# ABSTRACTS

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#### AN ASSOCIATION OF SERUM VITAMIN D, IL-4 LEVEL AND VDR GENE POLYMORPHISM IN CAD WITH AND WITHOUT T2DM

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Introduction: Coronary artery disease (CAD) is a leading cause of death in developed countries and is rapidly assuming epidemic proportions in developing countries as well. It has been shown that lower vitamin D levels appear to predict an increased risk of CAD mortality in patients with Type 2 Diabetes mellitus (T2DM). Coronary atherogenesis leading to CAD is an immunological phenomenon caused by foam cells i.e. transformed macrophages at the lesion site. Apart from the traditional role of vita D in calcium homeostasis lot of recent experimental evidences are available on role of vita D levels, VDR gene polymorphism, vitamin D binding protein gene polymorphism in immune reaction as immuno modulators and now-a- days are being considered as risk factors in generating coronary atherogenesis leading to CAD particularly in association with T2DM. Recent studies also provide that IL-4 exerts proinflammatory effects on vascular endothelium and may play a critical role in developing coronary atherosclerosis.

*Aims and Objectives:* So we set our aims for this study to investigate the association of vita D , VDR gene polymorphism and serum IL-4 levels in CAD with or without T2DM.

*Materials and Methods:* The study involves two groups of patients suffering from CAD with T2DM (n=40) and CAD without T2DM (n=40) attended emergency or coronary care unit of Lok Nayak Hospital, New Delhi. A total of 6ml of blood sample was collected for estimation of serum vita D and IL-4 levels by chemiluminescence immuno assay method and VDR gene polymorphism (exon 1l, rs 2228570) by PCR-RFLP using *Fok1* restriction enzyme. Other relevant routine blood biochemistry tests were done by Beckman coulter fully automated analyzer using commercially available kits.

**Results and Discussions:** Serum vita D levels were decreased in both groups of patients, more significantly decreased in the presence of T2DM in CAD patients. Serum IL-4 levels were significantly higher in CAD with T2DM group as compared to CAD without T2DM group. No association could be found between VDR gene polymorphism (*Fok1*) and risk of CAD in T2DM and non T2DM individuals. No significant correlation was found between vitamin D and IL-4 levels in the patients of both groups. No significant association was observed between low

25-hydroxy vitamin D levels with VDR genotypes (*Fok1*) in both groups of patients.

**Conclusions:** The association between VDR *Fok1* polymorphism, vitamin D and inflammatory markers needs to be further explored in diabetic CAD patients. A bigger study involving a much larger number of patients would help to generalize the results of this study.

#### EVALUATION OF ANTIMICROBIAL THERAPY AND PATIENT ADHERENCE IN DIABETIC FOOT INFECTIONS

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Background and Objectives: Diabetic foot infections are one of the most common problems in diabetic patients. Foot Infection in patients with diabetes is become more severe and takes longer to cure than infections in patients without diabetes. In some-cases, can reduce the severity of complications and also improve overall quality of life of patients especially by using a multidisciplinary team approach. The effectiveness of antibiotics depends not only on efficacy and appropriateness of usage but also on patient adherence to intended regimen. Hence this study was aimed to assess the evaluation of antimicrobial therapy and patient adherence in diabetic foot infections. It is also aimed to evaluate the medication adherence in Diabetic foot infections and to evaluate the time for streamlines therapies from empirical therapy to definitive therapy after culture reports are obtained. This study also asses the appropriateness of empiric antibiotic therapy for Diabetic foot infections.

*Method:* This study is a Prospective observational study conducted in Kasturba hospital, Manipal Consisting of 89 patients with diabetic foot infections and they were evaluated about the medication adherence and time for stream-lines therapies from empirical to definitive therapy and also check's the appropriateness of empirical therapy for DFI.

**Results:** Out of 89 patients, Did adherence for 50 patients among that 40% was found medium adherence, 40% was found low adherence and 20% was found high adherence. The prescribing of empiric antibiotic therapy is Inappropriate. The time for prescribing empirical therapy <12hrs is (62.9%), in between of 12 -24hrs was found to be 24.7%, in between 24-48hrs was found to be 7% and not given empirical therapy was found to be 5.4%. Definitive therapy was given around 64% patients and not given in 36% patients.

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**Conclusion:** Foot infections in patients is common, and frequently leads to lower limb amputation unless a rationale, Multidisciplinary approach to therapy is taken. This study shows the importance of following the hospital antibiotic policy and prescriptions prescribed by the physician to be adhered to prevent emergence of resistant pathogens and rationalize the use of antibiotics. Antimicrobial resistance is emerged as increased worrisome situation globally; there is need in awareness and education among public and health care professionals. Similarly in India it is an important public issue, its need priority as it has socioeconomic impact.

#### IMPROVING INDIVIDUALIZED T2D MANAGEMENT: EFFECT OF MEDICAL EDUCATION ON PCP KNOWLEDGE AND COMPETENCE

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Medscape Education; Developed through independent educational grants from AstraZeneca

**Background:** Although a glycated hemoglobin (A1c) level <7.0% is associated with health benefits in patients with type 2 diabetes (T2D), 52% of patients are not meeting recommended A1c targets. Successful individualized T2D treatment requires a thorough understanding of new cardiovascular outcomes trial (CVOT) data, standard and newly available therapies, and how these therapies best fit into modern practice. We sought to determine if online continuing medical education (CME) could improve the clinical knowledge and competence of primary care physicians (PCPs) regarding the use of newer therapies in T2D management.

**Methods:** The effect of three educational interventions focusing on the role of SGLT2 inhibitors in the treatment of T2D was analyzed to determine efficacy of online education. The activities were presented in the form of video discussions between 2 or 3 experts in the field of diabetes management. We assessed the effects of education using a repeated pairs, pre-/post-assessment study design. The assessment instrument assessed responses to knowledge-and case-based questions. McNemar's chi-squared test assessed if the mean post- assessment score differed from the mean pre- assessment score. *P* values are shown as a measure of significance; *P* values <.05 are statistically significant. The activities launched online between August 17, 2016 and November 9, 2016, and data collected through December 20, 2016.

*Results:* In total, 825 PCPs participated. Significant overall improvements were seen for all activities, including:

- Compared with baseline, 27% more PCPs (P <.001) correctly recognized recent CVOT data for SGLT2 inhibitors
- Compared with baseline, 19% more PCPs (P < .001) correctly identified the rationale for taking renal function into consideration prior to initiating SGLT2 inhibitor therapy
- Compared with baseline, 9% more PCPs (*P* =.002) correctly identified precautions to ask with patients about before initiating SGLT2 inhibitor therapy
- Compared with baseline, 6% more PCPs (*P* =.003) correctly identified SGLT2 inhibitor therapy as the next best step in an individualized T2D treatment plan in a case scenario

Continued educational gaps identified by low post-assessment knowledge/competence:

- 44% of PCPs failed to recognize recent CVOT data related to SGLT2 inhibitors
- 21% of PCPs failed to select the rationale for assessing kidney function prior to initiating SGLT2 inhibitor therapy
- 15% of PCPs failed to accurately address DKA risk in a patient with T2D on SGLT2 inhibitor therapy

*Conclusion:* This study demonstrates the success of a targeted multi-component educational intervention at improving knowledge and competence of PCPs regarding the use of SGLT2 inhibitors in the treatment of T2D. Additional education is needed related to CVOT data and addressing risks associated with SGLT2 inhibitors. Additional studies are needed to assess if improved knowledge and competence translates into improved appropriate use of these therapeutic options in the clinic setting.

#### UNCONTROLLED HYPERTENSION AND ASSOCIATED FACTORS AMONG HYPERTENSIVE PATIENTS AT JIMMA UNIVERSITY SPECIALIZED HOSPITAL, ETHIOPIA

#### Mr. Bekele Tesfaye (BSc, MSc in Adult Health Nursing); Professor Tefera Belachew (MD, MSc, PhD); Mr. Temamen Tesfaye (BSC, MSc, Assistant Professor)

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**Background:** Hypertension, including poorly controlled blood pressure, is the major global health problem which affects one billion people worldwide. However, limited studies have been conducted in Ethiopia. The aim of this study was to determine the prevalence of uncontrolled hypertension and associated factors among adult hypertensive patients at Jimma University Teaching and Specialized Hospital.

*Method:* Institution based cross-sectional study was conducted at the chronic illness clinic of Jimma University Specialized and Teaching hospital from March 09 to April 13, 2016. A total of 345 hypertensive patients were selected using systematic sampling technique. Data were collected using structured questionnaire through face to face exit interview and chart review. Data were analyzed using SPSS version 20.0 software. The bivariate and multivariable analysis were done to identify factors of uncontrolled hypertension.

**Result:** More than half 52.7% of the patients had uncontrolled hypertension. Lack of awareness of hypertension related complications (AOR=2.140, 95%CI=1.272-3.600, p-value=0.004), non-adherent to smoking abstinence (AOR=3.935, 95%CI=1.065-14.535, p-value=0.004), non-adherent to alcohol abstinence (AOR=2.477, 95%CI=1.074-5.711, p-value=033), Khat (Catha edulis) chewing (AOR=2.518, 95%CI=1.250-5.073, p-value=0.010), overweight (AOR=2.241,CI=1.239-4.053,P-value=0.008), middle age (AOR=7.893,95%CI=1.860-33.493, P-value=0.008) (AOR=9.944,95%CI=2.523-39.188, and old age P-value=0.001 were significant predictors of uncontrolled hypertension.

*Conclusion:* The prevalence of uncontrolled hypertension was high at Jimma University Teaching and Specialized hospital among patients with hypertension. Unhealthy life-styles were major factors. Continuous health education on lifestyle practices and hypertension related complications in each follow-up visit through nurses, physicians and pharmacists are very essential to avert the problem.

### DIABETES MELLITUS IS ASSOCIATED WITH SLEEP DISTURBANCE IN THE OLDEST OLD

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Sleep is an essential biological process and sleep disturbance is a common health problem that has substantial consequences like low quality of life, cognitive impairment and increased mortality in older people. The prevalence of sleep problems increase with age and there are well known risk factors for sleep disorders in older adults. The aim of this study is to investigate whether the presence of diabetes mellitus is associated with sleep problems in oldest old patients. A retrospective cohort analysis was performed us-

ing health records of patients admitted to outpatient clinic of our department. Demographic characteristics, comorbid conditions and presence of well-known risk factors for sleep disturbance were recorded. Ninety-nine patients over 85 years of age were included in the study. Mean age was 88.45±4 and 55.6% (n=55) was male. Twenty one percent of the patients had diabetes mellitus. Patients that declared they had sleeping problem was 35.4% (n=35). 34% of the patients experiencing sleep disturbance had diabetes while 14% of those not experiencing (p=0.02). Also nocturia was higher among patients with sleep problem (p=0.02). There was no statistically significant difference between sleep disturbance and gender (p=0.8), history of dementia (p=0.8), depression (p=0.06), hypertension (p=0.2), heart failure (p=0.27), chronic obstructive pulmonary disease (p=0.8), and Parkinson disease (p=0.55). The Odds Ratio (OR) of the significant risk factors in the logistic regression were diabetes mellitus (OR[95%CI] = 3,4 [1,2–9,7]), depression (OR[95%CI] = 3,3 [1,3-8,5]) and nocturia (OR[95%CI] =5 [1,2-20,4]). In addition to well known risk factors our findings highlight the importance of diabetes mellitus in the development of the sleep disturbance in the oldest old.

#### PREDICTION MODEL OF MORTALITY AMONG PATIENTS WITH DIABETIC KETOACIDOSIS

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**Background:** Diabetes Mellitus (DM) is a major cause of premature mortality globally. One of its acute complication is Diabetic Ketoacidosis (DKA). DKA is a medical emergency wherein abrupt and correct management could prevent patient mortality. Prediction of mortality from DKA could be done using patient's demographics, clinical profile and laboratory parameters. However, locally, there is no prediction model developed yet to predict mortality.

**Objective:** This study aims to create an assessment tool that could accurately predict the risk of mortality among DKA patients within the first 24 hours of admission and correlate patient's demographics, clinical profile and laboratory parameters with improvement of survival rate.

*Methods:* This is a retrospective, cohort study which included 129 admitted adult DKA patients. Statistical analysis used was logistic binary regression. Receiving operating characteristic (ROC) curve was done to validate prediction models.

*Results & Analysis:* 6 variables identified to predict mortality are patient's age >/= 60 years, severe DKA, non- insulin dependent status, GCS <15, non-normal platelet count and non-normal estimated creatinine clearance. Prediction models developed included and omitted age profile. Cutoff scores of prediction models were validated with the ROC curve. Cut-off score with age was 5 with sensitivity of 73.91% and specificity of 74.70% and the area under the curve is 0.751 which is significant (p=0.0001). On the other hand, cut-off score of the prediction model without age is 4 with sensitivity of 65.22% and specificity of 67.47% and the area under the curve is 0.719 which is significant (p=0.0001).

*Conclusion:* This study was able to prove that mortality in DKA can be predicted within the first 24 hours of admission using patient's demographics and significant clinical profile in the prediction models developed.

#### USABILITY COMPARISON OF ARKRAY TECHLITE® AND BD ULTRA-FINE<sup>™</sup> PEN NEEDLES

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Arkray USA

**Background:** Pen needles (PNs) are required for insulin injections using pen devices. Pen needles should be easy to use, affordable and users should feel confident in their insulin dose delivery. Purpose: This study evaluated patient usability preferences of the ARKRAY TechLITE® Pen Needles (Needle Gauge 32 and Needle Length 4mm) compared to BD Ultra-Fine<sup>TM</sup> Pen Needles (Needle Gauge 32 and Needle Length 4mm).

*Methods:* A clinical study was conducted with 20 participants having Type 1 or Type 2 diabetes mellitus with experience injecting insulin by pen at least once per day for a minimum of 2 months. The participants were directed to make 3 injections with the ARKRAY TechLite® Pen Needle (PN) and 3 injections with the BD Ultra-Fine<sup>TM</sup> PN into a simulated skin tissue pad. Following all 6 injections, a usability preference survey was completed by the participants rating the PN in a linear fashion from greatly preferring the ARKRAY PN to no difference to greatly preferring the BD PN.

**Results:** The average age of the participants was 60 years (19-88) with an average of 7.5 years of insulin pen use (0.2-20). In comparison to the BD PN, the results were as follows: Ease of Attaching the PN to the Pen 65% (13/20) of the participants preferred the ARKRAY TechLite  $\mbox{ PN}$  or observed no difference; Ease of Insertion and Amount

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of Thumb Force Required 85% (17/20) of the participants preferred the ARKRAY TechLite <sup>®</sup> PN or observed no difference; Feeling Confident of having Delivered a Full Dose and Time it Took to Make the Injection 95% (19/20) of the participants preferred the ARKRAY TechLite <sup>®</sup> PN or observed no difference; Ease of Pen Needle Removal and Overall Preference 75% (15/20) of the participants preferred the ARKRAY TechLite <sup>®</sup> PN or observed no difference.

**Conclusion:** The ARKRAY TechLite<sup>®</sup> Pen Needle performed as good as or better than the BD Ultra-Fine<sup>TM</sup> Pen Needle for each of the preference characteristics studied (Ease of PN Attachment to the Device, Thumb Force, Ease of Insertion, Full Dose Confidence, Perceived Injection Time, and Ease of PN Removal from Device, and Overall Preference), and is an affordable pen needle option.

#### ALONE OR TOGETHER?

#### Fatih Mehmet Cilingir, MD

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Abstract: In our study, our aim was to examine the coexistence and frequency of chronic diseases. A total of 1117 middle and elderly patients were included in the study. Patients were grouped according to the presence or absence of diabetes mellitus, hypertension, chronic obstructive pulmonary disease (copd), osteoporosis. 331 (29.6%) of patients had diabetes. 198 patients (59.8%) of diabetic patients also had hypertension. At the same time, the presence of hypertension was statistically significant in diabetic patients (p: 0.000). Sixty (5.4%) of the patients had osteoporosis. Twelve (3.6%) of diabetic patients also had osteoporosis. The presence of osteoporosis at the same time in diabetic patients was not statistically significant (p: 0.093). There were 124 (11.1%) patients with copd. 38 (11.5%) of diabetic patients also had copd. At the same time, the presence of copd in diabetic patients was not statistically significant (p: 0.793). 530 patients (47.4%) had hypertension. 198 patients (37.4%) of hypertensive patients also had diabetes. At the same time, the presence of dm was statistically significant in hypertensive patients (p: 0.000). 38 (30.6%) of patients with copd also had diabetes. At the same time, the presence of diabetes was not found statistically significant in patients with copd (p:0.793). Twelve (20.0%) of osteoporotic patients also had diabetes. The presence of diabetes at the same time in patients with osteoporosis was not statistically significant (p:0.093). Mortality and morbidity rates can be reduced by controlling frequent diseases.

#### FEMALE RATS DISPLAY GREATER RESPONSIVENESS TO LEPTIN OVEREXPRESSION AND DECREASED SUSCEPTIBILITY TO LEPTIN RESISTANCE COMPARED WITH MALES

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Abstract: Brains of females are more sensitive to the acute catabolic actions of leptin. However, gender differences in the long-term physiological responses to central leptin overexpression or leptin receptor blockade are unknown. To this end, we centrally delivered a viral vector to overexpress leptin (Leptin), a neutral leptin receptor antagonist (Leptin-Antagonist), or green fluorescence protein (Control). We examined chronic changes in food intake, body weight and body composition over 26 days in male and female rats. Females displayed greater and sustained responses to Leptin whereas males rapidly lost physiological effects and developed leptin resistance confirmed by lower acute leptin-mediated phosphorylation of STAT3 (P-STAT3). Surprisingly, despite persistent physiological responses, Leptin-females also exhibited reduced acute leptin-mediated P-STAT3, suggesting an onset of leptin resistance near time of death. In line with this interpretation, cumulative food intake was less in Leptin-females, but food consumption on day 26 was unchanged from Controls. Both Leptin-Antagonist groups gained similar percentages of their initial body weight and fat mass, whereas only Leptin-Antagonist-females gained lean body mass. Consequently, lean/fat mass ratio with Leptin-Antagonist was preserved females and decreased in males, suggesting a deterioration of body composition in males. In summary, this study establishes that females are more responsive to long-term central leptin overexpression than males and that leptin antagonism may be more detrimental to males. More importantly, females were less susceptible to leptin resistance than males suggesting that either female hormones mitigate or male hormones exacerbate leptin resistance or both.

#### A NOVEL FUNCTION FOR ZIP7 (SLC39A7), BY DIRECTLY SEQUESTERING (BUFFERING) ZINC TO MAINTAIN ENDOPLASMIC RETICULUM ZINC HOMEOSTASIS

#### John Adulcikas; Shaghayegh Norouzi; Lawrence Bretag; Sukhwinder Sohal; Stephen Myers

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Abstract: The endoplasmic reticulum (ER) is a cellular structure that is essential for the production and localization of proteins in cells. Aberrant processes associated with changes in ER structure and function leads to cellular stress, a process that underpins several important metabolic diseases such as cardiovascular disease, obesity and type 2 diabetes. In this context, the ER contains high concentrations of the metal ion zinc that, under normal physiological responses, maintains ER function. Changes in zinc concentrations and distribution in the ER leads to abnormal processes that typify many disease states. Physiological zinc concentrations are maintained by zinc transporter proteins that transport zinc into cells and subcellular organelles (ZnTs), or release zinc from subcellular organelles or the cell (ZIPs). One specific protein that is localized to the ER is ZIP7. This transporter possesses protective activity against ER stress and is a critical 'gate-keeper' of zinc release from the ER during processes that require cellular maintenance. However, it is not known how ZIP7 achieves this protective activity while maintaining cellular function. A preliminary scan of the amino acid structure of ZIP7 revealed several potential binding sites for zinc. Accordingly, we hypothesize that ZIP7 can sequester zinc through a mechanism that binds this metal ion in the ER and thereby produces a protective effect on this cellular structure. Understanding the mechanism of how ZIP7 is protective of ER stress could offer exciting new targets that are amenable to therapeutic intervention in the treatment of cellular stress-related disease.

#### ZINC INDUCES INSULIN SIGNALLING CASCADE IN HUMAN SKELETAL MUSCLE CELL LINE

#### Shaghayegh Norouzi; John Adulcikas; Sukhwinder Sohal; Stephen Myers

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*Abstract:* Insulin resistance (IR) is a medical disorder that is associated with the development type-2 diabetes (T2D). T2D occurs predominately due to pancreatic beta-cell failure. Elevated blood glucose as a consequence of IR, causes the pancreatic beta cells to produce more insulin resulting in hyperinsulinaemia. Although until the maintenance of  $\beta$ -cell compensatory function, IR per se does not stimulate type-2 diabetes, the boosted demand for insulin affects the  $\beta$ -cell secretion and its endoplasmic reticulum, and the stress of endoplasmic reticulum causes in  $\beta$ -cell failure in type 2 diabetic patients. Previous studies have suggested that the essential trace element, zinc, is a crucial component of insulin signaling and glucose metabolism and it may delay the onset of T2D among patients with IR. However the potential mechanisms by which zinc can improve insulin signaling and thus glycemic control, is not understood. Our study evaluated the insulin-like effects of zinc on the insulin signalling cascade in human skeletal muscle cells to further investigate the role of zinc in the management of IR and T2D. We identified that, zinc exhibited insulin-mimetic activity on the protein expression of key markers implicated in insulin signaling including Akt, SHP-2, ERK1/2, P38 and GSK3ß. Zinc also increased the gene expression of glucose transporter Glut-4 and increased glucose consumption in human cells. Accordingly, understanding how zinc regulates processes involved in insulin signalling may present opportunities to reduce or better manage insulin resistance and the progression of T2D.

#### EFFECT OF HIGH DOSE VITAMIN D SUPPLEMENTATION ON BETA CELL FUNCTION IN OBESE ASIAN-INDIAN CHILDREN AND ADOLESCENTS, AGED 11-17 YEARS: A RANDOMIZED, DOUBLE-BLIND, ACTIVE CONTROLLED STUDY

#### Shweta Varshney\*; Rajesh Khadgawat\*; Monita Gahlot; Ashok Jaryal; Nandita Gupta\*; V Sreenivas

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**Background:** Vitamin D deficiency has been shown to be associated with insulin resistance. In an attempt to explore this association, studies of vitamin D supplementation in insulin resistant subjects have not shown consistence results. Few of the important limitations of these studies are higher baseline mean vitamin D level, low dose and smaller duration of supplementation. We planned a study to investigate the effects of high dose vitamin D supplementation on beta cell dysfunction in obese children and adolescents. Objective: To study the effects of high dose vitamin D supplementation on beta cell function and cardiovascular risk factors in Asian-Indian obese children and adolescents, aged 11-17 years.

*Methods:* A prospective, randomized, double blind activecontrolled study, was carried out to investigate the effects of high dose vitamin D supplementation (Cholecalciferol -4000 IU per day) in comparison to daily requirement dose (Cholecalciferol - 400 IU/day) for 12 months. Both the doses of vitamin D were calculated on daily basis but given as once a month, single, oral dose (120,000 IUvs 12,000 IU once a month). Life style modification advice were given to both the groups before randomization (computer based randomization in 1:1). Beta cell functions were assessed by, disposition index (The primary outcome of the study, product of insulinogenic index and whole body insulin sensitivity; measured by oral glucose tolerance test) which was measured before and after 12 months of supplementation. As secondary outcomes, lipid profile, inflammatory cytokines (serum hsCRP, IL-6, TNF-alpha) and cardiovascular risk factors (aortic pulse wave velocity and radial pulse augmentation index) were also assessed before and after supplementation of vitamin D. Safety parameters, serum calcium, and urinary calcium creatinine ratio were assessed every two monthly.

Results: A total of 189 obese children and adolescents were recruited (Mean age: Boys - 12.94±1.51; Girls 13.13±1.72) After life style modification advice, were randomized into two groups, Group A (Intervention goup) and group B (control group). No significant difference in any of the clinical and biochemical parameters were seen at baseline. The mean serum vitamin D level of the study population was 9.21±7.54 ng/ml (Intervention group- 8.36±5.45) Control Group- (9.01±5.59). At baseline, 94.7% subjects (Intervention group- 94.7%; Control Group- 94.6%) were vitamin D deficient (serum 25OH Vit.D < 20 ng/mL). Only four subjects had serum vitamin D level >30 ng/ml. After 12 months of supplementation, there was a significant increase in serum 250HD level in intervention group in comparison to controls (26.89±12.23 vs. 13.14±4.66 ng/ ml, p<0.001). No significant difference in disposition index (primary outcome) as well as other parameters of insulin resistance and sensitivity were seen after 12 months of supplementation. Similarly, no significant difference in BMI, HbA1c, fasting blood glucose, lipid profile, inflammatory cytokines and pulse wave velocity were observed after 12 months. None of the study subjects in both groups developed hypercalcemia and hypercalciuria, suggesting safety of intervention.

*Conclusion:* Supplementation with vitamin D in doses of 4000 IU per day for 12 months in Asian-Indian children and adolescents did not affect beta cell function as well as cardiovascular risk factors.

#### INDIVIDUALIZING T2D MANAGEMENT: A CLINICAL LOOK AT THE EFFECT OF CME ON PHYSICIAN PERFORMANCE

Amy T. Larkin, PharmD; Kelly Hanley; Anne Le, PharmD

Medscape Education

#### Name of contact person for the group: Amy Larkin, PharmD

**Background:** Despite the recognized benefits of glycemic control in type 2 diabetes (T2D, nearly two thirds of patients with diabetes fail to achieve goals for glycemic control (ie, a glycated hemoglobin [A1c] level of <7%). Improvements in diabetes management are critical to increase the proportion of patients who meet glycemic goals. We sought to determine if online continuing medical education (CME) could improve the clinical performance of primary care physicians (PCPs) and diabetologists/endocrinologists (D/E) regarding the use of newer therapies in T2D management.

*Methods:* The educational activity was a 30-minute online video discussion between 3 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs pre-/post-assessment and McNemar's chi-squared test. P values are shown as a measure of significance; P values <.05 are statistically significant. Cramer's V determined the effect size (<0.05 no effect; 0.06-0.15 small effect, 0.16-0.30 medium effect, >0.30 large effect). The activity launched online December 21, 2015 and data collected through April 26, 2016.

**Results:** In total, 305 PCPs and 34 D/E completed the study. Overall, the education had a medium educational on both PCPs (V=0.285) and D/E (V=0.244). At baseline, 19% of PCPs and 32% of D/E answered all 3 case-based questions correctly; on post-assessment this increased to 60% for PCPs and 62% for D/E. Statistically significant improvements were seen for all 3 case-based questions, ranging from 41%-68% relative improvements for PCPs and 30%-41% relative improvements for D/E). Additionally, 38% of PCPs and 15% of D/E reported increased confidence posteducation.

*Conclusion:* This study demonstrates a significantly positive effect of this clinically relevant, video-based panel discussion among both PCPs and D/E.

#### STATIN AND FENOFIBRATE INHIBIT RAGE

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**Objective:** Statins demonstrated lipid lowering effects. Statins and feno-fibrate are anti-inflammatory and vasculoprotective in diabetes mellitus (DM). Therefore, we hypothesized statins and feno-fibrate may potentially inhibit RAGE [Receptor Advanced Glycation End products] interaction with AGE [Advanced Glycation End products].

*Methods:* It has been observed that AGEs increase the progression of retinopathy in patients in the early stages of retinopathy. The reason behind the complication progression induced by AGEs is the ligand - receptor binding with the Receptor Advanced Glycation End products. The binding interaction leads to an increase in the release of pro-inflammatory molecules. By identifying drugs to bind with RAGE, this could prevent the ligand receptor binding between RAGEs and AGEs and potentially prevent further progression of Diabetic Retinopathy. The following study analyzed drug targets based on their hydrophobicity, as to whether they will be able to bind with RAGE. A docking program, AutoDock Tools and AutoDock Vina, were both used to determine the binding affinity and rmsd values of the drug targets.

**Results:** Atorvastatin, a statin drug, and Fenofibrate, a Fibric Acid drug, were drug candidates that were able to bind to RAGE. They had high hydrophobicity and greater negative affinity. Metformin, a popular drug for diabetes treatment, did not show successful binding with RAGE. Metformin had low hydrophobicity and a low negative affinity.

*Discussion:* These results suggest that Statin drugs and Fibric Acid drugs have great potential to bind with RAGE, and can play a role in the prevention of Diabetic Retinopathy. Further elucidating its mode of action in epidemiological studies will help to refine how best to use statins and fenofibrate in the management of diabetic retinopathy.

#### WEIGHT LOSS AFTER GASTRIC BANDING SURGERY NEITHER PREVENT THE ARTERIAL STIFFENING NOR IMPROVE THE ENDOTHELIAL FUNCTION: A 4-YEAR CLINICAL STUDY

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*Objective:* Obesity is an independent risk factor for atherosclerotic disease. However, weight loss is not always associated with lower cardiovascular outcomes. Our aim was to evaluate the long-term effect of weight on arterial stiffness and endothelial function as independent markers of cardiovascular outcomes in morbidly obese patients who underwent laparoscopic adjustable gastric banding (LAGB) surgery. Subjects: Forty-Eight Caucasian subjects aged between 20 and 69 years, with morbid obesity who underwent LAGB and completed 4 years follow-up.

*Measurements:* Measurements were performed at baseline, 1 year and 4 years after LAGB for body mass index (BMI), waist circumference (WC), arterial blood pressure (ABP), metabolic factors: leptin, adiponectin, glucose, HbA1c, insulin, C-reactive protein (CRP). Endothelial function was evaluated as reactive hyperemic index (RHI). Arterial stiffness was determined by cardio – ankle vascular index (CAVI).

Results: BMI reduced from baseline 46.48±7.06 kg/m2 to  $39.78 \pm 7.36$  kg/m2 (p<0.001) after 1 year and to  $37.29 \pm 7.49$ kg/m2 (p=0.012) at the end point. We also observed WC, glucose, insulin, HbA1c, leptin, CRP values reduction. The significant reduction in ABP was observed only after 4 years comparing with the baseline (166.79±22.13 mmHg vs 161.81±25.46 mmHg, p=0.039). After one year follow up, an increase in mean CAVI values was observed  $(6.58 \pm 1.77 \text{ m/s to } 7.03 \pm 2.00 \text{ m/s, } p=0.014)$ . During all the study period there was no statistical significant improvement on RHI (2.01 $\pm$ 0.54 vs 2.07 $\pm$ 0.51, p= 0.948 vs 2.05±0.42, p=0.086). Correlation between  $\Delta RHI$  and  $\Delta$ diastolic BP (r=0.435, p=0.023),  $\Delta$ adiponectin (r=0.546, p=0.007) was found suggesting link between endothelial function, BP and adiponectin.  $\Delta CAVI$  inversely and significantly correlated with waist circumference (r=-0.493, p<0.001), body weight (r = -0.340, p = 0.021) and BMI (r =-0.323, p = 0.034).

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**Conclusion:** Weight reduction induced by LAGB was associated with significant improvement of metabolic parameters, as well as arterial stiffness but not with the endothelial function. Based on the results there might be an early time window during weight loss when CV risk may increase and if so, more intensive monitoring is needed during this time.

#### PREVALENCE OF PREDIABETES IN PATIENTS WITH LIVER FAILURE BEFORE THE TRANSPLANTATION

#### Ömercan Topaloğlu; İbrahim Şahin

Inonu University Medical Faculty, Department of Endocrinology and Metabolism

**Background:** It is well known about the prevalence of dysglycemia is very common in patients with liver diseases. However, the prevalence of prediabetes among liver transplantation(LT) candidates was not documented very well. Aim It is well known about the prevalence of dysglycemia is very common in patients with liver diseases. However, the prevalence of prediabetes among liver transplantation(LT) candidates was not documented very well. We aimed to investigate the prevalence and possible risk factors related to prediabetes in patients with liver failure before the LT.

*Method:* 101 adult patients waiting LT were included in the study. Data of the patients were analyzed retrospectively. Patients with a history of diabetes and aged less than 18 were excluded were not included in the study. Clinical and demographic features of the patients and preoperative fasting blood glucose (FBG) levels were analyzed.

**Results:** Prediabetes and diabetes were diagnosed in 34 (33.7%) and 6 (5.9%) patients, respectively, as regards to preoperative FBG levels. The prevalence of prediabetes were positively correlated with age but not related to body weight (p=0.001 and p=0.881, respectively. In patients whom LT were indicated for chronic viral hepatitis and other chronic liver diseases had increased mean age compared to acute liver failure (p=0.004). The prevalence of prediabetes and diabetes were lower in the patients with acute liver failure compared to chronic liver failure(p=0.004).

**Discussion:** Prevalence of prediabetes seems to be increased in liver disease. This increase is higher in patients chronic viral hepatitis and other chronic liver diseases. Our results indicate that age is one of the important risk factor for the development of prediabetes.

#### PREPONDERANCE OF INSULIN RESISTANCE SYNDROME IN ADULTS AND OLD AGE HUMAN FROM 5 DISTRICTS IN RAJASTHAN ACCORDING TO ATP III DEFINITION

#### Dr. Nitin Kumar; Dr. Sheekha

Vivekananda Global University; Rajasthan, India

**Background and Aim:** In 2016-17, the Third Report of the National Cholesterol Education Program Adult Treatment Panel (ATP III) prospective a new explanation for insulin resistance syndrome (IRS). The aim of this study was to estimation the ubiquity of IRS in numerous districts in western India in Rajasthan using ATP III fact.

*Material and Methods:* All studies of IRS prevalence in subjects 18 years of age or older, explained by ATP III, were comprised. Research was done up to August 2013 in Internet database. Studies in certain populations (off-spring from diabetics, workers with high physical activity, athletes), and also studies with the same population were prevent (the study with the greater population was chosen). Studies in populations with intense age ranges were also excluded. Certainly, studies from 5 districts were analyzed: Alwar, Dausa, Jaipur, Bharatpur and Karoli.

*Results:* Data of 8492 subjects were temperate. The prevalence of IRS was variable (15.8% - 40.9%). comprehensive prevalence was 30.3% (CI 96%: 14.9 - 27.7; n=67398). The dissemination by sex was very comparable (25.3% [CI: 15.8 - 26.9] and 23.4% [CI: 16.2 - 29.6] in men and in women, appropriately; p>0.07.

*Conclusions:* The vogue of insulin resistance syndrome in the 5 districts conscious was high and variable by ATP III definition. It is essential to determine the comprehensive vogue of this syndrome because it is a dominant trouble of public health.

#### A RANDOMIZED DOUBLE BLIND CONTROLLED TRIAL TO INVESTIGATE THE EFFECTS OF VITAMIN D SUPPLEMENTATION ON MATERNAL AND NEW-BORN BABY'S VITAMIN D STATUS IN ASIAN-INDIAN SUBJECTS

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*Introduction:* High prevalence of vitamin D deficiency (VDD) has been well documented during pregnancy.

Maternal vitamin D status has been linked to maternal and fetal outcomes. It is hypothesized that supplementation of vitamin D during pregnancy may improve these outcomes. We planned a study to investigate the efficacy of vitamin D supplementation, given in early stage of pregnancy, on maternal, fetal and newborn parameters.

Material & Method: This randomized double blind active controlled clinical trial was carried out in pregnant subjects attending antenatal clinic, AIIMS. The inclusion criteria were age between 18-40 years, singleton pregnancy with gestational age between 12-16 weeks. Any subject who had high risk pregnancy, or any systemic disease, or received vitamin D supplementation in doses exceeding 600 IU in last three months, on any medication known to affect metabolism of vitamin D were excluded. Similarly, after screening, any subject with serum vitamin D level (S.VitD) >100 ng/ml or serum calcium more than upper limit of normal were also excluded. Sample size for this study was calculated based on primary outcome of improvement of vitamin D status of mother at the time of delivery. Subjects randomized into four groups in ratio of 1:1:1:1(Group 1 active control group received 600 units of vitamin D per day; Group 2 – 1000 units/day; Group 3 – 2000 units/day; Group 4 - 4000 units per day). All groups received 1000 mg of elemental calcium (in two divided doses), and similar nutritional and lifestyle advice for standard management of pregnancy. Doses of vitamin D were calculated on daily basis but given orally, once a month, supervised in hospital. The primary outcome of the study was changes in vitamin D status of mother and newborn. Secondary outcomes of the study were weight gain during pregnancy, blood pressure, preterm labor, pre-eclampsia, fetal growth, newborn's anthropometry, and insulin resistance in mother as well as in cord blood. Safety of intervention was assessed by regular monitoring of urinary calcium creatinine ration and serum calcium levels.

**Results:** Total 243 subjects completed the study and were analyzed. High prevalence of vitamin D deficiency was seen in study population. Of total 243 subjects, 93.6% of subjects had VDD (S.VitD <20 ng/ml) while 97.5% subjects had S.VitD level <30 ng/ml. No significant difference was seen in S.VitD level among all four groups. Improvement in S.VitD level after supplementation is shown in Table -1. Among cord S.VitD status, 77.8% babies in group 1, 47.1% in group 2, 17.8% in group 3 and 6.2% in group 4 were VDD. Apart from S.VitD level, no significant difference was observed among all four groups in any other maternal, fetal and newborn parameters (maternal wt gain, pre-eclampsia, fetal growth, newborn's anthropometry, and insulin resistance in mother as well as in cord blood).

*Conclusion:* Our study shows that supplementation of vitamin D in mother improves vitamin D status of newborn.

However, vitamin D supplementation during pregnancy did not shown any effect on any other maternal, fetal and newborn parameter. Parameters:

	Group 1	Group 2	Group 3	Group 4
Dose of Vit D	600 IU/Day	1000 IU/Day	2000 IU/Day	4000 IU/Day
Baseline S. Vit D	9.09±5.69	7.51±3.91	10.63±7.67	8.89±7.4 S.
vit D 24-28 wks	11.87±7.79	19.03±6.87	22.38±7.52	30.68±10.67 S
vit D at delivery	11.4±9.95	20.34±8.66	27.45±10.64	37.17±12.4
Cord blood S.vit D	12.49±12.95	22114±9.17	30.67±14.15	41.38±14.71

All values are in ng/ml.

#### **RELATIONSHIPS BETWEEN BODY FAT DEPOTS AND INSULIN SENSITIVITY IN PEOPLE WITH AND WITHOUT TYPE 2 DIABETES**

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Abstract: Obesity is defined by the World Health Organization as a body mass index (BMI)  $\geq 30$  kg/m<sup>2</sup>. However, the occurrence of metabolic complications (e.g., hypertension, dyslipidemia) in obese individuals is highly variable, and numerous studies have shown a relatively weak relationship ( $R^2 = 0.1-0.2$ ) between BMI and insulin sensitivity. It has been suggested that this is due to differences in body fat distribution. The contribution of liver versus muscle to systemic insulin resistance has also been reported to be variable. In the present study, we enrolled overweight and obese individuals with (DM, n=13) and without (ND, n=16) type 2 diabetes. We measured insulin sensitivity with a 2-h oral glucose tolerance test, calculating the insulin sensitivity index (ISI) according to Matsuda. We also quantified regional adipose tissue depots (leg fat [LF], visceral fat [VF] and trunk fat [TF]) and total body fat (TBF) using the combination of dual energy X-ray absorptiometry and single-slice (L2-L3) abdominal CT scans. Results: There was no difference between DM and ND in age (52±2 v 47±3 y), BMI (34±1 v 32±1 kg/ m<sup>2</sup>), TBF (40±2 v 40±3 kg), TF (25±1 v 23±1 kg), or LF  $(10\pm1 \text{ v } 11\pm1 \text{ kg})$ , all p=NS. However, the DM group had greater VF (328±18 v 230±22 cm<sup>3</sup>, p<0.005) and borderline lower ISI (2.0±0.3 v 2.9±0.3, p=0.06). In DM, ISI did not correlate with TBF, TF or VF, but there was a borderline correlation between ISI and LF (R=0.53, p=0.06) and a strong negative correlation between ISI and the VF:LF ratio (R=-0.75, p=0.003). In ND, there was no correlation between ISI and VF, LF or VF/LF ratio, but a negative correlation between ISI and both TF (R=-0.64, p<0.01) and TBF (R=-0.51, p=0.04). These results indicate that in DM, lower body fat is positively associated with insulin sensitivity, and that the relative size of the VF depot in relation to lower body fat may be an important predictor of insulin resistance. In contrast, in ND individuals it appears that subcutaneous fat (but not VF) is most closely associated with insulin resistance. These differences may be due to differences in the regulation of regional lipolysis between groups. Whether these findings relate to discordance between hepatic and skeletal muscle insulin sensitivity will require further investigation.

#### NOVEL STRATEGIES FOR IMPROVING ADHERENCE IN T2D: EFFECT OF LIVE CME AT IMPROVING PHYSICIAN KNOWLEDGE AND CONFIDENCE

#### Amy T. Larkin, PharmD; Michael LaCouture; Teresa Marshall; Anne Le, PharmD

#### Medscape Education

**Background:** About half of patients with type 2 diabetes (T2D) fail to achieve adequate glycemic control, putting them at risk for microvascular and macrovascular complications.[NCQA 2015] Medication nonadherence is also highly prevalent among patients with T2D, leading to increased morbidity and mortality.[Cooke 2010; Frois 2014] We sought to assess the knowledge baseline of endocrinologists and the effect of a highly interactive, live continuing medical education (CME) satellite symposia on the clinical knowledge of diabetologists/endocrinologists (D/Es) regarding novel strategies for improving adherence in patients with T2D.

Methods: A live, interactive satellite symposium including a panel discussion was held at the American Diabetes Association (ADA) 2017 Scientific Sessions titled, Novel Approaches to Improving Adherence in T2D. We assessed the effects of education using a repeated pairs pre-/postassessment study design. During the symposium, participants were given iPads to use for answering pre/post questions, case-based questions, and other polling questions throughout the symposium, as well as completing the postactivity evaluation. Prior to utilizing the iPads, participants had to enter a valid email address, which allowed them to be included in this outcomes study. The assessment instrument collected responses to knowledge- and confidencebased questions. Pearson's chi-squared test assessed if the mean post- assessment score differed from the mean pre- assessment score. P values are shown as a measure of significance; P values <.05 are statistically significant. The activity was presented on June 10, 2017, and data collection continued until the end of the symposium. The activity was posted online as an enduring June 26, 2017, and can be found at http://www.medscape.org/viewarticle/880922.

**Results:** Significant overall improvements were seen for all questions (baseline vs post-assessment), including: Identification of adherence as the biggest barrier to GLP-1 receptor agonist efficacy in the real world [36% (N=224) vs 65% (N=128); P <.001]; Accurately describing the safety of ITCA 650 to that of available GLP-1 receptor agonists [47% (N=211) vs 65% (N=119P=.002]; Correctly identifying a doubling of A1c with ITCA 650 compared with sitagliptin [45% (N=211) vs 71% (N=117); P <.001]; Compared with baseline, 16% more participants would be "very likely" to consider using an implantable GLP-1 receptor agonist continuous delivery device in their patients who struggle with adherence (N = 225/127, P = 0.003); Continued educational gaps identified by low post-assessment knowledge/competence: 35% of participants still failed to recognize adherence as the biggest barrier to achieving GLP-1 receptor agonist efficacy in the real world; 35% of participants still failed to identify the safety of ITCA 650 compared to currently available GLP-1 receptor agonists; 29% of participants still failed to recognize improved efficacy of ITCA 650 over sitagliptin.

*Conclusion:* This study demonstrates the success of this live interactive satellite symposium with panel discussion on improving knowledge of novel strategies for improving adherence in patients with T2D. Additional education is needed in this area to further improve knowledge, followed by assessments of and activities directed at improving competence for improving adherence in T2D patients. Sources of support: Developed through independent educational grants from Intarcia Therapeutics, Inc.

## **CVOT UPDATES: HOW KNOWLEDGEABLE ARE PHYSICIANS?**

Amy T. Larkin, PharmD; Colleen S. Healy, MA; Teresa Marshall; Anne Le, PharmD

Medscape Education

*Background:* 52% of patients are not meeting recommended A1c targets of <7% .[Ali 2013; Stark Casagrande 2013] and are at heightened risk for heart attack, stroke, and microvascular complications.[CDC 2014] Furthermore, cardiovascular (CV) disease is the major cause of morbidity and mortality for patients with diabetes, as common coexisting conditions increase CV risk.[ADA 2015; Go 2013; Halter 2014] However, clinicians show limited knowledge of combinations of agents with complementary MOAs and poor awareness of recent clinical trial data that may influence patient care.[Berlie 2012] We sought to assess the knowledge baseline and the effect of a live continuing medical education (CME) satellite symposia on the clinical knowledge and confidence of diabetologists/endocrinologists (D/E) regarding CVOT data for T2D agents and combination therapy for T2D management.

Methods: A live, interactive satellite symposium including a panel discussion was held at the American Diabetes Association (ADA) 2017 Scientific Sessions titled, Individualized T2D Plans in the Midst of CVOTs Galore: Applying the Data in a Practical Sense. We assessed the effects of education using a repeated pre-/post-assessment study design. During the symposium, participants were given iPads to use for answering pre/post questions, as well as completing the post-activity evaluation. Prior to utilizing the iPads, participants had to enter a valid email address, which allowed them to be included in this outcomes study. The assessment instrument collected responses to knowledge- and confidence-based questions. Pearson's chi-squared test assessed if the mean post- assessment score differed from the mean pre- assessment score. P values are shown as a measure of significance; P values <.05 are statistically significant. The activity was presented on June 9, 2017, and data collection continued until the end of the symposium.

Results: Significant overall improvements were seen for all questions, including: Compared with baseline, there was a 30% increase in participants who reported being "very confident" applying CVOT data to practice (N = 294/174, P <.001); At baseline, 46% (N=296) of participants correctly identified that CVD-REAL showed a significant decrease in hospitalization for heart failure regardless of CVD status with SGLT2 inhibitors use, increasing to 59% (N=154) at post-assessment (P = .008); Compared with baseline, there was a 35% increase in participants being "very confident" using fixed-dose combination therapy in patients with T2D (N = 289/161, P <.001). Continued educational gaps identified by low post-assessment knowledge/competence: 41% of participants still chose an incorrect outcomes form CVD-REAL, signifying additional education on this trial results, as well as guidance on clinical application.

*Conclusion:* This study demonstrates the success of a live, interactive satellite symposium with panel discussion on improving knowledge and confidence in applying CVOT data to practice and utilizing combination therapy in patients with T2D. Additional education is needed regarding CVOT data to improve and then reinforce knowledge related to CVOT data and its impact on practice. Sources of support: Developed through independent educational grants AstraZeneca.

#### APPLYING CVOT DATA TO PRACTICE: EFFECT OF LIVE CME AT IMPROVING PHYSICIAN KNOWLEDGE AND CONFIDENCE

#### Amy T. Larkin, PharmD; Jess Dropkin; Anne Le, PharmD

#### Medscape Education

**Background:** Cardiovascular disease (CVD) is the major cause of morbidity and mortality for patients with diabetes. [ADA 2015] Given the heightened CV risk associated with diabetes, ideal therapies would both reduce CV complications and facilitate the achievement of euglycemia. [Menon 2014] Data from CV outcomes trials (CVOTs) have been released in recent years, and continue to emerge. We sought to assess the baseline knowledge and the effect of a live continuing medical education (CME) satellite symposium on the clinical knowledge and confidence of diabetologists/endocrinologists (D/E) and primary care physicians (PCPs) regarding application of CVOT data.

Methods: A live case-based, interactive satellite symposium, "Individualized T2D Plans in the Midst of CVOTs Galore: Applying the Data in a Practical Sense," was presented at the American Diabetes Association (ADA) 2017 Scientific Sessions. We assessed the effects of the symposium education using a pre-/post-assessment study design. During the symposium, participants were given iPads to use for answering pre/post questions, as well as completing the post-activity evaluation. The pre-/post-assessment instrument included both knowledge- and confidence-based questions. Pearson's chi-squared test assessed whether the mean post- assessment score differed from the mean pre- assessment score. P values are shown as a measure of significance; P values <.05 are considered statistically significant. The activity and data collection occurred June 10, 2017. The activity was posted online June 26, 2017 at http://www.medscape.org/viewarticle/881977.

Results: In total, 307 clinicians attended the symposium. Significant overall improvements were seen in all but one area: 18% increase in participants (N = 299) being "very familiar" and "somewhat familiar" with CVOT data published in the past 2 years on the newer antihyperglycemic agents (P = 0.004), Additionally, 10% fewer participants reported being "not familiar" with this CVOT data (P = 0.007); At baseline, 60% (N=169) of participants correctly identified the EMPA-REG 14% reduction in primary MACE end point, increasing to 70% (N=110) at post-assessment (P=0.101); 25% increase in participants being "confident" or "very confident" applying recent CVOT data in treatment of their patients with T2D and CVD or at elevated risk for CVD (N = 180/110, P < 0.001), Additionally, 14% fewer participants reported being "not confident" applying CVOT data to practice (P < 0.001). Ongoing educational gaps identified by low post-assessment knowledge/competence levels include: 34% of participants still reported being only familiar or less than familiar with recent CVOT data, demonstrating a need to reinforce this information in this audience; 30% of participants still failed to identify primary outcomes of EMPA-REG compared to other recent CVOT results; 30% of participants reported being only confident or less than confident applying CVOT data, demonstrating a need for additional education on clinical application in a case-based format.

**Conclusion:** This study demonstrates the success of a case-based, interactive live satellite symposium on improving knowledge and confidence in clinical application of CVOT data in patients with T2D. Additional education is needed in this area to further improve knowledge, reinforce knowledge, and further improve confidence applying data to practice. Sources of support: Independent educational grants from Boehringer Ingelheim and Lilly Diabetes Alliance.

#### THE RELATIONSHIP BETWEEN INSULIN AND LEVELS OF LIVER ENZYMES IN PATIENTS WITH METABOLIC SYNDROME

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**Objective:** Therefore; the aim of the study was to evaluate the relationships between insulin and levels of four liver enzymes such as aspartate aminotransferase (AST), alanine transferase (ALT)), gamma glutamyl transpeptidase (GGT) and alkaline phosphatase (ALP) in patients with metabolic syndrome (MS).

*Methods:* One hundred patients had MS and 100 patients without MS as control were included in the study. Metabolic syndrome was diagnosed according to the National Cholesterol Education Program Adult Treatment Panel III criteria.

**Results:** The mean age of patients had MS was  $59.0\pm6.0$  years (age range of 20-80 years). And also, it was found to be  $51.9\pm7.0$  years (age range of 20-80 years) in control. 69 of the 100 patients had MS (69%) showed 1 to more abnormal liver enzymes. The levels of the 4 liver enzymes were all higher in the group with MS than in the group without MS (all P < 0.05). With the increase of the number of elevated MS components the serum levels of ALT, AST, and GGT were elevated accordingly. Mean levels of HOMA were found to be  $3.4\pm0.3$  and  $2.0\pm0.8$  in patients with MS and without MS, respectively. Multivariate regression analysis showed that, among the above-mentioned variables, only HOMA-IR and was independently correlated with both ALT and GGT.

*Conclusion:* Most patients with MS have abnormal liver enzymes. And also, the percentage of high ALT and GGT in patients with insulin resistance. Key words: liver enzyme, metabolic syndrome

#### EICOSAPENTAENOIC ACID INHIBITS HIGH DENSITY LIPOPROTEIN (HDL) OXIDATION IN VITRO AS COMPARED TO DOCOSAHEXAENOIC ACID

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**Background:** The omega-3 fatty acid eicosapentaenoic acid (EPA) reduces oxidation of ApoB-containing particles in vitro and in patients with hypertriglyceridemia. EPA may produce these effects through an antioxidant mechanism, which may facilitate LDL clearance and reduce endothelial dysfunction. We hypothesize that EPA antioxidant effects may extend to HDL, potentially preserving certain atheroprotective functions.

*Methods:* HDL was isolated from human plasma, separated into test samples of 200  $\mu$ g/mL, and incubated at 37°C in the absence (vehicle) or presence of EPA and/or DHA; 5.0 or 10.0  $\mu$ M each. Samples were then subjected to copper-induced oxidation (10  $\mu$ M).

**Results:** HDL oxidation (MDA formation) was inhibited similarly by EPA and DHA up to 1h. EPA (10  $\mu$ M) maintained significant HDL oxidation inhibition of 89% (0.622  $\pm$  0.066  $\mu$ M; *p*<0.001) at 4h, with continued inhibition of 64% at 14h, vs. vehicle (5.65  $\pm$  0.06 to 2.01  $\pm$  0.10  $\mu$ M; *p*<0.001). Conversely, DHA antioxidant benefit was lost by 4h. At a lower concentration (5  $\mu$ M), EPA antioxidant activity remained at 81% (5.53  $\pm$  0.15 to 1.03  $\pm$  0.10  $\mu$ M; *p*<0.001) at 6h, while DHA lost all antioxidant activity by 4h. The antioxidant activity of EPA was preserved when combined with an equimolar concentration of DHA.

*Conclusion:* EPA pretreatment prevented HDL oxidation in a dose-dependent manner that was preserved over time, while DHA activity was quickly lost. These results suggest unique lipophilic and electron stabilization properties for EPA with respect to inhibition of HDL oxidation. These antioxidant effects of EPA may enhance atheroprotective functions for HDL.



**Figure 1.** Separate effects of EPA or DHA at 5  $\mu$ M and 10  $\mu$ M on copper-induced oxidation of human HDL through 14 hours and combined effects of EPA/DHA 5/5  $\mu$ M through 6 hours.

#### CIRCULATING LEVELS OF ADIPOKINES AND miR-21 ARE ASSOCIATED WITH BIRTH WEIGHT IN MEXICAN ADOLESCENTS

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**Background:** The microRNA miR-21 is involved in numerous pathophysiological processes, including development, cancer, inflammation and cardiovascular diseases. Recent studies supported its important role on obesity development. The aim of this study was to assess the association of circulating miR-21 and adipokines with birth weight in obese Mexican adolescents.

*Methods:* 108 subjects between 10 to 16 years were included. The adolescents were grouped according to their body mass index (BMI) and birth weight (BW): eutrophic subjects with normal weight and normal birth weight (E-NBW, n=39), obese subjects with normal birth weight (O-NBW, n=32), with lower birth weight (O-LBW, n=12), and with high birth weight (O-HBW, n=25). A blood sample was taken for standard biochemical analysis. The levels of insulin, adiponectin and leptin were measured by ELISA and miR-21 was evaluated by RT-qPCR.

**Results:** The obese adolescents showed significant higher levels of leptin compared with eutrophic subjects, and the highest levels of leptin was observed in the subjects O-LBW. Meanwhile, the subjects O-LBW and O-HBW demonstrated higher levels of insulin compared with subjects E-NBW. The circulating levels of miR-21 were significantly increased in the subjects O-NBW compared with the subjects O-HBW and the subjects E-NBW (O-NBW: 7.7 X10-3± 9 X10-3, O-HBW: 3.4X10-3± 2.1 X10-3, E-NBW: 2.2X10-3± 1.3 X10-3, respectively, p=0.05).

*Conclusions:* Our present study showed different circulating levels of miR-21 and adipokines in adolescents with different birth weight, indicating their possible epigenetic modifications in the development of adolescence obesity.

#### EVALUATION OF PERFORMANCE OF THE ASSURE® LANCE LOW FLOW 25G AND MICRO FLOW 28G SAFETY LANCETS FOR PAIN PERCEPTION, BLOOD VOLUME, AND EASE OF USE

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ARKRAY USA

**Background:** Single use safety lancets reduce the risk for needle stick injuries. Their primary use is in the institutional settings for residents with diabetes requiring capillary fingerstick blood glucose measurements. Purpose: This study was conducted to evaluate the performance of the Assure® Lance 25G Low Flow and 28G Micro Flow Safety Lancets with respect to pain perception, blood volume, and ease of use.

*Method:* Ten laboratory professionals used the 25G and 28G Safety Lancets to collect and measure capillary samples from 25 subjects. The subject's perceived pain was recorded on a scale 0 (no pain) to 10 (intense pain). An ease of use questionnaire (7 questions) was completed by the laboratory professionals using a scale of 1 (excellent) to 5 (poor).

**Results:** The 25G Safety Lancet provided an average pain rating of 1.8 (range 1 - 4) and the 28G an average of 0.9 (range 0 - 4). Since the two lancets are exactly the same size and shape, they were rated as one entity for usability on a scale from 1 to 5. The 10 laboratory professionals gave the Safety Lancets an average usability rating by property of 1.7 (range 1.5 - 2.0).

*Conclusion:* Overall, the 25G and 28G Assure® Safety Lancets demonstrated low perceived pain with the average pain rating significantly less for the thinner 28G Safety

Lancet (0.9 vs. 1.8). Both Safety Lancets provided an adequate blood volume (100% of the time). The laboratory professionals reported that both Assure Lance Safety Lancets were easy to use.

#### 24 HOURS CHRONOMICS OF AMBULATORY BLOOD PRESSURE MONITORING IN ROTATING NIGHT SHIFT NURSING PROFESSIONALS AND ITS RELATION WITH SALIVARY CORTISOL & 6- SULFATOXY MELATONIN LEVELS: A CASE CONTROL STUDY

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Abstract: The present study was aimed to investigate effect of night shift on 24 hours chronomics of BP/HR in terms of Double amplitude, Acrophase and Hyperbaric index and its relation with circadian rhythm of salivary cortisol and 6-sulfatoxy melatonin in night shift nurses and actual day workers. 56 night shift nurses, aged 20-40 years, performing day and night shift duties were recruited from the Trauma Center, KGMU, India, and 56 age sex matched actual day workers were also enrolled as controls. BP and HR were recorded by ABPM at every 30 min intervals in day time and each hour in night time during shift duties. Highly significant difference was found in double amplitude (2DA) of among between night (23.10  $\pm$  14.68) and day shift  $(34.27 \pm 16.44)$  (p < 0.0005). In night shift, hyperbaric index (HBI) of mean SBP was found to be increased at 00-03 am (midnight) while during day shift, peak was found at 06-09 am. HBI of mean HR was found to be increased at 18-21 pm during night shift while in controls, peak was found at 09-12 & again 15-18 pm of SBP, DBP & HR. Alterations in Acrophase of BP/HR were very common among night shift workers and Ecphasia was found in few nights shift workers. Difference was found in night cortisol levels among night  $(4.08 \pm 3.28)$  vs day shift (2.62) $\pm 2.37$ ), while in comparison to night shift or day shift with controls  $(1.82 \pm 1.18)$  these difference was significant (p < 0.05). Alteration in mean morning melatonin level was also found during night shift. Reverse pattern of Acrophase and HBI of BP & HR along with salivary cortisol during night shift represents desynchronization. It indicates that the circadian rhythm was disrupted during night shift and recovery occurs during day shift.

#### TO STUDY OF INDUCIBLE NITRIC OXIDE SYNTHASE MUTANT AND ENDOTHELIAL DYSFUNCTION ALONG WITH PRO-INFLAMMATORY MARKERS IN CORONARY ARTERY DISEASE

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#### Delhi University Faculty of Medical Sciences

**Objective:** The prevalence of coronary artery disease (CAD) in North Indian population varies from 7 to 10%. Patho-physiological processes in coronary artery disease are influenced by genetic factors. Vascular function and endothelial derived factors are affected by pro-inflammatory cytokines which leads to the activation of Inducible nitric oxide synthase (iNOS) during inflammation. The aim of this study was to look for a relationship between the C150T polymorphisms of the iNOS and endothelin dysfunction in Coronary Artery Disease (CAD) and correlation with pro-inflammatory markers.

*Methodology:* 150 Angiographically confirmed coronary artery disease patients attending the cardiac clinic of G B Pant hospital, New Delhi and 90 healthy people with no known risk factors for CAD were enrolled in this case-control study. Blood samples were collected and analyzed for nitric oxide (Methew et al), endothelin-1, inflammatory markers (by Elisa), iNOS (C150T) gene polymorphism (by PCR RFLP).

**Results:** Patients with CAD had increased levels of, IL-2, IL-6, and TNF- $\alpha$ , endothelin-1 and decreased level of nitric oxide as compared with healthy people (p<0.0001). Significant positive correlation was seen between endothelin-1 and cytokines levels and negative correlation was found between NO and cytokines levels CAD patient (p<0.001). C150T iNOS genotype distributions in patients with CAD (C 150 T: CC: 87.3%, CT: 12.6%, TT: 0%) was found to be significantly different from those in patients without CAD (C 150 T: CC: 96.6 %, CT: 3.3 %, TT : 0%). Significant differences were found in genotype/allele (C150T) distribution between two groups.

*Conclusion:* Raised levels of pro-inflammatory markers may have a role in the development of coronary heart disease. A larger group studies are required to establish the link of these markers with the disease. Endothelial dysfunction is characteristic features of coronary artery disease and the iNOS C150T polymorphism may contribute by affecting NO levels.

#### FIXED-RATIO COMBINATIONS FOR T2D MANAGEMENT: IMPROVING CLINICAL KNOWLEDGE, COMPETENCE, AND CONFIFDENCE OF CDES VIA LIVE, INTERACTIVE EDUCATION

#### Amy T. Larkin, PharmD; Michael LaCouture; Teresa S. Marshall; Anne Le, PharmD

#### Medscape Education

**Background:** As the number of available and emerging therapies to treat type 2 diabetes (T2D) increases, the role of Certified Diabetes Educators (CDEs) in caring for patients with T2D continues to expand. We sought to assess the effect of a live, certified continuing education satellite symposia on the clinical knowledge, competence, and confidence of CDEs regarding new GLP-1 receptor agonist and basal insulin fixed-ratio combination (FRC) strategies for improving adherence in patients with T2D.

*Methods:* A highly interactive satellite symposium – Strategies to Improve Adherence to Insulin FRC In T2D Patients: Are You Up to Speed? – that included a panel discussion and iPads for interactivity was held at the American Association for Diabetes Educators (AADE) 2017 Annual Meeting. We assessed the effects of that education using a repeated pairs baseline/post-assessment study design, consisting of knowledge-, competence-, and confidence-based questions. Pearson's chi-squared test assessed the extent of any difference between the mean post-assessment score and the mean baseline score. P values were calculated as a measure of significance; P values <.05 being statistically significant. The data were collected throughout the symposium held on August 6, 2017.

Results: Overall improvements from baseline to postassessment were seen for all questions, including: Identification of FRC therapy efficacy compared to individual components [44% (N=264) vs 72% (N=259); P <.001] • Accurate selection of clinical use of GLP-1 receptor agonist and basal insulin FRC products [53% (N=290) vs 82% (N=267); P <.001] • Correct clinical management of a patient with a FRC therapy [90% (N=281) vs 99% (N=276); P <.001] • Compared with baseline, in a Likertstyle question, 56% more participants self-selected the top 2 tiers of confidence ("confident" and "very confident") in their use of injectable FRC products in their patients with T2D (N = 326/281, P < .001) An ongoing educational gap identified by low post-assessment knowledge/competence was: • 28% of participants still failed to recognize the efficacy of FRC products compared to their individual components

*Conclusion:* This study demonstrates the success of this live, highly interactive panel discussion satellite symposium at improving knowledge, competence, and confidence of CDEs related to new FRC product use in practice to improve adherence.

#### AWARENESS AND PRACTICE OF DIABETIC FOOT CARE AMONG DIABETIC PATIENTS ATTENDING TO FAMILY MEDICINE DEPARTMENT IN PMMH

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King Khalid University

*Aim of the study:* The current research aimed at identifying deficits at diabetic patients practice and awareness regarding their foot care.

*Methodology:* A descriptive cross sectional survey design was conducted including 207 diabetic patients attended the PMMH during the period between November 2016 and April 2017 in PMMH, Taif, Saudi Arabia. A self-administered questionnaire was used for data collection and then data was analysed using SPSS version 22.

**Results:** The study was conducted on 207 diabetic patients who completed the questionnaire with age ranged from 20-75 years and 57.5% were females. All of the included patients complained of one or more foot problems such as feeling of heaviness, tightness pain or numbness. Generally 30% of the patients did healthy practices and 19.8% of the patients had satisfactory level of awareness regarding their foot care. Patients who have no familiar couple (unmarried) were more aware and recorded better practice than others.

**Conclusions and Recommendations:** The current survey covers that despite the variety at duration of diabetes among the studied patients as more than half of the patients with diabetes for more than 10 years and all of them have one or more foot problems but they recorded very poor practice and awareness regarding foot care. Health education sessions and posters and may be educational videos are required to improve patients practice and awareness.

#### FULL CIRCLE: DIABETIC KETOACIDOSIS, HYPERTRIGLYCERIDEMIA AND ACUTE PANCREATITIS: A CASE REPORT

#### Pamela Ann T. Aribon, M.D., Patricia D. Maningat M.D.

St. Luke's Medical Center - Global City

*Abstract:* The triad of Diabetic Ketoacidosis, Hypertriglyceridemia and Acute Pancreatitis is a rare occurrence and literatures are limited.

Case Report: A previously healthy, 33-year-old male, presented at the emergency department with epigastric pain and restlessness. Biochemical markers showed the presence of hyperglycemia (483 mg/dL), ketonemia (40 mg/dL, 2+), metabolic acidosis with an arterial blood gas pH of 7.09, bicarbonate of 5.2 and a high anion gap of 24, diagnostic of Diabetic Ketoacidosis. On further work up, triglyceride was severely elevated at 3,220 mg/d, amylase (439U/L) and lipase (5,803 U/L) were elevated as well, leading to the suspicion of acute pancreatitis. An abdominal CT scan was done confirming the diagnosis. Patient was admitted at the Intensive care unit and was successfully treated with insulin therapy, aggressive, careful hydration and supportive management. HemoglobinA1c was 14.6 indicating that the patient may have chronic diabetes mellitus. Islet cell antibody, anti-GAD (glutamic acid decarboxylase) was done which was low at 0.37 U/ml excluding the possibility of type 1 diabetes mellitus. Insulin resistance leads to decreased glucose uptake, increase glucose production and increase lipolysis causing hyperglycemia. Increase lipolysis can lead to ketosis, hyperglycemia and hypertriglyceridemia, which eventually leads to diabetic ketoacidosis. Severely elevated triglyceride levels can lead to acute pancreatitis which may aggravate and complicate the clinical course of patients with DKA.

*Conclusion:* This case illustrates that Diabetic Ketoacidosis, Hypertriglyceridemia and Acute Pancreatitis can co-exist and that prompt recognition is warranted to screen patients for severe hypertriglyceridemia induced acute pancreatitis in patients with Diabetic Ketoacidosis.

#### ASSOCIATION OF ATHEROGENIC INDEX OF PLASMA (AIP) WITH NON-LIPID PARAMETERS, AND INFLUENCE OF SREBP-SCAP PATHWAY GENETIC POLYMORPHISMS ON AIP REDUCTION BY ROSUVASTATIN THERAPY IN SAUDI METABOLIC SYNDROME PATIENTS

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Background: Metabolic Syndrome is an assemblage of risk factors and metabolic irregularities comprising of dyslipidemia, increased blood pressure, deranged plasma glucose or insulin resistance, chronic inflammatory and hypercoagulable state with an increased risk of diabetes and cardiovascular events. The atherogenic dyslipidemia of metabolic syndrome predispose to atherosclerotic vascular disease and the Atherogenic Index of Plasma (AIP) is an important predictive marker. Statins are first-line medications for treating dyslipidemia. Therapeutic response to statins is highly variable and genetic factors play an important role. SREBP-SCAP pathway is a vital regulator of cholesterol homeostasis and polymorphisms in this pathway have influenced therapeutic response of rosuvastatin in our previous studies. Objective: To evaluate the association of Atherogenic Index of Plasma (AIP) with non-lipid parameters, and investigate the effects of SNPs (rs12487736, rs192087293, rs2228314) in SREBP-SCAP pathway on AIP reduction with rosuvastatin therapy in Saudi metabolic syndrome patients.

**Methodology:** Metabolic syndrome patients (n=153) of either sex, according to modified NCEP-ATP III criteria were administered standardized diet and rosuvastatin 10 mg OD for 24 weeks. Lipids and other associated non-lipid parameters were measured before and after treatment and AIP score calculated. Genotyping was performed by pyrosequencing. Statistical analysis was done by spss.ver.19

**Results:** 142 patients completed the study. Overall, the pretreatment AIP scores were  $0.277\pm0.122$  ( $0.206\pm0.088$  for females and  $0.318\pm0.120$  for males, p=0.001), there was no significant association of AIP scores with age, genotype and blood pressure while the associations with gender (p=0.001), BMI (p=0.04), Waist-Hip ratio (p=0.01), and Fasting Blood Sugar (p=0.005) were significant. AIP scores categorized into high and low risk depicted that males are 4 times more likely to be in high risk (>0.21) category (OR=4, CI=1.38-11.55, p=0.01) than females. The overall mean percentage change in AIP scores was -49.79±40.45, but the difference between two genders or among various genotype groups was not significant. Likewise, the reduction in absolute AIP scores was highly significant after rosuvastatin therapy (Z= -7.059, p=0.001), however, there was no significant difference between various genotype groups in contrast to our previous reports which showed a large and significant effect of SCAP (GG), SREBP-1a (GG) and SREBP-1a (-delG) genotypes on total cholesterol reduction. Generalized linear model showed no significant effect of any fixed factors (gender, genotypes) and covariates (age, BMI, WHR, FBS and BP), and any interaction of variables, on mean percentage reduction of AIP scores by rosuvastatin therapy. The SCAP (G/G, A/G, and A/A), SREBP-1a (G/G, -del/G and –del/del) and SREBP-2 (G/G, C/G and C/C) genotypes distribution were not in Hardy Weinberg Equilibrium.

*Conclusion:* Significant reduction of AIP with rosuvastatin was observed without any effect of studied SNPs and other non-lipid parameters. Nevertheless; male gender, obesity, and fasting blood sugar were significantly associated with AIP. This paper contains the results and findings of a research project that is funded by king Abdulaziz city for science and technology (KACST) (Grant no. ARP-34-129)

#### IMPACT OF WEIGHT LOSS ON INSULIN RESISTANCE AND METABOLIC PARAMETERS IN OBESE PATIENTS

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**Objectives:** Insulin resistance is abnormal biological response to endogenous or exogenous insulin. This study aims to evaluate the changes in metabolic parameters and insulin resistance after a -at least 5%-of weight loss in obese patients.

*Material and Method:* 50 patients admitted to Istanbul Training and Research Hospital Obesity Outpatient Clinic and achieved 5% or more weight loss and didn't have diabetes or were not on insulin sensitizing or antiobesity drugs, were included in the study. Body mass index (BMI), fasting blood glucose (FBG), triglyceride (TG), high density lipoprotein (HDL) and fasting insulin levels were measured and insulin resistance was calculated with the formula of HOMA-IR (homeostatic model assessment-insulin resistance) at baseline and after at least 5% of weight loss and metabolic improvement was evaluated.

**Results:** 86% (43 patients) of patients were female and 14% (7 patients) of patients were male. Mean BMI, FBG, TG, HDL, fasting insulin and HOMA-IR levels showed improvement at different levels after at least 5% of weight loss compared to baseline values (Table 1). While 36% (18 patients) of patients had metabolic syndrome before weight

loss, the percentage decreased to 18% (9 patients) after at least 5% of weight loss. Table 1: Parameters Searched Mean values before at least 5% of weight loss Mean values after at least 5% of weight loss BMI (kg/m2) 40.57  $\pm$  4.05 36.66  $\pm$  4.35 FBG (mg/dl) 92.70  $\pm$  17.70 91.80  $\pm$  13.00 Fasting insulin(uU/ml) 17.80  $\pm$  5.98 14.73  $\pm$  3.93 TG (mg/dl) 140.50  $\pm$  73.41 115.80  $\pm$  41.13 HDL(mg/dl) 53.40  $\pm$  10.81 56.20  $\pm$  12.66 HOMA-IR 4.25  $\pm$  1.48 3.05  $\pm$  0.53 [(Body mass index (BMI), fasting blood glucose (FBG), triglyceride (TG), high density lipoprotein (HDL), HOMA-IR (homeostatic model assessment-insulin resistance)].

*Discussion:* Insulin resistance is associated with, type 2 diabetes, obesity, metabolic syndrome, hypertension, hyperlipidemia, coronary heart disease and polycystic ovary syndrome. Improvement in insulin sensitivity in obese patients, will decrease the morbidity and mortality of related diseases, contribute to public health and decrease health costs.

#### INSULIN RESISTANCE AND CARDIOMETABOLIC RISK IN OBESE MEXICAN ADOLESCENTS

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**Background and aims:** Early metabolic alterations are present in obese adolescents, insulin resistance (IR) and increased oxidative stress (OS) both seem to be prominent features in the cardiometabolic risk associated with obesity (1, 2). The Mexican population is particularly susceptible to develop metabolic alterations related to increased body fat (3). Biomarkers for obesity-related cardiovascular outcomes are limited in obese Mexican adolescents. The aim of the present study was to assess the association between IR, inflammation and oxidative stress in obese Mexican adolescents.

*Methods:* 83 Mexican adolescents were recruited and grouped according to HOMA-IR and BMI. Anthropometric, biochemical, and metabolic variables (interleukin-6 (IL-6), total human adiponectin), were determined. Chi square and t test were used for data analysis.

**Results:** Obesity, dyslipidemia, IL-6 and CRP were significantly higher in the IR group than in the non-IR group. Obese adolescents showed increased insulin levels, HOMA-IR, inflammatory markers, and triglycerides; while having lower HDL-C, and adiponectin when compared to normal-weight adolescents. Anthropometric markers of Obesity positively correlated with IR and inflammatory markers while negatively correlating with adiponectin levels. These findings emphasize the relevance of infantile obesity as a risk factor of insulin resistance and subsequent metabolic alterations underlying cardiovascular disease in obese children.

Conclusion: Early IR, subclinical inflammation, dyslipidemia and hypoadiponectinemia, characterizes obesity in Mexican adolescents. These factors may predispose future coronary heart disease and diabetes mellitus development in early adulthood. Refereces: 1. Sinaiko AR, Steinberger J, Moran A, Prineas RJ, Vessby B, Basu S, Tracy R, Jacobs DR Jr. Relation of body mass index and insulin resistance to cardiovascular risk factors, inflammatory factors, and oxidative stress during adolescence. Circulation. 2005; 111:1985-1991. 2. Reaven GM. Role of insulin resistance in human disease. Diabetes 1988; 37:1595-1607. (doi:10.2337/diab.37.12.1595). 3. Breslin WL, Johnston CA, Strohacker K, Carpenter KC, Davidson TR, Moreno JP, Foreyt JP, and McFarlin BK. Obese Mexican American Children Have Elevated MCP-1, TNF-a, Monocyte Concentration, and Dyslipidemia. Pediatrics 2012; 129:e1180-e1186.

#### COULD WE PREDICT THE DEVELOPMENT OF GLYCEMIC DYSREGULATION AFTER LIVER TRANSPLANTATION?

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Inonu University Medical Faculty

*Introduction:* "New Onset Diabetes After Transplantation" (NODAT) and prediabetes are important factors contributing to cardiovascular complications, infections, morbidity and mortality in transplant patients. Besides Liver Transplantation(LT), NODAT may also be determined in kidney, lung and bone marrow transplantation. We aimed to identify the possible risk factors for the development of NODAT and prediabetes in LT patients.

*Methods:* Adult patients underwent to LT between May 2014-May 2015 in our hospital were included in our study. The data were achieved by electronic files. The patients who were already known as diabetic or whose preoperative glucose levels were above the upper limits of normal were excluded. Sociodemographic features, preoperative and

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postoperative fasting blood glucose(FBG) levels, postoperative complications and infections were analyzed.

Results: NODAT was determined in 40 of total 81 patients (49.3%) according to the postoperative 4th week FBG levels. In all age groups, postoperative 1st day, 1st and 4th week mean FBG were found to be higher than preoperative mean FBG(p<0.001); moreover, postoperative mean FBG elevation continued in 3rd,6th and 12th months in group of 40-64 years-old (p<0.001). Significant postoperative mean FBG elevation comparing to preoperative levels continued in all follow-up visits in both genders(p<0.001). In all groups of body mass index(BMI), postoperative FBG elevation was significant on the 1st day, and in the 1st and 4th month (p<0.001); however, this elevation continued to the 3rd month in the group of BMI 25-30kg/m2(p<0.05), to 6th month in the group of BMI>30kg/m2(p<0.05). Postoperative FBG elevation continued to 6th month in patients undergoing LT due to acute liver failure or other causes (Budd-Chiari, autoimmune hepatitis, criptogenic cirrhosis)(p<0.05), to 12th month in patients undergoing LT due to viral hepatitis. Postoperative FBG elevation continued to 1st month in patients using tacrolimus in addition to corticosteroid and trimethoprim-sulfamethoxazole, however, FBG elevation continued to 12th month in patients using everolimus. The presence of infections according to blood culture results did not cause any differences according to the development of dysglycemia. In patients complicated with postoperative bilioma and/or thrombosis, mean FBG was elevated in all follow-up visits, however, in uncomplicated patients, FBG was found to be higher in only 1st day, 1st and 4th week, and 3rd month.

*Discussion:* We showed that the risk of glycemic dysregulation after LT was increased in the patient groups of 40-64 years-old or BMI>30kg/m2, patients underwent LT due to viral hepatitis, patients using everolimus postoperatively, and complicated patients. Moreover, we determined that dysglycemia continued longer in these groups.

#### ASSOCIATION OF GLUCAGON-TO-INSULIN RATIO AND NONALCOHOLIC FATTY LIVER DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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**Objective:** Although the importance of islet  $\alpha$ -cell dysfunction in the pathogenesis of type 2 diabetes has been reappraised, data on whether increase or decrease of glucagon relative to insulin is related with glucose metabolism parameters or metabolic diseases such as nonalcoholic fatty

liver disease (NAFLD) in clinical settings are very limited. Therefore, we investigated the association between glucagon-to-insulin ratio (G/I ratio) and presence of NAFLD and metabolic parameters in T2DM.

*Methods:* This retrospective, cross-sectional study was performed with data obtained from 230 T2DM patients (mean age, duration of DM, and BMI :56 years, 8 years, and 25 kg/m2, respectively). Participants were assessed for serum fasting and postprandial G/I ratio and divided into tertiles. NAFLD was defined as ultrasonographically detected fatty liver.

**Results:** The patients in the lowest tertile of fasting G/I ratio had higher BMI, visceral and subcutaneous fat thickness (VFT, SFT), and HOMA-IR and shorter duration of DM. Fasting and postprandial G/I ratios were negatively correlated with BMI, VFT, SFT, fasting c-peptide, and HOMA-IR. In addition, postprandial G/I ratio was positively correlated with HbA1c levels, FBG, and HDL-C. Subjects with HbA1c>8% showed significantly higher mean G/I ratio than those with HbA1c<8%. Prevalence of NAFLD was significantly decreased across tertile of fasting and postprandial G/I ratio. Low G/I ratio was significantly associated with presence of NAFLD by both unadjusted analysis and after multivariate adjustment (OR,95%[CI]:3.24[1.4-7.51], 2.59[1.03-6.55], respectively).

*Conclusion:* Our results suggest that the high glucagon relative to insulin may contribute to hyperglycemia, whereas low glucagon relative to insulin may contribute to NAFLD in T2DM.

#### **RELATIONSHIP BETWEEN HBA1C, HEPATIC STEATOSIS WITH BODY IRON PARAMETERS IN PATIENTS TYPE 2 DIABETES MELLITUS**

#### Dr. Ruhsen Ozcaglayan

*Abstract:* Body iron deposits are associated with insulin resistance. High ferritin levels were reported to have a higher risk of developing type 2 diabetes mellitus than people with normal ferritin levels. This study was to investigate the association between the body iron deposits, HbA1c and grade of non-alcoholic fatty liver disease (NAFLD) on ultrasonography (US) in patients with type 2 diabetes mellitus (T2DM). We investigated whether there was a difference between body iron stores in patients with type 2 diabetes mellitus and healthy individuals and the relationship between body iron deposits, HbA1c and fatty liver using US. NAFLD was defined as ultrasonographically detected fatty liver and was graded as normal, mild, moderate, and severe fatty liver 50 complicated type 2 diabetes mellitus

patients, 55 healthy persons were retrospectively screened for HbA1c, ferritin, iron, TDBC levels and sonographic hepatic steatosis A total 105 of subjects 65 (62%) were diagnosed with NAFLD on US, of which 32 (50%) had moderate-to-severe grade of NAFLD. It was observed that iron deposits measured by serum ferritin correlated positively with HbA1c in all subjects. Serum ferritin level were statistically higher in patient which had moderate –to severe grade compare to mild-to moderate grade of NAFLD. There is a significant increase in ferritin levels in diabetic patients compared healthy individuals, and a higher risk of developing type 2 diabetes in healthy persons with high ferritin levels and sonographic moderate –to severe grade of NAFLD may be a better guide for follow-up and treatment regimens than for those with normal ferritin levels.

#### DETECTION OF EARLY OCULAR PRECLINICAL CHANGES IN DIABETIC PATIENTS

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*Objective:* The aim of the study is to evaluate ocular pulse amplitude (OPA), intraocular pressure (IOP) and average choroidal thickness (CT) of the eye using dynamic contour tonometry (DCT) and optical coherence tomography (OCT) in diabetic patients and to investigate the relationship of these parameters with each other and with glycated haemoglobin (HbA1c) and blood lipid levels.

*Methods:* In total, 89 diabetic patients were included in the study. IOP and OPA measurements of the patients were conducted using DCT, whereas CT measurements were performed using SD-OCT and enhanced-depth imaging OCT (EDI-OCT).

**Results:** There was an increase in IOP (p = 0.00) and OPA (p = 0.616) as well as a decrease mean CT (p = 0.831) in diabetic patients compared with the control group. There was a significant negative correlation between mean CT and Triglyceride level (p = 0.001, r = -0.241); a nonsignificant negative correlation between CT and glucose, HbA1c and total cholesterol levels; a significant positive correlation between CT and high-density lipoprotein level (p = 0.013, r = 0.185) and a nonsignificant positive correlation between CT and low-density lipoprotein level.

*Conclusion:* It was observed that there was a decrease in CT in diabetic patients when DCT and EDI SD-OCT were used together. The Triglyceride and HbA1c levels were determined to have a negative effect on CT, whereas high-

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density lipoprotein had a positive effect. As the changes in CT may represent early preclinical condition in diabetic patients, they are of importance in clinical follow-up.

#### ELIGIBILITY VARIES BETWEEN THE 4 SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITOR CARDIOVASCULAR OUTCOMES TRIALS: IMPLICATIONS FOR THE GENERAL TYPE 2 DIABETES US POPULATION

#### Eric T. Wittbrodt; James E. Eudicone; Kelly F. Bell; Devin Enhoffer; Keith Latham; Jennifer Green

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**Background:** In 2008, US FDA issued guidance to industry for evaluating cardiovascular (CV) risk of type 2 diabetes (T2D) medications. While the CV outcomes trials (CVOTs) for each class of agents are similar in purpose, patient enrollment criteria vary, and extrapolation of trial data to the general population is a challenge. The objective of this study was to assess the proportion of adults with T2D who would been eligible for the 4 sodium-glucose cotransporter-2 inhibitor (SGLT-2i) CVOTs.

*Methods:* A cross-sectional retrospective cohort analysis was conducted. The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey designed to measure objective health data from patients, and health and health behavior surveys were fielded. Patient characteristics, physical examination, and laboratory test results from the two most recent waves of NHANES with available data relevant to this study were included: 2009-2010 and 2011-2012, in which 10,537 and 9,756 individuals were interviewed and examined, respectively. Weighted analysis estimated the proportions of US T2D patients who met the enrollment criteria for CANVAS (canagliflozin), DECLARE (dapagliflozin), EMPA-REG (empagliflozin), and VERTIS CV (ertugliflozin).

**Results:** This analysis indicates that 59.2% of adults with T2D would meet entry criteria for any of the 4 SGLT-2i CVOTs (Table). The DECLARE trial eligibility criteria were the most generalizable to the T2D population.

	Trial Identifiable Individuals with a Diagnosis of T2D	Individuals who meet Trial Criteria	% of Individuals with T2D who meet Trial Criteria
DECLARE	25,253,826	14,661,401	58.1%
CANVAS	23,941,512	3,613,205	15.1%
EMPA-REG	23,519,202	1,678,371	7.1%
VERTIS CV	23,519,202	1,247,256	5.3%
Any SGLT-2i CVOT	25,253,826	14,960,901	59.2%
No SGLT-2i CVOT	25,253,826	10,292,926	40.8%

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*Conclusion:* Study enrollment criteria vary greatly between the SGLT-2i CVOTs. The generalizability of the results of each CVOT to the overall T2D population must be interpreted in the context of the characteristics of the enrolled patients.

#### ETHYL ACETATE FRACTION OF SENNA ALATA FLOWER MODULATES DIABETES MELLITUS, DYSLIPIDEMIA AND OXIDATIVE STRESS IN DIABETIC RATS MODEL

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Abstract: Herbal remedies have been known to be efficacious in diabetes mellitus management for many years. Senna alata flower is one of the plants used in Nigeria traditional medicine for the management of diabetes and its associated complications. Thus, this study gives insight into the bioactive fractions of Senna alata flower. Crude aqueous extract of SAF (20.45 g) was partitioned using various solvents. Male Wistar rats (42) were randomized into six groups. Rats in group 1, the control, received distilled water. Rats in groups II-VI were made diabetic by alloxan induction. The untreated diabetic control group was in group II; groups III-V were treated with 75 mg/kg body weight of the solvent partitioned fractions from Senna alata flower aqueous extract while group VI received 2.5 mg/kg of glibenclamide. The fractions from Senna alata flower aqueous extract had varying anti-diabetic and anti-oxidant activities. Worthy of note is ethyl acetate fraction which reduced the fasting blood glucose level significantly to 66.57 mg/dL. Total cholesterol, triglyceride, LDL-cholesterol, VLDL- cholesterol levels were as well reduced to 165.62, 72.11, 47.81, 14.42 mg/dL respectively. However, there was significant increase in HDL-cholesterol level to 105.56 mg/dL and carbohydrate metabolism enzymes activities. Moreover, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase and glucose 6-phosphate dehydrogenase activities increased most significantly in the ethyl acetate fraction treated group.

*Conclusion:* Ethyl-acetate (EtoAc) fraction from Senna alata flower contains antioxidant and anti-diabetic principles as evident in the positive alterations in enzymes linked with Diabetes mellitus.

#### HEALTH CARE UTILIZATION AND COSTS IN PATIENTS WITH T2D TREATED WITH DAPAGLIFLOZIN OR SITAGLIPTIN IN A US MANAGED CARE SETTING

#### Wittbrodt E.T.; Parker E.D.; McPheeters J.

AztraZeneca Pharmaceuticals, Optum

**BACKGROUND:** Dapagliflozin (DAPA), an SGLT-2 inhibitor, and sitagliptin (SITA), a DPP-4 inhibitor, are commonly prescribed add-on oral anti-diabetic (OAD) therapies. Health care utilization and costs (HCRU) in patients with type 2 diabetes (T2D) initiating treatment with DAPA or SITA in a real-world setting were examined.

**METHODS:** This retrospective cohort study used a large health plan database with pharmacy, medical claims, and enrollment information for patients with T2D filling an initial prescription for DAPA or SITA on an index date between Jan 2014–Oct 2015. After 1:1 propensity-score matching, all-cause and T2D-related HCRU were assessed 6 months pre- and 12 months post-index (follow-up). Cost ratios were estimated using generalized linear models adjusted for baseline costs. Subgroup analyses based on preindex OAD monotherapy or insulin use were conducted. Patients receiving OAD monotherapy or insulin pre-index were included in subgroup analyses.

**RESULTS:** Of the 3,269 DAPA and 8,702 SITA patients identified, 2,722 from each cohort were matched. Cohorts were well-matched on demographics, Charlson Comborbidity Index, pre-index diabetes medications, and all-cause HCRU. Follow-up ambulatory visits were lower in DAPA vs SITA patients. Statistically significant differences in all-cause follow-up total costs were not observed. Compared with SITA, all-cause pharmacy costs were higher in DAPA, and all-cause-medical costs were lower in DAPA. Results were similar in the subgroup of patients who received OAD monotherapy pre-index.

**CONCLUSION:** Real-world evidence shows that in wellmatched T2D new-user cohorts, higher all-cause pharmacy costs of dapagliflozin were offset by lower all-cause medical costs resulting in no difference in total costs.

#### ADIPONECTIN, TNF-ALFA, INTERLEUKINE-6 AND CK-18 FRAGMENT LIVER EXPRESSION OF OBESE PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Federal University of Pernambuco and Keizo Asami Imunopatology ans laboratory

Abstract: Adipose tissue is metabolically active and secretes adipokines such as adiponectin. Hypoadiponectinemia is typical to obese patients although, in the liver seems to have a distinct behavior, acting as an important key in the mechanisms of fibrosis protection. This study aims to evaluate the expression of adiponectin, Interleukin-6, TNF- $\alpha$ and CK-18 fragment in the liver of patients with severe obesity undergoing bariatric surgery.

*Methods:* In this experimental study sixty-two patients with liver biopsy were selected between 2014-15. Patients with secondary causes of liver disease and consumption of alcohol were excluded. Histology was performed by an expert pathologist. NAFLD was classified according to NAS score. Quantitative PCR for IL-6, TNF- $\alpha$ , Adiponectin and CK-18 fragment was performed. SPSS software, version 20.0, was used. The study was approved by Ethics Committee.

**Results:** Fifty-two patients were included, with an average age of 38 years old, with a mean BMI of 40,74 Kg/m<sup>2</sup>. Among the patients studied, 42 (80.8%) had hepatic steatosis and 10 patients (19.2%) had NASH. More expression of adiponectin (p = 0,012), TNF- (p = 0,015), IL-6 (p = 0,009) and the CK-18 fragment (p = 0,016) were observed in the liver fragment of patients with NASH.

*Conclusion:* Significant expression of adiponectin along with significant expression of TNF-, IL-6, and CK-18 fragment in the hepatic tissue were correlated positively in patients with NASH in this study.

## IS VISCERAL ADIPOSITY INDEX CORRELATED WITH INSULIN RESISTANCE?

#### Şakir Özgür Keşkek

#### City Hospital

**Objective:** Increase in visceral adipose tissue correlate with increased gluconeogenesis, increased free fatty acid levels, and insulin resistance. The Visceral Adiposity Index (VAI)

is a determiner of fat distribution and function. The aim of this study was to investigate the association between VAI and insulin resistance in patients with metabolic syndrome.

*Methods:* A total of 61 subjects from both genders, with a minimum age of 18 years old, were included in this case control study. The study group was comprised of 30 subjects with insulin resistance and the control group was comprised of 31 healthy subjects. Insulin resistance was measured using homeostasis model assessment using the Oxford (HOMA-IR) calculator. The VAI was calculated by (WC/(39.68+(1.88\*BMI))\*( TG/1.03)\*(1.31/HDL) for males and VAI = (WC/ (36.58+(1.89\*BMI))\*( TG/0.81)\*(1.52/HDL) for females. The MedCalc V17.4 software (Belgium) was used for all statistical analyses.

**Results:** Groups were comparable according to the age and sex (p=0.401, p=0.968). HOMA-IR levels were  $4.03\pm1.2$  and  $2.1\pm0.2$  in subjects with insulin resistance and healthy subjects, respectively. The difference was statistically significant (p<0.001). There was no statistically significant difference between the groups according to the VAI (2.67±1.72 vs. 2.55±1.82, p= 0.544). Additionally, VAI was not correlated with HOMA-IR (p=0.812, r= -0.04).

*Conclusion:* Visceral adipose tissue is a metabolically active organ and it is an independent risk factor for metabolic alterations and development of cardiovascular diseases. In this study we have not found a correlation between VAI and HOMA-IR in subjects with insulin resistance.

#### CLINICAL AND ECONOMIC OUTCOMES IN TYPE 2 DIABETES PATIENTS TREATED WITH FIXED-DOSE VERSUS LOOSE-DOSE COMBINATION ANTI-HYPERGLYCEMIC THERAPIES

#### Eric T. Wittbrodt; Anna Vlahiotis; Jalpa Patel; Kelly F. Bell; Ellen Riehle

#### AstraZeneca, Truven Health Analytics

**Background:** The objective was to compare adherence and clinical and economic outcomes between patients initiating fixed-dose combination (FDC) and loose-dose combination (LDC) anti-hyperglycemic regimens in a contemporary, real-world setting.

*Methods:* This retrospective, observational study used claims data from Truven Health MarketScan Commercial and Medicare Supplemental Databases (2013-2015) to identify and compare T2D patients initiating metformin-containing FDC or LDC oral anti-hyperglycemic regimens, and patients were followed for 12 months for adher-

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ence and T2D-related cost outcomes. Among the patient subset with laboratory data, A1C values in the year before and after treatment initiation were analyzed.

Results: The 22,456 FDC patients and 21,172 LDC patients were well balanced on key baseline characteristics, including mean age, sex, and among the subset of patients with laboratory data, proportions of patients with baseline A1C values <7.0%. A majority of FDC patients initiated on branded products (80%) and a metformin/dipeptidyl peptidase-4 (DPP-4) inhibitor regimen (77%), and a majority of LDC patients initiated on metformin/sulfonylurea (73%) and 23% on branded products. Odds of adherence were significantly greater for FDC patients (Figure). The proportion of patients achieving A1C<7 at 12 months was 7% higher in the FDC cohort (37% vs. 30%, p=0.001). Mean T2D-related pharmacy costs were higher in FDC patients (FDC: \$2,142 vs. LDC: \$917; p<0.001), but T2D-related medical costs were significantly lower (FDC: \$1,483 vs. LDC: \$1,717; p<0.001).

*Conclusion:* This study demonstrates real-world evidence that FDC anti-hyperglycemic regimens are associated with higher adherence, lower T2D-related medical costs, and improved A1C outcomes compared with LDC regimens.

#### COMPARISON OF LOW-DOSE LIRAGLUTIDE USE VERSUS OTHER GLP-1 RECEPTOR AGONISTS IN PATIENTS WITHOUT TYPE 2 DIABETES

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#### AstraZeneca

**Background:** The objective was to compare the use of low-dose liraglutide (1.2 and 1.8 mg, L-LD, Victoza) with the other GLP-1 receptor agonists (GLP-1 RAs) in patients without a type 2 diabetes (T2D) diagnosis. The hypothesis was that L-LD use would be greater in patients without T2D than for the other marketed GLP-1 RAs (albuglutide, dulaglutide, exenatide) in the period after high-dose liraglutide (3 mg, L-HD, Saxenda) was approved for obesity in 2014.

*Methods:* This cohort study included adult T2D patients with > 1 year of history in the Optum Humedica database and > 1 prescription for a GLP-1 RA between December 2014 and March 2016. Patients using insulin, with type 1 DM, and prescriptions for L-LD and another GLP-1 RA in the prior 12 months were excluded. Proportions of patients without a diagnosis of T2D who were prescribed L-LD versus the other GLP-1 RAs were compared. **Results:** We identified 11,245 patients taking L-LD and 4,134 patients taking other GLP-1 RAs. The proportion of patients with L-LD prescriptions and without T2D increased from 11.8% in December 2014 to 37.5% in March 2016 (p<0.0001). During this same period, the proportion of patients without T2D prescribed other GLP-1 RAs decreased from 8.6% to 4.5% (p=0.10).

*Conclusion:* Use of L-LD in patients without T2D increased 3-fold in the 16 months after approval of L-HD for obesity and decreased for the other GLP-1 RAs. Increased payer scrutiny of L-LD use is warranted as part of a comprehensive evaluation of reimbursement policies for obesity treatments.

#### THE RELATIONSHIP BETWEEN INSULIN RESISTANCE AND C-REACTIVE PROTEIN IN OBESITY

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Aydin State Hospital

*Objective:* To determine the relationship between insulin resistance and CRP in patients with and without non-obese individuals. C-reactive protein may predict the development of type 2 diabetes mellitus, metabolic syndrome and cardiovascular diseases.

*Methods:* Two hundred fifty-five patients, between the age of 25-66 years were enrolled in the study. Heights, weights, body mass indexes (BMI), waist circumferences, fasting blood glucose (FBG), total cholesterol, triglyceride, LDL-c, HDL-c, CRP and insulin levels were measured.

**Results:** Of all the patients, 132 (51.7%) were female, 123 (48.2%) were male; 53 of them were of (20.7%) normal weight, 83 (32.5%) were overweight and 119 were (46.6%) obese. There was a significant difference between FBG, TG, HDL-c levels and BMI (p<0.05). The significant difference were found between insulin, insulin resistance, CRP and obesity (p<0.05). Consequently, HOMA-IR and CRP levels was found as the basic factors on obesity.

*Conclusion:* High FBG, TG, insulin, insulin resistance, CRP and low HDL-c levels were found to be correlated with obesity. This correlation leads to many diseases, notably diabetes mellitus and cardiovascular diseases.

#### PROTECTIVE EFFECTS OF PRUNELLA VULGARIS ON DIABETIC NEPHROPATHY: IMPROVEMENT OF GLOMERULAR FIBROSIS AND INFLAMMATION

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Abstract: Diabetic nephropathy is the most common complication and leading cause of mortality associated with diabetes. Prunella vulgaris (APV), well-known traditional medicinal plant, is used for the cure of abscess, hypertension and urinary diseases. In human mesangial cell, APV regulated TGF-B/Smad signaling pathway and decreased connective tissue growth factor (CTGF) and collagen IV, fibrosis biomarkers under high glucose (HG) condition. Moreover, APV suppressed inflammatory factors such as intracellular cell adhesion molecule-1 (ICAM-1) and monocyte chemoattractant protein-1 (MCP-1) as well as NF-KB/ROS signaling. In streptozotocin (STZ)-induced diabetic rat models, APV significantly decreased blood glucose, blood urea nitrogen and ameliorated plasma creatinine. APV reduced the PAS positivity staining intensity and basement membrane thickening in glomeruli of diabetic rats. These results suggest that APV significantly have protective effect against diabetic renal dysfunction including inflammation and fibrosis through disturbing TGF- $\beta$ /Smad signaling. Therefore, APV may be potential therapies targeting glomerulosclerosis leading to diabetic nephropathy.

#### BENEFICIAL EFFECT OF KOREAN RED GINSENG ON HYPERTRIGLYCERIDEMIA IN HIGH FAT/CHOLESTEROL DIET RAT

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College of Oriental Medicine and Professional Graduate School of Oriental Medicine

*Abstract:* Korean Red Ginseng (RG) are used as a traditional treatment for improve blood circulation. This experimental study was designed to investigate the inhibitory effects of RG (from JinAn) on lipid metabolism in high fat/cholesterol diet (HFCD)-induced hypertriglyceridemia. Sprague Dawley rats were fed the HFCD diet with/without fluvastatin (Flu, positive control) 3 mg/kg/day, and RG 125 or 250 mg/kg/day, respectively. All groups received regular

diet or HF diet, respectively, for 13 weeks. The last three groups treatment of Flu and RG125, and RG250 orally for a period of 9 weeks. Treatment with low or high doses of RG markedly attenuated plasma levels of triglycerides and augmented plasma levels of high-density lipoprotein (HDL) in HFCD-fed rats. RG and Flu also led to an increase in lipoprotein lipase activity in the HFCD group. On the other hand, RG and Flu led to a decrease in fatty acid synthase and free fatty acid activity in the HFCD group. Treatment with RG suppressed increased expressions of PPAR-α and AMPK in HFCD rat liver or muscle. In addition, the RG attenuated triglyceridemia by inhibition of PPAR-y and FABP protein expression levels and LXR and SREBP-1 gene expression in liver or muscle. The RG significantly prevented the development of the metabolic disturbances such as hypertriglyceridemia and hyperlipidemia. Taken together, the administration of RG improves hypertriglyceridemia through the alteration in suppression of triglyceride synthesis and accentuated of triglyceride decomposition. These results suggested that JinAn Red Ginseng is useful in the prevention or treatment of hypertriglyceridemia-related disorders such as triglyceride metabolism.

#### VISCERAL ADIPOSITY INDEX IN SUBJECTS WITH SEXUAL DYSFUNCTION

#### Şakir Özgür Keşkek

#### City Hospital, Adana, Turkey

**Objective:** Increase in visceral adipose tissue can lead to inflammation, insulin resistance, diabetes and hypertension, which are associated with sexual dysfunction. The Visceral Adiposity Index (VAI) is a determiner of fat distribution and function. The aim of this study was to investigate the association between VAI and sexual dysfunction in male patients.

*Methods:* A total of 35 male subjects were included in this case control study. The study group was comprised of 18 subjects with sexual dysfunction and the control group was comprised of 17 healthy subjects. Sexual dysfunction was diagnosed according to Arizona sexual experiences scale. The VAI was calculated by (WC/(39.68+(1.88\*BMI))\*(TG/1.03)\* (1.31/HDL). The MedCalc V17.6 software (Belgium) was used for all statistical analyses.

**Results:** Groups were matched according to the age  $(35.2\pm6.1 \text{ vs. } 34.0\pm6.5, \text{ p}=0.578)$ . The scores of Arizona sexual experiences scale were  $19.7\pm3.2$  and  $7.2\pm1.6$  in subjects with sexual dysfunction and healthy subjects, respectively. The difference was statistically significant (p<0.001). There was no statistically significant difference

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between the groups according to the VAI ( $1.95\pm0.96$  vs.  $1.48\pm0.72$ , p= 0.113).

*Conclusion:* In this study, we have found comparable VAI levels in both groups. Although VAI is associated with insulin resistance and diabetes which lead to sexual dysfunction, in this study we have not found any relationship between VAI and sexual dysfunction. Patients with sexual dysfunction should be checked for all causes in addition to the metabolic disturbances like insulin resistance.

				35.2±6.1		
Sexua tion (+	l dysfunc- -) N=18	Healthy N=17	n Age	34.0±6.5 0.578 Arizona	19.7±3.2 7.2+1.6	<0.001
VAT	1 05±0 06	1 48±0 72	0 113			
VAI	1.9J±0.90	1.40±0.72	0.115			

#### AN IMBALANCE OF THE HORMONES OF FATTY TISSUE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS DEPENDING ON THE BODY MASS INDEX

#### Zhuravlyova L.; Ogneva E.; Lavrynenko O.

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Abstract: 70 patients with DM-2 with normal weight and obesity were investigated. All patients were divided into 2 groups: group 1 (n=20) patients with DM-2 and normal body weight and group 2 (n=50) patients with DM-2 and obesity. The controls (n=20) were apparently healthy individuals. The BMI, levels of resistin and TNF- $\alpha$  were determined. The mean level of resistin was significantly (p<0.001) increased in all groups in comparison with the controls ( $4.87\pm0.11$  ng/ml), the level in group 2 ( $10.0\pm0.11$ ng/ml) was significantly different from that in group  $1(8.06\pm0.23 \text{ ng/ml})$ . The mean level of TNF- $\alpha$  also was significantly (p <0.001) increased in all groups of patients (group 1 - 86.4 ± 1.21 pg / ml, group - 2 96.65 ± 0.72 pg / ml) in comparison with the controls  $(24.19 \pm 1.06 \text{ pg} / \text{ml})$ , the level in group 2 was significantly (p < 0.001) different from that in group 1 group. In both groups of patients group the direct correlation was established between resistin and BMI (r = 0.36, p < 0.05 - group 1, r = 0.84, p < 0.05 - group 2) and between TNF- $\alpha$  and BMI (r = 0.39, p < 0.05 – group 1, r = 0.69, p < 0.05 - group 2). There is an imbalance in the production of fatty tissue hormones in patients with DM-2. This hormonal imbalance is manifested by an increase of the level of resistin and TNF- $\alpha$ . Obesity is the leading etiological factor in the pathogenesis of molecular-cellular mechanisms of interaction of immune and metabolic processes in patients with DM-2.

#### INSULIN RESISTANCE AND VITAMIN D LEVELS IN PATIENTS WITH POLYCYSTIC OVARY SYNDROME

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**Background:** Polycystic ovary syndrome (PCOS) is the most common endocrine disorder among women between the ages of 18 and 44. Due to the tendency towards central obesity and other symptoms associated with insulin resistance, PCOS was found to be associated with cardio-vascular diseases. Epidemic studies have suggested that vitamin d deficiency is also associated with insulin resistance. Vitamin d supplementation leads to an improvement in insulin release, insulin receptor expression, and insulin sensitivity. In this study, we aimed to investigate the vitamin d level in patients with PCOS.

*Methods:* A total of 216 female subjects were included in this cross-sectional cohort study. The study group comprised 109 patients with PCOS according to the Rotterdam criteria and the control group comprised 107 healthy subjects. 25(OH)D and insulin levels and HOMA-IR of the groups were calculated. MedCalc 17.9.5 software (MedCalc, Belgium) was used for all statistical analyses.

**Results:** Groups were matched according to the age (29.7 $\pm$ 3.4 vs. 29.6 $\pm$ 3.5 p=0.790). The mean insulin level and HOMA-IR was higher in patients with PCOS (20.8 $\pm$ 16.5 and 4.8 $\pm$ 4.4 vs. 8.4 $\pm$ 5.3 and 1.6 $\pm$ 1.2, respectively, p<0.001). The frequencies of hypovitaminosis D were 91% and 89% in PCOS and healthy groups, respectively. 25(OH)D levels were lower in patients with PCOS (8.7 $\pm$ 10.3 vs. 9.8 $\pm$ 8.9 p=0.039) (Table 1).

*Conclusion:* The prevalence of insulin resistance was reported in 70-80% of PCOS patients in previous studies. The coexisting hypovitaminosis D could exacerbate the metabolic abnormalities such as insulin resistance in the PCOS, leading to its increased CVD risk. It is essential to screen all the PCOS patients for 25(OH)D deficiency.

	PCOS (N=109)	Healthy group (N=107)	р
Age (year)	29.7±3.4	29.6±3.5	0.790
Insulin (µU/mL)	20.8±16.5	8.4±5.3	<0.001
HOMA-IR	4.8±4.4	1.6±1.2	<0.001
25(OH)D (ng/mL)	8.7±10.3	9.8±8.9	0.039

Table 1 shows the age and biochemical tests of the groups.

#### DIABETES INFLUENCES ON CARDIOVASCULAR DISEASE IN DEVELOPING COUNTRIES RESEARCH BASED

Dr. Mahmood Rueen Mustafa, Internal Medicine Specialist, Cardiologist

Masood Mustafa Curative Children Hospital

*Abstract:* According to the tittle above we focused on influences of Diabetes on Cardiovascular Disease in Developing Countries Research Based. This research is conducted actually on 347 patients with DM. The Consequences of Diabetes fully investigated based on scheduled doctor, lab and other per necessary examination.

#### NEW METHOD FOR THE ESTIMATION OF INSULIN SENSITIVITY FROM THE ORAL GLUCOSE TOLERANCE TEST

#### Francesca Piccinini; Richard N. Bergman

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Abstract: The minimal model used the intravenous glucose tolerance test (IVGTT) to estimate parameters determining glucose tolerance [first phase insulin response, insulin sensitivity (SI), glucose effectiveness (SG)]. Others have attempted to extend this method to the oral glucose tolerance test (OGTT). Glucose and insulin patterns are similar to each other during the OGTT; therefore, changes in unrelated processes (glucose absorption rate, renal glucose clearance, glucose effectiveness) can result in false calculated values of SI per se. To make SI calculation from the OGTT correct we have designed a new OGTT protocol. Changes were 1) a lower glucose dose (25 g), 2) administration of exogenous insulin during the test (0.03 U/kg at 60 min), and 3) used simplified assumptions regarding glucose absorption. Method was tested using data for subjects with normal, moderately reduced (impaired glucose tolerance), and very reduced SI (type 2 diabetes). Results were compared in terms of plausibility, precision of parameter estimates [standard deviation (SD)], ability to predict data, parsimony, and randomness of weighted residuals. This refined method, with oral glucose dose reduction and insulin injection, provides accurate estimates of both SI and SG, (see table for normal and type 2 diabetes subject values) independently of changes in processes other than insulin resistance itself.

		Oral glucose mini- mal model	New Protocol
	Preal value (SD)	Pest value (SD)	Pest value (SD)
Normal subject			
SI (10 <sup>-4</sup> min <sup>-1</sup> per μU/ml)	9	8 (3)	9 (1)
SG (min <sup>-1</sup> )	0.025	0.038 (0.010)	0.033 (0.006)
Type 2 diabetes subject			
SI (10 <sup>-4</sup> min <sup>-1</sup> per μU/ml)	3	4 (5)	3.6 (2)
SG (min <sup>-1</sup> )	0.010	0.012 (0.015)	0.013 (0.007)

#### KIOM-2015E ALLEVIATES DEXTRAN SODIUM SULFATE-INDUCED COLITIS BY IMPROVING INTESTINAL BARRIER FUNCTION AND REDUCING INFLAMMATION

#### Kwang-Youn Kim; Jin-Yeul Ma\*; Kwang-Il Park\*

Korea Medicine (KM)-Application Center, Korea Institute of Oriental Medicine

Abstract: Ulcerative colitis (UC) is one of inflammatory bowel disease (IBD) and is caused by diverse factors, including the extent and duration of intestinal inflammation. We investigated effect of KIOM-2015E on expression of tight junction proteins and the levels of inflammatory in a mouse model of dextran sodium sulfate (DSS)-induced of acute colitis. KIOM-2015E (100 mg/kg) was orally administered once per day to BALB/C mice with colitis induced by administration of 5% DSS in drinking water. KIOM-2015E recovered the loss of body weight and disease activity index (DAI) and the abnormally short colon lengths in DSS-induced model of acute colitis. Moreover, KIOM-2015E significantly inhibited the decrease of zonula occluden-1 (ZO-1), occludin in colonic tissue relative to a DSS-treated control group. KIOM-2015E also significantly inhibited the expression of interleukin (IL)-6 and tumor necrosis factor- $\alpha$  in level of serum relative to the control group. Collectively, these data suggest that KIOM-2015E protects colitis principally by improving intestinal barrier function and promoting anti-inflammatory responses. In turn these effects inhibit macrophage infiltration into the colon and thus may be a candidate treatment for IBD.

#### SOCIAL SUPPORT IS ASSOCIATED WITH DECREASED DEPRESSION IN PATIENTS WITH CHRONIC ILLNESS

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**Background:** The positive correlation between chronic illness and depression has been well studied. The aim of this research was to understand how social support and personal life satisfaction affect depression in patients with chronic disease.

*Methods:* Patients at the Western University Patient Care Center with an array of chronic diseases such as diabetes and hypertension were surveyed at their medical appointments with questionnaires assessing their level of depression, social support, and personal life satisfaction. Depression was measured with the Patient Health Questionnaire (PHQ-9), social support with a survey from the RAND Corporation, and life satisfaction with Ryff's Scales of Psychological Well-Being. Data was collected and a statistical analysis was performed to compare depression with social support and depression with life satisfaction.

**Results:** Of the 45 completed surveys, it was found that increased overall social support was associated with decreased levels of depression (p<0.0013) in these patients with chronic disease. This was particularly true for emotional support (p<0.0014), affectionate support (p<0.0076), and positive interaction (p<0.0028), as opposed to tangible support (p<0.1022). On the other hand, our data showed that personal life satisfaction was not significantly associated with depression in these patients (p<0.134).

**Conclusions:** Patients with chronic illness that have increased social support may have a lower risk of depression. Our results shed light on the importance of considering the integration of social support as part of the overall treatment plan for patients with chronic disease. This may lead to a positive impact on their emotional and physical health.

	No or mild depression	Mild depression	Moderate or severe depression	P-value
Age	54.44 ± 12.29	$49.62 \pm 19.57$	$60.17 \pm 4.88$	0.3166
Emotional support subscale	$4.17\pm0.81$	3.58 ± 0.83	2.71 ± 1.14	0.0014
Tangible sup- port subscale	$4.01 \pm 0.85$	3.63 ± 1.25	3.08 ± 0.75	0.1022
Affectionate support subscale	$4.45\pm0.97$	3.9 ± 1.07	3 ± 0.94	0.0076
Positive inter- action subscale	4.28 ± 1.08	3.33 ± 1.27	2.56 ± 1.22	0.0028
Social Support total score	$4.2 \pm 0.75$	$3.6 \pm 0.91$	$2.81 \pm 0.87$	0.0013
Life satisfac- tion total score	35.42 ± 4.35	34.15 ± 6.54	30.67 ± 5.01	0.134

#### C-REACTIVE PROTEIN AND ALL-CAUSE MORTALITY IN U.S. ADULTS: AN ANALYSIS OF GENDER AND RACE/ETHNICITY NHANES 1999-2006

#### Michael Richardson<sup>1</sup>; William Boyer<sup>2</sup>; James Churilla<sup>1</sup>

<sup>1</sup>University of North Florida; <sup>2</sup>California Baptist University

**Background:** Evidence suggests that elevated C-reactive protein (CRP) concentrations are associated with incident cardiovascular disease (CVD) and mortality. However, the prognostic value of elevated CRP concentrations when examining all-cause mortality risk has not been previously examined utilizing a nationally representative sample of U.S. adults stratified by gender and race/ethnicity.

**Purpose:** Examine the relationship between elevated (CRP) and all-cause mortality across gender and race/ethnicity in a nationally representative sample of U.S. adults.

*Methods:* Study sample (n=4,736) included adults (30-79 years of age) who participated in the 1999-2006 NHANES. A dichotomous elevated CRP concentration variable was created (> 3 to 10 mg/L, yes/no). Mortality, using continuous NHANES data linked to the National Death Index, was defined as death from any cause. SAS 9.4 survey procedures were used for all analyses.

**Results:** Following adjustments for age, education, smoking, alcohol consumption, CVD, waist circumference, and aerobic physical activity, significantly higher risk for all-cause mortality was revealed in non-Hispanic Black males (Hazard Ratio [HR] 2.04, 95% Confidence Interval [CI] 1.28-3.25) and Mexican American Females (HR 2.24, 95% CI 1.26 – 3.98). The HR in non-Hispanic White males approached but did not reach statistical significance (HR 1.32, 95% CI 0.95 – 1.83, p=0.09).

*Conclusion:* The current analysis adds to the paucity of evidence suggesting that elevated CRP concentrations are associated with an increased risk for all-cause mortality. Additionally, our study is one of the first to examine CRP and mortality utilizing a nationally representative sample of U.S. adults, stratified by gender and race/ethnicity.

#### IMPAIRED GLUCAGON RESPONSE TO LONG ORAL GLUCOSE LOAD IN PATIENTS WITH HEART FAILURE

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**Background:** Sodium glucose transporter 2 inhibitors (SGLT2-I) has reported to decrease the rate of heart failure (HF) hospitalization. One possible the reason of favorable effect of SGLT2-I is its ability to induce the glucagon secretion, which is known to increase cardiac output. However dynamic of the glucagon is not precisely evaluated in patients with HF. We investigated the change of glucagon concentration after long oral glucose tolerance test (OGTT) in patients with HF.

*Methods:* We enrolled 11 HF and 19 non-HF patients with non-DM (70 y/o, HbA1c  $6.0\pm0.2\%$ ). 4-h OGTT were performed at the stable condition. Blood samples were collected at pre to 4-h and evaluated serum glucose, insulin and glucagon.

**Results:** We newly diagnosed 57% dysglycemia and 33% reactive hypoglycemia. Although dynamics of glucose and insulin were not different between the patients with or without HF, in patients with HF, area under the curve (AUC) during 4-h of the glucagon was lower than that in patients without HF. When divided into 2 groups according to the left ventricular ejection fraction (LVEF), AUC of the glucagon was significantly lower in patients with lower LVEF ( $28\pm6\%$ ) than that in higher LVEF ( $65\pm6\%$ ) (AUC glucagon; lower group:  $8070.9\pm564.5$  vs higher group  $9329.7\pm1708.6$  mol  $\cdot$  min/L, p=0.041).

*Conclusion:* Glucagon secretion is decreased in patients with HF than in patients without HF. It is suggested that glucagon secretion is related cardiac function. SGLT2-I is thought to protect HF exacerbation by improving the glucagon secretion.

#### FAMILIAL PARTIAL LIPODYSTROPHY FROM THE PATIENTS' PERSPECTIVE

#### Halter Rob; Hubbard Brant; Digenio Andres; Gilstrap Alan; Stratton Andra

Akcea Therapeutics

**Background:** Familial Partial Lipodystrophy (FPL) is a rare genetic disorder characterized by selective loss of adipose tissue and metabolic abnormalities (hypertriglyceridemia, insulin resistance and diabetes). Although the physical manifestations of FPL are well-documented, the impact of FPL on a patient's quality of life is not wellcharacterized in the literature. This study is believed to be the first assessment of this impact on patients with FPL.

*Methods:* A panel of patients diagnosed with FPL participated in a facilitator-led question and answer panel that focused on quality of life and medical consequences of FPL.

**Results:** Ten patients with a mean age of 46.8yr (range 30-71yr) participated in the discussion. Patients reported seeing an average of 10 doctors (range 2 to 20) before diagnosis. One hundred percent of patients reported being diagnosed as adults, yet 5/10 patients reported first symptoms as children. Ninety percent (9/10) of patients reported insulin resistance with overt diabetes, leading to depression in 8/10 reporting patients. Sixty percent (6/10) reported feeling ashamed at their looks and feeling abnormal. Many (5/9) women reported severe body image issues, starting in puberty, related to changes in body fat deposition. In high school, 50% (5/10) reported being bullied; one attempted suicide twice. Eighty percent (8/10) reported anxiety, fear and worry about their health, 7/10 feeling sad, down, blue, and 5/10 reported sleep issues.

*Conclusion:* Patients with FPL reported a decreased quality of life beyond the physical manifestations of FPL and experience a multitude of psychosocial symptoms.

#### NUTRIENT CORRECTION OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH 2 TYPE DIABETES MELLITUS AND NON-ALCOHOLIC FATTY LIVER DISEASE

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**Objective:** To determine the changes in the oxidative stress (OS) activity in terms of lipid peroxidation (LP) in compliance with the proposed dietary patterns using the average daily rate of number of advanced glycation end products (AGE). We examined 23 patients with type 2 diabetes mellitus (DM) and non-alcoholic fatty liver disease (NAFLD) at the age of  $54.7\pm2.2$  with disease duration of  $8.09\pm1.54$ years. BMI was 35.9±3.26 kg/m2. Patients were in a state of carbohydrate metabolism decompensation. The level of glycosylated hemoglobin was 7.5±0.3%. Significant decrease of OS manifestations according to LP products including diene, triene, oxydiene, tetraene conjugates was revealed. It indicates the high specificity of the limited use of AGE in food for patients with DM type 2 and NAFLD. Dietary recommendations are therapeutic measures in view of reducing the oxidative stress. We receive data concerning prescriptive reduction of triglyceride levels on the background of dietary observation, even without additional use of lipid stabilizers and hepatoprotectors. It indicates the effectiveness of the proposed dietary regimens. The importance of limited AGE consumption, especially in patients with DM type 2 and NAFLD, was proved, since in this category of patients a greater number of endogenous AGE is formed than in patients without diabetes. Thus, it is proposed a food scheme for the content of AGE in products that may be consumed in limited, moderate amounts or not recommended for consumption. The expediency of conduction of native correction in patients with type 2 diabetes with NAFLD has been proved.

#### FRUCTOSE RESTRICTION REDUCES D-LACTATE LEVELS IN OBESE LATINO AND AFRICAN AMERICAN CHILDREN: CORRELATIONS WITH IMPROVED LIPID PROFILES

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**Background:** Fructose is an important lipogenic molecule. It increases both fatty acid synthesis and triose phosphate fluxes, which generate methylglyoxal (MG), implicated in diabetes pathogenesis. MG is detoxified to D-lactate which is a surrogate marker of whole body MG production. We hypothesized that fructose restriction leads to decreased MG and therefore D-lactate production.

**Objective:** We determined the effect of 9 days of a fructosetose- but not calorie- restricted diet on D-lactate levels in obese children with high habitual dietary sugar intake. Design/Methods: Twenty high sugar consumer obese children BMI z-score  $2.4 \pm 0.1$ ), (average fructose intake >50 g/day), had all meals provided for 10 days with the same caloric, CHO and macronutrient composition as their standard diet (reducing fructose from 12 to 4% of total caloric intake). D-lactate was measured with a specific enzymatic assay. Insulin, lipids, glucose were measured using standard methods on Day 0 (high fructose) and Day 10 (low fructose).

**Results:** D-lactate levels were significantly reduced (38%) after fructose restriction from 6.0 +/- 2 umol/l to 3.7 +/- 1.5 umol/l; p<0.0001). D-lactate levels at baseline correlated positively with TG, LDL-C, and TG/HDL-C ratio (r=0.39, 0.55 and 0.36 respectively, p<0.01) and negatively with HDL-C, r=0.3, p<0.05. Percent changes (Day 0-Day 10) in D-lactate levels correlated positively with percent changes in TG, LDL-C, and TG/HDL-C ratio (r=0.43, 0.36 and 0.36 respectively, p<0.01).

*Conclusions:* This is the first mechanistic evidence for a link between fructose consumption, MG fluxes, and therefore, glycation, which is a key contributor to diabetes complications.

#### OXIDATIVE STRESS IS ASSOCIATED WITH METABOLIC SYNDROME AND ATHEROGENIC LIPID PROFILES, AND METHIONINE SULFOXIDE LEVELS PREDICT CARDIOVASCULAR EVENTS IN BOTH ACCORD AND VADT SUBSETS

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**Background:** Oxidative stress (OS) plays a role in metabolic syndrome (MS) associated insulin resistance and cardiovascular disease (CVD) in diabetes. Since OS is difficult to measure in the clinical setting, we developed methods to determine blood levels of two unique oxidative endproducts (OPs), lysine derived 2-AAA and methionine derived MetSO. To determine if these OPs predict cardiovascular events, we studied their relationship with incident events in subsets of the ACCORD and VADT. We also assessed the relationship of OPs with prevalence of MS, atherosclerotic lipid profiles (ALPs) and inflammatory-cytokine markers.

*Methods:* We studied 271 matched participants (135 cases, 136 controls) from ACCORD and 445 participants from the VADT. The primary outcome was the first occurrence of cardiovascular events. We measured plasma levels of OPs by liquid chromatography-mass spectrometry.

**Results:** 97% (ACCORD) and 91% (VADT) met NCEP-ATP-III criteria for MS. 2-AAA rose progressively with increasing numbers of MS criteria in both studies (p<0.005). Higher 2-AAA was also significantly associated with ALP (higher triglycerides total and small dense LDL, and lower HDL) and higher CRP and PAI-1. Importantly, incident CVD cases had lower MetSO than controls (ACCORD:  $1.64\pm0.80 \text{ vs.}1.90\pm0.80 \mu\text{M}$ , p=0.007; VADT:  $0.94\pm0.33$ vs.  $1.03\pm0.35 \mu\text{M}$ , p=0.02), while those protected from CVD had higher MetSO.

*Summary:* The OP 2-AAA was related to MS and inflammation; while MetSO was inversely related to incident CVD events in type 2 diabetes patients in both populations. These OPs may provide useful biomarkers for metabolic disease and CVD risk in diabetes, and deserve further study in larger populations.

#### IMPACT OF TOUJEO® COACH PROGRAM ON PATIENT ADHERENCE AND PERSISTENCE

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**Background:** The Toujeo® COACH program was launched in 2015 with the goal of supporting and educating patients prescribed insulin glargine 300 U/mL (Gla-300). The study objective was to assess program impact on clinical and economic outcomes for patients with type 2 diabetes (T2D).

**Methods:** A retrospective cohort study was conducted linking data from the Toujeo® COACH program to the QuintilesIMS Integrated Data Warehouse from 2/1/2016 through 7/31/2016. Overall inclusion criteria were:  $\geq 1$ pharmacy claim for Gla-300 (first claim as index date), continuous database activity for  $\geq 180$  days preceding the 6-month pre-index, pharmacy stability in the 6-month pre-index,  $\geq 1$  diagnosis code for T2D, and  $\geq 18$  years. Exclusion criteria were:  $\geq 1$  pharmacy claim for another basal insulin  $\leq 14$  days preceding index and data quality issues. Patients categorized to a 'COACH participant' cohort based on participation criteria were directly matched to a 'Non-COACH' cohort. Persistence and adherence were measured for 6-months of follow-up.

**Results:** Each of the two matched cohorts included 544 patients. A significantly higher proportion of patients in the COACH participant cohort were persistent (78.5% vs. 65.8%; p<0.0001) and adherent (85.7% vs. 77.2%; p=0.0003) to their index Gla-300 medication compared with Gla-300 patients in the matched Non-COACH cohort. In multivariate adjusted analyses, the odds of being adherent to index medication were 1.99-times higher (Odds Ratio (OR): 1.99; p=0.0002) and the risk of discontinuation of index medication was 48% lower (Hazards Ratio (HR): 0.52; p=0.0002) for patients in the COACH participant cohort.

*Conclusion:* COACH participation was associated with significantly higher 6-month adherence and persistence to Gla-300. Sponsorship: This study was funded by Sanofi.

#### BLOOD PRESSURE CHANGES ACROSS 52-WEEK TREATMENT WITH LORCASERIN: A POST HOC ANAYLSIS OF PHASE 3 CLINICAL TRIALS

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Abstract: Blood pressure (BP) changes might be a safety concern for some patients (pts) on weight loss therapy. We aimed to assess the effect of lorcaserin (LOR) on longitudinal blood pressure changes across 52-weeks of treatment, and progression to hypertension (HTN) among patients with pre-HTN. Vital signs BP data was pooled for population with and without type 2 diabetes (DM) from 3 phase III trials. Longitudinal BP assessment was conducted using mixed model repeated measure (MMRM). Shifts in % pts who had pre-HTN at baseline and attained normal BP, no change in BP and HTN at 52 weeks were also assessed. Across 52-week treatment we observed modest, but statistically significant reduction in SBP with LOR (N=3095) vs. Placebo (N=3038) among non-DM pts: -0.97 mmHg (-0.35, -1.59 95% CI; p=0.002; Figure), but not significant in those with DM (LOR N=251, PBO N=248). Further, we found that by 1-year among pts with P-HTN at baseline (SBP/DBP: LOR N=629/465, PBO N=557/442), numerically greater proportion of LOR patients had normal BP and fewer LOR patients converted to HTN vs PBO (SBP: LOR 44.5% vs PBO 35.7% normal, LOR 6% vs PBO 8.1% HTN; DBP: LOR 55.9% vs PBO 47.7% normal, LOR 5.2% vs PBO 9% HTN), while numerically greater PBO pts remained on P-HTN (SBP: 49.4%, 56.2%; DBP: 38.9%, 43.2% LOR vs PBO, respectively). We observed modest reduction in SBP in non-DM but not DM pts on LOR treatment. Numerically greater proportion of LOR pts with baseline P-HTN shifted toward normal BP compared with PBO.

*Figure 1.* Placebo-adjusted blood pressure changes in non-DM and DM populations after Lorcaserin treatment across 52-week time (MMRM analysis).



#### THE IMPLANTATION AND REMOVAL OF THE ENDOBARRIER AFFECTS GLUCOSE HOMEOSTASIS IN A LEAN CANINE MODEL

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Abstract: Placed endoscopically, the EndoBarrier covers the first 60 cm of the small intestine with a nonpermeable liner, mimicking intestinal bypass. This device has been shown to improve glucose metabolism in obese humans with type 2 diabetes. Seven lean, male mongrel hounds with normal glucose homeostasis underwent an intravenous glucose tolerance test (IVGTT) at baseline (BL), week 1 and week 6 after the EndoBarrier implant (I1 and I6, respectively), and week 1 and week 6 after removal (R1 and R6, respectively). Following implant, there was a decrease from BL in glucose tolerance as reflected in the 10-19 min Kg value (BL: 3.18, I1: to 2.12, I6: 2.23 %/ min) that was reversed following removal (R1: 4.37, R6: 4.02 %/min). This accompanied a trend to decrease in glucose effectiveness (BL: 0.052, I1: 0.028, I6: 0.043 1/ min), which reversed following removal (R1: 0.065, R6: 0.042 1/min). Trends to increase above baseline for SI (BL: 4.15, R1: 6.82, R6: 4.45 1/10^4 U/mL/min) and AIRg (BL: 501, R1: 524, R6: 518 µU/mL) occurred following removal, despite no changes during implant. Interestingly, EndoBarrier placement impacted the rate at which glucose levels returned to basal (40-70 min) following the nadir after the insulin bolus. This rate of return was retarded after implant (BL: 1.22, I1: 0.16, I6: 0.30 mg/dL/min) but returned to BL following removal (R1: 1.09, R6: 0.51 mg/ dL/min). Further studies to elucidate the mechanism are ongoing.

#### GENERALIZABILITY OF GLP-1 RA CARDIOVASCULAR OUTCOMES TRIALS ENROLLMENT CRITERIA TO THE US TYPE 2 DIABETES POPULATION

#### Eric T. Wittbrodt; Jennifer Green; Keith Latham; Devin Enhoffer; James M. Eudicone; Kelly F. Bell

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**Background:** Assessment of cardiovascular risk of antidiabetic agents with randomized controlled cardiovascular outcomes trails (CVOTs) is mandated by FDA guidance. The study designs for CVOTs vary, including enrollment criteria, which impact the generalizability of study populations to the general T2D population. This cross-sectional retrospective cohort study estimated the proportion of US adult T2D patients who would be eligible for enrollment in each of the 7 ongoing or concluded GLP-1 receptor agonist (GLP-1 RA) CVOTs.

*Methods:* This study used patient characteristics, medications, examination, and laboratory test results from the representative 2009–2010 and 2011–2012 National Health and Nutrition Examination Survey (NHANES) database. Utilizing a weighted analysis to estimate these proportions in the US population, we identified individuals who would meet the eligibility criteria for enrollment in the following CVOTs: EXSCEL (exenatide QW), LEADER (liraglutide), ELIXA (lixisenatide), REWIND (dulaglutide), HARMONY (albiglutide), SUSTAIN-6 (semaglutide), and FREEDOM-CVO (ITCA-650).

**Results:** In only two CVOTs (EXSCEL and REWIND) would more than 1 in 5 adult T2D patients in the US have been eligible, while for the other 5 CVOTs from 8% to 15% would have been eligible. A majority of US adults with T2D (64.3%) would have qualified for enrollment into at least one of the GLP-1 RA CVOTs, while very few (1.0%) would have qualified for all CVOTs.

*Conclusions:* This analysis indicates that among GLP-1 RA CVOTs, the proportion of US adults with T2D who would have met enrollment criteria varies substantially. Among individual CVOTs, EXSCEL was the most inclusive of the 7 trials.

Identifiable Individuals with a Diagnosis of T2D in US	Individuals who meet Trial Criteria in US	% of Individuals with T2D who meet Trial Criteria
24,062,453	11,347,155	47.2%
23,941,512	5,364,783	22.4%
23,941,512	3,698,585	15.5%
23,941,512	3,063,663	12.8%
23,941,512	2,815,927	11.8%
23,941,512	1,907,129	8.0%
23,941,512	1,538,856	6.4%
24,062,453	15,482,386	64.3%
24,062,453	4,912,193	35.7%
24,062,453	250,426	1.0%
	Identifiable Individuals with a           Diagnosis of T2D in US           24,062,453           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           23,941,512           24,062,453           24,062,453           24,062,453	Identifiable Individuals with a Diagnosis of T2D in USIndividuals who meet Trial Criteria in US24,062,45311,347,15523,941,5125,364,78323,941,5123,698,58523,941,5123,698,58523,941,5122,815,92723,941,5121,907,12923,941,5121,538,85624,062,45315,482,38624,062,4534,912,19324,062,453250,426

#### THE INFLUENCE OF HEALTH EDUCATION IN CALIFORNIA MIDDLE AND HIGH SHOOLS ON ADULT INACTIVITY, OBESITY AND DIABETES RATES

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*Objectives:* Healthy life style habits are developed during adolescence. We hypothesized that health education (HE) in California middle and high schools may influence adult inactivity, obesity and diabetes rates.

*Methods:* We used 2015 CDC California adult inactivity, obesity and diabetes rates as well as 2015 California Dept. of Education HE data. We calculated the percent of schools that offer HE in each county, and compared the disease rates in counties where more than 60% of the schools offer HE (Group A) with counties where less than 40% of the schools offer HE (Group B). Student t-tests was used to compare the differences.

**Results:** 3155/6310 (50%) schools offered HE. The 20 counties in Group A were Amador, Butte, Colusa, Del Norte, Glenn, Inyo, Los Angeles, Marin, Mariposa, Modoc, Mono, Orange, Riverside, Sacramento, San Francisco, San Luis Obispo, Santa Cruz, Sierra, Yuba and Yolo, and 22 counties in Group B were Contra Costa, El Dorado, Fresno, Imperial, Kern, Kings, Madera, Merced, Monterey, Napa, Nevada, Plumas, San Bernardino, San Diego, San Mateo, Santa Clara, Shasta, Sonoma, Stanislaus, Tehama, Trinity, Tuolumne; (82.5 $\pm$ 15% vs 24 $\pm$ 13% respectively). The adult inactivity rates were significantly higher in Group B counties (16.3% vs. 17.8%, p=0.02). Availability of HE did not influence adult obesity (23 $\pm$ 3% vs. 24 $\pm$ 4%) and diabetes (8 $\pm$ 1% vs. 8 $\pm$ 1%) rates.

*Conclusions:* Adult inactivity is higher in CA counties where fewer schools offer HE. Effective and widely available HE is needed to lay the foundations of a healthy life style.

#### THE IMPACT OF HAVING A FAMILY MEMBER WITH DIABETES ON DIETARY HABITS

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**Background:** Poor diet and obesity are the main risk factors for pre-diabetes and type-2 diabetes. We assessed whether having a family member with diabetes influences the dietary habits of an individual.

*Methods:* We used data from a previous survey conducted among adults that assessed their awareness of daily CDC sodium intake recommendations. Chi-square test was used to assess the differences.

Results: Out of 74 subjects who completed the survey, 43 (58%) had a family member with diabetes; 81% (35) of those who had a diabetic family member were between the ages of 18-35 years and 72% were female. 16% were Asians, 53% were Caucasians and 30% Hispanic/Latino. Most individuals who had a family member with diabetes did not track daily calorie (22 out 43; 51 %), sodium (27 out of 43, 63%), cholesterol (28 out of 43; 65.2%) or fat intake (28 out of 43; 65.2%). There were no demographic differences (age, gender) or socioeconomic differences (highest level of education in the family, family average annual income) between subjects with family history of diabetes compared to those without; however more Asian (87.5%) and Latino subjects (76.5%) had a family member with diabetes diagnosis as compared to Caucasian subjects (48.9%; p=0.048).

*Conclusion:* Having a family member with diabetes does not influence the dietary habits of the individual. This may be due to a lack of understanding of the risks associated with the development diabetes. Better education is needed.

#### HEALTH CARE COSTS AMONG TYPE 2 DIABETES PATIENTS FOLLOWING NEW USER INITIATION OF DAPAGLIFLOZIN VERSUS DIPEPTIDYL PEPTIDASE-4 INHIBITORS: A NATIONWIDE STUDY OF TYPE 2 DIABETES PATIENTS IN SWEDEN

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Abstract: To describe healthcare costs of type 2 diabetes patients up to 18 months following initiation of dapagliflozin or DPP-4i. All new users of dapagliflozin or DPP-4i, on top of existing glucose lowering treatment, during 2013-2015 were identified and followed in the mandatory Swedish Prescribed Drug-, National Patient- and Cause of Death Registers. Individual patient-level data were linked using unique personal identification numbers. Patients receiving dapagliflozin were propensity score matched (1:3) with DPP-4i patients. Actual costs for hospital care (hospitalizations and outpatient hospital visits) and drug dispenses were extracted and cumulatively calculated per patient during follow-up. The matched population included 15,996 patients; 3,999 new users of dapagliflozin and 11,997 new users of DPP-4i. The groups were well balanced. Mean age at baseline was 62.0 years, 22.8% had a cardiovascular disease, and mean total 12-month pre-baseline total healthcare cost was \$2,981. At 18 months, total mean cumulative cost was numerically lower in the dapagliflozin group versus the DPP-4i group; \$6,042 versus \$6,363, difference -\$321 (95%CI -\$757 to \$107; p=0.128). The dapagliflozin group was associated with significantly lower hospital costs; -\$510 (-\$942 to -\$92; p=0.016), and significantly higher drug costs, \$190 (\$137 to \$244; p<0.001). Hospital costs related to cardiovascular disease were numerically lower for dapagliflozin, -\$122 (-\$304 to \$65; p=0.230). Initiation of dapagliflozin was associated with a lower relative risk (0.78 vs DPP-4i; p=0.042) for all-cause mortality. In this observational study, new use of dapagliflozin was associated with a similar total healthcare cost and lower risk of all-cause mortality compared to DPP-4i.



#### HEALTHCARE COSTS AMONG TYPE 2 DIABETES PATIENTS FOLLOWING NEW USER INITIATION OF DAPAGLIFLOZIN VERSUS SULFONYLUREA: A NATIONWIDE OBSERVATIONAL STUDY IN SWEDEN

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Abstract: To describe healthcare costs of type 2 diabetes patients up to 18 months following initiation of dapagliflozin or sulfonylurea. All new users of dapagliflozin or sulfonylurea, on top of existing glucose lowering treatment, during 2013-2015 were identified and followed in the mandatory Swedish Prescribed Drug-, National Patient-, and Cause of Death Registers. Individual patientlevel data were linked using unique personal identification numbers. Patients receiving dapagliflozin were propensity score matched (1:3) with sulforylurea patients using >90 variables. Actual costs for hospital care (hospitalizations and outpatient-hospital visits) and drug dispenses were extracted and cumulatively calculated per patient during follow-up. The matched population included 11,928 patients; 2,982 new users of dapagliflozin and 8,946 new users of sulfonylurea. The groups were well balanced. Mean age at baseline was 61.9 years, 21.5% had a cardiovascular disease, and mean total 12-month pre-baseline total healthcare cost was \$2,679. At 18 months, total mean cumulative costs in the dapagliflozin and sulfonylurea groups, respectively, were similar; \$5,573 vs \$5,506, difference \$67 (95%)

CI -\$360 to \$527; p=0.696). The dapagliflozin group was associated with significantly lower hospital costs; -\$821 (-\$1,238 to -\$372; p=0.002), and significantly higher drug costs; \$889 (\$836 to \$945; p<0.001). Hospital costs related to cardiovascular disease were lower for dapagliflozin; -\$217 (-\$410 to -\$21; p=0.030). Initiation of dapagliflozin was associated with a lower relative risk (0.68 vs sulfonylurea; p=0.012) for all-cause mortality. In this observational study, new use of dapagliflozin was associated with a similar total healthcare cost and lower risk of all-cause mortality compared to sulfonylurea.



#### HEALTHCARE COSTS AMONG TYPE 2 DIABETES PATIENTS FOLLOWING NEW USER INITIATION OF DAPAGLIFLOZIN VERSUS INSULIN: A NATIONWIDE OBSERVATIONAL STUDY IN SWEDEN

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To describe healthcare costs of type 2 diabetes patients up to 18 months following initiation of dapagliflozin or insulin. All new users of dapagliflozin or insulin, on top of existing glucose lowering treatment, during 2013-2015 were identified and followed in the mandatory Swedish Prescribed Drug-, National Patient- and Cause of Death Registers. Individual patient-level data were linked using unique personal identification numbers. Patients receiving dapagliflozin were propensity score matched (1:3) with insulin patients. Actual costs for hospital care (hospitalizations and outpatient hospital visits) and drug dispenses were extracted and cumulatively calculated per patient during follow-up. The matched population included 15,540 patients; 3,885 new users of dapagliflozin and 11,655 new users of insulin. The groups were well balanced. Mean age at baseline was 61.4 years, 19.2% had a cardiovascular disease, and mean total 12-month pre-baseline total healthcare cost

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was \$2,205. At 18 months, total mean cumulative cost was significantly lower in the dapagliflozin group versus the insulin group; \$5,191 versus \$5,948, difference -\$757 (95% CI -\$1,149 to -\$403; p<0.001). The dapagliflozin group was associated with significantly lower hospital costs; -\$1,367 (-\$1,756 to -\$1,030; p<0.001), and significantly higher drug costs; \$610 (\$559 to \$657; p<0.001). Hospital costs related to cardiovascular disease were numerically lower for dapagliflozin; -\$145 (-\$311 to \$30; p=0.120). Initiation of dapagliflozin was associated with a lower relative risk (0.46 vs insulin; p<0.001) for all-cause mortality. In this observational study, new use of dapagliflozin was associated with lower risk of all-cause mortality compared to insulin.



#### ACCESS TO DIABETES CARE IN THE RETAIL PHARMACY SETTING: COMPTON EXPERIENCE

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**Background:** Patients from lower socioeconomic backgrounds are at higher risk for diabetes and access to healthcare is challenging for those patients. Retail pharmacies are trained to provide diabetes care and education. We assessed whether individuals who attended 2016 and 2017 Back to School and Health Fairs in Compton, California received diabetes education and care at local retail pharmacies.

*Methods:* The survey was administered to adult subjects visiting a nonprofit educational booth, in the language they feel most comfortable in communicating (i.e. English or Spanish). Chi-square test was used to assess the impact of confounding variables on the utilization of retail pharmacy for health education.

**Results:** 119 subjects (n=99, 84% Hispanic, n=16, 13%: African American, n=4, 3% Other) participated in the study, 33 patients (27.7%) had diabetes. 13 out of 33 (39%)

received diabetes care in local retail pharmacy. 7 out of 33 (21%) was educated about glucometer use, and 17 out of 33 (52%) received vaccines in the retail pharmacy. Patients who were male (p=0.04), African American (p=0.002) whose primary language was English (p=0.001), had health insurance (p value=1.4 x 10-5) and received other medical care at a retail pharmacy (p value= 0.014) were more likely to get diabetes care in the pharmacy setting.

*Conclusions:* In our study 61% of the diabetic patients did not receive diabetes counseling from their local pharmacist. Retail pharmacies can help close the diabetes health-care access gap in the lower socioeconomic settings.

#### ACANTHOSIS NIGRICANS: THE VISIBLE SIGNAL OF A SILENT SPECTRUM IN POLYCYSTIC OVARY SYNDROME

#### Márcio Augusto Ávila, MD, PhD;

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**Context:** Evidence is accumulating that the vocalization of cardiovascular risk in polycystic ovary syndrome (PCOS) is under the pathology and wide scope of severity concerning ponderal status and defective homeostasis. Objective: To further understand the interrelations of acanthosis nigricans (AN) with metabolic dysfunction in PCOS, expressing the morbid enlacements of disturbed weight and insulin sensitivity.

*Method:* A hundred consecutive patients affected by PCOS, diagnosed according to the consensus of Rotterdam (2003), in agreement with the complete phenotypic picture (hyperandrogenism, ovulation dysfunction, polycystic ovaries typed), and the metabolic syndrome (MS) classification assigned (Grundy et al., 2005), became eligible for the cross-sectional prospective study. Excess weight and resonances of insulin resistance (Schwartz, 1994) related to AN were screened by means of body mass index (BMI), abdominal circumference (AC), and homeostatic model assessment of insulin resistance (HOMA-IR). The coefficient of determination (denoted by R2) and the significance p-value (<0.05) corroborated the statistical analysis.

**Results:** Prevalence of AN (53%) was dominant in the neck, over 90% (apart or in combination with other areas). Prevalence of SM reached 36% (86.1% associated with AN). Mean values of BMI, AC and HOMA-IR related to AN were 36.23±8.87 kg/m2, 102.96 cm, 2,23, respectively. The highly significant p-value=6.113×10-13 and

moderate association (R2=41.2%) between AN and BMI prevailed with respect to the other variables, ie: AC (p-value= $5.236.\times1012$ ; R2=38.0%) and HOMA-IR (p-value=0.0003567; R2=11.7%).

*Conclusion:* The proteiform presentation of PCOS implies that coexistence of AN and metabolic dysfunction encompass the relevance ascribed to the significance of underlying mechanisms of the disease.

#### OVEREXPRESSED GENES LIPE, ADIPOQ Y G0S2 IN PRIMARY ADIPOCYTES DERIVED FROM VISCERAL ADIPOSE TISSUE OF PATIENTS METABOLICALLY HEALTHY BUT OBESE AND METABOLICALLY UNHEALTHY AND OBESE

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*Introduction:* Obesity is a chronic disease(1), which progresses with an increase in the size of the adipocyte producing molecular and cellular changes that later cause a change in systemic metabolism. Excess food, low physical activity and environmental factors interact with genetic susceptibility producing a positive energy balance(2). Phenotypically, there is a clear difference between metabolically healthy but obese (MHO) and metabolically unhealthy and obese patients (MUO). The objective is to find the difference in the gene expression profile of adipocytes from these phenotypes of obese patients.

*Material and Methods:* Morbid obese patients undergoing bariatric surgery divided into two groups phenotypically by metabolic syndrome (NCEP-ATP III) criteria: MUO and MHO. A biopsy of visceral adipose tissue (VAT) was taken to make a primary adipocyte cell culture. RNA was obtained for microarrays.

**Results:** LIPE (Lipase); ADIPOQ (Adiponectin) and G0S2 showed a significant and reproducible elevation during the multiple comparison analysis of RNA transcribed from primary adipocyte genes of MHO (n = 5, considered as control) vs. MUO (n = 7, considered as a comparator).

*Conclusions:* According to profile comparison, MUO was characterized by overexpression of ADIPOQ (involved in all the diseases associated with adiponectin deficiency)(3), LIPE (hydrolyzes stored triglycerides to free fatty acids, non-alcoholic fatty liver, dyslipidemia) and G0S2 (regula-

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tion of adipocyte size and lipolysis control)(4). These results suggest the participation of these different genes on the pathophysiology of the metabolic risk attributed to the MUO phenotype.

**References:** 1. WHO: Report of a WHO Consultation. 10 facts on obesity: World Health Organization; Updated May 2017. 2. 2. Bray G.A., Kim K., Wilding J.P.H. 2017 Obesity Reviews vol: 18 pág. 715-723 3. Juárez-Rojas JG, et al. 2017 Arch Med Res; 48 -1, 73 4. Skopp A, et al. Arch Physiol Biochem 2016;122(2):47-5

Overexpression of MHO-1 vs. MUOs



**Fig1.** Overexpression levels of LIPE, ADIPOQ y G0S2 of different patients MUO vs. MHO-1.



Overexpression of MHO-2 vs. MUOs

**Fig 2.** Overexpression levels de LIPE, ADIPOQ y G0S2 of different patients MUO vs MHO-2.

Tabla 1. Genes overexpressed in primary adipocytes of VAT.
Analysis of times of overexpression on the control
(MHO vs MUO)

	MHO vs. MUO Representative Comparison	MHO vs. MUO Representative Comparison 2
LIPE	10.24	5.25
ADIPOQ	6.11	7.335
G0S2	2.01	2.07

#### MEDIATORS OF LOCAL HEPATIC METABOLIC DAMAGE AND NAFLD IN PATIENTS WITH OBESITY AND METABOLIC RISK

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**Background:** The metabolic syndrome (MS) is associated with an increased production of nitrogen metabolites that favor the development and progression of non-alcoholic fatty liver disease (NAFLD). Among the population that presents obesity, there is a phenotype with a high metabolic risk known as metabolically unhealthy obese (MUO), similar to the criteria of MS, even in its high prevalence of NAFLD, as opposed to the phenotype known as metabolically healthy obese (MHO). Aim: This study evaluated the hepatic concentration of nitrogen metabolites in relation to the severity of NAFLD in patients with a metabolic risk phenotype. We hypothesize that nitrogen metabolites are higher in advanced stages of NAFLD in patients with the MUO phenotype.

*Methods:* This observational, cross-analytical study included candidates for bariatric surgery, with a liver biopsy available for the diagnosis and staging of NAFLD. Two groups were formed (MHO vs MUO, based on the MS criteria) and also according to the NAFLD progression (steatohepatitis F0-F1 vs F2-F4). The hepatic concentration of nitrogen metabolites was determined by enzymatic kinetics assays.

**Results:** NAFLD progression was associated with the metabolic phenotype. Regarding the metabolites of metabolic damage, the hepatic ammonium concentration was related to the progression of NAFLD in the MUO phenotype. Citrulline and hepatic nitrites were only related to the metabolic phenotype, regardless of the NAFLD condition.

*Conclusions:* The mediators of local hepatic metabolic damage, selectively related to the progression of NAFLD, were identified in patients with metabolic risk phenotype. This suggests their potential as new prognostic and therapeutic targets.



**Graph 1.** The levels of ammonium, citrulline and nitrites in each gram of liver were assessed from an initial sample of 200mg of this tissue, as a result of several enzymatic kinetics tests. This graph represents the levels of ammonium. The MHO AR group was not included due to lack of patients. Abbreviations: MHO, metabolically healthy obese; MUO, metabolically unhealthy obese; LR, low-risk steatohepatitis with fibrosis of stages 0 to 1; HA, high-risk steatohepatitis with fibrosis of stages 2 to 4.

#### HYPOGLYCEMIA RISK ASSOCIATED WITH BASAL INSULIN USE IN TYPE 2 DIABETES (T2DM): THE LIGHTNING STUDY

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**Background and Aims:** The Lightning study aims to utilize real-world electronic health record data, representative of the general population and real-life practice, to assess hypoglycemia rates in patients with type 2 diabetes (T2DM) prescribed first- (glargine 100 U/mL [Gla-100], detemir [IDet]) or second-generation (degludec [IDeg], glargine 300 U/mL [Gla-300]) basal insulin (BI) analogs.

*Methods:* We collected data for BI treatments between April 1, 2015 and December 31, 2016. This preliminary analysis focuses on patients switching BIs, to validate findings from previous real-world Gla-300 studies. Propensity score matching (PSM) for variables including BI start date, diabetes duration, patient demographics, comorbidities and baseline HbA1c ensured similar baseline characteristics between treatment groups, minimizing potential confounders. Period of BI use was the unit of analysis. Main endpoints: severe hypoglycemia event rate and HbA1c change from baseline to 76-180 days follow-up. **Results:** Severe hypoglycemia rates were significantly lower in patients switching from any BI to Gla-300 vs those switching to Gla-100 (p=0.009) or IDet (p=0.002), and comparable vs those switching to IDeg (p=0.370) (Figure). Between-treatment difference in HbA1c reduction was  $\leq 0.09 \%$  for all comparisons.

*Conclusions:* Findings from the Lightning study PSM analysis indicate significantly lower rates of severe hypoglycemia for Gla-300 vs first-generation BIs and comparable rates vs IDeg, without compromising HbA1c reduction, in patients with T2DM switching from any previous BI. These results are consistent with previous randomized controlled trials and other real-world analyses of Gla-300. Further analyses are planned to correlate the different incidence of severe hypoglycemia with clinical and economic outcomes.



Figure: Estimated rates of severe hypoglycemia

#### INTERRELATIONS BETWEEN CUTANEOUS PROFILE AND METABOLIC DYSFUNCTION IN POLYCYSTIC OVARY SYNDROME

#### Roberto Bueno de Paiva, MD;

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*Introduction:* The cutaneous presentation (acne, hirsutism, acanthosis nigricans, androgenic alopecia) performs a profile that concerns the interrelations between endocrine and metabolic dysfunction in polycystic ovary syndrome (PCOS) Objective: To examine the association between the cutaneous profile and contingent features of metabolic dysfunction in the course of PCOS.

*Method:* One hundred patients affected by PCOS diagnosed according to consensus of Rotterdam (2003), under full phenotype expression (hyperandrogenism, ovulation dysfunction, polycystic ovaries typed), and metabolic syndrome (MS) with respect to the classification proposed

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by Grundy et al. (2005) were investigated. In addition, the presence of hirsutism, score  $\geq 8$  (Hatch et al., 1981), acne (Slayden et al., 2001), acanthosis nigricans (AN) (Schwartz, 1994), and androgenic alopecia (AGA) (Quinn et al., 2014), comprise the cutaneous evaluation. Insulin resistance was assessed by glucose/insulin ratio (G/I>6.4) (Carmina and Lobo, 2004). The p-value (<0.05) corroborated the statistical analysis.

**Results:** The prevalence of hirsutism, acne, AN, and AGA were 72%, 49%, 53%, and 18%, respectively. The prevalence of MS reached 36% and its correlation with cutaneous profile was exclusively significant with AN (p-value <0.01). Concerning G/I ratio, the p-value pointed out significance with hirsutism (0,04) and AN (<0,01). The average age, the mean body mass index and waist circumference were 25.72 ( $\pm$ 4.87), 30.63 ( $\pm$ 9.31), and 92.09 ( $\pm$ 18.73) respectively. Among the components of MS, the values of HDL-C (76%) prevailed.

*Conclusion:* Although the spectrum of cutaneous profile interests the space of public health, in the context of metabolic dysfunction - AN (primarily) and hirsutism are the protagonists.

#### CLINICAL VARIABLES ASSOCIATED WITH MODERATE-SEVERE MULTIMORBIDITY IN PATIENTS WITH TYPE 2 DIABETES

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**Purpose of Study:** Type 2 diabetes (T2D) affects 9.3% of Americans. Most suffer from multimorbidity, defined as having 2 or more comorbid medical conditions. We aimed to identify clinical variables associated with moderate-severe multimorbidity.

*Methods:* A retrospective, IRB-approved registry review was conducted on de-identified data from patients referred to Western Diabetes Institute (WDI) at Western University of Health Sciences, Pomona, California, between 6/1/2014 and 6/30/2016. The number (N) of moderate-severe comorbidities were categorized as either "low" (N=0-2), "intermediate" (N=3-4), or "high" (N=5-8). Nine of 13 clinical variable domains of the Diabetes Cross-Disciplinary Index (DXDI©) were used, including glycemic (HbA1c), low-density lipoprotein (LDL), and blood pressure (BP) control; CKD stage; retinopathy stage; periodontal health status; foot health; and BMI. Each domain is graded from 1 (good control or health/absence of disease) through 5 (poor control or advanced disease). Levels 1 and 2 were bundled and classified as "mild"; level 3 as "moderate"; and levels 4 and 5 as "severe".

**Results:** Data on 161 patients were evaluable. Over half (56.5%, n=91) were female, 81.9% (n=127) were Hispanic, and mean age was  $56.5 \pm 12.3$  years. A statistically significant association was detected between N of moderate-

severe comorbidities and "severe" DXDI© levels for LDL (p=0.0372), BP control (p=0.0465), CKD (p=0.0153), retinopathy (p=0.0014), foot disease (p=0.0698), and BMI (p=0.0497). No association was found for level of glycemic control or status of periodontal health (p>.05).

*Conclusions:* Multimorbidity in patients with T2D is associated with greater severity of measurable clinical variables, such as poor LDL, BP control, CKD, retinopathy, foot disease, and BMI.

Clinical Variables	DXDI© level	Low number of comorbidities %(N)	Intermediate number of comorbidities %(N)	High number of comorbidities %(N)	p-value
	Mild	56.1% (46)	37.8% (31)	6.1% (5)	
Glycemic Control (HbA1C)	Moderate	62.5% (10)	25.0% (4)	12.5% (2)	0.7
(1101110)	Severe	50.8% (32)	39.7% (25)	9.5% (6)	
	Mild	43.7% (59)	50.4% (68)	5.9% (8)	
Low Density Lipoprotein Level	Moderate	44.4% (8)	38.9% (7)	16.7% (3)	0.037
	Severe	0% (0)	75% (6)	25.0% (2)	
	Mild	54.6% (53)	43.3% (42)	2.1% (2)	
Blood pressure Control	Moderate	50.0% (12)	41.7% (10)	8.3% (2)	0.047
Connor	Severe $0\%$ (0) $75\%$ (6) $25$ Mild $54.6\%$ (53) $43.3\%$ (42) $2.1$ Moderate $50.0\%$ (12) $41.7\%$ (10) $8.2$ Severe $37.5\%$ (15) $47.5\%$ (19) $15$ Mild $45.0\%$ (59) $48.9\%$ (64) $6.1$ Moderate $21.7\%$ (5) $52.2\%$ (12) $26$ Severe $42.9\%$ (3) $57.1\%$ (4) $0.0$ Mild $45.5\%$ (60) $49.2\%$ (65) $5.2$ Moderate $14.3\%$ (2) $71.4\%$ (10) $14.5\%$	15.0% (6)			
	Mild	45.0% (59)	48.9% (64)	6.1% (8)	
CKD Stage	Moderate	21.7% (5)	52.2% (12)	26.1% (6)	0.015
	Mild         45.0% (59)         48.9% (64)           Stage         Moderate         21.7% (5)         52.2% (12)           Severe         42.9% (3)         57.1% (4)           Mild         45.5% (60)         49.2% (65)	0.0% (0)			
	Mild	45.5% (60)	49.2% (65)	5.3% (7)	
Retinal Health/ Retinopathy	Moderate	14.3% (2)	71.4% (10)	14.3% (2)	0.001
	Severe	6.7% (1)	66.7% (10)	26.7% (4)	
	Mild	62.3% (33)	34.0% (18)	3.8% (2)	
Periodontal Health/ Disease	Moderate	61.5% (32)	36.5% (19)	1.9% (1)	0.542
	Severe	57.1% (32)	33.9% (19)	8.9% (5)	
	Mild	45.5% (55)	47.1% (57)	7.4% (9)	
Foot Health/Disease	Moderate	52.2% (12)	43.5% (10)	4.4% (1)	0.070
	Severe	17.7% (3)	58.8% (10)	23.5% (4)	
	Mild	44.6% (25)	46.4% (26)	8.9% (5)	
BMI	Moderate	70.9% (39)	21.8% (12)	7.3% (4)	0.0497
	Severe	66.0% (33)	28.0% (14)	6.0% (3)	

DXDI levels: Mild = 1 and 2, Moderate = 3, Severe = 4 and 5

Comorbidities: Low = 0-2, Intermediate = 3-4, High = 5-8

#### REAL-WORLD EVIDENCE DEMONSTRATES COMPARABLE CLINICAL OUTCOMES OF SWITCHING FROM INSULIN GLARGINE 100 U/ mL (GLA-100) TO INSULIN GLARGINE 300 U/mL (GLA-300) VS INSULIN DEGLUDEC (IDEG) IN PATIENTS WITH TYPE 2 DIABETES (T2D)

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**Background:** This study compared clinical outcomes of T2D patients switched from using Gla-100 to Gla-300 or IDeg in a real-world clinical setting.

Methods: This retrospective, observational study used electronic medical records (EMRs) from the Predictive Health Intelligence Environment database. Inclusion criteria: adults with T2D; switched to Gla-300 or IDeg from using Gla-100 during 6 months before the switch (index date: first switch between 03/01/2015-12/31/2016); active in EMR for  $\geq 12$  months prior to index date and followed for 6 months after; A1C measures during 6 months before switching (Gla-300, n=2,893; IDeg, n=853). Gla-300 and IDeg switchers were propensity score matched 1:1 on baseline characteristics. Endpoints were A1C change, hypoglycemia (ICD-9/ICD-10 and/or plasma-glucose level ≤70 mg/dL) incidence and event rate (all hypoglycemia and hypoglycemia associated with hospitalization/emergency department service [hospitalization/ED-related]) during follow-up. A1C change was analyzed in a patient subgroup with A1C measures at both baseline and 3-6 months' follow-up in the matched cohorts.

**Results:** During follow-up, switching to Gla-300 (n=810) and IDeg (n=810) showed comparable hypoglycemia incidence (all: 11.9% vs 12.7%, respectively, P=0.45; hospitalization/ED-related: 4.4% vs 3.8%, respectively, P=0.80). Adjusted for baseline hypoglycemia, Gla-300 and IDeg showed similar hypoglycemia event rate during follow-up (all: P=0.88; hospitalization/ED-related: P=0.82). A1C decreased significantly from 8.95% to 8.46% for Gla-300 (n=364) and from 8.98% to 8.49% for IDeg (n=370) (both cohorts: P<0.01) during follow-up (comparable A1C reduction in both groups, P=0.97).

*Conclusion:* In a real-world setting, T2D patients on Gla-100 switching to Gla-300 or IDeg showed comparable glycemic control, hypoglycemia incidence and hypoglycemia event rate.

#### DISCOVERY OF NOVEL DIABETES-DAMAGED PROTEINS (E.G. PKG-I-ALPHA) THAT NORMALLY PROMOTE PANCREATIC BETA-CELL SURVIVAL/REGENERATION AND ANGIOGENESIS/ENDOTHELIAL CELL SURVIVAL AND PROTECT AGAINST OBESITY/FAT CELL DIFFERENTIATION AND INFLAMMATION, BY USING A NEW ULTRASENSITIVE ROBOTIC CAPILLARY ISOELECTRIC FOCUSING (cIEF) TECHNOLOGY

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Abstract: Current proteomic technologies (Westerns, ELISAs, Mass-Spec) have limitations that hamper identification of novel/previously-unrecognized proteins, especially lower-abundance proteins like receptors and cell-signaling mediators. Westerns and Mass-Spec lack high sensitivity, thus requiring large sample-sizes, and ELISAs, although sensitive, often lack specificity because of off-target-binding by antibodies. Our lab helped pioneer new/robotic cIEF technology (NanoPro-1000) for proteomic analysis. NanoPro-1000 has clear advantages: 1,000- and 100,000-times higher sensitivity than Westerns and 2-D gel/Mass-Spec, respectively, thus able to analyze extremely small samples (<100 cells). Previouslyunrecognized proteins below detection-limits of Westerns and Mass-Spec can now be identified/effectively characterized. Unlike ELISAs, off-target binding of antibodies can be detected and removed from analysis. Using cIEF technology, we identified a novel protein, PKG-I-alpha, promoting pancreatic-beta-cell/vascular-endothelial-cell survival and regeneration. Previously, PKG-I-alpha was identified in smooth muscle, mediating vasodilation/antihypertensive and penile-erectile actions of nitric oxide (NO). Importantly, PKG-I-alpha functional/kinase activity is damaged by oxidative stress from chronic inflammation, high glucose and high lipids during type-1 and type-2 diabetes, contributing to diabetic complications (cardiovascular diseases and erectile dysfunction). PKG-I-alpha also prevents inflammation in obesity-associated fat cells and M1-macrophages. Using cIEF, we found that pre-adipocytes express high-level PKG-I-alpha, which dramatically decreases during differentiation into pro-inflammatory fat cells. Lastly, our recent data using cIEF show that PKG-Ialpha is expressed at much higher levels in alpha-cell line (alpha-TC1), compared with relatively low-levels in betacell line (beta-TC6), suggesting that protection of alphacells and vulnerability of beta-cells during pathogenesis of diabetes may relate to differences in cytoprotective PKG-I-alpha, illustrating the value of using ultrasensitive cIEF technology.

#### THE IMPACT OF A DIABETES PREVENTION PROGRAM IN THE CLINICAL SETTING: ACTIVATING THE PATIENTS

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*Background:* Currently there is an epidemic of obesity and diabetes in the USA.

*Methods:* In a pilot study, we enrolled patients attending a Family Medicine Clinic in Ventura County, California, educated them on the pathogenesis of diabetes mellitus (DM), the consequences and prevention. We then conducted a survey to assess the impact of education. Chi-square test was used to determine the factors influencing patient response.

Results: 25 patients were enrolled, 17 (68%) were female; the average age was 40.7 ±13.7 years. 4% was AA, 12% was Asian, 16% was Caucasian and 68% was Hispanic/Latino. 64% reported annual income <\$40K. 52% reported "some college" as the highest level of education in their family; 36% reported Associate-Degree or Bachelor-Degree. 17 (68%) did not have diabetes, 3 (12%) had Type1 DM and 5 (20%) had Type2 DM. 23 (92%) of the patients reported that "they learned something". 18 (72%) stated that they will change their life style and 19 (76%) stated that they will share the information they learned with family and friends. The age, gender, ethnicity, family education, income, history of heart disease, stroke, diabetes or obesity did not influence the impact of the education. 79% with and 21% without a diabetic family member reported that they worry (p=0.04).

*Conclusion:* Regardless of having a family member with DM, patients respond to diabetes prevention education in the clinical setting and majority is willing to share the information with friends and family. An educational program may be implemented to activate the community to prevent DM.

#### PREVALENCE OF NONALCOHOLIC FATTY LIVER DISEASE AS ASSESSED BY VIBRATION CONTROLLED TRANSIENT ELASTOGRAPHY IN AN URBAN LOS ANGELES DIABETES AND METABOLISM CLINIC

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Abstract: Nonalcoholic fatty liver disease (NAFLD) represents a spectrum of liver disease from simple steatosis to nonalcoholic steatohepatitis (NASH). The prevalence of NAFLD in the general population has been reported at approximately 25%, with higher rates in patients with features of 'metabolic syndrome' or frank type 2 diabetes. Progression from simple steatosis to NASH may occur in up to 25% of patients, and persistent hepatic inflammation can progress to fibrosis, cirrhosis, and in some cases hepatocellular carcinoma. In the present cross-sectional analysis, we assessed hepatic steatosis and fibrosis, using Vibration Controlled Transient Elastography (VCTE) with Controlled Attenuation Parameter (CAP) (FibroScan<sup>®</sup>, EchoSens, Paris, France) in an urban Los Angeles diabetes and metabolism clinic. Results of FibroScans conducted from January 2nd, 2017 through September 30th, 2017 are reported. 576 patients underwent FibroScans during this timeframe. Patient characteristics included mean (±SD) age 53.9±10.6 y, BMI 31.4±6.0 kg/m2, 51.6% female, 94.5% Hispanic, 78.4% type 2 diabetes. Mean (±SD) CAP and Liver Stiffness Measure (LSM) were 291.8±57.2 dB/m (range 100-400 dB/m) and 6.2±3.5 kPa (range 2.1-34.3 kPa), respectively. 77.7% of patients had a CAP ≥250 dB/m, indicative of significant hepatic steatosis. 12.6% of patients had a LSM between ≥7.5-9.9 kPa and 9.0% had a LSM ≥10.0 kPa, indicative of F2 and F3/F4 fibrosis, respectively. Additional data including NAFLD risk scores and liver biopsies are currently being assessed. This analysis demonstrates a high prevalence of NAFL and NASH - as assessed by VCTE with CAP - in an obese and largely Hispanic population in Los Angeles, CA.

#### THE SIMPLEST WAY TO FOUND PEOPLE WITH METABOLIC SYNDROME AND RELATED COMPLICATIONS IS THE DIRECT ANALYSIS OF WAIST CIRCUMFERENCE CUT-OFF, WHICH PREDICTS THE PRESENCE OF METABOLIC SYNDROME AND OBESITY RELATED COMPLICATIONS, A STUDY IN THE WOMEN COLOMBIAN POPULATION

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*Objective:* To find the best cut-off of waist circumference (WC) to recognize Metabolic Syndrome-Obesity Related Complications (MS-ORC) in Colombian Women. A cut-off for WC has been recommended by IDF to Latin-Americans use the South-Asians cut-off (80 cm) due to lack of regional Studies. A trial in 278 Latin-American women proposed WC 90-92 cm corresponding VFA> 100 cm2. We rate a group of Colombian women in order to determine the best WC cut-off that detect MS-ORC included in Metabolic Syndrome criteria, without consideration of VFA.

**Design and Methods:** Subjects were 526 Colombian Women, edad 18-85 average 50.3 years-old, Body-massindex 27.05+/-6.49 kg/mt, patients from Endocrinology practice. Anthropometric parameters. Hyperglycemia, Dyslipidemia and Hypertension were evaluated as MS-ORC included criteria, According IDF definition. Established optimal WC threshold by means of receiver operating characteristic (ROC) curves for discriminate which women presented 2 or more MS-ORC.

**Results:** The waist cut-point better discriminates Colombian women was 80.5 cm to identify 2 MS-ORC, with sensitivity 84.2%, specificity 56.6%, PPV 57,7% and NPV 83,6%. The sensitivity and NPV of WC cut-off point (80.5 cm) identify subjects with MS-ORC above 80%. Contrary WC value of 92cm suggested by the VFA study, showed lower sensitivity (75.9%) but higher specificity (74.5%). These results are clinical less useful, so we propose continue using South-Asians WC initially IDF suggested. Conclusions: This study demonstrates that the first consideration to determine the WC cut-off must be the clinical utility, easily and cost-less find the high-risk patients. By serendipity the best cut-off is the original IDF recommendation.

WC	≥ 80.5 (cm)	< 80.5 (cm)	≥ 88 (cm)	< 88 (cm)
Age (years)	52.8 (±14.2)	46.4 (±13.2)	53.8 (±13.5)	48.25 (± 14.1)
BMI (kg/m²)	29.6 (±.4.8)	23.0 (± 2.6) †	31.3 6. (± 5.0)	24.5 (± 3.2) †
SBP (mmHg)	131.5 (± 18.3)	120.8 (± 15.2) †	134.6 (± 19.5)	122.9 (± 15.4) †
DBP (mmHg)	80.6 (± 9.4)	76.1 (± 8.7)	81.6 (± 9.3)	77.2 (± 9.0)
HDL (mg/dl)	51.4 (± 15.5)	58.5 (± 14.6)	51.24 (± 17.3)	56.03 (± 14.1)
TG (mg/dl)	149.2 (± 74.9)	114.7 (± 53.6) †	156.6 (± 80.5)	123.2 (± 58.5)‡
GLU (mg/dl)	99.7 (± 26.1)	86.6 (± 15.3)†	102.7 (± 28.8)	89.7 (± 17.8) †

WC Waist circumference; GLU, fasting glycaemia; HDL, cholesterol HDL; BMI Body mass index; SBP Systolic Blood pressure, DBP Diastolic Blood pressure, TG, triglycerides. p < 0.001, p < 0.005 for difference between groups.

#### CVD-REAL STUDY FINDINGS IN THE CONTEXT OF THE CURRENT SGLT-2I CARDIOVASCULAR OUTCOME TRIALS (CVOT)

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**Background:** Randomized, placebo-controlled, CVOTs of SGLT-2i have reported consistent cardiovascular (CV) and renal benefits in patients with T2D and elevated CV disease risk, suggesting a class effect.

*Methods:* CVD-REAL is the first large, multinational, observational, comparative effectiveness study assessing CV outcomes, including all-cause mortality (ACM), CV mortality (CVM), major adverse CV events (MACE), and hospitalization for heart failure (HHF) in a broad population of patients with T2D initiating SGLT-2i or other glucose-lowering drugs (oGLDs). We review the baseline characteristics and main findings of CVD-REAL in the context of the SGLT-2i CVOTs.

**Results:** Results from CVD-REAL were consistent with the SGLT2-i CVOTs (Table). The baseline characteristics differed, with lower prevalence of established CV disease in CVD-REAL studies (13–25%) than EMPA-REG OUTCOME (>99%) or CANVAS (66%). Additionally, in CVD-REAL the comparison was to an active comparator group, compared to placebo plus standard of care in the CVOTs.

*Conclusions:* The findings from CVD-REAL suggest that the benefits reported in the SGLT-2i CVOTs may be applicable to a broader T2D population in the real-world. CVD-REAL illustrates that properly designed and powered observational studies can effectively complement evidence from RCTs.

HR (95%CI)	<b>CVD-REAL</b> (N=309,056)	CVD-REAL Nordic (vs. oGLD) (N=91,320)	<b>CVD-REAL Nordic</b> (vs. DPP-4i) (N=34,328)	EMPA-REG OUTCOME (N=7,020)	<b>CANVAS</b> (N=10,142)
HHF	0.61 (0.51-0.73)	0.70 (0.61-0.81)	0.63 (0.50-0.81)	0.65 (0.50-0.85)	0.67 (0.52-0.87)
ACM	0.49 (0.41-0.57)	0.51 (0.45-0.58)	0.73 (0.59-0.90)	0.68 (0.57-0.82)	0.87 (0.74–1.01)
MACE	-	0.78 (0.56-0.90)	0.71 (0.56-0.90)	0.86 (0.74–0.99)	0.86 (0.75-0.97)
CVM	-	0.53 (0.40-0.71)	0.74 (0.44–1.23)	0.62 (0.49-0.77)	0.87 (0.72–1.06)

#### STUDY DESIGN AND METHODS OF THE CVD-REAL STUDY – A MULTINATIONAL STUDY IN PATIENTS WITH TYPE 2 DIABETES WHO ARE NEW USERS OF AN SGLT-2 INHIBITOR OR OTHER GLUCOSE-LOWERING DRUGS

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**Background:** CVD-REAL is a multinational, comparative effectiveness study of cardiovascular (CV) outcomes, including major adverse CV events, CV death, all-cause death and heart failure, in patients with T2D who are new users of SGLT-2 inhibitors versus other glucose-lowering drugs. More than 1.3 million patients were included, and the results from the primary and secondary analyses were recently presented at international congresses and published as manuscripts. Questions regarding the methodology and the generalizability of the results have highlighted the need for a more detailed description of how the data were extracted and analyzed. The aim of this presentation is to describe the CVD-REAL study design and methods, with emphasis on the challenges of analyzing data from multiple countries and data sources.

*Methods and Results:* The study was conducted in two phases; an initial descriptive phase including assessment of data quality, comparability and statistical power, as well as non-parsimonious propensity score matching; followed by a comparative phase addressing the endpoints. Important considerations in the study design included the use of health registers, definitions of study groups, inclusion and exclusion criteria, assessment of study group comparability, propensity score derivation and matching, specifications of on-treatment follow-up times and events, and the between-group comparisons and meta-analyses.

*Conclusions:* CVD-REAL is an example of how realworld, comparative effectiveness studies, including patients from across world regions, can complement CV outcome trials in the understanding of the outcomes associated with treatment with different glucose-lowering drugs.

#### A HIGH IMPACT CARDIOVASCULAR PREVENTION PROGRAM FOR LOW-INCOME LATINO PATIENTS

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**Background:** Heart disease is the number one cause of death in Ventura County with a crude death rate of 107 per 100,000, a risk of dying equivalent to one for every 994 persons. The county ranks 20th in CA for deaths due to heart disease and falls short of meeting Healthy People 2020 objectives (CA Department of Public Health). With proper clinical care and a healthy lifestyle, heart disease can be managed to prevent premature death and medical complications.

*Methods:* To improve the health outcomes of low-income, uninsured Latinos suffering from or at high risk of heart disease through culturally competent, patient-centered services and programs including: early detection through community health screenings; access to preventative care and medical specialists; healthy lifestyle support; oneon-one socio-emotional support; empowerment through improvement of food environments and leadership experiences for low-income, Latino high school interns serving as community health workers. Health assessment data and laboratory clinical measures were conducted. A qualitative pre/post survey using a likert scale measured changes in knowledge, attitudes and behaviors.

Results: 252 patients were enrolled, 199 were female and 53 were male; the average age was 39 years. 100% were Hispanic/Latino. 100% reported annual income <\$30K and have an FPL classification of very low income. The majority are low-literacy in any language, with over 60% not completing middle school. About 100 have Type 2 diabetes, 100% are at risk for cardiovascular disease and presented with at least two risk factors at the beginning of the program. Sample of key 1-year results included below: 54% (110 out of 204) participants reduced their BMI levels by an average of 0.5 points from 31.9 to 31.4, 39% (58 out of 147) participants reduced their systolic pressure by 5 points. 55% (81 out of 147) participants reduced their diastolic pressure by 2 points, Average BP at baseline = 129/76 (n=208), average at the end of one year 124/74 (n=208), 71% (98 out of 138) participants reduced their cholesterol levels by an average of 29 points or maintained their levels within normal range, 80% (110 out of 138) participants increased their HDL levels by an average of 47 points or maintained their levels within normal range. 78% (107 out of 138) participants reduced their LDL levels by an average of 56.6 points or maintained their levels within normal range. 64% (88 out of 138) participants reduced their Triglyceride levels by an average of 44.7 points or maintained their levels within normal range. 46% (63 out of 138) participants reduced their glucose levels by an average of 31.5 point or maintained their levels within normal range. 46% (63 out of 138) participants reduced their HGBA1C levels by 0.5 points or maintained their levels within normal range.

On a scale from 1 to 6, 4.2 say they eat fruits and vegetables 4-5 times day, 3-4 times a week, up 2.1 points from the pre test score. On a scale from 1 to 6, 3.5 say they eat fish, chicken, or turkey instead of meat, up 2.1 points from the pre test score. 67% (100 out of 147) of participants drink more than 4 glasses of water a day. 40% (57 out of 143) participants exercise more than 3X a week, up 23% since pre test score. 44% (62 out of 143) participants exercise 1-2X a week, up 34% from pre test score. 22% (31 out of 143) exercise every day, up from 17% in the pre test score.

*Conclusion:* Sustainable, positive health outcomes can be achieved with culturally sensitive, culturally competent cardiovascular health programs and services that take into consideration the many barriers and challenges faced by low-income Latino adults as we demonstrate in our multi-year findings. Adjusting traditional health and clinical models of care and prevention programming is essential for improved outcomes.