (BMI), waist and hip circumferences, waist-to-hip ratio (WHR), and lipid profile were measured. Triglyceride was higher in high visceral fat to subcutaneous fat ratio group (V/S ratio≥0.4) than in low V/S ratio group (V/S ratio<0.4) ($p < 0.001$), and HDL-C was lower in high V/S ratio group than in low V/S ratio group ($p < 0.001$).). In pearson's correlations, Total abdominal fat was correlated with HDL-C ($r = -0.192$, $p < 0.001$), and Triglyceride ($r = 0.121$, $p < 0.002$). Visceral fat was correlated with HDL-C ($r = -0.305$, $p < 0.001$) and Triglyceride ($r = 0.235$, $p < 0.001$). Subcutaneous fat was also correlated with LDL-C ($r = 0.080$, $p < 0.04$). But Visceral to subcutaneous fat ratio, which is known to be related with cardio-metabolic risk, was not correlated with Lipid profile (Total cholesterol, Triglyceride, HDL- and LDL-cholesterol). High Visceral fat to subcutaneous fat ratio group (V/S ratio≥0.4) have higher Triglyceride, and lower HDL-C than those in Low V/S ratio group. Further prospective studies with long-term follow-up are required to establish a correlation between CT indices of abdominal fat distributions and lipid metabolism

PI-18

Role of androgen in gender differences in adipocyte fatty acid binding protein induced by body fat content and distribution

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Objectives: Adipocyte fatty acid binding protein (A-FABP) is a transport protein in mature adipocytes. Clinical investigations have indicated women have higher levels of A-FABP than men. In consideration of sex hormones and body fat content and distribution, the present study aimed to identify factors related to gender differences in serum A-FABP levels.
Methods: Serum A-FABP levels were measured by a sandwich enzyme-linked immunosorbent assay. An automatic bioelectrical impedance analyzer was used to measure the fat mass and percentage of the total body, trunk, arms, and legs.
Results: A total of 507 participants were enrolled, including 194 men, 132 premenopausal women, and 181 postmenopausal women. Serum A-FABP levels increased in the order from men to premenopausal women to postmenopausal women for participants in both body mass index (BMI) categories ($BMI < 25.0\ kg/m^2$ or $BMI \geq 25.0\ kg/m^2$; all $P < 0.05$). Spearman correlation analyses showed that the indexes of the total and segment body fat were correlated with serum A-FABP levels significantly in both genders (all $P < 0.001$). Total testosterone (TT) and sex hormone-binding globulin (SHBG) displayed negative associations with serum A-FABP levels in men (all $P < 0.001$). In pre- and postmenopausal women, TT, free testosterone (FT), and bioavailable testosterone (BAT) were positively associated with serum A-FABP levels (all $P < 0.001$), whereas SHBG was negatively ($P < 0.001$ and $P = 0.001$, respectively) associated with serum A-FABP levels. Multiple stepwise regression analyses showed the trunk FM was an independent and positive factor of serum A-FABP levels in our sample of men and pre- and postmenopausal women. For men, TT was associated independently and inversely with serum A-FABP levels. For pre- and postmenopausal women, BAT and TT were independent and positive factors associated with serum A-FABP levels, respectively. After adjustment for the factors related to serum A-FABP levels, the associations described above remained significant.
Conclusion: Serum A-FABP levels increased following the order of men, premenopausal women, and postmenopausal women progressively. Androgen was identified as an independent and negative factor of serum A-FABP levels in men and an independent and positive factor of serum A-FABP levels in women. Based on its effects on fat content, especially trunk fat, androgen may contribute to gender differences in serum A-FABP levels.

PI-19

Controlled attenuation parameter (CAP) have close relationship with the prevalence and the severity of NAFLD in a T2DM population

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Background: The severity of non-alcoholic fatty liver disease (NAFLD) in type 2 diabetes mellitus (T2DM) population compared with that in normal glucose tolerance (NGT) individuals has not yet been assessed by a quantitative method. We investigated the prevalence and the severity of NAFLD in a T2DM population using controlled attenuation parameter (CAP).
Methods: Subjects who underwent testing for biomarkers related to T2DMand CAP using Fibroscan® during a regular health check-up were enrolled. CAP values of 250 dB/m and 300 dB/m were selected as the cutoffs for the presence of NAFLD and for moderate to severe NAFLD respectively. Biomarkers related to T2DM included fasting glucose/insulin, C-peptide, HbA1c, glycoalbumin, and HOMA-IR.
Results: Among 340 study participants (T2DM, n = 66; pre-diabetes, n = 202; NGT, n = 72), the proportion of subjects with NAFLD increased according to the glucose tolerance status (31.9% in NGT; 47.0% in pre-diabetes; 57.6% in T2DM). The median CAP value was significantly higher in subjects with T2DM (265 dB/m) than in those with pre-diabetes (245 dB/m) or NGT (231 dB/m) (all $P < 0.05$). Logistic regression analysis showed that subjects with moderate to severe NAFLD had a 2.4-fold (odds ratio) higher risk of having T2DM than those without NAFLD ($P = 0.02$; 95% confidence interval, 1.13–4.86), and positive correlations between the CAP value and HOMA-IR ($\rho = 0.407$) or C-peptide ($\rho = 0.402$) were demonstrated.
Conclusion: Subjects with T2DM had a higher prevalence of severe NAFLD than those with NGT. Increased hepatic steatosis was independently associated with the presence of T2DM, and insulin resistance induced by hepatic fat may be an important mechanistic connection.

PI-20

Correlation between insulin sensitivity and pathohistological findings in non-alcoholic fatty liver disease

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While the association of the prevalence of non-alcoholic fatty liver disease (NAFLD) with impaired glucose metabolism has been reported, the association between the severity of NAFLD and glucose tolerance remains to be clarified. We previously reported that the stages of severity in histological findings (Matteoni's classification) independently affect insulin sensitivity/resistance in NAFLD. In this study, correlation between insulin sensitivity and pathohistological findings of liver specimens in detail in patients with NAFLD. Glucose tolerance of 131 Japanese patients [sex: male/female = 73/58; age (y): 46.4 ± 16.5 (mean ± SD); BMI: 29.0 ± 5.2] in our hospital diagnosed as NAFLD by histological findings of liver biopsy specimen was examined by using 75-g OGTT [normal: n = 47; impaired glucose tolerance: n = 51; diabetes (DM): n = 33]. In DM, 29 patients did not take any antidiabetic medication and 4 patients took oral hypoglycemic agents (nateglinide: n = 2; voglibose: n = 2). Based on the OGTT data, QUICKI, which reflects insulin sensitivity in both liver and skeletal muscle, Matsuda Index (MI), which mainly reflects insulin sensitivity in skeletal muscle, and Hepatic insulin resistance index (HRI), which mainly reflects insulin resistance in liver were calculated. Pathohistological findings were scored according to Fibrosis Score by Brunt et al. (F) (0–4) and NAFLD Activity Score (NAS) (0–8) composed of scores for steatosis (NAS-S) (0–3), lobular inflammation (NAS-I) (0–3), and ballooning (NAS-B) (0–2). Stepwise multiple regression analysis was performed to predict indices of insulin sensitivity/resistance. Analysis using QUICKI as a dependent variable and sex (female = 0, male = 1), BMI, age, F, and NAS-T as independent variables shows that BMI (β = –0.401), F (β = –0.263), NAS-T (β = –0.193), and sex (β = –0.158) are predicting factors (R2 = 0.346). Analysis using QUICKI as a dependent variable and sex, BMI, age, F, NAS-S, NAS-I, and NAS-B as independent variables shows that BMI (β = –0.410), F (β = –0.296), and NAS-S (β = –0.150) are predicting factors (R2 = 0.315). Analysis using normally-distributed log-e-transformed MI (log-e MI) and log-e-transformed HRI (log-e HRI) as a dependent variable and sex, BMI, age, F, and NAS (NAS-T or NAS-S, NAS-I, and NAS-B) as independent variables shows that BMI (β = –0.456) and F (β = –0.336) (log-e MI: R2 = 0.356) and BMI (β = 0.495) (log-e HRI: R2 = 0.245) are predicting factors, respectively. These findings indicate that although adiposity is correlated with insulin sensitivity in both liver and skeletal muscle, fibrosis in liver histology is an important factor to predict insulin sensitivity in skeletal muscle independent of adiposity in NAFLD.

PI-21

Circulating soluble IL-6 receptor levels and visceral adipocyte size are associated with insulin resistance in morbidly obese subjects

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Background: Morbid obesity is related to chronic inflammation and many related metabolic complications. Interleukin (IL)-6 plays a pivotal pathophysiological role in obesity, and IL-6 trans-signaling via the soluble IL-6 receptor (sIL-6R) has a major pro-inflammatory effect. The aim of this study was to investigate the associations between sIL-6R, adipocyte size and insulin resistance in morbidly obese individuals.
Methods: We measured levels of sIL-6R, high-sensitivity C-reactive protein (hs-CRP), and lipid parameters and estimated insulin resistance using homeostasis model assessment (HOMA-IR) before the patients underwent bariatric surgery. Mesenteric adipose tissue was collected during surgery, adipocyte size and levels of membrane bound IL-6 receptor (mIL-6R) were evaluated. In total, 35 adults (20 men and 15 women) were recruited.
Results: The subjects with high HOMA-IR (≥2.4) had higher fasting glucose/insulin, triglycerides, sIL-6R, adipocyte size and lower high-density lipoprotein (HDL) cholesterol and mIL-6R than those with low HOMA-IR (<2.4). Adipocyte size positively correlated with sIL-6R (r = 0.559, P = 0.001) and HOMA-IR (r = 0.773, P = <0.001) independent of age, sex, body mass index (BMI), waist and use of diabetic drugs. In addition, every 1 ng/mL increase in sIL-6R concentration corresponded to a 10.9% decrease in the likelihood of maintaining lower insulin resistance. Furthermore, a sIL-6R level of 77.45 ng/mL was a reasonable cutoff level to predict lower insulin resistance in morbidly obese subjects.
Conclusion: Circulating sIL-6R and adipocyte size are more closely associated with insulin status than waist circumference or BMI in morbidly obese adults. sIL-6R may be a useful biomarker to predict insulin status among morbid obese subjects.

PI-22

Inhibition of local macrophage growth ameliorates obesity-associated adipose tissue inflammation, insulin resistance and hepatic steatosis in HFD-fed mice

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Objective: Chronically increased activity of the innate immune system has been implicated in the pathogenesis of the insulin resistance associated with obesity and type 2 diabetes. Although the tissue macrophage has been demonstrated proliferating in the adipose tissue and the liver, the roles of the macrophage proliferation in the development of insulin resistance and hepatic steatosis are largely unknown.
Research design and methods: To verify the direct evidence of involvement of tissue macrophage proliferation for adipose tissue inflammation and hepatic steatosis, we generated a transgenic mouse whose macrophage proliferation is specifically suppressed by inducing the expression of cyclin dependent kinase inhibitor, p27kip under the regulation of the scavenger receptor promoter/enhancer (mac-p27Tg). The mac-p27Tg mice were fed High-Fat Diet (HFD) to assess the impact on adipose tissue inflammation, insulin resistance and hepatic steatosis.
Results: Glucose and insulin tolerance tests in HFD-fed mac-p27Tg indicate significantly enhanced glucose clearance and insulin sensitivity compared with the control littermates. Macrophages were less accumulated in mac-p27Tg adipose tissue. The crown-like structure formation was significantly reduced in mac-p27Tg along with decreased inflammatory cytokine mRNA expression in adipose tissue. The triglyceride content in the liver was significantly decreased in HFD-fed mac-p27Tg mice compared with the controls. Azan staining showed significant reduction of liver fibrosis in mac-p27Tg liver. The mRNA expression of fibrosis markers (collagen1a1, alpha-SMA) and the NADPH oxidase (p22phox) were significantly decreased in mac-p27Tg liver.

Conclusions: The excess inflammatory response in the adipose tissue and the formation of hepatic steatosis were ameliorated by macrophage growth inhibition. In addition, the inhibition of macrophage growth resulted in the suppression of obesity-associated insulin resistance. These results suggest that the local macrophage proliferation could be the common pathophysiological feature in formation and progression of dietary-induced insulin resistance and the formation of hepatic steatosis.

PI-23

The weight changes of type 2 diabetes patients with non-insulin antidiabetic drugs: a meta-analysis

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This meta-analysis is to clarify the weight changes in type 2 diabetes mellitus (T2DM) patients with different non-insulin antidiabetic treatment. Studies were identified by a literature search of Medline, Embase, and others from the time that recording commenced until December 2015. The meta-analysis was performed by computing the weighted mean difference (WMD) and 95% confidence interval (CI) for a change from baseline to the study endpoint for placebo versus non-insulin antidiabetic drugs.

Totally 206 randomized controlled trials were judged to be appropriate for inclusion in the meta-analysis. There is no significant weight change from baseline (WMD −0.63 kg; p \0.08) in the metformin group (2,353 participants) compare with placebo. The alpha-glucosidase inhibitor group (2,424 participants) has a significantly greater decrease in the weight change from baseline (WMD −0.53 kg; p\0.006) compare with placebo. The Glucagon-like peptide-1 analogue group (5,246 participants) has a significantly greater decrease in the weight change from baseline (WMD −1.49 kg; p\0.00001) compare with placebo. The sodium-glucose cotransporter 2 inhibitor group (8,193 participants) has a significantly greater decrease in the body weight (WMD −1.95 kg; p\0.00001) compare with placebo. The dipeptidyl peptidase-4 inhibitor group (16,579 participants) has a significant increase in the body weight (WMD 0.25 kg; p\0.00001) compare with placebo. The thiazolidinedione group (7,768 participants) has a significantly greater increase in the weight change from baseline (WMD 2.46 kg; p\0.00001) compare with placebo. The sulphonylurea group (1,768 participants) has a significantly greater increase in weight change from baseline (WMD 2.23 kg; p\0.00001) compare with placebo. According to this meta-analysis, the weight changes in different treatments in type 2 diabetes were comprehensively concluded.

PI-24

Association between adolescent pregnancy and sarcopenic obesity in postmenopausal women: The KNHNES 2009–2010

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Objective: The objective of the present study was to determine whether there was an association between age at first childbirth and sarcopenic obesity in postmenopausal women.
Research design and methods: This study was based on data from the Korean National Health and Nutrition Examination Survey (KNHANES), conducted by the Korean Ministry of Health and Welfare, from 2009 to 2010. Out of 19,491 participants, the analysis included data for 2,196 postmenopausal women. Subjects were subdivided according to their age at first childbirth as follows: ≤19 years, 20–24 years, 25–29 years, and ≥30 years. Multivariate logistic regression analyses were used to identify whether or not there was an independent association between the age of women at first childbirth and sarcopenic obesity by adjusting for confounding factors.
Results: The prevalence rates of nonsarcopenic nonobesity, nonsarcopenic obesity, sarcopenic nonobesity, and sarcopenic obesity were 48.6%, 16.1%, 15.0%, and 20.3%, respectively. Sarcopenic obesity prevalence differed significantly between the subgroups and increased with earlier age at first childbirth, with 11.7% in subjects ≥30 years at first childbirth and 30.7% in subjects ≤19 years at first childbirth. After fully adjusting for confounding factors, including chronic diseases, sociodemographic influences, lifestyle differences, serum 25(OH)D levels, and reproductive issues, women ≤19 years at first childbirth were significantly associated with sarcopenic obesity (odds ratio [OR] 1.719 [95% CI 1.091–2.711]).
Conclusions: Women's age at first childbirth influenced the sarcopenic obesity risk in postmenopausal women, and adolescent pregnancy was independently associated with a higher risk of sarcopenic obesity in postmenopausal women.

PI-25

Hinokitiol improves insulin action in 3T3-L1 adipocytes

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In recent decades, obesity has become a worldwide epidemic disease. Obesity leads to chronic inflammation and insulin resistance which are associated with the development of type 2 diabetes mellitus, hypertension and cardiovascular disease. Hinokitiol, a phytochemical isolated from Chamaecyparis obtusa Siebold & Zucc. var. formosana (Hayatya) Rehder, has shown anti-cancer, anti-bacterial and anti-inflammatory functions. Previous data of ours have demonstrated that Hinokitiol decreases adipogenesis as evidenced by reduction of lipid droplets and triglyceride level as well as modulation of adipogenesis related marker expression. Although Hinokitiol reduces adipogenesis, effect of Hinokitiol especially in insulin action on differentiated 3T3-L1 adipocytes is not clear. Differentiated 3T3-L1 adipocytes treated with test concentration of Hinokitiol of up to 5 μM still had more than 90% of the cell viability of cultures treated with Dimethyl sulfoxide vehicle control. Moreover, Hinokitiol did not change the mRNA expression of of peroxisome proliferator-activated receptor γ, glucose transporter type 4 (GLUT4), adipocyte protein 2 and adiponectin in differentiated 3T3-L1 adipocytes. Notably, pre-treated with Hinokitiol significantly improve insulin action in differentiated 3T3-L1 adipocytes. Specifically, insulin-induced protein kinase B and Akt substrate of 160 kDa phosphorylation and membrane GLUT4 protein expression as well as glucose uptake is enhanced by Hinokitiol treatment. Based on these above findings, Hinokitiol may improve adipocytes insulin action and have a health benefits on obesity related insulin resistance.

PI-26

Prebariatric screening for diabetes and cardiovascular risk in an interdisciplinary obesity center discloses unexpected gender differences

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Question: Type 2 diabetes prevalence is higher in men, but diabetic women lose more years of life. Obesity prevalence is only slightly higher, but bariatric obesity treatment is much more frequent in women. We therefore performed a gender-specific evaluation of both systematic diabetes screening and atherosclerotic cardiovascular risk assessment in an obese cohort qualifying for bariatric surgery.
Methods: 315 consecutive patients (65% women) who qualified for bariatric surgery according to current guidelines and a local

modification of the Edmonton obesity staging system (EOSS) were analyzed. In addition to HbA1c and fasting plasma glucose (FPG), a 75 g oral glucose tolerance test was performed in all non-diabetic subjects. In patients with known or newly diagnosed diabetes, 10-year atherosclerotic cardiovascular disease risk was assessed using established tools (ASCVD, UKPDS-risk score, ARRIBA).

Results: [mean ± SEM; female vs. male] Among the 143 (80 female/63 male) patients with known or newly diagnosed diabetes, age (50.3 ± 1.5 vs. 49.0 ± 1.8 years), BMI (48.2 ± 1.4 vs. 47.9 ± 1.6 kg/m^2) and diabetes duration (7.4 ± 1.3 vs. 7.8 ± 1.3 years) were not different between men and women. In contrast, we detected pronounced gender differences in the prevalence of known diabetes (29.1 vs. 50.5%), rate of newly diagnosed diabetes cases (33 vs.14.5%) and HbA1c (7.18 ± 0.2 vs. 8.15 ± 0.3%; p = 0.01). Clinical atherosclerosis was 2.8 times more prevalent (10.4 vs. 28.8%) and estimated 10-year atherosclerotic cardiovascular disease risk was significantly higher (factor 5.9/3.1/2.7 – ARRIBA/ASCVD/UKPDS) in the male cohort.

Conclusions: Systematic prebariatric screening discloses both higher than expected diabetes prevalence in men and higher than expected numbers of newly detected type 2 diabetes in women. The rampant notion of diabetic women having the same or even higher atherosclerotic cardiovascular disease risk as compared to diabetic men, is apparently inapplicable in the context of very high BMI. In fact, obese diabetic men have 2.5 times more clinical atherosclerosis and three to six times higher 10-year atherosclerotic cardiovascular disease risk, than women. Thus, in contrast to published perception, female preponderance among qualifyers for bariatric surgery may be a misallocation of resources and a waste of bariatric risk reduction potential. Taken together, key aspects of prebariatric screening strategies are diabetes in obese women and ASCVD in obese men.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; ARRIBA, absolute and relative risk reduction in general practice.

PI-27

Increased overall mortality and presenting more advanced TNM stage of well differentiated thyroid cancer patients with type 2 DM

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Obesity, type 2 diabetes mellitus (DM) had been known increased risk of certain cancers. Metformin treatment in these patients may have better outcome. The purpose of our study is to realize the characteristics of type 2 DM patients with well differentiated thyroid cancer patients. In addition, we had compared clinical features and therapeutic outcome of thyroid cancer with and without type 2 DM.

A retrospective analysis of adult thyroid cancer patients with or without type 2 DM admitted between January 2001 and December 2010 was performed at an institution. A total of 1,687 well-differentiated thyroid cancer patients with different histological patterns were enrolled. Among these subjects, 260 were type 2 DM patients. Patients with thyroid cancer and type 2 DM were significantly older than non-DM patients. The mean follow-up period of these patient were 6.1 ± 6.1 years. Thyroid cancer in type 2 DM was showed larger tumor size, and more advanced TNM stage than non-DM group. In addition, disease-specific mortality was higher in the type 2 DM group (2.7% vs. 1.2%); but the difference was not statistical difference. Overall mortality was higher in type 2 DM patients (6.2% vs. 1.5%, p = 0.001). Thyroid cancer patients with type 2 DM showed a higher percentage of secondary primary cancers than those without DM (8.5% vs. 3.0%). In conclusion, type 2 DM diagnosed as thyroid cancer need to be underwent more aggressive surgical procedure and postoperative other modalities treatment.

PI-28

Effect of bariatric surgery on diabetic nephropathy in obese type 2 diabetes patients in a local retrospective 2 year study

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Background: Numerous studies have examined the benefits and risks of Bariatric Surgery (BS) versus conventional therapy in the treatment of obese patients with type 2 diabetic mellitus (T2DM). BS has been shown to result in improvements in weight reduction, glycemic control, and even remission of diabetes. However, not many studies have looked at changes in microvascular complications after BS. Local data in this area is particularly lacking.

Objective: To evaluate the effect of BS on Diabetic Nephropathy (DN) in obese T2DM subjects as measured by changes in urine albumin-to-creatinine ratio (uACR) or urine protein-to-creatinine ratio (uPCR).

Subjects and methods: This was an observational retrospective cohort study. Data of 46 multi-ethnic obese T2DM subjects who were followed up for 2 years were retrieved from our hospital database of all BS done from January 2011 to December 2014 (n = 150). Glomerular filtration rate (eGFR) was computed using the modified MDRD formula and chronic kidney disease (CKD) stage was categorized based on KDIGO 2012 clinical practice guidelines. Conversion of uPCR to uACR was done by multiplying by 88.4: g/day = ×88.4 mg/mmol. (KDIGO 2013).

Results: Surgery performed included sleeve gastrectomy, Roux-en-Y gastric bypass and lap-band gastric bypass. Of the 46 subjects with T2DM, 23 had normal uACR and glomerular filtration rates (eGFR) >60 mL/min (1.73 m^2) before the operation, including 1 who died. 1 patient with eGFR in CKD3a range had normal uACR before and after the operation. 8 had missing data ie no uACR results either before or after surgery. Only 14 T2DM patients had pre and post BS uACR data available for analysis. Of these 14 patients, 9 had GFR >60 mL/min (1.73 m^2) before and after BS. 2 each had CKD stage 3a and stage 3b and 1 had CKD stage 4 before and after BS. In the 14 T2DM patients, the median uACR before and after BS was 10.4 mg/mmol (Interquartile range (IQR) 7.2–92.3) and 2.8 mg/mmol (IQR 0.9–22.9) (p = 0.009).

12 out of the 14 subjects (85.7%) showed improvement of uACR after surgery. The remaining 2 showed worsening of uACR results, with one of them showing only insignificant increase (from 4.90 mg/mmol to 7.24 mg/mmol).

Conclusions: Our data suggests that BS improves DN in obese T2DM subjects. Larger studies and randomized controlled trials, looking at local patients of different ethnic groups and for longer duration, are needed to confirm our data on renal profiles before and after BS.

PI-29

Prevalence, clinical characteristics, and risk factors of sarcopenia in overweight patients with type 2 diabetes

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Aims: The coexistence of excessive accumulation of body fat and loss of skeletal muscle increase the risk of physical disability, morbidity, and mortality. The early detection and prevention of sarcopenia are important in the management of overweight/obese patients with type 2 diabetes, because the combination may be particularly harmful to diabetic patients. Thus, we analyzed the clinical characteristics and risk factors of sarcopenia in overweight diabetic patients.
Materials and methods: The subjects of this study were 570 patients (325 men and 245 women) with type 2 diabetes aged 40 years or older, consisting of 299 lean (BMI < 25 kg/m^2), 178 overweight (25–30 kg/m^2, obese class I by Japanese criteria), and 93 obese (≥30 kg/m^2) individuals. Patients with malignant disease, massive proteinuria, severe liver disease and chronic pancreatitis were excluded. Body composition was measured with a multi-frequency bioelectrical impedance analyzer. Sarcopenia was defined as a skeletal muscle index (total appendicular muscle mass/height2) <7.0 kg/m^2 in men and <5.7 kg/m^2 in women.
Results: The prevalence of sarcopenia was 31.6%. Although sarcopenic subjects had a lower BMI than non-sarcopenic subjects (21.4 ± 2.8 vs. 27.4 ± 4.9 kg/m^2, $p < 0.0001$), 18 sarcopenic subjects were overweight. Sarcopenic overweight patients were older than non-sarcopenic overweight patients (69.5 ± 11.2 vs. 62.7 ± 10.9 years, $p = 0.002$). There was no significant difference in HbA1c, FPG, IRI, CPR, HOMA-IR, FT3, FT4, or TSH levels. Sarcopenic overweight subjects had more fat mass in spite of a slightly lower BMI. Tuning fork vibration time at the medial malleolus was significantly shorter in sarcopenic subjects (9.7 ± 4.5 vs. 13.0 ± 4.2 sec, $p = 0.003$). The difference remained significant after the adjustment of age. Furthermore, the vibration time was correlated with the skeletal muscle index ($p < 0.0001$). A multiple regression analysis showed that, in addition to age and gender, vibration time was an independent contributor to the skeletal muscle index. A fecal fat test was positive in 69% of sarcopenic overweight subjects and in 38% of non-sarcopenic overweight subjects ($p = 0.029$). There was no significant difference in the rate of having exercise habits.
Conclusion: Here we showed that sarcopenia is a common complication of type 2 diabetes even in overweight patients. Diabetic neuropathy may accelerate sarcopenia directly or indirectly through the reduction of exercise. Furthermore, subclinical malabsorption may be involved in the development of sarcopenia in diabetic patients. The appropriate management of peripheral neuropathy and the improvement of digestive function may be beneficial in prevention and treatment of sarcopenia in diabetic patients.

PI-31
Role of novel variants of PGC-1α in the pathogenesis of obesity

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Peroxisome proliferator-activated receptor γ coactivator-1α (PGC-1α) is a transcriptional coactivator that regulates various metabolic processes, including mitochondrial biogenesis and thermogenesis. Given that mitochondrial dysfunction and impaired thermogenesis are often observed in individuals with insulin resistance and obesity and that the abundance of PGC-1α is reduced in skeletal muscle of such affected animals and humans, PGC-1α has been implicated in the pathogenesis of these health problems. We have recently identified variants of PGC-1α (PGC-1αb/c) generated by transcription from an alternative promoter. These variants are robustly induced in skeletal muscle by acute exercise. Mice specifically lacking the novel variants (PGC-1αb/cKO) developed age-dependent obesity and insulin resistance. Abundance of total PGC-1α in skeletal muscle was not altered in PGC-1αb/cKO mice, likely because the canonical isoform is predominant under static conditions. However, increases in total PGC-1α abundance and energy expenditure in response to exercise were attenuated in PGC1-αb/cKO mice, likely contributing to their obesity-prone phenotype. Among various exercise-mimetic stimuli, a β2 agonist clenbuterol most specifically and potently up-regulated PGC-1αb/c in skeletal muscle, and the exercise-induced up-regulation of PGC-1αb/c in skeletal muscle was inhibited by a β-adrenergic antagonist propranolol. Furthermore, clenbuterol-induced oxygen consumption was attenuated in PGC1-αb/cKO mice. These data indicate that the β2 adrenergic signaling is largely responsible for exercise-induced induction of PGC1-αb/c. The expression of PGC-1αb/c induced by clenbuterol was impaired in skeletal muscle of obese model mice including db/db mice and high fat-fed mice. Furthermore, the increase in energy expenditure in response to β2 adrenergic stimuli was impaired in such obese model mice. In skeletal muscle of obese animals, the expression of β2 adrenergic receptor (Adrb2) mRNA was decreased and the percentage of methylated CpG sites in the Adrb2 promoter was increased as compared to non-obese mice, suggesting that the epigenetic regulation of Adrb2 likely contributes to the development of adrenaline resistance via the downregulation of Adrb2 in skeletal muscle. Our results thus indicate that exercise-induced expression of PGC1-αb/c plays an important role in the control of energy expenditure during exercise and that impaired induction of PGC1-αb/c in skeletal muscle of obese animals, which is at least partly induced by the downregulation Adrb2, leads to the impaired energy expenditure during exercise.

PI-32
Pioglitazone ameliorates hepatic steatosis via enhancing cytosolic- and autophagy-related lipolysis dominantly mediated by PPAR

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Aims: Impaired cytosolic- and autophagy-lipolysis evidently contribute to the development of obesity and insulin resistance. Pioglitazone has been shown to lessen hepatic steatosis in human studies. However, the molecular mechanism is still unclear. Enhancing hepatic lipolysis is supposed to elucidate the intracellular lipid regulation by pioglitazone. The study investigated the modulation of cytosolic- and autophagy-related lipolysis by pioglitazone in a mouse model of high fat diet and cell model treated by palmitic acid.
Methods: Male C57BL/6 mice were divided into (1) chow diet, (2) high fat diet and (3) high fat diet co-administered with pioglitazone 100 mg/kg/day for 8 weeks. Hepatic steatosis was measured by hepatic triglyceride content and Oil-red O staining. Expression of the genes and proteins [(Atg 7, LC3, lysosomal acid lipase (LAL), adipose triglyceride lipase (ATGL) and hormone-sensitive lipase (HSL)] related to autophagy- and cytosolic-lipolysis were compared among groups. The AML12 liver cell model was used to test the regulation by small interfering RNA (siRNA) of PPARγ and PPARα.
Results: Our results showed that a high fat diet induced prominent hepatic steatosis and diminished expression of autophagy-related proteins 7 (Atg7) and LC3. These

abnormalities were significantly reversed by pioglitazone. The protein expressions reflecting the macroautophagy process, involving vesicle elongation (Atg7), phagolysosome fusion (LC3) and lipophagy-specific lysososmal lipolysis (LAL) were significantly and consistently enhanced well by pioglitazone. Hepatic expressions of the ATGL and HSL were significantly stimulated, which mainly distributed over hepatocytes rather than Kupffer cells. The SiRNA assay of the AML12 liver cells demonstrated the lipolysis was both modulated both by PPARα and γ activation. However, the autophagy-lipolysis was dominantly dependent to PPARα activation.

Conclusion: Our study suggests that pioglitazone did alleviate hepatic steatosis via enhancing lipophagy and cytosolic lipolysis of hepatocytes.

PI-35

Adipocyte fatty acid binding protein (A-FABP) is a potential mediator of heart dysfunction and failure related to obesity

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Obesity predisposes to the development of diabetes, hypertension and dyslipidemia, which are the risk factors for the development of cardiac artery disease and ischemic cardiomyopathy. It is also an independent risk factor for the development of heart failure. Adipocyte fatty acid binding protein (A-FABP) is an adipokine that mainly expressed in adipocytes and macrophages and can be released into the circulation. Emerging clinical evidence suggest that A-FABP is a key link between obesity and cardiac dysfunction as elevated circulating A-FABP levels are positively associated with cardiac contractile dysfunction of obese subjects as well as left ventricular mass and myocardial performance index in patients with obstructive sleep apnea syndrome. Circulating A-FABP is also significantly increased in Chinese subjects with heart failure and is independently associated with the deterioration of heart function. Here we investigate the pathological role of A-FABP in cardiomyopathy associated with obesity using A-FABP knockout (KO) mice and their wildtype (WT) littermates.

A-FABP KO mice and their WT littermates were fed with standard chow (STC) or high fat high cholesterol diet (HFHC) for 24 weeks with or without treatment of selective A-FABP inhibitor BMS309403 (BMS). The circulating level and cardiac expression of A-FABP were markedly elevated in WT mice after prolonged HFHC diet feeding. A-FABP deficiency protected against HFHC diet induced- hypertension and -impairment of systolic and diastolic function in mice. Compared to WT mice, diet-induced cardiomyocyte hypertrophy, cardiac lipid accumulation and fibrosis were ameliorated in A-FABP KO mice. These protective actions of A-FABP deficiency were accompanied by reduced cardiac inflammation and endoplasmic reticulum (ER) stress. Consistently, HFHC diet-induced cardiomyocyte hypertrophy and cardiac collagen deposition were significantly diminished in WT mice treated with BMS.

In conclusion, A-FABP deficiency protects mice against cardiomyopathy and heart dysfunction associated with obesity. A-FABP may be the therapeutic target for the treatment of obesity-related cardiomyopathy.

Acknowledgement: This project is supported by RGC HKU 767913.

PI-36

The association between GFR and metabolic syndrome in Korean population

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Background: Metabolic syndrome (MS) is a cluster of cardiovascular risk factors and chronic kidney disease (CKD) is an increasingly common and progresses to end-stage renal disease with combined complications. The aim of our study was to investigate the relationship between CKD and key components of MS.

Methods: We recruited 2,403 Korean adults Goryeong region in KoGES_Multi-Rural (MR) communities cohort study from February 2006 to March 2009. Metabolic parameters, clinical characteristics, biochemical markers were obtained in each subject. The MS was defined by the National Cholesterol Education Program Adult Treatment Panel III criteria as three or more of five components where the cut-off point of waist circumference (WC) was modified for Korean as ≥90 cm in men and ≥80 cm in women according to the recommendation by WHO West Pacific Region. CKD was defined as an estimated glomerular filtration rate (GFR) less than 60 mL/min/1.73 m^2.

Results: Among 2,403 subjects (Mean age 61.62 ± 9.97), prevalence of MS and CKD were 44.9% (1,078 cases) and 9.2% (222 cases). The presence of CKD according to GFR was significantly associated with key components of MS including WC, blood pressure, HDL, triglyceride, and fasting glucose levels ($P < 0.01$). The prevalence of CKD was 67.6% in the subjects with MS. The incidence of CKD was significantly higher in subjects who was diagnosed as MS compared to subjects without MS (13.9% vs 5.4%, $p < 0.05$).

Conclusions: This study shows that CKD according to was significantly associated with the components of the MS, suggesting metabolic syndrome may be an independent risk factor for developing CKD.

Acknowledgement: This work was supported by the Research Program funded by the Korea Centers for Disease Control and Prevention (2006-E71009-00, 2007-E71002-00, 2008-E71004-00, 2009-E71006-00).

PI-38

N-acetylcytein improves high-fat-induced overweight and fat accumulation, insulin resistance and glucose intolerance through reducing mitochondrial ROS in visceral fat

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Obesity, especially accumulation of visceral fat (VF), is a major risk of diabetes and related cardiovascular diseases. Mitochondrial reactive oxygen species (ROS), a critical source of intracellular oxidative stress, is associated with excessive fat accumulation in VF. However, whether intervention reducing mitochondrial ROS is able to reduce obesity and diabetes progression remain elusive. Here we present that antioxidant N-acetylcystein (NAC) reduced VF mass, VF oxidative damage, insulin resistance and glucose intolerance in an obesity mouse model induced by high fat high sugar (HFHS) diet. C57BL6 mice fed for six months were divided to three groups: control diet (CD), HFHS or HFHS combined with NAC (HFHS + NAC). HFHS diet significantly induced overweight, VF accumulation, VF oxidative damage, VF mitochondrial ROS and development of insulin resistance as well as glucose intolerance. Importantly, HFHS + NAC showed reduction in HFHS-caused overweight, VF accumulation, VF oxidative damage, VF mitochondrial ROS

and ameliorated insulin resistance and glucose intolerance. Throughout six months both HFHS and HFHS + NAC groups showed a dramatic increase of mitochondrial bioenergetics, measured as oxygen consumption rate by the Seahorse XF24 Extracellular Flux Analyzer. Compared to CD group at six month, HFHS group exhibited a significant increase of mitochondrial biogenesis associated with induced mitochondrial ROS, which was not observed in HFHS + NAC group. In light of this study, we suggest that anti-oxidative NAC reduces obesity and mitigates insulin resistance and glucose intolerance through reducing mitochondrial ROS, oxidative damage and changing mitochondrial bioenergetics of VF. Notably, our study shed light on the therapeutic effect of mitochondrial ROS-repressing anti-oxidant on obesity-prevention and development of diabetes.

PI-39

Short leukocyte telomere length is associated with the FTO rs9939609 polymorphism in non-obese individuals

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The fat mass and obesity-associated (FTO) gene polymorphism rs9939609 has been associated with body weight and adiposity in many studies. Obesity contributes to limited life expectancy and short telomere length, a cellular marker for biological age. Our study aimed to evaluate the association between FTO rs9939609 risk variant and leukocyte telomere length, and to investigate if this relationship is modified by the status of obesity.

A total of 2,133 participants were recruited from the Korean Genome and Epidemiology Study. Leukocyte telomere length was determined using real-time quantitative polymerase chain reaction methodology. The FTO rs9939609 polymorphism was genotyped using DNA samples collected at baseline. The proportion of the TT, TA, and AA genotypes were shown as 76.7, 21.5, 1.8%, respectively. The mean body mass index (BMI) was significantly higher in carriers with the A-risk allele than in those with TT genotype (25.1 vs. 24.6 kg/m^2, P = 0.002). In 1,184 subjects without obesity (BMI < 25 kg/m^2), BMI, waist circumference and visceral fat area were higher in those with the FTO risk allele than in non-carriers. In contrast, none of them were associated with FTO risk allele in those with obesity. Leukocyte telomere length was significantly shorter in carriers with the FTO risk allele compared with non-carriers after controlling for age, sex, BMI, smoking, alcohol, exercise, hypertension, diabetes and cardiovascular disease (P < 0.01). In particular, such significant association between the FTO risk allele and telomere length appeared only in non-obese subjects (P = 0.03). In stepwise multivariate linear regression analyses, the independent risk factors affecting shorter leukocyte telomere length were higher age, lower high-density lipoprotein cholesterol levels and the presence of the FTO risk allele. This finding was evident only in those without obesity.

The FTO rs9939609 polymorphism is the independent risk factor not only for obesity but also for biological aging in non-obese population.

PI-40

Fatty liver changes after gastric cancer surgery

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Type 2 diabetes mellitus (T2DM) has been dramatically improved after bariatric surgery especially Roux-en-Y gastric bypass method. Immediate improvement of hepatic insulin sensitivity is suggested one of main mechanism. The procedures of gastric cancer surgeries are very similar with bariatric surgery. However, there is no study about the fatty liver change after gastric cancer surgery. Therefore we evaluated the fatty liver changes after gastrectomy for gastric cancer according to the types of surgery.

From a total 374 patients who underwent gastric cancer surgery in Kosin University Gospel Hospital form 1 January to 31 December of 2013, 212 patients had early gastric cancer (EGC). We evaluated hepatic steatosis for only EGC patients using Hounsfield unit (HU) on non contrast computed tomography (CT) imaging. Spleen and liver ratio of HU was calculated at previous to operation, 6 months, 12 months and 24 months. We compared the preoperative results and postoperative results according to the types of surgery: Billroth I (B I), Billroth II (B II) and Roux-en-Y gastric bypass (RYGB).

Among the total 212 EGC patients, 62.3% (132) underwent surgery with B I, 21.7% (46) with B II and 16% (34) with RYGB. Initial results of HU of liver, HU of spleen and spleen and liver ratio were not different among the three groups. After surgery, only patients with RYGB had significant changes of spleen and liver ratio at 6 months, 12 months and 24 months compared to the preoperative results (from −6.0 to −9.7, −9.2 and −10.4, p = 0.03). In 26 patients who had higher HU levels of spleen than liver initially, spleen and liver ratio also significantly decreased from 7.6 to −4.7 at 6 mo., −4.3 at 12 mo. and −4.2 at 24 mo. (p < 0.001).

In this study we identified that even in normal patients who had high HU of liver than spleen had significant changes of hepatic steatosis after RYGB. The patients initially had fatty liver had also significant decrease of spleen and liver ratio. These results suggested that RYGB could be better choice for patients with gastric cancer and metabolic disease coincidentally.

PI-41

Hypoglycemia occurred in one case after liver transplantation and bariatric surgery

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Secondary diabetes frequently occurs after liver transplantation under immunosuppression therapy. The accumulated incidence is reported around 50% after immunosuppression therapy, ex., tacrolimus. However, hypoglycemia is an important issue with emergent life-threatening risk more than hyperglycemia. It is so rare that hypoglycemia occurred in cases after successful liver transplantation. Here, we reported a case of severe hypoglycemia occurring one year after liver transplantation and treated by tacrolimus and mycophenolate mofetil.

This 42 year-old man is a case with morbid obesity (126 kg, BMI 44.6 kg/m^2) and he received the gastric bypass bariatric surgery in December, 2012. Then, he lost his body weight to 81 kg (BMI 28.7 kg/m^2) one year later. This patient was also a heavy drinker and chronic hepatitis B complicated with liver cirrhosis and decompensated liver failure. Then, liver transplantation was performed successfully in April, 2015. Immunosuppression therapy was combined with tacrolimus and mycophenolate mofetil thereafter. However, frequent symptomatic hypoglycemia (<50 mg/dL) happened during admission for management of the rejection. The blood glucose was kept in the range of 55–90 mg/dL in fasting state and 60–130 mg/dL postprandially under dextrose infusion.

The baseline evaluation revealed A1C 4.6%, ACTH 64.47 pg/mL, cortisol 3.55 μg/dL to exclude out adrenal insufficiency and organ failure. OGTT was performed and blood glucose was 78 mg/dL (baseline), 196 mg/dL (1st hour), dropped to 37 mg/dL (2nd hour) with C-peptide 7.97 ng/mL and insulin:

4.34 uIU/mL. Postprandial hyperinsulinemia related hypoglycemia was defined because of absence of pancreatic lesion detected by triple-phase spiral computed tomography. The hypoglycemia was well corrected by cortisone acetate 75 mg/day and dietary adjustments to keep normal blood glucose level ranged from preprandial 80–100 mg/dL to postprandial 83–120 mg/dL.
Secondary diabetes was frequently induced by immunosuppression therapy, especially tacrolimus. But hypoglycemia in case of liver transplantation always hints the poor prognosis for the transplanted liver. However, our case was well handled by the steroid treatment and dietary adjustments even complicated by hypoglycemia. Hypoglycemia after bariatric surgery is reported rare (<1%) but often arises within 3 years after operation. The dumping effect may be caused by the enhanced GLP-1 effect and pancreatic nesidioblatosis. Therefore, the exaggerated GLP-1 secretion and improved insulin sensitivity may rationally contribute to the hypoglycemia in our patient.

PI-42

The effects of aerobic exercise training on chemerin, apelin, and visfatin in obese young males

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Objective: Recent evidence suggests that adipose tissue is not only a passive reservoir for excess energy but also an active endocrine organ which secretes more than 600 bioactive molecules, namely, adipokines. Among newly identified adipokines, visfatin, chemerin and apelin are reported to be associated with obesity and type 2 diabetes mellitus. We investigated the exercise-induced changes in novel adipokines related to obesity and insulin resistance and their correlations with the changes in body fat composition and metabolic parameters after exercise.
Study design and methods: Forty young obese Korean males were randomly assigned to control and exercise group, who received 8-week supervised exercise training program. Body fat compositions and various metabolic parameters and adipokines were assessed before and after exercise.
Results: Significant reductions of body weight, total and truncal fat, and waist circumference and significant improvement in insulin resistance, systolic blood pressure, and LDL-cholesterol were observed in Exercise group (all $p < 0.001$). Serum visfatin, chemerin, and apelin levels were decreased after exercise ($p < 0.005$). Changes in body fat composition were significantly associated with changes in adipokines, and multiple linear regression analyses showed theses adipokines to be independent predictors of changes in insulin resistance, and in case of chemerin, fasting glucose as well.
Conclusions: Aerobic exercise led to improvements in insulin resistance and glucose homeostasis independent of changes in body composition and conventional adipokines, and visfatin, chemerin and apelin seem to be involved in the etiology of obesity and insulin resistance.

Using Big Data for Research and Care in Diabetes

PJ-01

Efficacy of exercise on HbA1c, lipid profiles and BMI changes in diabetic patients participating shared care programs

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Aim/introduction: Exercise for diabetics is very economic, benefits for their well beings, and can effectively lower blood sugar and blood lipid levels. We analyze the efficacy of type, duration, and frequency of exercise in patients with diabetes mellitus joining our diabetes health care improvement programs less than two years on the changes of A1C, bl.
Method/material: From January 2012 to June 2014, a total of 227 diabetic subjects entering our "diabetes health care improvement programs" for more than 2 years were retrieved for analysis. We excluded those were lost to follow-up, unfinished at any stage of the programs, and did not do exercise. Exercise groups are defined as exercising once a week, and for at least 10 minutes a time. We recorded the types, duration, and frequency of their exercise. The causes were collected in those with no exercise. We compared the changes in A1c, blood lipid profiles, and BMI between two groups. Statistical methods were Bivariate T-test and for Independent-Samples. ood lipid profiles, and BMI.
Results: About 80.7% had a walk in exercise group; the portions of exercise group had a duration more than 30 minutes a time is about 54%; 55.3% of exercise group had a frequency of 7 times a week.
Causes of non-exercise group were no time (40.9%), especially in the hot weather (accounting for 3%). The lipid profile changes in non-exercise group versus exercise group were 0.032 ± 0.232 mg/dL and -0.045 ± 0.316 mg/dL in total cholestereols ($p = 0.04$); -0.095 ± 0.623 mg/dL and -0.414 ± 1.203 mg/dL in triglycerides ($p = 0.01$); and 0.076 ± 0.35 mg/dL and -0.047 ± 0.463 mg/dL in LDL ($p = 0.31$).
The aging subjects had more exercise frequencies ($p = 0.03$). The more stronger strength of the exercise, the more time the subjects did the exercise ($p < 0.001$), which also correlated with the reduction of the levels of cholesterol ($p = 0.009$), and LDL ($p = 0.03$).
Conclusions: Our study suggests exercise helped reduce blood lipid profiles, but did not significantly improve the A1C, BMI and HDL levels. It may be associated with oral hypoglycemic agents and insulin use. Most people have no time to exercise, and may be related to work and no family support. Hot weather can also affect the motivation for exercise.

PJ-02

Mortality and causes of death from 2002 to 2013 in a national sample of diabetic patients in Korea

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Objective: We investigated the mortality rate (MR), causes of death and standardized mortality ratio (SMR) in Korean diabetic populations using data from the Korean National Health Insurance Service (NHIS) National Sample Cohort 2002 to 2013.
Research design and methods: From 1,000,000 NHIS National Sample Cohort, we identified 29,807 diabetic subjects (aged more than 30 years) from 2002 to 2004. Individuals having diabetes were defined if anti-diabetic drugs were prescribed with the presence of ICD-10 codes (E11 to E14) as diagnosis. Specific causes of death were classified into the following categories according to ICD-10 codes: diabetes, malignant neoplasm, disease of the circulatory system, and other causes. Among deaths due to the circulatory system, deaths due to ischemic heart diseases and cerebrovascular diseases were further analyzed.
Results: A total of 7,103 (23.8%) deaths were recorded. MR tended to increase with age. The MR ratio for men versus women was highest in their 40s to 50s. The overall SMR was 2.32 and SMRs attenuated in the elderly. Causes of death ascribed to diabetes, malignant neoplasm; ischemic heart

disease; cerebrovascular disease; and other causes were 22.0, 24.8, 6.2, 11.2 and 31.3%, respectively. The SMRs according to the each cause of death were 9.73, 1.76, 2.60, 2.04 and 1.89, respectively.
Conclusion: Approximately 78.0% of the diabetes-related deaths would not be ascribed to diabetes in Korea. The diabetic men have higher risk of dying than women, and diabetic patients have excess mortality when compared with the general population. For underlying causes of death not listed as diabetes, malignant neoplasm was the most common causes of death in Korea.

PJ-03
Impact of intensified frequent clinic visit on glucose control
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This protocol aimed at exploring how HbA1C was improved in different groups of patients with uncontrolled blood glucose (A1C < 9.9%, A1C < 10.9%, A1C > 11%) after they received care. The protocol was implemented between January 1, 2015 and March 31, 2015 at a metabolism clinic of a teaching hospital in southern Taiwan where patients with Type 2 diabetes featuring HbA1c≧9% attended visits on a monthly basis, had their dose adjusted, and attended diabetes care programs; the improvement of their HbA1c after three visits was analyzed to see if < 9% is achieved. Recruitment was done adopting the purposive sampling approach and a total of 905 patients showed improvement. Statistical method: Data were analyzed with ANOVA and it was found that the group of patients with A1C > 11% before they received intervention (n = 115) showed the most reduction by 4.5% ± 1.9%. Significant difference was observed among the three groups ($p < .001$). The two groups, with and without diabetic care, were then analyzed again; improvements did not reach significance in either group. With the "doctor-adjusted dose regimen", the two groups, with and without consistent doses (addition and no addition of doses), were analyzed; results showed improvement but no difference in the reduction of HbA1c. This protocol can help patients re-examine their uncontrolled blood glucose; they should take on an approach where they receive treatment provided by the doctor through monthly visits, have their dose adjusted and take part in diabetes care programs in order to understand the right countermeasures they should adopt and to further adjust their attitude and behavior for the ultimate goal of improving blood glucose control efficacy.

PJ-04
The analysis of diabetic patients' blood pressure difference before and after the doctor visit
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Purpose: It was found in the study that when subjects focused on related clues concerning their physical condition and disorders, it would also have an effect on the action they took in response to the disease. Data were collected and analyzed to understand the difference and reflect actual quality of care.
Methodology: Data were collected over a period of two weeks, that is, from September 21, 2015 to October 2, 2015. Five hundred subjects were enrolled. They followed the clinic procedure by checking in first at the waiting room to have their blood pressure taken. After the doctor visit, they went to another room for health education. Then, a health educator with a nursing background would take blood pressure from their right hand for two consecutive times (same as that done at the waiting room) to get a mean value. Data obtained before and after the doctor visit were registered and analyzed.
Result: Overall, there was significant difference in terms of presence of a hypertension history or not among the three age groups and their SBP values obtained at the hospital and at home ($p < 0.05$). The DBP values, on the other hand, showed significant difference in only the group <50 years old between that obtained at the hospital and that obtained at home ($p < 0.05$). For people with hypertension, those with SBP < 140 and >141 could maintain or improve to be <140, accounting for 60.5% of all; and those with DBP < 90 and DBP > 91 could maintain or improve to be <90, accounting for 93.5%. For those without hypertension, SBP was improved more significantly and the maintenance rate was better (85.5%). In other words, besides measuring blood pressure correctly, conditions and a mechanism for measuring blood pressure again should be established to reflect the actual quality of care. Among people with hypertension, 43% would monitor their own blood pressure (40% as is shown in the national survey). Data obtained from self monitoring of blood pressure help ensure effective safety required for adjusting medication. Therefore, encouraging patients to measure blood pressure at home is equally important in both health education and monitoring of blood glucose.

PJ-05
The impact of hemoglobin A1c on low-density lipoprotein cholesterol estimation by different formula in diabetic patients
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Background: The Friedewald formula (FF) is the main method for estimation of low-density lipoprotein cholesterol (LDL-C). Several modified formulae, including Martin and our recently developed formulae, had been developed in past years to improve the accuracy of estimated LDL-C. Because LDL-C control is an important goal for prevention of cardiovascular disease in diabetes, we aimed to evaluate the accuracy of various LDL-C estimation formulae in diabetic patients with different levels of hemoglobin A1c (HbA1c).
Methods: This is a cross-sectional study enrolled outpatients diabetes subjects who had full lipid profiles examinations, including measurements of total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and directly-measured LDL-C (dLDL-C) in the same blood sample between January 2004 and October 2014 at two hospitals in central Taiwan. Patients with TG level greater than 400 mg/dL or TC greater than 300 mg/dL were excluded. In FF formula, LDL-C = TC − HDL-C − (TG/5) (mg/dL); Lee and Hu formula: LDL-C = 0.75×TC − 25 (mg/dL); Martin formula: LDL-C = TC − HDL-C − (TG/3.1 to 11.9 according to strata-specific median TG: very low-density lipoprotein cholesterol ratio). The performance of each formula was compared in different levels of HbA1c. The concordance was defined by the proportion of correct classification in each dLDL-C category (<70, 70–99, 100–129, 130–159, 160–189, ≥190 mg/dL). Accuracy by different formulae in different HbA1c levels were compared by Chi-sqaure test.
Results: A total of 31,814 diabetic subjects were included in analysis. The overall concordance in each dLDL-C category according to our Lee and Hu formula were 66.6%, 66.8%, 65.2%, 64.1% for HbA1c<6.5%, 6.5–8%, 8–9%, ≥9 respectively. (P0.004). The corresponding concordance for FF were 63.6%, 56.8%,

55.7%, and 54.8. ($P < 0.001$). The overall concordance with Martin LDL-C was 70.0% for HbA1c < 6.5 vs. 67.6% for HbA1c between 6.5–8 vs. 67.7% for HbA1c between 8–9 vs. 67.3 for HbA1c ≥9 ($P < 0.001$). The accuracy of Lee and Hu formula was slightly inferior to the Martin formula, but better than FF, especially in subjects with high HbA1c level ($P < 0.001$, respectively).
Conclusion: High HbA1c was associated with poor accuracy in LDL-C estimation. The Lee and Hu formula cost less and maybe a simple form to estimate LDL-C in clinical practice.

PJ-07
Tramadol is a risk factor for hypoglycemia in diabetic patients in Taiwan
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Aim: To evaluate the association between tramadol and hypoglycemia in diabetic Taiwanese.
Method: Our study data were derived from a subset of the National Health Insurance Research Database. Diabetic patients aged 20 years or older with prescribed tramadol prescription were in the tramadol group, compared to nontramadol group.
Results: During a mean follow-up of 2 to 2.7 years for these two groups, the overall incidences of hypoglycemia (per 1,000 person-y) were significantly higher in tramadol group. According to the multivariable analyses, the tramadol group exhibited a significantly greater risk of hypoglycemia.
Conclusion: Tramadol use increases hypoglycemia in diabetic Taiwanese.

PJ-08
Associations between type 2 diabetes and peptic ulcer disease in Taiwan
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Purpose: To evaluate the association between type 2 diabetes mellitus (T2DM) and peptic ulcer disease (PUD) in Taiwan.
Methods: Patients diagnosed with T2DM for the first time between 2000 and 2005 was included and excluded patients diagnosed with PUD before the index date. Only patients who were treated for PUD by using proton-pump inhibitors, H2-receptor antagonists, or both were included. Distributions of sex, age, comorbidity, and medication were compared between the T2DM and non-T2DM groups to determine whether T2DM was a risk factor for PUD.
Results: During the study period, the T2DM group exhibited a significantly higher risk of developing PUD than did the non-T2DM group. After stratification by comorbidity, the significant association of the T2DM group with the increased risk of PUD development is still in our study.
Conclusion: This cohort study shows that T2DM increases the risk of developing PUD in Taiwan.

PJ-10
Meta-analysis of the insulin dosage in Chinese type 2 diabetes patients receiving insulin treatment
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Aim: To evaluate the insulin dosage in Chinese type 2 diabetes patients receiving various kinds of insulin treatment.
Methods: The MEDLINE, EMBASE, CNKI and Wan Fang databases were searched and qualified studies were included. The inclusion criteria were as following: (1) randomized controlled trial in type 2 diabetes patients; (2) Chinese participants; (3) insulin treatment in one arm or both arms in the trial; (4) study duration more than 12 weeks.
Results: Totally 88 qualified studies were included. According to randomized controlled trials, in patients receiving basal bolus insulin treatment, daily insulin dosage for the long-acting insulin analog in combination with rapid insulin analog was 28.30 u/day, daily insulin dosage for the NPH combined with regular insulin was 42.16 u/day, daily insulin dosage for the NPH combined with rapid insulin analog was 39.41 u/day. In patients receiving basal insulin with oral hypoglycemic agents treatment, daily insulin dosage for the long-acting insulin analog was 18.33 u/day, daily insulin dosage for NPH insulin was 16.34 u/day. In patients receiving premixed insulin treatment, daily insulin dosage for premixed insulin analog with oral hypoglycemic agents was 26.41 u/day, daily insulin dosage for premixed insulin analog alone was 36.14 u/day, daily insulin dosage for premixed human insulin with oral hypoglycemic agents was 29.91 u/day, daily insulin dosage for premixed human insulin alone was 38.42 u/day.
Conclusion: This meta-analysis was the first meta-analysis focused on the insulin dosage in Chinese type 2 diabetes patients which provided more comprehensive clinical evidence on the insulin dosage among different insulin treatments in treating Chinese type 2 diabetes patients.

PJ-11
Insulin resistance distribution and cut off value in Korea: From the 2008–2010 Korean national health and nutrition examination survey
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The subject of this study is to identify the distribution of HOMA-IR in Korea. And we investigated the cut off values of HOMA-IR that related with prevalence rate of metabolic syndrome, especially according to gender and menopause state.
We analysed the data of Korean National Health and Nutrition Examination Survey in 2008–2010. We conducted this study for participant aged 20 years or older and excluded the subject who had diabetes or fasting serum glucose >126 mg/dL. Finally, 11,121 participants were gathered and they were classified into three groups (4,911 men, 3,597 premenopausal women, 2,613 postmenopausal women). We used modified Adult Treatment Panel III criteria to define metabolic syndrome.
In our study, the mean HOMA-IR was 2.11(2.07–2.15) for men, 2.0(1.97–2.04) for premenopausal women, and 2.14(2.2–2.19) for postmenopausal women. Incidence of metabolic syndrome was 20.6% in men, 8.9% in premenopausal women, and 40.4% in postmenopausal women. The first cut off values for metabolic syndrome in men, premenopausal women and postmenopausal women is 2.23(sensitivity 70.6%, specificity 66.9%), 2.39(sensitivity 72.3%, specificity 76.4%) and 2.48 (sensitivity 51.9%, specificity 80.2%), respectively. The prevalence rate of metabolic syndrome associated to first HOMA-IR cut off value is 22.9% in men, 13.7% in premenopausal women and 51.6% in postmenopausal women. The second cut off value was around 3.2 in three groups. The prevalence rate of metabolic syndrome associated to second HOMA-IR cut off value is 50.8% in men, 42.5% in premenopausal women and 71.6% in postmenopausal women.
In conclusion, first cut off value of HOMA-IR were 2.2–2.5 and second cut off value of HOMA-IR were 3.2 in Korea. And cut off values of HOMA-IR for metabolic syndrome was different in accord with gender and menopausal status. When we estimated the HOMA-IR and prevalence of metabolic syndrome, we should consider to gender and menopausal status of participants.

PJ-12

Comparisons of placebo effect of hypoglycemic drugs between Asian and Caucasian type 2 diabetes patients

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Aim: It was hypothesis that the placebo effect might be different between different ethnicity. The aim of this study is to compare the placebo effect of hypoglycemic treatment between Asian and Caucasian type 2 diabetes patients.
Methods: The MEDLINE®, EMBASE®, CENTRAL were searched and qualified studies were included. References were collected until Dec. 2015. All the studies were double blind, placebo-controlled randomized trials in type 2 diabetes patients; study length of ≥12 weeks with the efficacy evaluated by changes in HbA1c from baseline in groups.
Results: 250 studies compared a placebo with an active hypoglycemic agent either in Asian (n = 40) or in Caucasian (n = 210), placebo effect in HbA1c was comparable between Asian (0.09%, 95%CI, 0 to 0.18%) and Caucasian (−0.02%, 95%CI, −0.15 to 0.10%), placebo effect in FPG was comparable between Asian (0.21 mmol/L; 95% CI, 0.07–0.34 mmol/L) and Caucasian (0.1 mmol/L; 95% CI, −0.09 to 0.29 mmol/L), placebo effect in weight was also comparable between Asian (−0.22 kg; 95% CI, −0.48–0.03 kg) and Caucasian (−0.02 kg; 95% CI, −0.48–0.44 kg). 40 studies compared a placebo with an AGI either in Asian (n = 25) or in Caucasian (n = 17), placebo effect in HbA1c was comparable between Asian (−0.13, 95%CI, −0.31 to 0.04) and Caucasian (0.08, 95%CI, −0.11 to 0.27). 83 trials compared a placebo with a TZD either in Asian (n = 38) or in Caucasian (n = 46), placebo effect in HbA1c was superior in Asian (−0.33, 95%CI, −0.64 to −0.03) to that in Caucasian (0.12, 95%CI, −0.03 to 0.27). 57 trials compared a placebo with a DPP-IV inhibitors either in Asian (n = 20) or in Caucasian (n = 39), placebo effect in HbA1c was comparable between Asian (0.02, 95%CI, −0.19 to 0.23) and Caucasian (−0.13, 95%CI, −0.26 to 0.01). For SU treatment, metformin treatment as well as SGLT2 inhibitors treatment, no enough studies were found for the comparisons between Asian and Caucasian population.
Conclusion: Results from this meta-analysis indicated that the placebo effect in hypoglycemic drugs was comparable between Asian and Caucasian type 2 diabetes patients.

PJ-13

Safety and efficacy comparison of different insulin regimens in T2DM patients: A meta-analysis

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To compare the safety and efficacy in T2DM patients treated with different insulin regimens, we searched the following databases: MEDLINE, EMBASE, CENTRAL. References were collected until Dec. 2015. The main search concepts were type 2 diabetes, NPH insulin, long acting insulin analogs, human regular insulin, rapid insulin analogs, premixed insulin, premixed insulin analogs, randomized controlled trials (RCTs), and clinical trials. Inclusion criteria were: (1) T2DM patients aged >18 years; (2) RCTs with at least 4 weeks of follow-up; (3) different insulin regimens were evaluated and compared.
A total of 74 articles were included in this review. (1) NPH insulin versus long acting insulin analogs therapy (twenty-two studies): Treatment with long acting insulin analogs was associated with a significantly greater decrease in HbA1c and FPG level, a significantly lower increase in body weight, and a significantly lower risk of hypoglycemia. Treatment with NPH insulin was associated with a significantly lower insulin dosage. No statistically significant difference was found in terms of all-cause mortality between two groups. (2) Human regular insulin versus rapid insulin analogs therapy (nine studies): Treatment with rapid insulin analogs was associated with a significantly greater decrease in HbA1c. No statistically significant difference was found in FPG change, body weight change, insulin dosage, rate of hypoglycemia, and all-cause mortality between two groups. (3) Premixed insulin versus premixed insulin analogs therapy (six studies): Treatment with premixed insulin was associated with a significantly greater increase in body weight. No statistically significant difference was found in HbA1c change, FPG change, insulin dosage, rate of hypoglycemia, and all-cause mortality between two groups. (4) Premixed insulin versus basal insulin therapy (twenty studies): Treatment with premixed insulin was associated with a significantly greater decrease in HbA1c level, and a significantly greater increase in body weight. Treatment with basal insulin was associated with a significantly lower insulin dosage, and a significantly lower risk of hypoglycemia. No statistically significant difference was found in FPG change, and all-cause mortality between two groups. (5) Premixed insulin versus basal-bolus/bolus insulin therapy (twenty-one studies): Treatment with basal-bolus/bolus insulin was associated with a significantly greater decrease in FPG change. No statistically significant difference was found HbA1c change, body weight change, insulin dosage, rate of hypoglycemia, and all-cause mortality between two groups.
Results from this meta-analysis comprehensively evaluated the glucose control and the hypoglycemic rate as well as all-cause mortality in different kinds of insulin treatment.

PJ-14

Metformin as an anticancer agent in breast cancer therapy by regulating tumor associated macrophage polarization and function

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Background: Accumulated evidence suggests that diabetic patients treated with metformin had a significantly lower risk of developing cancer or a lower cancer mortality. Recent evidence suggested that the phenotype of TAMs varies from M1 to M2 with the stage of tumor progression. However, it is not known if metformin is involved in TAMs phenotype switch to affect tumor malignant behaviors.
Material and methods: We used the THP-1 macrophage cultured with breast cancer conditioned medium as tumor microenvironment model.
Results: We found that metformin significantly switched from M2 to M1 phenotype in breast cancer conditioned medium, by reduced expression of CD206, down-regulation of M2 marker mRNA, and enhanced expression of CD16, up-regulation of M1 marker mRNA. But metformin not be direct influence THP-1 macrophage polarization. Moreover, we found that metformin can affect cytokines secretion in the breast cancer, by reduced expression of IL-4, IL-10, IL-13, and induced IFN-γ through AMPK-NF-κB signaling to regulate, and then affect macrophage polarization. Administration of CC, another inhibitor of AMPK, also blocked the switched from M2 to M1 phenotype. In tumor tissue, the percentage of M2-like macrophage was decreased and M1-like macrophage was increased in the metformin group.
Conclusion: These findings suggest that metformin treatment can induce cytokines secretion and expression by AMPK-NF-κB pathway in breast cancer and then affect TAM polarization.

PJ-15

LDL-C/APOB and HDL-C/APOA-1 ratios predict incident chronic kidney disease in a large apparently healthy cohort

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Introduction: The objective of this study was to evaluate the ability of lipid variables to predict the development of chronic kidney disease (CKD). We investigated the longitudinal association between lipid profiles and incident CKD in a large apparently healthy cohort.
Materials and methods: A retrospective longitudinal analysis of 10,288 subjects who had participated in comprehensive health check-ups at least four times over a 7-year period was conducted. The risk of incident CKD associated with lipid variables was analyzed using adjusted hazard ratio (HR) for CKD per 1 standard deviation (SD) increase in lipid level. The development of CKD was defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2.
Results: Over a mean follow-up of 56.5 ± 14.3 months, 356 (3.5%) subjects developed CKD. The multivariate adjusted HRs for incident CKD per 1 SD increase in baseline lipid level were 1.29 (95% confidence interval [CI], 1.17–1.41) for triglycerides (TG), 0.77 (0.68–0.88) for high-density lipoprotein cholesterol (HDL-C), 1.22 (1.12–1.32) for the TG/HDL-C ratio, 0.82 (0.73 to 0.92) for the low-density lipoprotein cholesterol/apolipoprotein B (LDL-C/apoB) ratio, and 0.74 (0.66–0.83) for the HDL-C/apoA-1 ratio. No longitudinal association was found between incident CKD and baseline total cholesterol, LDL-C, non-HDL-C, the LDL-C/HDL-C ratio, apoB, apoA-I, or the apoB/apoA-I ratio.
Conclusion: The LDL-C/apoB and HDL-C/apoA-1 ratios as well as TG and HDL-C concentrations independently predicted an increased risk for developing CKD. Our findings suggest that particle size rather than the number of HDLs and LDLs contribute to the development of CKD.

PJ-17

The function of betatrophin in the prediction of nonalcoholic fatty liver and its progress

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Objective: To study the function of betatrophin in the prediction of nonalcoholic fatty liver (NAFLD) and its progress.
Methods: A total of 249 subjects based on ultrasonic quantitative determination of fat content (LFC) were divided into three groups, Control, (LFC < 9.15%, n = 84), low liver fat content, (9.15% ≤ LFC ≤ 20%, n = 82), high liver fat content, (LFC > 20%, n = 83). Anthropometric and biochemical examinations were performed. Betatrophin and clinical factors were measured by Elisa Kit.
Results: Serum Betatrophin were showed significant differences in the three groups ($p < 0.01$). Adjusted by gender, age, the Betatrophin levels were positively correlated with LFC ($r = 0.231$, $p < 0.01$). Multivariate linear regression analysis showed that the serum Betatrophin levels were independent factors affecting the LFC ($P < 0.05$).
Conclusion: Betatrophin is an independent risk factor for NAFLD and its progress. Checking serum Betatrophin will help clinical doctors to identify NAFLD earlier and improve the prognosis.

PJ-18

The association between hyperglycomia and hearing impairment in a Taiwanese adult population

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Aim: There were some studies to explore the relationship between hyperglycemia and hearing impairment, and the results were inconsistent. The aim of this study was to investigate the association between different glycemic status and hearing impairment in a Taiwanese population.
Methods: From April 2002 to August 2009, participants undergoing a comprehensive health check-up were evaluated by audiometric testing. Hearing impairment were assessed from the pure tone average of thresholds over low frequencies (500, 1,000, 2,000 Hz) and high frequencies (3,000, 4,000, 6,000 Hz), and defined for mild or greater severity (pure tone average >25 decibels hearing level). All subjects were divided into 3 groups, including normal glucose tolerance (NGT), pre-diabetes (pre-DM), and diabetes mellitus (DM). A multiple logistic model was used for analyzing the relationship between hearing impairment and different glycemic status, with adjustment for other variables.
Results: Of 4,995 recruited participants, 239 subjects (4.8%) had low frequency hearing impairment, while 460 subjects (9.2%) had high frequency hearing impairment. The prevalence of low frequency hearing impairment was 3.9%, 5.1%, and 9.7% in NGT, pre-DM, and DM group, and those of high frequency hearing impairment was 6.8%, 11.8%, and 19.7%, respectively, Multivariate analysis revealed a positive association between diabetes and high frequency hearing impairment (odds ratio [OR] = 1.75,95% confidence interval [CI] = 1.19–2.57, $p = 0.004$), but not between pre-diabetes and high frequency hearing impairment (OR = 1.13,95% CI = 0.83–1.53, $p = 0.45$) after adjusting for other variables. In addition, older age (age ≥ 40–<60, OR = 4.61, 95%CI = 2.84–7.49, $P < 0.001$; age ≥ 60 years, OR = 17.70, 95% ci = 9.74–32.18, $p < 0.001$), body mass index ≥25 vs. <23 (OR = 1.64, 95% CI = 1.10–2.44, $p = 0.01$), and smoking (OR = 1.52, 95% CI = 1.04–2.22, $p = 0.03$) were the associated factors of high frequency hearing impairment.
Conclusions: Diabetes mellitus, but not pre-diabetes, is an important associated factor of high frequency hearing impairment, in addition to older age, obesity, and smoking.

PJ-19

The association of serum uric acid and pre-diabetes in a Taiwanese population

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Background/aims: Individuals with diabetes mellitus (DM) and pre-DM, including impaired fasting glucose (IFG) and glucose tolerance (IGT), had a high risk of cardiovascular and all- cause mortality. Hyperuricemia has been reported to be a risk factor for coronary heart disease and often co-present with obesity, hypertension and hyperlipidaemia. Hyperuricemia is also an established risk factor for DM but not pre-DM. Therefore, the aim of this study was to investigate the relationship between serum uric acid and pre-diabetes in a Taiwanese population.
Methods: A total of 7,469 adults were recruited for the final analysis after exclusion of individuals with a history of DM, chronic kidney disease, and those with newly-diagnosed DM, and current usage of medication for DM, hypertension, hyperlipidemia, hyperuricemia, heart disease, and cerebral vascular disease. Subjects were classified into three groups according to their glycemic status: (1) normal glucose tolerance: Fasting plasma glucose (FPG) < 5.6 mmol/L and 2-h PG < 7.8 mmol/L; (2) isolated IFG: FPG of 5.6–6.9 ol/L and 2-h PG

<7.8 mmol/L; (3) IGT: 2-h PG of 7.8–11.0 mmol/L and FPG <7.0 mmol/L. Categories of serum uric acid level were defined by gender-specific quartiles.
Results: There were significant differences in age, gender, education level, body mass index, waist circumstances, systolic and diastolic blood pressure, FPG,2-h PG, uric acid, lipid profiles, and the prevalence of hyperuricemia (upper quartile), hypertension, hypertriglyceridemia, low HDL-C, family history of diabetes, cigarette smoking and alcohol drinking among three groups. Based on multinomial regression analysis, highest quartile of uric acid level was positively associated with IGT (OR = 1.39, 95%CI: 1.12–1.74), but not IFG (OR = 1.46,95%CI: 0.97–2.18), after adjusting for age, gender, body mass index, hypertriglyceridemia, low HDL-C, education level, family history of diabetes, cigarette smoking, alcohol drinking and regular exercise.
Conclusions: Increased serum uric acid may increase a higher risk of IGT but not IFG.

PJ-20

The association of gastric Helicobacter pylori infection, diabetes and pre-diabetes in a Taiwanese population

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Aims: Emerging literatures revealed Helicobacter pylori (H. pylori) infection playing a role in extra-gastric diseases. Some of previous studies demonstrated higher prevalence of H. pylori infection in diabetic patients, but others revealed no difference. Association between glycated hemoglobin levels and H. pylori immunoglobulin G antibodies was also reported. However, there was little evidence about relation between gastric H. pylori infection and pre-diabetes.
Methods: This cross-section study enrolled 19,694 participants with health examination in the National Cheng Kung University Hospital from July 1997 to October 2007. Biopsy was performed in 1,866 subjects out of 11,653 subjects who underwent esophagogastroduodenoscopy (EGD). Finally 1,285 subjects were available for analysis after exclusion criteria consisting of age <18 years old, biopsy of esophagus or duodenum, endoscopic diagnosis of cancer proven by histopathological examination, prior upper gastrointestinal tract surgery, prior Helicobacter eradication therapy, use of non-steroid anti-inflammatory drugs and incomplete data. H. pylori infection was defined as H. pylori present in samples of gastric biopsy by EGD. Diabetes mellitus (DM) was defined as fasting plasma glucose (FPG) ≧126 mg/dL, 2 hour-post load glucose (2 h-PG) ≧200 mg/dL, or a positive DM history. Pre-diabetes was defined as FPG of 101–125 mg/dL or 2 h-PG of 141–199 mg/dL without DM.
Results: DM was diagnosed in 238 (18.5%) and pre-diabetes in 318 (24.7%) of the 1,285 subjects. There were significant differences in age, gender, education level and the prevalence of hypertension, prehypertension, H. pylori infection, hepatitis C infection, hypertriglyceridemia, low HDL-C, C-reactive protein >8.0 mg/L and family history of DM among subjects with normal blood glucose, pre-diabetes and DM. Multivariate analysis showed age, obesity, family history of DM, hypertension and hypertriglyceridemia were significantly related to both pre-diabetes and DM H. pylori infection were positively associated with DM (odds ratio 1.42, 95% confidence interval 1.01–2.01), but not pre-diabetes (odds ratio 1.02,95% confidence interval 0.77–1.36), in addition to male gender, education level, prehypertension and low HDL-C.
Conclusions: Gastric H. pylori infection may increase the risk of DM, but not pre-diabetes. In clinical practice, we recommend to monitor plasma glucose level in subjects with gastric H. pylori infection.

PJ-21

Gait speed as a predictor of all-cause mortality in community-dwelling elderly people in Japan: The Mima cohort study

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Background: Japan's aging rate is currently the highest in the world. The number of people with diabetes is increasing due to urbanization, aging, and increasing prevalence of obesity and physical inactivity. The aim of the Special Health Check-up (SHC) and Guidance System initiated in 2008, targeting people 40–74 years of age, was to detect those with Metabolic Syndrome and to offer lifestyle modification services that lead to the reduction of type 2 diabetes and diabetes-related death. The Mima Cohort Study was looking for its own important themes to focus on for their public health activities.
Objectives: To identify factors related with death among the general population in Mima City.
Method: 3,752 community-dwelling people (mean age 63.5 +/−8.2 (SD) years old, 1,623 male and 2,129 female) in Mima City who took SHC from 2009 to 2014 were followed up for a mean period of 2.4 years (9,059 person-years). Association between deaths and factors tested by SHC was analysed.
Results: 104 subjects (72 male and 32 female) died during the study period, including 42 from cancers, 10 from cardiac events, 8 from stroke, and 44 from other causes. For males, multiple Cox proportional hazards regression models adjusted for age showed all-cause death was positively associated with estimated glomerular filtration rate (eGFR) less than 45 mL/min/1.73 m^2 [hazard ratio (HR) 4.6 (95% confidence interval 2.1–10.1)], history of stroke [HR 3.8 (1.7–8.1)], high-density lipoprotein cholesterol (HDL-C) levels less than 40 mg/dL [HR 3.0 (1.7–5.5)] and AST more than 40 [HR 2.5 (1.2–5.4)], and negatively associated with self-reported fast gait speed [HR 0.45 (0.26–0.79)]. In subgroup analysis, the model showed the association between all-cause death and self-reported fast gait speed was seen only in the group aged 65–74 [HR 0.33 (0.16–0.67)]. For females, the model didn't show any association between death and these factors. However, univariable Cox proportional hazards regression models showed a positive association between all-cause death and being aged 65 and over [HR 7.3 (2.6–21.0)], proteinuria [HR 5.1 (1.9–13.1)], eGFR less than 45 mL/min/1.73 m^2 [HR 3.8 (1.1–13.0)], and taking medication for diabetes [HR 3.8 (1.4–9.9)].
Conclusion: Several factors relating to kidney disease, HDL-C, medical history, and gait speed were associated with deaths in men over a short period of time. These factors should be themes for public health activities in Mima City. Beyond trying to improve laboratory findings for preventing early deaths, walking fast may also be important, especially for elderly people.

PJ-22

Increased risk of heart failure in diabetic patients of Taiwan: Age- and sex-stratified population-based study

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Background and aims: Diabetes is regarded as a coronary heart disease (CHD) equivalent, but the risk of heart failure (HF) between diabetic patients and non-diabetic subjects has scarcely been compared before. This study used a nationally representative cohort selected from National Health Insurance to compare the relative hazard of heart failure in diabetic patients and non-diabetic subjects.

Methods: 500,424 diabetic patients from ambulatory care claims and 500,424 age- and sex-matched control subjects from registry of beneficiaries were linked to inpatient claims (1997–2008) to identify the admissions for HF (ICD-9: 428). With Cox proportional hazard regression mode, we compared the relative hazards of HF in relation to diabetic patients and control subjects under various age- and sex-stratifications.
Results: Compared with the control subjects, diabetic patients had increased hazards of HF [adjusted hazard ratio (aHR): 2.30, 95% confidence interval (CI) 2.28–2.33]. After adjustment of various coronary heart diseases such as acute myocardial infarction, unstable angina, angina pectoris, chronic ischemic heart disease, hypertension, hypertensive disease, procedures of percutaneous transluminal angiography and coronary artery bypass surgery in the model, aHR attenuated to 1.79 (95% CI 1.77–1.81). In both genders, the diabetic patients aged <45 years had highest risks of HF, and the respective relative risks for diabetic men and women aged <45 years were aHR: 8.07 (95% CI 7.03–9.26) and aHR: 12.18 (95% CI 10.14–14.64).
Conclusions: Optimal control of blood sugar and aggressive management of cardiovascular risk factors are crucial in reducing subsequent risk of heart failure especially in young diabetic patients.

PJ-23

Inverse relationship between serum osteocalcin levels and nonalcoholic fatty liver disease in postmenopausal Chinese women with normal blood glucose levels

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Aim: Osteocalcin is involved in the progression of nonalcoholic fatty liver disease (NAFLD) in animal models and humans. In this study we investigated the relationship between serum osteocalcin levels and NAFLD in postmenopausal Chinese women.
Methods: A total of 733 postmenopausal women (age range, 41–78 years) with normal blood glucose levels were enrolled in this cross-sectional study. Women taking lipid-lowering or anti-hypertensive drugs were excluded from enrollment. Serum osteocalcin levels were assessed using an electrochemiluminescence immunoassay. Each subject's fat liver degree was assessed through ultrasonography, and each participant's fatty liver index (FLI) was calculated to quantify the degree of liver steatosis.
Results: The median level of serum osteocalcin in the total enrolled subjects was 21.99 ng/mL (interquartile range, 17.84–26.55 ng/mL). Subjects with NAFLD had significantly lower serum osteocalcin levels than those without NAFLD (18.39 ng/mL [range, 16.03–23.64 ng/mL] vs. 22.31 ng/mL [range, 18.55–27.06 ng/mL], $P < 0.001$). Serum osteocalcin levels decreased significantly with incremental changes in the FLI value divided by the quartile (P-value for trend <0.001). The serum osteocalcin levels showed a significant negative correlation with the FLI values, even after adjusting for confounding factors (standardized $\beta = -0.124$, $P < 0.001$). Binary logistic regression analysis identified an individual's serum osteocalcin level as an independent risk factor for NAFLD (odds ratio, 0.951; 95% confidence interval: 0.911–0.992; $P = 0.020$).
Conclusion: Serum osteocalcin levels were inversely correlated with NAFLD in postmenopausal Chinese women with normal blood glucose levels.

PJ-25

Hyperglycemic crisis is associated with subsequent major adverse cardiovascular events: A nationwide population-based study

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Objective: Hyperglycemic crisis is associated with significant morbidity and mortality but the association between hyperglycemic crisis and long term cardiovascular outcomes was elusive. The purpose of this study is to discuss the association between hyperglycemic crisis and subsequent major adverse cardiovascular events (MACE).
Participants and methods: The population-based cohort study using data from 1996 to 2012 in the Taiwan National Health Insurance Research Database was conducted. A total of 2,171 diabetic patients with hyperglycemic crisis fit the criteria of analysis. The propensity score was used for matching the baseline characters and 8,684 patients were retrieved as the comparison cohort. The risk of subsequent MACE was compared between two groups.
Results: Six hundred and seventy-six events occurred in group with hyperglycemic crisis and the events rate was higher than those without hyperglycemic crisis (31.1% versus 24.1%, $p < 0.001$ by log-rank test). Subjects with Hyperglycemic crisis were associated with higher risk of subsequent MACE even after adjusting with all baseline characters (hazard ratio (HR) 1.76, 95% confidence interval (CI) 1.62–1.90, $p < 0.001$). After age-stratification, the junior patients with hyperglycemic crisis had higher risk of MACE than senior group (HR 2.69 for age 20–39 years old versus HR 1.58 for age >65 years old).
Conclusion: Hyperglycemic crisis is associated with subsequent MACE, especially in young patients. Further plan of primary prevention of hyperglycemic crisis should be concerned in clinical practice.

PJ-26

Early menarche and increased risk of cardiovascular disease in Korean women

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Early menarche is strongly associated with adulthood obesity; however, the relationship between age at menarche and cardiovascular disease (CVD) in Korean women remains

poorly understood. Here, we investigated the association between early menarche and risk factors for developing CVD during adulthood using a nationwide population database.
In total, 12,336 women (weighted n = 17,483,406; weighted age, 45.7 years) who participated in the Korean National Health and Nutrition Examination Survey 2010–2013 were included in this study. Participants were scored using the National Cholesterol Education Program Adult Treatment Panel III criteria for metabolic syndrome. Risk of CVD was estimated using the 10-year Framingham Coronary Heart Disease Risk Point Scale (10-yr FRS).
Early menarche (≤11 years) was reported in 5.2% (weighted n = 917,493) of subjects. The weighted prevalences of metabolic syndrome and ≥20% 10-yr FRS were 23.6% (95% CI, 22.7–24.6) and 7.7% (7.1–8.3), respectively. Women with early menarche reported a significantly higher body mass index and waist circumference, along with a higher prevalence of hypertension, diabetes, and metabolic syndrome compared with those with later menarche (≥13 years). Furthermore, the prevalence of women with a ≥10% or ≥20% 10-yr FRS was higher in those with early menarche compared with other groups after adjusting for age, smoking, education level, and menstruation. Logistic regression analyses controlling for these and other confounding factors revealed odds ratios of 2.29 (95% CI = 1.25–4.19) and 1.78 (0.96–3.30) for ≥10% and ≥20% 10-yr FRS in women with early menarche, respectively, compared with those in the latest menarche group (≥17 years).
Taken together, this nationwide study revealed women with early menarche are at increased risks of metabolic syndrome and CVD. Early menarche may therefore represent an important marker for early preventive interventions.

PJ-27
Association of complete blood cell counts with metabolic syndrome in an elderly population

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Objective: The role of metabolic syndrome (MetS) in predicting cardiovascular diseases and diabetes has been repeatedly confirmed in many large cohort studies. As a non-traditional component, hematogram components are shown to be significantly related to MetS in many different age groups. However, little is known about the role of the hematogram among the elderly.
Methods: We enrolled 18,907 subjects over the age of 65 years who underwent regular health examinations. They were divided into three groups according to their ages: young old (YO: ≥65 and <74 years old), old old (OO: ≥75 and <84 years old), and oldest old (ODO: ≥85 years old). The MetS components were determined, and correlations between MetS and hematogram components were evaluated using Pearson and multivariate linear regression analyses. Here, the hematogram components were taken to be independent variables and were evaluated separately against the dependent variable (MetS components).
Results: While SBP and HDL-C became higher, most other MetS and hematogram parameters became lower in men as they aged. Fewer significant differences were noted among the women. In the YO and OO groups for both genders, not surprisingly the subjects with MetS had higher WBC and Hb. Interestingly, none of the hematogram components were different for subjects with or without MetS in the ODO group. The results of the multiple regression show that most of the relationships between hematogram and MetS components disappeared in the ODO groups. The WBC levels were mainly correlated with WC and TG. At the same time, Hb was found to be associated with BP, FPG, and LDL-C. Compared to WBC and Hb, PLT was least related to MetS, except in the cases of LDL-C and TG. Among the MetS components, it is interesting to note that BMI, LDL-C, and TG were consistently related to all the hematogram components in YO and OO men. However, only TG had the same consistency among YO and OO women.
Conclusions: This study's three major findings are as follows: 1. WBC and Hb are indeed associated with MetS, even among the YO and OO groups, regardless of gender; among the three hematogram components, Hb had the strongest and PLT had the weakest correlation with MetS; and TG is not the only component that had relatively higher r values, but it is also related to all hematogram components.

PJ-29
Plasma aldosterone concentration predicts the incidence of diabetes mellitus

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Objective: Genetic variation in aldosterone synthase is associated with diabetes. Suppression of intestinal and urinary glucose absorption by aldosterone through sodium-glucose cotransporters may be the key mechanism. However, it remains unknown if plasma aldosterone predicts the incidence of diabetes in human. In this study, we investigated if plasma aldosterone concentration is associated with the incidence of diabetes in a community-based prospective cohort without any medication for hypertension.
Research design and methods: We included 608 subjects without diabetes at baseline and followed them for an average of 4.01 years. Subjects who received medications for hypertension at baseline or during follow-up were excluded. Diabetes was diagnosed by results from an oral glucose tolerance test and hemoglobin A1c, and if the subject was taking medications for diabetes. Plasma aldosterone concentration at baseline was measured with an ELISA kit.
Results: During follow-up, 42 subjects (6.91%) developed type 2 diabetes. Plasma aldosterone concentration was negatively associated with body mass index ($r = -0.0978$, $p = 0.0162$), but was not correlated with glycemic indices, HOMA2-%B, or HOMA2-IR (all $p > 0.05$) at baseline. Plasma aldosterone concentration predicts the incidence of type 2 diabetes significantly, after adjusting for age, family history of diabetes, body mass index, HOMA2-%B, HOMA2-IR, and hemoglobin A1c (HR = 0.83 for every 10 pg/mL increase in plasma aldosterone concentration, 95%CI 0.692–0.986, $p = 0.034$; HR = 0.31 for subjects with plasma aldosterone concentration in the highest tertile, 95%CI 0.14–0.71, $p < 0.01$).
Conclusions: Plasma aldosterone concentration predicts the incidence of type 2 diabetes independently.

PJ-30
Angiopoietin-like protein 6 is associated with an inflammatory marker and low HDL cholesterol in type 2 diabetes

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Angiopoietin-like protein (ANGPTL) 6, a novel hepatokine, is known to modulate angiogenesis and metabolism. ANGPTL6 has been shown to be higher in metabolic syndrome than in healthy individuals. Recent clinical data suggest a potential role of ANGPTL6 in endothelial dysfunction. However, the functional role of ANGPTL6 in type 2 diabetes mellitus (T2DM)

has not been determined. Therefore, we analyzed plasma ANGPTL6 levels and other biochemical markers in patients with T2DM.
A total of 108 Korean patients with T2DM were enrolled. Subjects with known cardiovascular diseases, chronic kidney disease, or active infection were excluded. Plasma ANGPTL6 was quantified. We assessed vascular health status by measuring carotid intima-media thickness (IMT).
Plasma ANGPTL6 correlated positively with C-reactive protein (CRP; $r = 0.31$, $P < 0.01$) and resistin ($r = 0.28$, $P < 0.05$), and negatively with high-density lipoprotein (HDL) cholesterol ($r = -0.24$, $P < 0.05$). However, ANGPTL6 did not correlate with carotid IMT, adiponectin, or leptin. A multiple regression analysis showed that CRP and HDL cholesterol remained independently associated with ANGPTL6 after adjustment for age, gender, body mass index, and resistin.
Circulating ANGPTL6 concentrations are positively associated with inflammatory markers, and negatively with HDL cholesterol in subjects with T2DM. Further studies will be needed to explore the physiologic functions of ANGPTL6 in T2DM.

PJ-31

Association of serum uric acid concentration and microvascular complications in Taiwanese patients with type 2 diabetes mellitus

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Patients with type 2 diabetes mellitus (DM) may have chronic microvascular complications such as diabetic retinopathy (DR) and diabetic nephropathy (DN) in their life. In clinical studies, serum uric acid concentration was found to be associated with DR and DN. The goal of this study is to evaluate the relationship between the increase of serum uric acid level and the severity of microvascular complications in Taiwanese patients with type 2 DM. 385 patients with type 2 DM were enrolled for obtaining serum uric acid level, the status of DR severity, and the status of albuminuria severity by calculating urinary albumin-to-creatinine ratio (UACR). In multivariate logistic regression analysis, high uric acid was the risk factor of albuminuria (OR, 1.227; 95% CI = 1.015–1.482; p = 0.034) and DR (OR, 1.264; 95% CI = 1.084–1.473; p = 0.003). We also demonstrated that there was a higher concentration of serum uric acid in the more severe form of albuminuria and DR. In conclusion, increased serum uric acid level significantly correlated with the severity of microvascular complications in Taiwanese patients with type 2 DM.

PJ-32

A reduced risk of diabetes with aripiprazole exposure in schizophrenia patients: A population-based retrospective cohort study

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Objective: Aripiprazole exhibits protective effects for metabolic syndromes, but the association between aripiprazole use and the subsequent risk of diabetes in schizophrenia patients is unclear. This population-based study is aimed to assess the incidence and risk of diabetes among schizophrenia patients who received aripiprazole treatment.
Methods: Using a nationwide database, the Taiwan National Health Insurance Research Database, subjects who had first been diagnosed with schizophrenia between 2002 and 2013 were identified. The schizophrenia patients receiving aripiprazole were designated as the aripiprazole group. A 1:1 ratio was used to select age-, gender-, and index-year -matched control without aripiprazole use. Patients who had diabetes before enrollment were excluded. The 2 cohorts were observed until December 31, 2013. The primary endpoint was occurrence of diabetes.
Results: Among 15,974 newly diagnosed schizophrenia patients, we identified 3,462 patients with aripiprazole use, and 3,462 matched patients without aripiprazole use between January 2002 and December 2013. Of the 6,924 patients, 283 (4.09%) suffered from diabetes during a mean follow-up period of 4.39 years, including 119 (3.44%) from the aripiprazole cohort and 164 (4.73%) from the control group. In schizophrenia patients, the Cox multivariate proportional hazards analysis showed that the risk decreased with aripiprazole use 0.5884 (95% confidence interval (CI), 0.4970 to 0.6966; p < 0.0001).
Conclusions: Aripiprazole use was associated with a reduced risk of diabetes among schizophrenia patients.

PJ-34

The synergistic effect of serum albumin and globulin on the metabolic syndrome

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Serum albumin and globulin have been used as biochemical parameters indicating different metabolic status. The aim of this study is to clarify the association between serum albumin and/or globulin and the presence of metabolic syndrome (MetS).
A total of 24,185 adults aged ≥18 years underwent comprehensive medical health check-ups annually over 7-year period. Among them, 19,208 subjects were finally enrolled in the research. Multivariate logistic regression analysis was used to assess the risk of MetS according to the quartile of baseline level of serum albumin and globulin, also as continuous variables per 1 standard deviation (SD).
In a multivariate model adjusting for all possible metabolic risk factors, the highest quartile of serum albumin (OR 1.21, 95% Confidence Interval [CI] 1.04–1.41; p for trend = 0.015) and globulin (OR 1.47, 95% CI 1.27–1.70; p for trend <0.001) were associated with an enhanced risk of MetS compared with lowest tertile. However, serum albumin as continuous variables per 1 SD lost its significance on the risk of MetS in a fully adjusted model, while serum globulin were still significant. In the conditional logistic model adjusting for all covariates and dividing subjects into 4 groups (low albumin + low globulin; high albumin + low globulin; low albumin + high globulin; high albumin + high globulin) according to the median values of albumin and globulin levels, the synergistic effect of albumin and globulin on MetS was found when both of them were high (OR 1.42, 95% CI 1.22–1.47; p < 0.001), compared with those with low albumin and low globulin.
High serum albumin and globulin were independently associated with the presence of MetS. The synergistic effect of both high albumin and globulin on MetS was greater than either one alone.

PJ-35

Elucidating pharmacological beneficial functions of soybean extract on metabolism

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According to the Standard Tables of Food Composition in Japan, soybean contains protein (33%), carbohydrates (28%), lipids (19%), water (13%) and ash content (5%). Some ingredients of soybean have been reported to provide such beneficial effects as hypotensive activity, prevention of obesity, proliferation of lactobacillus bifidus, attenuation of osteoporosis and antioxidative action. Therefore, soybean has attracted our attention as an excellent functional food. Soybean is processed into various foods such as tofu, soy milk and soy sauce, as well as soybean oil, feedstuffs and fertilizer, and they have been used all over the world. For example, soy milk is a good alternative to cow's milk for vegetarians, lactose-intolerant people and consumers allergic to cow's milk thanks to its high-quality proteins and essential fatty acids with low amount of cholesterol, gluten or lactose. In Japan, consumption of soy milk was greatly increased from 2007 to 2012. Thus, not only soybean but also soy products are attracting much attention in recent years. Furthermore, it has been reported that an effect of suppressing cancer cell growth in components contained in soybean or soy products.

In this study, we examined the effect of soy extract in the experiments in vitro and in vivo for the purpose of elucidating pharmacological beneficial functions of soybean. The soy extract were administered orally at 100 mg/kg/day for 4 weeks to male ddY mice, and we measured body weight, food and water intake. We examined the glucose uptake activity of extract from soybean by using [3H]2-deoxy-D-glucose in myotube differentiated from C2C12 cells. In addition, we studied the expression levels of glucose uptake-related factors by Western Blotting. The body weight was decreased in the group of the extract from soybean compared to the control group, while food and water intake were almost same between groups. Further, soy extract increased the glucose uptake in a concentration-dependent manner in the myotube. However, the phosphorylation level of Akt and AMPK had not changed significantly. As a result, the extract of soybean induced weight loss and enhancement of glucose uptake in cultured cells as well as in vivo. Although the mechanism remains unknown, it is suggested that the extract of soybean has an anti-diabetic effect which may be independent of the Akt or AMPK.

PJ-36

Long term DPP4i use reduces joint pain in patients with type 2 diabetes. A study using the national health insurance

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Objective: The link between arthropathy in type 2 diabetes patients treated with DPP4 inhibitors (dipeptidyl peptidase 4 inhibitors) is rarely studied in Asians.

Research design and methods: A random sample of 1,000,000 subjects between January 1 2009 and December 31 2010 covered by the National Health Insurance Research Database (NHIRD) in 2000 was recruited. A total of 19,729 diabetes, type 2 patients who received oral anti-diabetic agents at least for 3 months or hospitalization with the diagnosis of Diabetes mellitus without joint pain were followed for 1 year. The definition of who received sitagliptin was patient with Sitagliptin use at least 1 month. There are 2,825 patients who received Sitagliptin and the other never used Sitagliptin. We used 1:3 for all comorbidities matching: 2,813 of Diabetes patients received Sitagliptin followed up till the end of study and 82 patients had the episode of joint pain (2.9%). On the other hand, 8,616 of Diabetes patients without using Sitagliptin followed up till the end of study and 315 patients had the episode of joint pain (3.7%).

Results: Under sitagliptin use, arthralgia appeared early after initiation of treatment: Cumulative defined daily dose (DDD) < 84. The risk of joint pain didn't increase significantly under Sitagliptin use followed up for 1 year. On the contrary, joint pain significantly decreased under Sitagliptin use ($P < 0.001$).

Conclusions: Its meaning of no increase of nonsteroidal anti-inflammatory drugs(NSAIDs) under sitagliptin use, on the contrary, NSAIDs cumulative DDDs significantly decreased after sitagliptin use within 1 year, the probable explanation may be under sitagliptin use, its exerts an anti-inflammatory action (1). If indeed DPP-IV and CD26 are proinflammatory, their inhibitors, like sitagliptin, could potentially be anti-inflammatory and possibly anti-atherogenic because atherosclerosis is a chronic inflammation of the arterial wall. Thus, sitagliptin may offer anti-inflammatory effect.

PJ-38

Congenital malformations in the first offspring of women with gestational diabetes mellitus in Taiwan – a nationwide survey

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Background: Recent literatures have shown that gestational diabetes mellitus (GDM) associated with the occurrence of congenital malformations (CMs) in their offspring. However the results were controversial. In Taiwan very few studies have been conducted in this regard.

Objective: This study aimed to analyze the CMs and health status of the first offspring from mothers with GDM using a national representative. The relation to different managements during pregnancy on the risk of CMs was also investigated.

Method: The dataset was obtained from the Birth Certificate Application, National Health Insurance Research Database, and the Birth Registration database during 2004 to 2009. Those who had delivered newborns (n = 188,798) before 2004, and those who have already been suffering from diabetes prior to pregnancy (n = 3,356) were excluded. A total 19,430 pregnant women with GDM were recruited for analysis, of whom 793 women were on insulin treatment while the remaining 18,637 women on diet control during their pregnancy.

Results: The prevalence of GDM in Taiwan is about 3.4% of the total 1st-preganant women. Among 19,430 GDM mothers, the average age was 31 years old, the average gestational age 38.3 weeks and the average birth weight of their offspring was 3,163 gm. When adjust for mother age, gestational weeks, urbanization, and CCI, the results showed that GDM mother

had an adjusted odds ratio (aOR) 1.18 higher risk for total congenital malformations in their first offspring in comparison with non-GDM mothers. The aOR for ear/face/neck defects, congenital heart defects, urinary/renal agenesis and limb defects were 1.49, 1.24, 1.42 and 1.31 respectively in their offspring for GDM mothers when compared to non-GDM mothers.
GDM mothers who were treated with insulin had higher risks for total CMs in their offspring when compared with GDM mothers who were on diet control. This was especially true in birth defects of nervous system defects, ear/face/neck defects, congenital heart defects, respiratory defects, oro-facial clefts, urinary/renal agenesis and chromosome abnormality.
Conclusion: GDM mothers confer higher risk for CMs in their first offspring when compared with non-GDM mothers. GDM mothers who were treated with insulin also having higher risks for total CMs than those who were on diet control, indicated that the severity of glycemic status might relate to the offspring outcome. The results of this study imply the mandatory for GDM management during pregnancy.

PJ-39

Relationship between pre-gestational diabetes and birth defects in the first offspring in Taiwan – a nationwide survey

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Background: The literature had shown that women with pre-gestational diabetes significantly increased birth defect (BD) in their offspring. In Taiwan the incidence of BD were around 0.2–0.45%. The relation between pre-gestational diabetes and BD in Taiwan however remains unknown at large.
Objective: By using a national representative, this study aimed to investigate the relation of BD risk in the first-offspring with singleton birth among pre-gestational diabetes, suspect-diabetes and non-diabetes mothers, and to explore the association among BD risk and maternal age, neonatal gender, gestational age, birth weight and Apgar score.
Methods: A dataset during 2004 to 2009 from National Health Insurance Research Database, the Birth Registration database and the Birth Certificate Application were applied. Pre-gestational diabetes was defined by three or more outpatient visits with diabetes diagnostic codes (ICD-9-CM 250) 300 days before delivery day or by one inpatient discharge code. Those with only one or two outpatient visits with diabetes diagnostic codes were deemed as suspect-diabetes, while those without any were non-diabetes. Those who had delivered newborns (n = 188,798) before 2004, and those who had been diagnosed as gestational diabetes (n = 19,430) were excluded. A total 3,356 pregnant women with pre-gestational diabetes, 60,909 with suspect-diabetes and 556,743 with non-diabetes were recruited for analysis. Maternal age, gestational weeks, urbanization and CCI were adjusted to obtain BD risk odds ratio (aOR).
Results: Offspring from women with pre-gestational diabetes significantly increased the risk of BD when compared to those from non-diabetes mothers (aOR 1.83). The defects included the nervous system, eyes, heart, respiratory system, orofacial cleft, GI system, urinary tract system and limb with aOR 1.82, 2.12, 1.94, 1.82, 2.40, 1.65, 1.75 and 2.15 respectively. Offspring from suspect-diabetes mother had only mild increased risk of heart defect (aOR 1.14) when compared to those from non-diabetes mothers. The decreased risk of BD was associated with the increase of gestation weeks, birth weight and the 1st, 5th–min Apgar score of newborn. The increase in maternal age, the increase in BD risk was found. In addition, the BD risk in boys was significantly higher than in girls.
Conclusion: Women with pre-gestational diabetes and higher maternal age raise the risk of BD in their offspring. Cautious prenatal counseling and comprehensive diabetes management are mandatory for these populations.

PJ-40

The relationship of glycemic exposure (HbAlc) to the risk of subclinical hypothyroidism in type 2 diabetes mellitus patients

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Background: Patients with subclinical hypothyroidism (SCH) sustain an obvious increase in cardiovascular event rates. Abundant evidence suggests a link between SCH and type 2 diabetes mellitus (T2DM). How is the relationship between glycemic control (HbA1c) with SCH in T2DM patients in Indonesia, is still unknown.
Objective: To determine the proportion of SCH in patients with T2DM and to know the relationship between HbAlc with SCH in patients with T2DM.
Methods: Two hundred and seventy-eight adult patients with T2DM were included in the study. Data retrieved from medical records and laboratory tests. Patients who have been diagnosed with T2DM at least 1 year, who had no previous history of thyroid disease from outpatient depatment of Cipto Mangun Kusumo Hospital, Jakarta, Indonesia, retrieved data of HbAlc and thyroid hormones. Those with normal free triiodothyronine (FT3), free thyroxine (FT4), and an increased TSH level were diagnosed with SCH.
Results: The proportion of SCH in patients with T2DM 7.2%, mostly aged over 60 years. There were no differences in the proportion between men and women. From the analysis reveals the T2DM patients with HbA1C > 7 had 3.664 times greater risk of developing SCH compared with T2DM patients with well glycemic control.
Conclusions: There was a significant relationship between HbAlc with SCH events in patients with T2DM.

PJ-41

Infection with hepatitis C virus increases the incidence of dialysis in patients with type 2 diabetes

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Background: Type 2 diabetes mellitus (T2DM) and hepatitis C virus (HCV) infection are unsolved public health issues, and patients with both these diseases are at a higher risk for chronic kidney disease. We aimed to investigate the influence

of HCV infection on the incidence of dialysis in patients with T2DM in Taiwan.
Research design and methods: This was a population-based retrospective study employed the Taiwan National Health Insurance Research Database covering the claim data between 1998 and 2012.
Results: Among a total of 1,940,005 patients with T2DM, 53,477 had HCV infection. In 2012, the incidence of dialysis among patients with T2DM was 308.1 per million person-years. Among those with diabetes, the incidences of dialysis with or without HCV infection were 379.7 per million person-years and 305.9 per million person-years, respectively. After adjusting gender, age, insured-premium salary, low-income households, urbanization levels, comorbidity and disease severity, the incidences of dialysis were significantly higher in T2DM patients with HCV infection than those without HCV throughout the observational period (p value = 0.0025). Although the incidence for HCV-associated dialysis was relatively stable, its trend continued rising during the past decade.
Conclusions: HCV infection increases the risk for dialysis in patients with T2DM. Prevention and early effective management of the infection to decrease the incidences of progression to chronic kidney disease and the subsequent burden of dialysis in patients with T2DM are clearly warranted.

PJ-42
Effects of hypoglycemia on soluble endoglin in patients with type 2 diabetes
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Background: Hypoglycemia can be associated with an increase in cardiovascular mortality in type 2 diabetes. But the impact of hypoglycemia on endothelial dysfunction is still unknown in patients with type 2 diabetes. Recently, it was reported that early decreased plasma soluble endoglin levels represent impaired endothelial function in patients with acute myocardial infarction. But there are no researches of the relation between endoglin and hypoglycemia.
Aim: We studied the relationship between hypoglycemia and plasma soluble endoglin in patients with type 2 diabetes.
Method: This is a cross-sectional study performed in patients with hypoglycemia with or without type 2 diabetes. Patients enrolled in the study from September 2011 to December 2012 were from Hallym University Medical Center and National Medical Center. We analyzed 117 patients with type 2 diabetes and 10 patients without diabetes visited emergency room for hypoglycemia. We excluded patients with malignancies. Markers of endothelial dysfunction and hypoxia, VEGF (vascular endothelial growth factor), EPO (erythropoietin), VCAM-1 (vascular cell adhesion molecule-1) and endoglin, were measured; the levels of soluble plasma endoglin were measured by enzyme-linked immunosorbent assay. The 10-year cardiovascular event risks in patients with diabetes were estimated using the UK Prospective Diabetes Study (UKPDS) risk engine.
Results: The levels of endoglin were significantly, negatively correlated with age. Endoglin levels in patients with type 2 diabetes were significantly lower than in non-diabetic controls during hypoglycemia after adjustment for age and sex (poster table 1). The difference remained marginally significant (4.47 ± 0.13 ng/mL vs 5.94 ± 0.48 ng/mL, p = 0.05) after adjusting for age, sex, body mass index, AST, ALT and systolic blood pressure (poster figure 1). But there were no significant differences on levels of VEGF, EPO and VCAM-1 between diabetic and non-diabetic patients during hypoglycemia. Plasma soluble endoglin levels in diabetic groups showed a significantly negative correlation with 10-yrear risk for fetal stroke calculated using UKPDS risk engine (r = –0.312, p = 0.039). However, this phenomenon was not seen on other vascular markers.
Discussion: This data suggest that plasma soluble endoglin is related to hypoglycemia and associated with vascular pathologies as endothelial dysfunction in patients with type 2 diabetes. Endoglin may therefore be considered as a new marker of hypoglycemic responsiveness in patients with type 2 diabetes.

PJ-43
The association of Sitagliptin treatment with all-cause mortality and renal outcomes in diabetic patients with chronic kidney disease
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Backgrounds: The association between Dipeptidyl peptidase 4 (DPP-4) inhibitors and cardiovascular outcomes was reported in large randomized control trials and cohort studies. However, limit data focus on renal outcomes. We investigated the effect of Sitagliptin on all-cause mortality and renal outcomes in a nationwide cohort of Chronic kidney disease (CKD).
Methods: Using data from the multidisciplinary team care pay for performance (P4P) program, a part of National Health Insurance Research Database, we identified CKD patients with diabetes mellitus (DM) between 2007 and 2011. We used intention-to-treat analysis and multivariate Cox proportional hazards to evaluate the association between Sitagliptin use and risks of death and renal outcomes, controlling for medical history, laboratory results, medications, and comorbidities. Patients were followed to death, end-stage renal disease, or the end of 2012. Residual confounding was assessed by sensitivity analysis.
Results: Cumulative mortality rates were lower for Sitagliptin-treated CKD patients with DM than for untreated patients (Incident rate ratio: 0.70, 95% confident interval [CI]: 0.58–0.85). Sitagliptin use was independently associated with lower all-cause mortality after multivariate adjustment (adjusted hazard ratio [aHR]: 0.80, 95% CI: 0.65–0.99). In multivariable analysis, Sitagliptin use was not significant difference in the risk of end-stage renal disease (aHR: 1.05, 95% CI: 0.91–1.20) in CKD patients with DM after adjusting for comorbidities, medications, and competing risk of mortality.
Conclusions: The Sitagliptin was associated with decreased risk of all-cause mortality but not end-stage renal disease in CKD patients with DM. More studies focus on kidney outcomes warrants further investigation.

PJ-45
Impaired fasting glucose and risk of cardiovascular mortality in Korean adults
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Background: To assess the association between impaired fasting glucose and overall and cardiovascular disease (CVD) mortality among Korean adults.
Methods: From the nationwide cohort provided by the National Health Insurance Service in Korea (2002–2013), subjects were stratified as normal glucose tolerance (NGT, fasting glucose <100 mg/dL), impaired fasting glucose (IFG) stage 1 (100–109 mg/dL), IFG stage 2 (110–125 mg/dL), and diabetes mellitus (DM) groups based on serum fasting glucose

level. Overall and CVD mortality risks were assessed by Cox regression analyses.
Results: When adjusted for age, sex, and body mass index, IFG stage 2 was associated with significantly higher all-cause mortality (HR, 1.26, 95% CI: 1.18–1.34), and CVD mortality (HR, 1.27, 95% CI: 1.08–1.49) compared to NGT. However, IFG stage 1 was not associated with increased risk of mortality from any causes. Among CVD category, mortality from ischemic stroke was significantly higher (HR, 1.60, 95% CI: 1.18–2.18) in subjects with IFG stage 2, but not mortality from ischemic heart disease. The ischemic stroke mortality in IFG stage 2 remained elevated when other CVD risk factors including smoking, physical activity, systolic blood pressure, and total cholesterol were adjusted for.
Conclusions: Higher degree of IFG (110–125 mg/dL of fasting glucose) was associated with increased all-cause and CVD mortality. The increased risk of CVD mortality in IFG was attributable to ischemic stroke, not ischemic heart disease among Korean adults.

PJ-46
Risk of melanoma in patients with diabetes mellitus: A nationwide retrospective cohort study in Taiwan
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Background: Increasing evidence suggests that certain types of cancers are more common in people with diabetes mellitus (DM). The risk of melanoma in patients with DM was seldomly reported in Taiwan.
Method: In this retrospective cohort study using Taiwan Longitudinal Health Insurance Research Database, 41,898 patients newly diagnosed as DM was matched with those without DM by age, sex, index date, and comorbidities (obesity, coronary artery disease, hyperlipidemia, hypertension, chronic kidney disease, and chronic obstructive pulmonary disease). The risk of melanoma in DM patients was analyzed by Kaplan-Meier survival analysis and Cox regression analysis.
Results: The number of melanoma patients was 6 in the DM cohort and 14 in the non-DM cohort. For the people in the subgroup of age ≥ 30 years, although the risk of developing melanoma was lower in the DM cohort than that in the non-DM cohort, the risk was only borderline significant by Kaplan-Meier survival analysis (log-rank test: 0.097). By univariable Cox regression, the risk of developing melanoma was lower but insignificant in the DM cohort [crude hazard ratio = 0.46, P = 0.106]. By Cox regression with multivariable adjustment, the risk of developing melanoma was also lower in the DM cohort, but without significance [adjusted hazard ratio (AHR) = 0.46, P = 0.11]. The only significant risk factor for developing melanoma was cardiovascular disease (AHR = 5.38, P = 0.001).
Conclusion: The present study indicated that there might be a lower incidence and risk of developing melanoma in DM patients. The non-significant result may be due to small number of melanoma patients. Cardiovascular disease was a significant risk factor for melanoma development even in young adults that warranted further investigation.

PJ-47
Association of severe hypoglycemia with incident atrial fibrillation in type 2 diabetes: a nationwide population-based cohort study
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The association between severe hypoglycemia (SH) and atrial fibrillation (AF) is not conclusive. The aim of this study was to investigate the association between AF and SH in type 2 diabetes using the Korean National Health Insurance Service cohort database from 2002 to 2013.
A National Sample Cohort (2002–2013) database consisting of 1,025,340 Koreans was released in 2014, and followed for maximum 11 years. Among them, we selected 421,626 subjects aged over 30 years. Thereafter, we selected patients with type 2 diabetes who prescribed anti-diabetic drugs with the presence of ICD-10 codes E11, E14, and who had not diagnosed with AF (I48) and SH [defined by ICD-10 (E16.x, E11.63, E13.63, E14.63) from the inpatients or emergency room claim dataset] from the year of 2002 to 2005. The patients who diagnosed with valvular heart disease (I34.x, I35.x, I36.x), and hyperthyroidism (E05.x) were excluded. As a result, a total of 43,627 subjects were included in our study. The main outcome was the development of AF occurred after SH. A Cox proportional hazards regression analysis was used to test the association between the development of AF and potential explanatory variables.
During the follow-up period, a total of 1,913 AF episode occurred in 43,627 subjects (4.3%). The incidence of AF in the study cohort was 2.3 times higher in the group with SH than the group without SH (5.2 vs. 12.0 per 1,000 person-years). The group who developed AF were older (60.9 ± 12.0 vs. 67.0 ± 10.7 years; P < 0.001), had a higher ratio of the presence of hypertension (61.7% vs. 81.7%; P < 0.001), and congestive heart failure (4.3% vs. 13.4%; P < 0.001). After adjustment for age, sex, social economic status, the presence of hypertension, and congestive heart failure, SH showed the significantly higher risk for AF [hazard ratio (HR) 1.45, 95% CI 1.01–2.10]. In addition, male sex (HR 1.42, 95% CI 1.29–1.55), the presence of hypertension (HR 2.01, 95% CI 1.78–2.26), congestive heart failure (HR 2.41 95% CI 2.11–2.76) were the significant predictive factors for the development of AF.
SH was associated with incidence of AF in Korean patients with type 2 diabetes. Further exploration of the underlying mechanism is necessary.

PJ-48
Effect of obstructive sleep apnea on chronic kidney disease – Systematic review and meta-analysis study
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Background: Obstructive sleep apnea (OSA) is substantially increased in patients with diabetes mellitus and contributes to cardiovascular diseases. However, OSA also characterized of episodic intermittent nocturnal hypoxia which may alter intra-renal hemodynamic, increase oxidative stress and result in renal function deterioration. Thus, the aim of this systematic review is to summarize the effect of obstructive sleep apnea on the development of chronic kidney disease (CKD).
Material and methods: Our study followed the PRISMA guideline. Two independent reviewers searched relevant articles from the database of Pubmed, Web of Science and CENTRAL and conducted the study selection and quality assessment. Data extraction was performed by the main author and checked by the other authors. Random effect model was used to estimates the effect summary.

Results: A total of 985 was initially identified (Pubmed = 420, Web of Science = 546, CENTRAL = 19). After removed duplicate articles (n = 292) and irrelevant articles (n = 669), there were 24 articles selected for full text review and 11 articles left to be included in present analysis. Overall, patients who are diagnosed of OSA had a higher chance of CKD with pooled odds ratio of 2.01 (95% C.I: 1.61–2.2); however, the risk was increased with pooled odds ratio of 2.46 (95% C.I: 2.0–3.03) in patients with diabetes mellitus. In addition, we found that OSA was consistently associated with a higher proteinuria/albuminuria and a worse renal function with pooled odds ratio of 2.44 (95% C.I: 2.12–2.80), 1.50 (95% C.I: 1.21–1.86) respectively.
Conclusion: Our report demonstrated that OSA is significantly associated with CKD, which may be particular important to patients with diabetes mellitus.

PJ-49

The development of human recombinant protein, GAPtin, for diabetes

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Obesity has become a growing epidemic that plaques people of different cultures worldwide. Obesity is such a major health concern because it leads to several fatal diseases. Obesity sufferers are prone to cardiovascular problems, diabetes, stroke and heart attack. To study these diseases such as obesity and diabetes, many reports reveals that some proteins and/or peptides could reduce the blood-glucose level and inhibit appetite. The major issues are the half-life is very short of critical polypeptides molecules, and they were very sensitive to proteinases and were degraded by these enzymes. In order to increase the half-life of these proteins, three polypeptides, Adiponectin, Glucagon-like peptide-1, Peptide YY, will be selected and genetic fused to form a fusion protein, GAPtin. The structural and biochemical assays will be performed to confirm the protein folding, protein sensitivities, and protein functions. In further, we proposed that the abilities of blood sugar control and appetite inhibition of these fusion proteins could be elevate by using animal studies. We hope that these recombinant proteins not only can be used in reducing blood-glucose levels of diabetes patients but also can prevent the obesity-related diseases. The air sensitivity of latter groups makes the expression and purification of such proteins challenging. Here we describe a method for the purification of the GAPtin protein under conditions. Our procedure consisted of three steps. Subsequent affinity chromatography on Ni-column, anion exchange on Q-column, and gel filtration on Superdex 200. Structure and functionality tests performed with mass spectrometry and circular dichroism spectroscopy assays approved the success of the purification procedure. We have already purified GAPtin protein.

PJ-50

Type 2 diabetes increases the risk for gout in Taiwan

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Through impaired kidney ammoniagenesis and because a low urine PH, type 2 diabetes may be the main factor of hyperuricemia and gout formation. It was hypothesized that type 2 diabetes should favor the formation of gout. Therefore, in a series of 257,156 patients with type 2 diabetes and 1,078,773 without type 2 diabetes. The proportion of gout was 13.4% in patients with type 2 diabetes and 11.3% in patients without type 2 diabetes (Adjusted HR 1.28 (1.23, 1.34), $P < 0.001$). Multivariable analysis included age (Adjusted HR 1.45 (1.37, 1.53), $P < 0.001$), sex (Adjusted HR 2.00 (1.93, 2.08), $P < 0.001$), and comorbidities of chronic liver disease and cirrhosis (Adjusted HR 1.20 (1.15, 1.26), $P < 0.01$), hypertension (Adjusted HR 1.86(1.78,1 .94), $P < 0.001$), hyperlipidemia (Adjusted HR 1.53(1.46, 1.59), $P < 0.001$), stroke (Adjusted HR 0.91(0.82, 1.01), $P > 0.05$), coronary artery disease (Adjusted HR 1.07(1.02, 1.13), $P < 0.001$), chronic kidney disease (Adjusted HR 1.44(1.35, 1.53), $P < 0.001$), and obesity (Adjusted HR 1.09 (0.93, 1.28), $P < 0.01$). All above variables except stroke had elevated hazard risk for gout formation significantly. There were still significant higher risks for gout between patients with type 2 diabetes and patients without type 2 diabetes after stratified by age, sex and comorbidity. Stepwise regression analysis identified type 2 diabetes as a strong factor that was independently associated with the risk for gout. The occurrence of gout was most apparent in obese men and in patients at the oldest age and hyperlipidemia. The 10-year cummulative incidence of gout for patients with type 2 diabetes was about 1.6 times that without type 2 diabetes. In conclusion, in view of the strong association between type 2 diabetes and gout formation, it is proposed that gout may be added to the conditions that potentially are associated with insulin resistance. Accordingly, it is suggested that patients with gout, especially if overweight, should be screened for the presence of type 2 diabetes or components of the metabolic syndrome.

PJ-51

Impact of metabolic status on the incidence of psoriasis: A Korean nationwide cohort study

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Background: Growing evidence suggests that obesity is a risk factor for incident psoriasis. This study was aimed to evaluate the association of obesity and metabolic status with the incidence of psoriasis.
Methods: A total of 418,057 adults were followed-up using a nationwide prospective cohort study in Korea. Participants were stratified based on the body mass index categories and metabolic condition.
Results: During the follow-up visit, 11,054 (2.6%) cases were found to have psoriasis. Diabetes, hypertension, hyperlipidemia, and obesity were all found to be risk factors for incident psoriasis. Subjects with the metabolically unhealthy non-obese phenotype (MUNO; hazard ratio [HR], 1.29; 95% confidence interval [CI], 1.22–1.37) and metabolically unhealthy obese phenotype (MUO; HR, 1.33; 95% CI, 1. 26–1.41) had a significantly higher risk of psoriasis incidence as compared to those with the metabolically healthy non-obese phenotype, after adjusting for age, sex, smoking, exercise, and income. The risk of psoriasis development was found to be high among those with the MUNO and MUO phenotypes in both sexes and all age groups.
Conclusions: The metabolic health status was significantly associated with an increased risk of psoriasis in both obese and non-obese individuals. However, further studies are needed to evaluate whether the control of metabolic parameters can lower the incidence of psoriasis.

PJ-52

Extra virgin olive oil does not cause post-prandial endothelial dysfunction unlike processed butter through protective mechanisms against oxidative stress

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It is well known that Traditional Mediterranean Diet (TMD), characterized by a high consumption of vegetables, legumes, grains, fruits, nuts and olive oil, reduces blood pressure and produces benefits on cardiovascular (CV) risk. Previous reports demonstrated that the intake of extra virgin olive oil (EVOO), rich in polyphenol compounds, exerted a protective effect

against postprandial oxidative stress and thus ameliorates endothelial dysfunction (ED) in a population with high CV risk such as metabolic syndrome and obesity. The aim of this study is to investigate whether a single administration of EVOO restores endothelial function and induces changes on endothelial physiology elements such as nitric oxide (NO) or 8-hydroxy-2′-deoxyguanosine (8-OHdG) in healthy subjects.
Fourteen apparently healthy subjects (10 men, 33 ± 8 years old, BMI 21.8 ± 2.4) were recruited by advertisement and informed consent was obtained from each subjects. The subjects were divided into two groups to receive either EVOO (30 mL) or processed butter (B: 30 g) in the morning after an overnight fast following a randomized crossover design with at least 1-week washout period. Brachial artery Flow-Mediated Dilatation (FMD), a surrogate marker for vascular endothelial function, was measured by use of a vascular ultrasound system equipped with an edge-tracking system and a pulsed Doppler flow velocimeter (Unex EF, Unex Co., Japan) before and 1, 2, 3 hours after an ingestion of either oil. Blood samples were obtained from the antecubital vein at the same time points as FMD for the measurements of serum nitrite and nitrate (colorimetric method by Griess reagent) and 8-OHdG (ELISA).
Results: Although FMD was significantly impaired after an ingestion of B (10.2 ± 4.1% at baseline to 6.9 ± 3.8% after 3 hours, $P < 0.01$), an ingestion of EVOO didn't bring about such an impairment of FMD (9.5 ± 3.2% at baseline to 8.2 ± 2.7% after 3 hours). Serum NO concentration decreased by processed B (46.8 ± 35.4 μmol/L at baseline to 35.3 ± 24.6 μmol/L after 3 hours, $P < 0.01$) in contrast to no significant change after EVOO ingestion. Furthermore, serum 8-OHdG concentration increased by processed B (0.16 ± 0.03 ng/mL at baseline to 0.18 ± 0.05 ng/mL after 3 hours, $P < 0.05$) with no significant change after EVOO ingestion.
Conclusion: Our results clearly demonstrated that processed B rich in saturated fatty acid caused post-prandial ED through an enhancement of oxidative stress, which may lead to future CV events. Unlike B, EVOO even composed of fatty acid didn't affect endothelial function probably due to neutral effects on oxidative stress produced by its polyphenol compounds.

PJ-53

Acarbose therapy and diagnosis of colorectal cancer in type 2 diabetes mellitus: A nationwide cohort study in Taiwan

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Background: Acarbose, an alpha glucosidase inhibitor, is anti-diabetic drug in clinical practice. It has been proposed that acarbose therapy may have beneficial and putative antineoplastic effect of the colon. However, there has been few clinical study investigating this potential benefit. Acarbose therapy is popular in Taiwan. We conducted a population-based cohort study to investigate long-term acarbose use and the incidence of colorectal cancer diagnosis in type 2 diabetes patients.
Methods: The study was conducted using the National Health Insurance Research Database of Taiwan (1,000,000 randomly sampled beneficiaries from the 25.68 million population in Taiwan in 2005). Acarbose-use was defined as prescription of acarbose for durations of at least 90 days every year continuously until the study end or the date of diagnosis of colorectal cancer. Patients prescribed with anti-diabetic drugs every year continuously and never with acarbose were in the non-acarbose group. Patients who were not prescribed with anti-diabetic drugs continuously or who were not ever prescribed with any anti-diabetic drugs were excluded. Patients with the diagnosis of colon cancer or rectal cancer before or in 2005 were excluded. Total 21,337 type 2 diabetes patients were included in the study. Follow-up duration was from 1 to 13 years.
Results: The incidence rate of colorectal cancer diagnosis was higher in the acarbose group than in non-acarbose group (598.2 vs. 434.9 per 100,000 person-years). The adjusted hazard ratio (HR) was 1.97 (95% confidence interval [CI] 1.58–2.47). The adjusted HR was 1.09 (95% CI 0.87–1.37) for acarbose use of 1–7 years and 2.76 (95% CI 1.33–5.73) for duration more than 8 years. Very high proportion of our cohort patients took metformin (92.87% of acarbose group, 91.02% of non-acarbose). Those who did not take metformin had similar incidence of colorectal diagnosis in both groups (acarbose vs non-acarbose, 1010.1 vs. 1109.8 per 100,000 person-years), but those who took metformin had significant difference (acarbose vs. non-acarbose, 565.2 vs. 383.3 per 100,000 person-years; $p < 0.001$). In our study cohort, metformin use was associated with lower incidence of colorectal cancer diagnosis.
Conclusion: Our finding suggests that acarbose in chronic long-term use might reduce the anti-colorectal cancer effect of metformin. However, further clinical study is indicated.

PJ-54

Increased levels of soluble fibrin in human plasma in type 2 diabetic patients

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Background and aims: A prothrombotic state characterized by activation of the coagulation system has been implicated in the pathogenesis of vascular complications in patients with diabetes mellitus. Recently, soluble fibrin (SF) established molecular marker reflecting hyper-coagulable states. However, plasma levels of SF are unclear in type 2 diabetic patients. Therefore, the current study aimed to evaluate plasma levels of SF in type 2 diabetic patients.
Materials and methods: The new onset type 2 diabetic outpatients (hemoglobin A1c was higher than 9.2%) were recruited from January 2014 through December 2015 (n = 53). We measured plasma levels of SF, plasminogen activator inhibitor-1 (PAI-1), D-dimer, prothrombin fragment 1 + 2 (F1 + 2), high sensitive C-reactive protein (hs-CRP) in the new onset type 2 diabetic outpatients.
Results: The average age of patients was 56.0 ± 14.6 years old (range from 23–80 years old, 36 male, 17 female). Also, the average hemoglobin A1c (HbA1c) of patients was 12.4 ± 2.0 (range from 9.2–17.1%). We detected high plasma levels of SF in about 55% of the new onset type 2 diabetic outpatients (range from 5 to 33 μg/mL). In healthy volunteers, plasma levels of SF were less than 5 μg/mL. Furthermore, the SF became less than 5 μg/mL when HbA1c decreased by treatment of diabetes. There was a positive correlation between plasma levels of SF and hs-CRP. However, we did not find any difference plasma levels of F1 + 2, PAI-1, and D-dimer in the new onset type 2 diabetic outpatients.
Conclusion: These results suggest that new onset type 2 diabetic patients have a hyper-coagulable states. Also, in the type 2 diabetic patients, the SF is thought to be useful as a marker knowing whether coagulation system is activated.

PJ-55

The association between body mass index and cardiovascular event in the Korean general population

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The relationship between body mass index (BMI) and mortality is still controversial. Furthermore, the association between BMI and cardiovascular events is not conclusive, and may differ by ethnicity. This study aimed to estimate the association between BMI and mortality and cardiovascular disease including ischemic heart disease and stroke in Korean general population.

This study was based on the sample cohort database released from the Korean National Health Insurance Service (NHIS), which is consisted of 1,025,340 subjects. We analyzed the adults over 30 years who had taken the national health examination at least once from 2002 to 2012. Hazard ratios of death and cardiovascular event were calculated using Cox's proportional hazards models with adjusting for age, smoking, alcohol drinking status, physical activity level, income level, and family history of cardiovascular disease.

During follow-up, 7,257 men and 3,801 women died, and 51,593 cardiovascular events (men: 26,684, women: 24,909) occurred. Subjects with a BMI $\geq 30\ kg/m^2$ and $<25\ kg/m^2$ showed a raised risk of death from overall mortality, and those with a BMI $< 25\ kg/m^2$ had an increased risk of cardiovascular mortality after adjustment for multiple variables. The lowest risk of mortality was appeared in subjects with a BMI of 25–27.4 kg/m^2. The cardiovascular events were lowest in subjects with a BMI 20–22.4 kg/m^2 and rose as the BMI was increased.

BMI showed a U-shaped association with overall mortality with lowest in subjects with slight obesity, whereas cardiovascular event exhibited a J-shaped pattern with lowest in normal weight subjects in Korean general population.

PJ-56

Fifteen-year trends in lifestyle modification in patients with diabetes mellitus: From KNHANES 1998–2013

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Healthy diet and adequate physical activity the initial, and often the primary, component in the management of diabetes mellitus. Furthermore, health-related behaviors such as alcohol consumption and smoking have been known to be related with risk of diabetic complication or cardiovascular disease. In this study, we investigated trends in the achievement of goal of lifestyle modification in the patients with diabetes mellitus in a representative Korean population.

From the Korea National Health and Nutrition Examination Survey (KNHANES) conducted in 1998, 2005, 2009, and 2013, daily intakes of total energy, carbohydrate, protein, fat, and sodium were calculated based on the food items consumed. Physical activity, alcohol consumption, smoking status, and sleep duration were assessed from the questionnaire.

A total of 4,625 patients with diabetes mellitus were analyzed. Patients from 2013 were more obese, however, age, gender, and glycemic control status were not different. From 1998 to 2013, diet in men had not changed. Only 30% consumed adequate amount of carbohydrate, and though group with moderate salt consumption slightly increased, most patients still exceeded the recommended intake. In women, consumption of carbohydrate was far much higher and especially in even non-obese women, only 13% showed adequate carbohydrate consumption. Most drastic change appeared in physical activity. With exception of 1998, analysis from 2005 to 2013 showed decrease in proportion of sustaining moderate physical activity and vigorous physical activity, especially in obese men. Though men having regular strength exercise increased a little, it decreased in obese group. In women, moderate physical activity decreased markedly regardless of obesity, which showed reflection of sedentary lifestyle. Despite of decrease in current cigarette smokers for 15 years, 40% of men still were smokers. Alcohol consumption showed decrease on the whole, but in men, one third still showed binge drinking and the fraction was higher in obese group. As for sleeping duration, men showed no significant difference, but in women, it decreased a little.

Despite the importance of diet and physical activity in diabetic patients is well known, actual dietary habit in diabetes patients did not improve significantly for 15 years and as for physical activity, they showed alarmingly insufficient level. There were some improvement in drinking and smoking habit, however, still many patients showed current smoking or binge drinking. Adoption and maintenance of a healthy lifestyle should be emphasized in people with diabetes.

PJ-58

Patterns of search queries of diabetes-related terms: An infodemiological study using Google trends

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Purpose: Google Trends has been used to explore the searching trends of various health outcomes and behaviors such as influenza, allergic diseases, dementia, multiple sclerosis, epilepsy, cancer screening, smoking cessation, and behavior change. The aim of this study was to investigate patterns of search queries of diabetes-related Chinese terms using Google Trends.

Methods: Google Trends (http://www.google.com.tw/trends/), which allows Internet users to examine trends of certain query terms by time, geographic location, and category was used to search for the following query terms in Chinese, "diabetes", "complications of diabetes", "prevention of diabetes", and "blood glucose". The observation period was limited to 10 years, containing 522 weeks from January 1, 2006 to December 31, 2015. The geographical region of the search trend was limited to Taiwan. The results were normalized to a range of 0 to 100, with 100 equals to the peak value over the study time period with respect to the search term. Cycle plots, including sequential plots and seasonal subseries plots, were used to visualize cyclical patterns in the data.

Results: Seasonality patterns were observed in the search query terms. For the query term "diabetes", two peaks appeared in March and May whereas one dip appeared in August. Similarly pattern appeared when the English term, with geographical location limited to Taiwan, was used. On the other hand, for the query "complications in diabetes", higher volume was observed around March and April with two dips in January, August, and October. For "prevention of diabetes", a peak appeared in May and a dip appeared in November. For "blood glucose", the search volume was lower in January and February.

Conclusions: Different seasonality patterns were observed depending on the diabetes-related query terms. Certain peaks can possibly be explained by the activities generated by health professionals and students in relation to the time of examination and major academic health conferences. While Google Trends holds potential for easy access to aggregated results of big data, there are limitations to its applicability to derive meaningful insights about population health behavior.

PJ-59

RBP2R expression and retinol homeostasis in the liver of diabetes

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Vitamin A (retinol) absorbed from small intestine and circulation, stored in liver, and secreted into circulation bound to serum retinol-binding protein (RBP4). A novel retinol transporter, RBPR2, expressed primarily in liver of mice, was found to potentially regulate retinol homeostasis in liver. We hypothesize that diabetes and obesity might affect RBPR2 and its signaling (CRBP1, RARs), and circulating RBP4 concentration. Here, we showed our results; (1) In the liver of high fat diet (HFD)-fed mice, RBPR2 mRNA, CRBP1 and RARα protein level markedly decreased while blood RBP4 concentration increased. (2) In the liver of db/db mice, CRBP1 and RARα protein level significantly decreased, but RBPR2 mRNA and protein markedly increased. (3) By using RBPR2 immunoprecipation method, RBP4 binding activity with RBP2R remarkably declined in high glucose-cultured clone 9 hepatic and HepG2 cells. (4) In RBPR2 immunoprecipation method, O-GlcNAc modification of RBP2R was found in HG-cultured HepG2 cells. (5) HG- induced RBP4 overproduction was attenuated by O-GlcNAc transferase siRNA in HepG2 cells. Thus, high fat feeding causes down-regulation of RBPR2 while diabetes enhances O-GlcNAc modification of RBP2R, and both reduce retinol homeostasis in liver and possibly affect circulating RBP4 concentration.

PJ-60

Long-term effectiveness of sulfonylureas in type 2 diabetes

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Background: Very long-term drug therapy is commonly needed for proper management of the type 2 diabetes (T2DM). Sulfonylureas (SU) have been widely and long used for T2DM treatment in Japan since insulin secretagougues are suitable for pathophysiology of Asian T2DM with predominant insulin secretory defect. There is, however, few clinical finding about the T2DM under very long-term treatment of SU. In this study, T2DM patients with decade SU treatment period are extracted by analyses of the dataset of prescriptions aiming to reveal the clinical features of very long-term SU using.
Method: The dataset which consists of 220,000 medical prescriptions for 15 years was reconstructed and analyzed. Patients who were continuously prescribed SU at least 10 years were extracted and investigated their clinical features.
Result: Fifty T2DM patients (72.9 ± 9.3 y.o.) were extracted. Dosages of SU were 47.6, 1.4 (gliclazide, glimepiride respectively) (mg/day). 1.4 ± 0.9 oral hypoglycemic agents other than insulin secretagogues were used as combination therapy. Recent HbA1c of extracted patients was 7.2 ± 0.9%.
Conclusion: Our results revealed that sulfonylureas have very long-term effectiveness for treatment of T2DM in relatively low-dose use. Analysis of reconstructed medical prescription records was very useful method for obtaining long-term clinical findings.

Endocrinology

PK-01

Dynamic risk estimates of outcome in patients with well-differentiated thyroid cancer after initial treatment

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Introduction: This study was conducted to evaluate the American Joint Cancer Committee (AJCC), American Thyroid Association (ATA) staging systems and response to initial therapy reclassification system for the prediction of long term disease status in patients with well-differentiated thyroid carcinoma (WDTC).
Patients and methods: Patients with WDTC (n = 356) treated with total or near-total thyroidectomy followed by 131I remnant ablation at Kaohsiung Chang Gung Memorial Hospital were retrospectively studied. A minimum of 5 years of follow-up was required and patients with anti-thyroglobulin (Tg) autoantibodies were excluded. Each patient was risk-stratified using the AJCC (stage I–IV) and 2009 ATA staging systems (low, intermediate, high risk) immediately after operation and first 131I remnant ablation, and response to initial therapy reclassification system (excellent response, biochemical incomplete, indeterminate, structural persistent) at 6–24 months after the first 131I remnant ablation. The clinical outcome at last follow-up is defined as no evidence of disease (NED) (suppressed Tg < 0.5 ng/mL, stimulated Tg < 1 ng/mL and no structural detectable disease), biochemical persistent disease (BPD) (suppressed Tg > 0.5 ng/mL or stimulated Tg > 1 ng/mL in the absence of structural disease), structural persistent disease (SPD) (locoregional or distant metastases with any Tg level), or recurrence disease (RD) (biochemical or structural disease identified after a period of NED).
Results: The mean age of the 356 patients was 41.5 ± 12.7 years and duration of follow-up was 12.3 ± 5.0 years. At the time of last follow-up, 78% (n = 279) of the patients were NED, 9.3% (n = 33) had BPD, 10.1% (n = 36) had SPD and 2.2% (n = 8) developed RD. SPD was identified in 6.7%, 9.5%, 16.7%, and 29.3% of stage I, II, III and IV patients, respectively ($p < 0.001$) according to AJCC classification. SPD was identified in 0.5%, 4.9%, and 28.3% of the low-, intermediate-, and high-risk patients, respectively ($p < 0.001$) according to ATA staging system. As using response to initial therapy re-classification system, the likelihood of finding SPD was 0.5%, 6.2%, 27.7% and 80% in patients with excellent, indeterminate, biochemical incomplete and structural incomplete response, respectively ($p < 0.001$).
Conclusions: Our results are consistent with ATA guideline that recommends a dynamic risk assessment to incorporate the response to therapy during follow-up in an ongoing process for individual patient.

PK-02

Consumptive hypothyroidism associated with hepatic hemangiomas

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The vast majority of hemangiomas never cause symptoms, however, huge and diffuse hepatic hemangiomas can cause consumptive hypothyroidism through the overproduction of type 3 iodothyronine deiodinase. Here, we reported a

premature female infant developed severe hypothyroidism due to diffused hepatic hemangiomas. At 3 days, a routine thyroid-stimulating hormone (TSH) screening test was normal. Nevertheless, the sizes and numbers of cutaneous hemangiomas were rapidly progressive after birth. At 4 weeks, she had poor feeding, lethargy, jaundice and constipation. Extremely high level of TSH, low levels of T3 and T4, and inappropriately high level of reversed T3 pointed to consumptive hypothyroidism. Abdominal image demonstrated multiple hepatic hemangiomas causing severe hepatomegaly. With the treatment of levothyroxine and propranolol, her thyroid function improved concurrently with significant involution of the hepatic hemangiomas at the age of 6 months. This case highlighted repeated thyroid function and image of abdomen are crucial, especially when encountering infants presenting simultaneously with rapid growth of cutaneous hemangiomas and unexplained symptoms of hypothyroidism.

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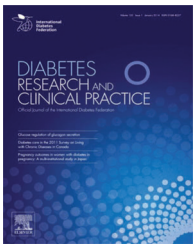

Author index

Publication information: *Diabetes Research and Clinical Practice* (ISSN 0168-8227). For 2016, volumes 111–122 are scheduled for publication. Subscription prices are available upon request from the Publisher or from the Elsevier Customer Service Department nearest you or from this journal's website (http://www.elsevier.com/locate/diabres). Further information is available on this journal and other Elsevier products through Elsevier's website (http://www.elsevier.com). Subscriptions are accepted on a prepaid basis only and are entered on a calendar year basis. Issues are sent by standard mail (surface within Europe, air delivery outside Europe). Priority rates are available upon request. Claims for missing issues should be made within six months of the date of dispatch.

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Abstracts of the 11th IDF-WPR Congress 2016 &
8th AASD Scientific Meeting
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