Posters

BASIC SCIENCE (PPB)

PPB1. MicroRNA expression profiling for the early detection of type 2 diabetes in South African women of mixed ethnic ancestry

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Background: MicroRNAs (miRNAs) are small, non-coding RNAs that regulate gene expression post-transcriptionally. Dysregulated miRNA expression patterns have been demonstrated during the development and progression of type 2 diabetes (T2D). This has attracted considerable interest in the potential use of circulating miRNAs as biomarkers to identify individuals at risk for T2D. The objective of this study was to determine whether miRNA expression profiles differ between T2D, impaired glucose tolerance (IGT) and normal glucose tolerance (NGT) women of mixed ethnic ancestry.

Methods: MiRNAs were extracted from the whole blood and serum of age-, gender- and ethnicity-matched women with newly diagnosed T2D (n=4), IGT (n=4) and NGT (n=4). The quantity and integrity of RNA samples were determined using nanodrop spectrophotometry and with the Agilent 2100 Bioanalyser, respectively. Blood-derived miRNAs were subjected to transcriptome sequencing, thereafter transcript levels of selected novel and annotated miRNAs were validated in the whole blood and serum of these women using quantitative real-time PCR (qRT-PCR). Target prediction analysis, gene ontology (GO) and Kyoto encyclopedia of genes and genomes (KEGG) pathway analyses were conducted to identify functional enrichment of genes predicted to be regulated by selected miRNAs.

Results: Sequencing identified 263 annotated and 151 novel miRNAs in the whole blood of women of mixed ethnic ancestry. The expression of five annotated miRNAs (miR-21, miR-27b, miR-98, miR-143, and miR-379) were differentially expressed (≥1.1-fold; p≤0.05) according to glucose tolerance. Of these, only the directional significant increase of miR-27b in women with IGT compared to NGT was confirmed in the whole blood (1.55-fold; p=0.07) and serum (2.0-fold; p≤0.05) of these women using qRT-PCR. Moreover, the expression of five novel miRNAs selected based on effect size (MYN08, MYN059) and randomly (MYNO22, MYN066 and MYN095) were confirmed by qRT-PCR in the same dataset. The expression of MYN059 was of particular interest due to its directional decreased expression in individuals with T2D compared to individuals with NGT (2.2-fold, $p < 0.05$). Functional enrichment identified 464 Gene Ontology terms and 5 significant KEGG pathways enriched by gene targets of miR-27b, and 153 GO terms and 12 KEGG pathways enriched by gene targets of MYNO59. Biological processes such as regulation of RNA transport and translation, immune responses, histone methylation and signal transduction, and biological pathways associated with glucose transport and insulin regulation were enriched by miRNA gene targets.

Conclusion: This study showed that annotated and novel miRNA profiles differ during T2D progression, and can discriminate between T2D, IGT and NGT in South African women of mixed ethnic ancestry. These miRNAs may offer potential as biomarkers for risk stratification and intervention strategies to prevent or delay T2D progression in this population, thus warranting further investigation of these differentially expressed miRNAs.

PPB2. Identification of polyphenolic compounds responsible for the anti-obesity properties of Cyclopia intermedia (honeybush) using high performance counter-current chromatography

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Background: Polyphenols have a range of health promoting effects against metabolic diseases such as obesity. We have previously showed that a polyphenol-enriched organic fraction of *Cyclopia intermedia* (*C. intermedia*) decreases lipid content in 3T3-L1 adipocytes and reduces bodyweight gain in obese db/db mice, demonstrating its potential as an anti-obesity nutraceutical. The aim of this study was to explore polyphenolic compounds responsible for the anti-obesity properties of a polyphenol-enriched organic fraction of *C. intermedia* by fractionation with high performance counter-current chromatography (HPCCC).

Methods: The organic fraction of *C. intermedia* was separated into four fractions using HPCCC, and their phenolic content was determined using quantitative high performance liquid chromatography-diode array detection (qHPLC-DAD). The effects of the four fractions on lipid content, lipolysis and cell viability were measured in differentiating 3T3-L1 pre-adipocytes and in mature 3T3-L1 adipocytes using the Oil Red O, glycerol release and adenosine triphosphate (ATP) assays, respectively. The expression of genes and proteins relevant to lipid and energy metabolism was assessed using quantitative real-time PCR and western blot analysis, respectively.

Results: The polyphenol-enriched organic fraction of *C. intermedia* was separated into four major fractions (F1 - F4) with different polyphenolic content and bioactivity. F1 and F4 decreased lipid content in both differentiating 3T3-L1 pre-adipocytes and in mature 3T3-L1 adipocytes, while F3 inhibited lipid accumulation in differentiating 3T3-L1 pre-adipocytes only, and F2 decreased lipid content in mature 3T3-L1 adipocytes only. F1, F2 and F3 stimulated

lipolysis in mature 3T3-L1 adipocytes. ATP quantification showed that F1 and F3 deceased cell viability by 24.4% ($P < 0.001$) and 21.5% ($P < 0.05$), respectively, in differentiating 3T3-L1 pre-adipocytes whereas F4 increased ATP content by 14.9% ($P < 0.05$) in mature 3T3-L1 adipocytes. At the molecular level, increased messenger RNA (mRNA) expression of hormone sensitive lipase (HSL) was observed in mature 3T3-L1 adipocytes treated with F1 (1.60 fold, $P < 0.05$) and F2 (1.61 fold, $P < 0.05$), while the mRNA expression of uncoupling protein 3 (UCP3) was increased by treatment with F1 (1.45 fold, $P < 0.05$) and F4 (1.52 fold, $P < 0.05$). Moreover, F4 increased the protein expression of peroxisome proliferator-activated receptor alpha (PPARα) by 1.55-fold ($P < 0.05$).

Conclusion: Chromatographic separation of a crude extract of *C. intermedia* showed that the anti-obesity effects of *C. intermedia* is mediated by more than one polyphenolic compound. Synergy between these compounds could lead to improved bioactivity, thus supporting the use of phenolic cocktails or crude plant extracts, rather than single compounds as nutraceuticals for obesity.

PPB3. Screening black South African females with Type 2 Diabetes Mellitus for mutations in the Peroxisome Proliferator-activated receptor gamma gene

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Background: Type 2 Diabetes Mellitus (T2DM) is a chronic metabolic disorder, which is caused by a combination of an inadequate response to insulin secretion and a resistance to insulin action. The peroxisome proliferator-activated receptor gamma (*PPARG*) gene has been identified as one of the major genes to have an impact on the risk of T2DM. The Pro12Ala polymorphism (rs1801282) is one of the most common mutations found within *PPARG* and has been described in many different populations.

However, it has not yet been established whether the Pro12Ala variant has a significant association with T2DM in the black, female South African population. The aim of this study was to screen for novel T2DM genetic variants in the *PPARG* gene and to determine the presence of the Pro12Ala polymorphism in black South African women with T2DM.

Methods: A descriptive case control study was performed on 184 black female South African participants that consisted of 93 T2DM diagnosed patients and 91 non-T2DM control participants. The two groups were individually matched according to age and body mass index (BMI). Genotyping of the *PPARG* gene SNP (rs1801282) was performed with Real-time PCR. Next Generation Sequencing (NGS) was used to identify novel polymorphisms and to detect the prevalence of previously described variants within the *PPARG* gene exon region.

Results: The Real-time PCR genotyping results of SNP (rs1801282) showed that 183 had the homozygous Pro/Pro genotype and only one had the heterozygous Pro/Ala genotype (n=184). The Ala/Ala genotype was not detected in this study population. Although the study sample is only a small representation of the total population, the results are in accordance with literature that the Ala12 *PPARG* allele probably appeared in human evolution after the first migration out of Africa.

Additionally, NGS results identified two variants. The one variant (rs41516544) has not been associated with clinical relevance. The other variant (rs3856806) is a well-described polymorphism and has been associated with having a protective effect against T2DM and was present in a control participant.

Conclusion: Ala12 *PPARG* genotype has been described as diabetes-protective in Caucasian populations and the pro12 *PPARG* genotype as being associated with insulin resistance and increased BMI. However, it seems unlikely that this SNP is useful as a diabetes associated risk predictor in the studied population.

In depth analysis of the NGS data revealed three synonymous polymorphisms in the *PPARG* coding region. Two of these variants were identical and found in a control and a patient; the other variant was found in a control sample. SNP (rs3856806) showed an association with T2DM in several populations, usually in combination with an additional variant indicating a common variant with a minor clinical effect. Nevertheless, this variant might be significant in its association to T2DM in the black South African population and should be investigated further.

PPB4. Identification of novel small molecule therapeutics targeting the Growth Hormone Releasing Hormone Receptor (GHRHR).

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Background: Growth Hormone (GH) is synthesised and secreted from the anterior pituitary and has a role in many physiological and pathophysiological processes. Disorders such as acromegaly and dwarfism can occur when too much (hyperpituitarism) or too little (hypopituitarism) is secreted. Regulation of GH secretion is controlled by two peptides, somatostatin and growth hormone releasing hormone (GHRH), which are released by the hypothalamus. GHRH is therefore considered to be a primary regulator of the pituitary GH axis, but also has various other important extra-pituitary effects. It elicits its effects through binding to the growth hormone releasing hormone receptor (GHRHR). Thus, GHRH and GHRHR are very important therapeutic targets although no non-peptide therapeutics currently exist targeting the GHRHR. GHRHR belongs to the G protein-coupled receptor (GPCR) family, which play a crucial role in signal transduction. Remarkable progress has been made in the structural biology of GPCRs over the last few years, opening up possibilities for applying structure-based approaches to GPCR drug discovery efforts, including *in silico* docking, a computational method of docking small flexible molecules to a protein structure.

Methods: Using *in silico* docking, 50 putative GHRHR interactive compounds have been designed using predicted models of the GHRHR extracellular and transmembrane domains. These have been synthesised and their *in vitro* activity tested using HEK 293-T cell lines expressing GHRHR. Agonist and antagonist activities of the compounds have been tested using a CRE-luciferase reporter assay which responds to cAMP, a second messenger produced upon GHRHR activation. GHRH and the antagonist JV-1-36 have been used as controls for GHRHR agonism and antagonism, respectively.

Results: Western blotting confirmed the expression of GHRHR in transfected HEK293-T cells. A CRE-luciferase assay then identified one agonist compound, which showed a significant level of

stimulation. No stimulation of this compound was found in cells not expressing GHRHR, confirming that the response was specific. Dose response curves provided information on the potency/efficacy of this compound in relation to GHRH. Several putative antagonists were also identified, which were able to reduce GHRH-induced stimulation of the receptor and their selectivity for the GHRHR has been confirmed.

Conclusion: GHRH and GHRHR are important therapeutic targets due to their role in many physiological processes and disorders. The development of agonists and antagonists for the GHRHR is therefore important. We have identified several small-molecule GHRHR interactive compounds, confirming the validity of *in silico* docking as an approach for GPCR-targeted drug development. The 'hit' compounds will be further refined through "in catalogue" screening, aiding in the process of producing new effective therapeutic compounds.

PPB5. Functional Characterisation of Gonadotropin-Releasing Hormone-Estrogen Conjugates as Potential Therapeutics for Prostate Cancer

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Background: Prostate cancer is estimated to be increasing at a rate of 2-3% worldwide according to the World Health Organisation. In many countries, it is one of the most common causes of cancer-related deaths, with a higher prevalence in developed countries as well as in Southern Africa, making it highly relevant in the South African context.

Prostate cancer is an androgen-dependent disease and androgen deprivation therapy (ADT) is a standard and effective treatment for prostate cancer that allows avoidance of more drastic measures such as orchiectomy. The hypothalamic-pituitary-gonadal axis controls reproduction and puberty, and in men is responsible for the production and regulation of androgens from the testes. Gonadotropin releasing hormone (GnRH) is the main hormone controlling this axis. Therefore, GnRH agonists (which down-regulate this axis and therefore reduce the level of androgens produced) are currently the foremost therapeutic option for ADT, and have the added benefit of intrinsic anti-proliferative activity. However, ADT is associated with negative side effects, many similar to that of post-menopausal women, such as loss of trabecular bone mass, hot flushes and loss of libido, due to a concomitant decrease in estrogens as well as androgens. It therefore is important to find novel treatments that remain efficacious against the disease but ameliorate the associated negative side effects and provide patients with an improved quality of life.

Methods: Estradiol and the phytoestrogen genistein were conjugated to a GnRH agonist by CPC Scientific (Sunnyvale, USA). Conjugates have been tested to determine whether both the GnRH and the estrogen moieties retain their respective activities. The ability of the conjugate to stimulate production of inositol phosphate in human embryonic kidney cells stably expressing GnRH receptor (GnRHR) was used as an indication to measure agonist activity at the GnRHR. T47D breast cancer cells expressing estrogen receptor and stably expressing an estrogen response element (ERE) driving the expression of a luciferase reporter gene were stimulated by the conjugates. Response was monitored by a luminometer to assess estrogen receptor activity. In each assay the conjugated molecule has been compared to its respective unconjugated counterparts as well as a vehicle control. Activities of 17 β-estradiol and genistein conjugates were also compared.

Results: Both the Genistein-GnRH analogue and the 17 β-estradiol-GnRH analogues were able to achieve comparable levels of stimulation to the GnRH analogue alone in cells expressing the GnRH receptor. Similarly, it was found that estrogen receptor activity is stimulated by both conjugates to the same degree as unconjugated estrogens. Both conjugated analogues gave similar responses in each assay.

Conclusion: The results demonstrate that the conjugates retain GnRH and estrogen activity. We now intend to examine their potential to alleviate ADT side effects associated with the treatment of PC. Their impact on prostate cancer cell proliferation will also be examined.

This study looks to use these innovative molecules to establish a base that will allow new therapies to be created to extend duration of action of current ADT treatment as well as reducing negative side effects traditionally associated with these treatments.

PPB6. The FOK1 polymorphism in the vitamin D receptor gene is associated with type 1 diabetes in the black South African population.

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Background: Type 1 diabetes (T1D) is characterised by the specific immune destruction of the insulin-producing β cells of the pancreas. Vitamin D has been shown to play an immuno-modulatory role in T1D, exerting its effect through the vitamin D receptor (VDR). Within T cells, VDR signaling down-regulates Th1 cytokine production shifting the immune response toward the Th2 pathway, therefore reducing β cell death. Low levels of vitamin D and polymorphisms in the VDR gene have been associated with T1D. Despite numerous studies investigating the role of vitamin D in T1D, there is no data from South Africa. We therefore aimed to investigate the association between the *Fok*I polymorphism (rs2228570; T > C transition) in the VDR gene and T1D in the South African black population.

Methods: Patients (n=163) were recruited from Chris Hani Baragwanath and Charlotte Maxeke Johannesburg Academic Hospitals. Controls (n=121) were recruited from South African National Blood Services blood drives. Anthropometric measurements were performed and a brief medical questionnaire completed. Vitamin D levels were measured by HPLC. All participants were genotyped for the rs2228570 polymorphism using PCR-RFLP.

Results: The rs2228570 polymorphism was found to be in Hardy-Weinberg equilibrium. The T allele frequency was significantly higher in the control group compared to T1D patients (0.23 vs. 0.16; p=0.037). Vitamin D levels were significantly higher in participants with the TT/TC genotype (65.41 ± 21.16 vs. 59.34 ± 20.67; p=0.02),

and this significance remained after adjusting for BMI and age. However, vitamin D levels were not significantly different between patients and controls, irrespective of genotype, when controlling for BMI and age (p=0.21).

Conclusions: The frequency of the T allele was found to be significantly higher in the control group suggesting that it is protective against the development of T1D. In addition, the T allele of the rs2228570 polymorphism was associated with higher circulating vitamin D levels, which have been shown to be protective of T1D in other populations. Interestingly, when comparing vitamin D levels in patients versus controls no statistical differences were seen between groups. This suggests that any possible protective effect of the T allele is not mediated via vitamin D, although this requires further investigation.

PPB7. Novel hypothalamic G protein-coupled receptors involved in the control of reproduction

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Background: Gonadotropin releasing hormone (GnRH) secreted from the hypothalamus is the master hormone regulator of the hypothalamus-pituitary-gonadal (HPG) axis, which controls puberty, fertility and reproduction. Several genes have been shown to impact GnRH activity, with defects in these causing reproductive dysfunction. For example, gene mutations in some hypothalamic G protein-coupled receptors (GPCRs) have been implicated in patients suffering from hypogonadotropic hypogonadism (HH), characterized by deficient GnRH activity. GPCRs are an extremely important family of signaling molecules involved in the majority of endocrine hormone signaling. A number of GPCRs are expressed in the hypothalamus and there is therefore much potential for them to impact the secretion and function of GnRH. Using DNA obtained from a cohort of European patients suffering from idiopathic HH, our intention was to identify novel GPCR gene mutations and determine whether they cause non-functionality of the receptor and therefore have the potential to be causative of reproductive dysfunction.

Methods: Patient blood has been collected and exome sequenced. Mutations in GPCRs located in the hypothalamus were identified and analysed *in silico* using six different bioinformatics tools to predict whether their mutations would be detrimental to receptor functionality. Based on these results and the genotypes of patients (i.e. whether or not mutations were homo- or heterozygous), receptors were selected for further examination. These selected mutant GPCRs have been cloned into a mammalian N-terminal epitope-tagging expression vector and their functionality tested *in vitro* after expression in HEK 293T cells. An inositol phosphate accumulation assay or CRE-luciferase reporter gene assay (which measure second messenger generation upon ligand stimulation) were used to compare mutant receptor activity to wild-type. As the majority of GPCR mutations cause protein misfolding, intracellular retention and loss of receptor expression at the cell surface, a receptor ELISA assay was also utilized to examine and compare wild-type/mutant receptor expression.

Results: Shortlisting of the identified mutations identified three GPCRs of interest: oxytocin receptor (OXR), neuropeptide Y4 receptor (NPY4R) and leucine rich repeating GPCR 5 (LGR5). In bioinformatics analyses the oxytocin receptor mutations showed a 50% chance of being non-functional and NPY4R 67%. Although the LGR5 mutations only showed a 33% chance of being non-functional, bioinformatics analyses have a high false-negative rate and mutations in this receptor were identified in more than one patient. These mutant receptors have now been expressed in mammalian cells and their functionality and expression compared to their wild-type counterparts.

Conclusions: Characterisation of novel GPCR mutations implicated in HH will provide insight into the physiological and pathophysiological roles of these receptors in the neuroendocrine control of reproduction, and may aid in the discovery of novel pathways or targets through which diagnostic tools or therapeutic agents for infertility and reproduction can be administered and developed. This is an ongoing study and we hope that more targets will be identified as additional European patient samples are collected. Fifteen South African patient samples have also been collected and are undergoing exome sequencing, thus expanding the cohort of samples for analysis.

PPB8. Systemic oxidative stress in obese black South African women and effect of exercise training

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Background: Oxidative stress is an imbalance between free radical production and antioxidant capacity, which results in the production and accumulation of reactive oxygen species (ROS). Progressive ROS production and accumulation together with inflammation are increased in obesity and are associated with insulin resistance (IR) and progression to type 2 diabetes. The formation of ROS and secretion of antioxidants are thought to be regulated by exercise training, which is used for the prevention and management of obesity. This study aimed to assess the association between circulating ROS and anti-oxidant markers and body composition in obese black South African (SA) women and to examine the effect of a 12-week aerobic exercise training programme on these markers.

Methods: Forty-five, obese and sedentary black SA women were randomised into a control (n=22) or experimental (exercise, n=23) group. Ten participants withdrew from the study throughout the 12 week intervention. The exercise group underwent 12 weeks of supervised aerobic and resistance training (40-60 min/day, 4 days/week). The control group refrained from any exercise training. Prior to and following the intervention, the following measures were taken: Physical fitness (VO_{2max}), anthropometry (weight, height), body composition and distribution (dual-energy x-ray absorptiometry; DXA), and serum for the analyses of thiobarbituric acid reactive substances (TBARS) concentration, oxygen radical absorbance capacity (ORAC), and catalase (CAT) activity.

Results: In both exercise and control baseline samples (n=45), TBARS and CAT showed no significant correlation with body composition and distribution ($p > 0.05$), BMI and VO_{2max} ($p > 0.05$). Furthermore, these samples also showed ORAC concentration to have a significant negative correlation with visceral fat area (VAT) ($r=-0.3$, $p=0.05$) in both groups at baseline. There was no significant group by time interaction between (exercise, n=20; control n=15)

for the oxidative stress parameters (TBARS p=0.27, CAT p=0.41, ORAC p=0.26). Finally, in the exercise intervention there was no correlation between exercise dose (number of sessions attended x Mean maximal heart rate) and change of oxidative stress parameters (CAT, Rho=-0.2; ORAC, Rho=-0.2; TBARS, Rho=-0.03).

Conclusion: These results show that exercise training without improvements in body composition was not sufficient to improve the oxidative stress parameters. Furthermore, the negative correlation at baseline between ORAC and VAT suggests that a reduction in VAT is required to stimulate an increase in antioxidant capacity. Finally, more studies looking at other oxidative stress markers and antioxidant activity are needed to confirm the relationship between VAT and oxidative stress and then, future projects targeting improvements in oxidative stress within obese populations could focus on interventions specifically designed for a reduction in fat-mass and VAT.

PPB9. Examining cell-surface expression of GPCR mutants in the HPG axis

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Background: Inactivating mutations in G-protein coupled receptors (GPCRs) at all levels of the hypothalamic-pituitary-gonadal (HPG) axis give rise to incomplete reproductive development and adult infertility. The majority of the mutations in GPCRs cause misfolding of the receptor and a failure to traffic to the cell surface. We have therefore sought for cell permeant small molecules, which can bind orthosterically, or allosterically to stabilize the nascent GPCR in the endoplasmic reticulum and chaperone the mutant GPCR to the cell membrane. These molecules are referred to as 'pharmacological chaperones'.

We have successfully used pharmacological chaperones to rescue the cell surface trafficking of mutant retained gonadotropin releasing hormone (GnRH) receptors, and luteinizing hormone (LH) receptors. Furthermore we and others have demonstrated that these receptors are functional when successfully trafficked to the cell membrane, including restoration of reproductive competency in mice harbouring a retained mutant GnRH receptor by the laboratory of Michael Conn. Pharmacological chaperones therefore have real therapeutic benefit in the treatment of a number of debilitating endocrine disorders caused by mutant GPCR misfolding.

We hypothesise that any small cell permeant molecule that can bind to a misfolded GPCR will have the potential to stabilise that receptor and increase cell surface expression. To test this hypothesis we have focused on the rescue of mutant kisspeptin receptor (GPR54/KISS1R) utilising an existing small molecule antagonist, thereby determining whether existing modulators of GPCR function can be 're-purposed' as pharmacological chaperones.

Methods: Wild-type or mutant receptors containing an extracellular N-terminal epitope tag were expressed in HEK293T cells. A cell-based ELISA assay utilising an antibody targeting the extracellular epitope tag was then employed to quantify cell surface (intact cells) and total (permeabilised cells) receptor expression and to determine effects of small molecule treatment on retained mutant GPCRs.

Results: Several naturally-occurring human GPR54 mutations were identified by literature searching. Receptors were cloned and GPR54 mutant receptors generated by site-directed mutagenesis. Cell surface expression of the mutant receptors has been quantified (and compared to wild-type receptor) and these data demonstrate differential cell surface expression of the mutant receptors.

Conclusions: GPR54 is an important regulator of reproduction in humans and dysregulation of GPR54 function has been demonstrated to cause infertility in patients harbouring GPR54 point mutations. These studies indicate that intracellular retention of GPR54 receptors could be contributory to/responsible for the reproductive phenotype, and that these retained receptors are valid targets for pharmacological chaperone rescue. These discoveries represent an advance towards personalized medicine for GPCR deficiencies in the human HPG axis.

PPB10. The effect of exercise training on ectopic hepatic, pancreas and skeletal muscle lipid content in black obese South African women

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Background: Obesity, increases ectopic lipid deposition, which is linked to other conditions such as type 2 diabetes (T2D), non-alcoholic fatty liver disease, hypertension and dyslipidaemia. Black South African women have a high prevalence of obesity (40%) and insulin resistance. Exercise training is used to prevent and/or manage obesity and T2D. However, the effect of exercise on pancreatic and skeletal muscle lipid content is inconclusive. The purpose of this study was to determine the effect of a 12-week exercise intervention on hepatic, pancreatic and skeletal muscle lipid content.

Methods: Forty-five, obese and sedentary black South African women (mean age 23 ± 3.5, y) were randomly assigned to an exercise (n=23) or control (n=22) group. The exercise group completed 12-weeks of aerobic and resistance exercises (40-60 min, 4 days per week), while the control group did not change their activity. Prior to and following the intervention, anthropometric measures were taken and hepatic, pancreatic and intra- (IMCL) and extra-myocellular (EMCL) (tibialis anterior and soleus) lipid content were measured by magnetic resonance spectroscopy (MRS) using a 3T Skyra (Siemens, Erlangen) whole-body scanner. MRS data were acquired using PRESS sequence with the following parameters: TR/TE 3000/33 ms, bandwidth 2000 Hz, 10 averages for each liver and pancreas scans and 80 averages for the calf scan. The voxel dimensions were 20×20×20 mm^3 for liver, 15×15×15 mm^3 for pancreas and 15×15×15 mm^3 for both soleus and tibialis muscles. Assessment of skeletal muscle fat contents was evaluated using LCModel. The absolute concentration of the different fat compartments, which include IMCL (at 1.3 ppm) and EMCL (at 1.5 ppm) for calf as well as hepatic and pancreas (methylene (-CH2-, 1.3 ppm), were reported relative to the water.

Results: The exercise (n=19) and control (n=15) groups were similar in baseline anthropometric and ectopic lipid content. The median hepatic and pancreatic lipid content was 0.6% (IQR 0.40 to 2.57) and 7.9% (IQR 3.67 to 20.4), respectively. At baseline, only 2 participants had a hepatic lipid content greater than 5% while 35% (n=12) of participants had a pancreatic lipid content of more than 10%. In

response to the 12-week exercise intervention the exercise group experienced a non-significant ($p > 0.05$) reduction in body weight (-0.39 ±1.55 kg) and BMI (0.31 ±0.10 kg/m^2). In contrast, the control group experienced a significant increase in body weight (0.98 ±1.3 kg, p=0.013). The exercise group showed a significant reduction in pancreatic lipid content (-6.05% ±0.13, p=0.05) compared to the control group. No within or between subject changes occurred in hepatic lipid content, tibialis anterior IMCL and EMCL content and soleus IMCL and EMCL content ($p > 0.05$).

Conclusion: This is the first study to determine that exercise training was associated with a reduction in pancreatic lipid content in obese black South African women. Contrastingly, hepatic and skeletal muscle IMCL and EMCL did not change in response to exercise. Further studies are required to determine the implications of the decrease in pancreatic lipid content on beta cell function.

PPB11. The effect of maternal exposure to alcohol and nicotine on the birth outcome and subsequent association with health outcomes at 5 years of age.

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Background: There is an alarming increase in cardiovascular related morbidity and mortality in South Africa. In addition, the prevalence of cardiovascular risk factors presenting in early childhood has shown an alarming increase. Both animal and human studies have demonstrated the effect of intra-uterine growth restriction on the development of chronic disease in later life. This research project was aimed at identifying the associations between environmental influences, in particular, alcohol and nicotine during pregnancy on birth outcome and on kidney size and hypertension at 5 years of age. The hypothesis for this study was that maternal lifestyle choices such as smoking and alcohol consumption during pregnancy have adverse effects on the development of the kidney and, hence, may increase the risk for developing hypertension later in life even during early childhood.

Methods: Data was collected at birth and at the age of 5 years from children within the Tygerberg Academic Hospital catchment area in Bellville, South Africa. Data collected included birth and placental weight at birth and anthropometric measurements (weight, height, sub-scapular and triceps skinfold thickness and waist circumference), blood pressure and ultrasound imaging of the kidneys at 5 years of age.

Results: In this study it was found that nicotine and alcohol exposure on its own did not have an effect on birth weight, kidney volume or any of the other measurements taken. However, nicotine and alcohol together had a significant impact on systolic blood pressure (p=0.035) at 5 years. However, no association was found between kidney volume and blood pressure ($p > 0.222$) and no significant difference was found between the different exposure groups and low birth weight and those who were born normal birth weight. However, birth weight proved to be significantly associated with BMI (p=0.033), waist circumference (p=0.048) and left kidney volume (p=0.019) at 5 years. Waist circumference is an indicator of abdominal fat content and consequently a known indicator of risk of cardiovascular disease. Correlations of waist circumference proved to be significant with BMI ($p < 0.05$), systolic blood pressure ($p < 0.05$) and left and right kidney volume ($p < 0.05$). In addition, some of the participants presented with risk factors for cardiovascular disease, including a high BMI, increased waist circumference and high blood pressure at 5 years of age.

Conclusions: This study demonstrated that the use of both nicotine and alcohol during pregnancy had a significant effect on increasing systolic blood pressure. As waist circumference is a strong indicator of cardiovascular disease, the significant association found with blood pressure and both right and left kidney size is an important finding. The mechanism behind these associations would need further investigation. The strong association between birth weight and waist circumference at 5 years may indicate an effect of intra-uterine growth restriction on organ development and/or function.

PPB12. Concomitant use of rooibos with hypoglycaemic and hypolipidaemic medications enhances their efficacy

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Background: Current oral therapeutics used to treat metabolic diseases such as diabetes often fail to prevent the progression of the disease and have side effects. Increasingly, natural products, perceived to be effective but with less side effects, are used as mono- or adjunctive therapies. Rooibos (*Aspalathus linearis*), an indigenous South African plant and its major phenolic constituent, aspalathin, has been demonstrated to have positive effects on glycaemia and dyslipidaemia. However, limited evidence exists on the effects of rooibos extract taken in combination with other hypoglycaemic and hypolipidaemic drugs. This study therefore aimed to investigate the effects of combination therapies of an aspalathin-enriched green rooibos extract (GRT) containing 12% aspalathin with the hypoglycaemic drugs, glyburide and pioglitazone, and the hypolipidaemic drug, atorvastatin, respectively, on blood glucose and lipid levels in a type 2 diabetic (*db/db*) mouse model.

Methods: Six-week-old male *db/db* mice together with their non-diabetic lean littermate controls (*db/+*) were divided into 11 experimental groups (n=6/group). *Db/db* mice were treated orally with pioglitazone (25 mg/kg), glyburide (5 mg/kg), atorvastatin (80 mg/kg) and GRT (100 mg/kg) as mono, and combination therapies. Untreated controls (both *db/db* and *db/+*) were given dimethyl sulfoxide (0.1%) and phosphate buffered saline. Intra-peritoneal glucose tolerance test was conducted after 3 weeks of treatment. At termination, blood was drawn and serum collected for serum lipid analysis while tissue was collected for histological analysis.

Results: Administration of GRT significantly reduced fasting plasma glucose (FPG) levels in *db/db* mice when compared to untreated controls (from 26.4 ± 4.1 to 18.7 ± 4.4, $p < 0.001$) without affecting body weight (BW). This effect was enhanced by pioglitazone co-treatment (15.3 ± 2.4, $p < 0.05$). Interestingly, the

hypoglycaemic drug, glyburide was not effective at improving FPG, either alone or in combination with GRT in *db/db* mice. As expected, atorvastatin monotherapy was effective at reducing cholesterol (2.9 ± 0.1, $p < 0.05$) and triglyceride levels (1.5 ± 0.2, $p < 0.05$). The hypo-triglyceridaemic effect of atorvastatin was enhanced when combined with both GRT and pioglitazone (0.7 ± 0.1, $p < 0.001$) in these diabetic mice.

Conclusion: Recent advances in combination therapy suggest that natural products can improve the efficacy of current drugs to prevent diabetes and associated complications. GRT showed a comparable effect to a known hypoglycaemic agent, pioglitazone in reducing FPG levels in diabetic *db/db* mice. In addition, its effect was significantly enhanced when combined with atorvastatin and pioglitazone in reducing triglyceride levels. This finding demonstrates additive and complimentary effects between GRT, pioglitazone and atorvastatin.

PPB13. Temperature Sensitivity of Selected Luteinizing Hormone Receptor Mutants

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Background: The luteinizing hormone receptor (LHR) is a G protein-coupled receptor (GPCR) found predominantly on the cells of the ovaries and testes and has an important role in the endocrine control of reproduction. Genetic mutation of the LHR, often cause reduced cell surface expression due to intracellular retention of the receptors. This retention is believed to be a result of the mutation causing misfolding of the receptor protein, which is detected by the endoplasmic reticulum (ER) quality control system and leads to targeting of the mutants for degradation. The intra-cellularly trapped mutants often retain a high binding affinity for ligand if the mutation has not affected the binding site. We, and others, have demonstrated that if the mutants can be rescued from the ER quality control system and expressed on the cell surface, they can transduce a signal upon activation. Pharmacological chaperones are cell permeant small molecules that can interact with retained receptors, aiding their folding and facilitating the rescue of cell surface expression of retained mutant receptors.

Temperature is also known to affect protein folding and previous studies have shown that cell surface expression of a subset of LHR retained mutants can be increased by growth of cells at sub-physiological temperatures. It is our aim to examine the effects of reduced temperature on the cell surface expression of a range of LHR mutants that have previously been found to be trapped intra-cellularly and correlate this with their ability to be rescued by an LHR pharmacological chaperone.

Methods: Selected naturally-occurring, LHR mutants which are retained to differing degrees were cloned into a mammalian expression vector and expressed in HEK293T cells. These receptors contain an N-terminal FLAG epitope tag allowing cell surface expression of the receptors to be determined through ELISA, by incubating the cells with an anti-FLAG antibody followed by a complementary secondary antibody conjugated to horseradish peroxidase enzyme (HRP). Cells expressing the receptors were incubated at 37ºC and 30ºC, in the absence or presence of pharmacological chaperone and cell surface (intact cells) and total cellular (permeabilised) expression of the receptors was determined. Crystal violet cell stain was used to adjust for differences in cell growth in the different conditions.

Results: As expected, the sub-physiological temperature affected the growth rate of the cells and therefore ELISA data was normalised using the crystal violet assay, to account for these differences in cell number.

The sub-physiological temperature also had differential effects on the mutant receptors cell surface expression with some correlation observed between cell surface expression at sub-physiological temperature and the rescue of cell surface expression by pharmacological chaperone.

Conclusion: The data presented describe a correlation between rescue of cell surface expression of retained LHR mutants at low temperature and pharmacological chaperone treatment. One interpretation of this data is that subsets of mutants have a propensity for rescue, possibly because they are less severely misfolded. This approach could be used to identify intra-cellularly retained GPCR mutants that have potential to be rescued by pharmacological chaperones, providing a frame of reference for drug development.

PPB14. Maternal exposure to alcohol and nicotine on birth outcome and subsequent risk factors for chronic disease: possible transgenerational effects.

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Background: Maternal exposure to alcohol and nicotine on birth outcome and subsequent risk factors for chronic disease: possible transgenerational effects. The increase in the prevalence of early signs of non-communicable diseases in children can partly be explained by the thrifty phenotype hypothesis, where poor pre-natal nutrition plays a vital role, resulting in a high prevalence of overweight, obesity as adolescents and adults. Rapid infant weight gain causes increased risk for diabetes and cardiovascular disease risk factors later in life. Small for gestational age offspring are often leptin and insulin resistant. Maternal high-energy diets during gestation cause offspring to have an impaired hypophagic response to insulin as adults, thus reducing the neuronal response to leptin and insulin resulting in hyperphagia. In addition, epigenetic modifications play a role in determining susceptibility to metabolic diseases.

Aims: This research project was aimed at identifying the associations of alcohol and nicotine during pregnancy, on birth outcome and current weight, BMI, central obesity, subcutaneous and visceral fat and hypertension at 5 years of age.

Methodology: A retrospective cohort study including 500 children aged 5 years was assessed using ultrasonography to determine kidney and pancreas size, visceral fat, aorta and carotid intima thickness. Anthropometric measurements, including weight, height, skinfold thickness, waist and hip circumference, as well as blood pressure, mean arterial pressure and heart rate were collected. The

association between maternal exposure to teratogens and these measurements was determined as well as the association between organ size and anthropometric measurements and blood pressure.

Results: In this study it was found that although there was no significant difference in birth weight between the different exposure groups, those who were exposed to both alcohol and nicotine had the lowest birth weight (2880 g (600)) with the nicotine group second lowest (2993 g (570)). The unexposed group had a mean birth weight of 3097 g (499). A similar trend was observed with placental weight where those exposed to both had a placental weight of 538 g (200) when compared to 641 g (132) in the unexposed group. Aorta intima thickness as a risk factor for chronic disease was significantly greater in the group exposed to alcohol when compared to the unexposed (0.577 mm (0.075) versus (0.520 mm (0.085). P/S ratio, a proxy for visceral fat, was almost significantly greater in exposed versus non-exposed (0.251 (0.146) versus 0.438 (0.384). The difference in pancreas head size almost reached significance if compared to those exposed versus the unexposed. Significant correlations were also observed between birth weight and blood pressure at 5 years of age as well as waist circumference and blood pressure at 5 years.

Conclusions: The results show that although the effects of maternal exposure to alcohol and nicotine during pregnancy on birth outcome was not significant it did seem to impact on early markers for chronic disease at 5 years of age. This might indicate that transgenerational effects may mask these effects at birth.

CLINICAL POSTERS (PPC)

PPC1. Titrating insulin in type 2 diabetes patients using a structured self-monitoring blood glucose regimen

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Background: Self-monitoring of blood glucose (SMBG) can inform on the timing of hyperglycaemia; however, there is currently no standardised approach to utilise these data to improve glycaemic control in type 2 diabetes patients. The objective of this study was to assess the efficacy of structured blood glucose testing in guiding an insulin titration algorithm in poorly controlled, insulin-treated type 2 diabetes patients.

Methods: This six-month, prospective study recruited 39 poorly controlled (HbA_{1c} ≥ 8.5%; 69.4 mmol/mol) type 2 diabetes subjects using twice-daily biphasic insulin from two state hospitals in Tshwane, South Africa. Patients were asked to perform structured SMBG over four weeks and return monthly for consultations where physicians titrated insulin doses using an algorithm guided by the data collected. The primary endpoint was trend in HbA_{1c} level measured at baseline, three and six months. Post-hoc analysis was performed to assess glycaemic control of study participants compared to those receiving standard treatment.

Results: Mean HbA_{1c} decreased over the study by 1.89% (95% CI: -2.46 to -1.33, p-value < 0.001). Mean SMBG and mean fasting plasma glucose (FPG) decreased by 1.6 mmol/L (95% CI: -2.5 to -0.6 mmol/L, p-value: 0.002) and 1.0 mmol/L (95% CI: -2.2 to -0.2 mmol/L, p-value: 0.024), respectively. Hypoglycaemic event rate (< 4.0 mmol/L) was 33.08 events per patient-year. Total daily insulin use increased by a mean 40.12 units.day-1 (SE: 7.7, p-value < 0.001); weight increased by an average 3.98 kg (95% CI: 2.56 to 5.41, p-value < 0.001) over the study period. Study participants were found to have a greater mean (SE) reduction of 0.777% (0.404) in HbA_{1c} compared to patients receiving standard care, which fell short of statistical significance (95% CI: -1.569 to 0.015%, p-value: 0.054) due to lack of power (56.5%) in the retrospective comparison.

Conclusions: Monthly algorithmic insulin titration guided by structured SMBG can improve glycaemic control in type 2 diabetes patients using insulin with moderate hypoglycaemic events and weight gain.

PPC3. Real world experience in type 2 diabetes management: patterns of treatment and control over nine years at Inkosi Albert Luthuli Central Hospital, Durban.

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Background: The Real World Experience (RWE) Study is a multi-national, multi-centre study evaluating patterns of treatment of diabetes and achievement of goals in clinical practice in diverse settings outside of Europe and North America. The Diabetes clinic at Inkosi Albert Luthuli Central Hospital (IALCH) in Durban was one of two sites in Africa participating in this study.

Aim: This study aimed to assess patterns of type 2 diabetes management and control at three time points over a nine year period.

Methods: The study was a retrospective observational study in which data was collected from all patient visits to the Diabetes Clinic at IALCH for the years 2006, 2012 and 2015. The data included demographic and anthropometric measures, classification and duration of diabetes, blood pressure and patterns of treatment. Laboratory measures included HbA_{1c}, serum lipids, serum creatinine and urine albumin-creatinine ratio. Renal function was assessed by isotope GFR. This analysis only includes data for subjects with type 2 diabetes.

Results: The study included a total of 601 subjects in 2006, 712 in 2012 and 681 in 2015, of whom subjects with type 2 diabetes comprised 77.7, 62.4 and 59.3%, respectively. The mean age of subjects with type 2 diabetes was 49.3 ± 17.5 years in 2006, 45.8 ± 19.9 in 2012 and 46.5 ± 20.4 in 2015; mean duration of diabetes was 13.2 ± 11.0, 12.9 ± 9.9 and 14.0 ± 10.3 years. Hypertension was present in 74.0, 67.6 and 63.7% and blood pressure ≤140/90 mmHg was achieved in 69, 72.1 and 52.0% (p=0.015 for 2006 vs. 2015). Insulin therapy was used in 57.8, 42.1 and 65.1% and of these, basal-bolus insulin was used in 20.1, 39.2 and 40.8%. The mean HbA_{1c} was 9.43 ± 2.30, 8.23 ± 1.80 and 8.35 ± 1.80% (p < 0.0001 for 2006 vs. 2012 and 2015). Optimal glycaemic control (HbA_{1c} < 7.0%) was achieved in 13.1, 28.6 and 26.5% of patients (p < 0.0001 for 2006 vs. 2012 and 2015). Mean LDL cholesterol was 2.58 ± 1.05, 2.22 ± 0.80 and 2.26 ± 0.87 mmol/l (p < 0.0001 for 2006 vs. 2012 and 2015).

Conclusion: Amongst subjects with type 2 diabetes attending a tertiary diabetes clinic in Durban, KwaZulu-Natal, there was significant improvement in attainment of glycaemic and lipid targets, although glucose control remains suboptimal in a large proportion of the clinic population.

PPC4. A Review of Obesity and Type 2 Diabetes in Zambia

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Background: Globally, there have been significant increases in both obesity and type 2 diabetes prevalence. In Zambia, most of the focus on nutrition and health has been on reducing micronutrient deficiencies, wasting and underweight malnutrition and not on the rising global projections of obesity and type 2 diabetes. The aim of this review was to identify and collate studies on the prevalence of obesity and type 2 diabetes conducted in Zambia, to summarise their findings and to identify areas that need further research.

Methods: The Medical Literature Analysis and Retrieval System (MEDLINE) database was searched for peer-reviewed articles on the prevalence of, and factors associated with obesity and type 2 diabetes amongst Zambian residents using a combination of search terms. The period of search was from 1 January 2000 to 31 December 2016. We explored the search terms to include all possible synonyms and spellings obtained in the search strategy. Additionally, we performed a manual search for other articles and references of peer-reviewed articles.

Results: In Zambia, the current prevalence of obesity and type 2 diabetes is estimated at between 13%-17% and 2.0% - 4.0% respectively. Risk factors such as the adoption of western dietary habits, the social stigmatisation associated with rapid weight loss due to tuberculosis and/ or the human immunodeficiency virus/

acquired immunodeficiency syndrome and rapid urbanization have all been blamed for fuelling the increased risk of obesity and type 2 diabetes. However, unlike traditional western populations, in Zambia those with no formal education were less likely to be obese than those who attained secondary or tertiary level education. Between 30% - 40% of those surveyed were unaware of their diabetes diagnosis and more than 60% were not on treatment despite a known diabetic status. Socio-demographic factors such as older age, female sex, urban dwelling, lack of tobacco use and marital status were associated with an increased risk of obesity, impaired glucose tolerance and type 2 diabetes.

Conclusion: Although the prevalence of obesity and type 2 diabetes in Zambia appears low, more representative studies focusing on parts of the country outside of the main industrial zone need to be conducted. National surveillance, monitoring and evaluation on all non-communicable diseases need to be prioritised and policies that address underweight, obesity and type 2 diabetes developed and the importance of adequate treatment emphasised to patients.

PPC5. Neonatal diabetes associated with transaminitis in a growth retarded infant

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Background: A neonate, born at 34 weeks gestation by caesarian section for foetal distress, was severely growth retarded at birth. Deranged liver functions were noted at birth with alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyl transferase (GGT) recorded as 102, 228, and 1078 U/L respectively. The GGT rose to a peak of 3877 U/L at 6 months of age. The clinical course of the neonate was associated with failure to thrive and intermittent hyperglycaemia (although keto-acidosis was not observed early in the phase of the disease). The insulin and C-peptide levels were < 0.5 and < 0.1 U/L respectively. A trial of glibenacamide failed to control the hyperglycaemia. Investigations for inborn errors of metabolism were normal.

Objective It was postulated that insulin deficiency in utero contributed to growth retardation. Wide fluctuations of blood glucose and poor weight gain characterised the post natal course. Furthermore, as there was paucity of subcutaneous fat, insulin could only be administered via the intravenous route as a continuous infusion.

Method: A review of the clinical case record. Permission was obtained from the parent to use the clinical record for presentation.

Results: A liver biopsy revealed marked glycogen deposition.

Conclusion: Association of neonatal diabetes with growth retardation suggested that insulin deficiency in utero most likely contributed to growth retardation. It is speculated that severe insulin deficiency contributed to the hepatopathy and consequent raised liver enzymes.

PPC6. Unusual presentation of acquired hypophosphataemic rickets

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Background: Acquired hypophosphataemic rickets is an unusual presentation in children and usually consequent on renal tubular damage. One of the factors important in phosphate homeostasis is FGF23. Healthy individuals maintain normal phosphate homeostasis by coupling FGF23 production with proteolytic cleavage. Iron deficiency stimulates FGF23 transcription and is a novel mechanism of FGF23 elevation. We present two children who presented with iron deficiency anaemia and hypophosphataemic rickets, which we postulate was due to elevated FGF23 levels.

Presenting problem: Two children, a 5 year old male (Case 1) and a 7 year old female (Case 2), presented with rachitic deformities of the lower limbs and a history of pica. Both children were stunted (HAZ score -2.59 and HAZ score -3.16) had genu valgum deformities at the knees, frontal bossing and pallor. Radiological findings confirmed the presence of active rickets and biochemical findings confirmed hypophosphataemic rickets and anaemia in both cases.

Clinical management: Both cases were treated with oral phosphate supplements, one alpha vitamin D and ferrous gluconate. The rickets healed and anaemia was resolving after 9 months on the above-mentioned treatment and after another 9 months of ferrous gluconate only.

Discussion: These two clinical cases highlight the association between iron deficiency anaemia secondary to pica and hypophosphataemic rickets in children. The biological intersection of iron and phosphate homeostasis through FGF23 is unknown and complex. Although FGF23 levels were not measured in these children, it is possible that elevated FGF23 levels as a consequence of chronic iron deficiency associated with pica were responsible for hypophosphataemia and rickets. The association between pica, iron deficiency and FGF23 needs further investigation.

PPC7. Tumour-induced Osteomalacia

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Tumor-induced osteomalacia (TIO), also known as oncogenic osteomalacia, is a rare paraneoplastic syndrome, commonly caused by over-secretion of fibroblast growth factor 23 (FGF-23) from a phosphaturic mesenchymal tumour. These tumours are usually benign and are typically small, thus proving a diagnostic challenge. FGF-23 is the commonest phosphatonin implicated in the pathogenesis of TIO. FGF-23 acts predominantly at the renal tubule and impairs phosphate reabsorption and 1-alpha hydroxylation of 25-hydroxyvitamin D (25-OHD). Thus, the biochemical hallmarks of TIO are severe hypophosphataemia secondary to phosphaturia and an inappropriately normal or low 1,25-dihydroxy vitamin D (1,25-OHD).

We describe a 52 year old female presenting with a 14 year history of progressive proximal muscle weakness and myalgia. She had been wheelchair bound for the previous ten years, with a significant loss of height since the onset of symptoms. She was previously healthy, with no family history of metabolic bone disease. Clinical examination revealed a proximal myopathy, short stature with marked kyphoscoliosis and pectus carinatum.

Initial biochemical evaluation revealed severe hypophosphataemia of 0.28 mmol/L (reference range [RR] 0.8-1.4 mmol/L), but normal

serum calcium and magnesium. Renal function was normal. Parathyroid hormone (PTH) was elevated at 66 pmol/L (RR 1.5-7.6 pmol/L), with a reduced 25-OHD of 31.41 nmol/L (RR < 50 pmol/L - deficient; > 72.50 pmol/L - sufficient) and an inappropriately normal 1,25-OHD. Alkaline phosphatase (ALP) was markedly elevated at 460 IU/L (RR 42-98 IU/L), with a bone specific ALP of 305 IU/L (RR 14-42 IU/L). Muscle enzymes were normal. Tubular maximum reabsorption for phosphate (TmP), corrected for glomerular filtration rate (GFR) (TmP/GFR) was reduced at 0.22 (RR > 0.8).

X-rays demonstrated numerous rib fractures and 'pseudo-reactivation' of the growth plates. The bone scan was in keeping with metabolic bone disease. In view of the hyperparathyroidism, a parathyroid sestamibi scan was done and was negative. Despite phosphate and 1-alpha vitamin D replacement, hypophosphataemia persisted. A working diagnosis of TIO was considered and further investigations were carried out to confirm the diagnosis.

The FGF-23 level was elevated at 1121 pg/ml (RR approximately 11.7-48.6 pg/ml). ^{68}Gallium DOTATATE PET/CT showed a soft tissue density inferior to the metatarsophalangeal joints of the second and third digit of the right foot. The CT and MRI features of this mass were suggestive of a Morton's neuroma.

The tumour was surgically resected and the histology was compatible with a phosphaturic mesenchymal tumour. Phosphate levels normalized one week postoperatively.

Due to the lack of awareness of this condition, there is often a prolonged lag time between the onset of symptoms and diagnosis. The clinical and biochemical presentation of TIO is important to recognise, as it is one of the endocrine neoplasms with an extraordinary and debilitating presentation, yet can have a very gratifying outcome if cured. Treatment of choice is surgical excision of the tumour, with a wide margin, to prevent recurrence.

PPC8. Addison's Disease in South Africa: An Electronic Survey of Physicians' Perception of Patients' Characteristics and Patterns of Management Practices

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Background: The burden and management of Addison's disease (AD) in South Africa (RSA) have not been well documented. We aimed to identify the disease attributes, patients' characteristics and patterns of clinical management of patients with established AD in RSA "through the eyes of the practising physicians".

Methods: An online survey of a large pool of medical practitioners held by a reputable commercial provider was undertaken. The questionnaire covered respondents' profiles, patient demographics, aetiology, presentation and therapy.

Results: Respondents: A total of 704 responses were received, 303 provided a complete questionnaire and of these 156 respondents confirmed that they do treat patients with hypoadrenalism. They were mostly non-endocrine specialists (49.4%) or primary care doctors (43.6%) and 7.1% were endocrinologists. Two thirds were senior doctors. One third were in government or university hospitals and the remainder were in private practice. Most respondents (83.9%) were practicing in large cities.

Patients: The physicians' responses were based on their experiences with 1140 patients with AD (535 males, 605 females). Other causes of hypoadrenalism were pituitary disease, long term steroid use and adrenalectomy in 343, 402 and 209 patients respectively. The majority were between 16-60 years of age (219, 291 and 175 patients within the age groups 16-30, 31-45 and 46-60 years respectively). Reported "non-mutually exclusive" causes of primary hypoadrenalism included autoimmune disease (19.9%), tuberculosis (31.1%), AIDS (22.3%), malignancy (6.6%), Genetic (3.2%) and adrenoleukodystrophy (2.0%). Observed associations included hypothyroidism (135/156; 86.9%), type 1 diabetes (105/156; 67.3%), pernicious anemia (52/156; 33.3%), premature ovarian insufficiency (42/156; 26.9%) and Graves' disease (22/156; 14.1%). Most patients presented with a constellation of the classical symptoms in varying combinations, however 128 patients (11%) presented in Addisonian crisis. Many patients were reportedly treated with hydrocortisone only (31.1%) and the rest (17.9%) on a combination of hydrocortisone and fludrocortisone. Several formulations of steroid replacement therapy are used including in decreasing frequency prednisolone, hydrocortisone, cortisone acetate, dexamethasone and betamethasone.

Patterns of clinical management: Many respondents (45%) perceived management of Addison's disease as easy, 36% found it difficult and 14% found very difficult. More physicians reported adjusting the dose of steroid replacement according to body weight (63.1%) than those using a fixed dose therapy (30%) and a minority adjusted doses according to body surface area (6.9%). Too many patients in the previous 5 years were not using any form of identification indicating that they have Addison's disease and need steroids in case of emergency. Numerous difficulties with diagnosing, managing and obtaining suitable treatment were identified including limited access to medications, diagnostic facilities and language and cultural barriers.

Conclusions: We report the first survey of South African physicians' perceptions of Addison's disease including their observations on disease burden, patients' characteristics and aspects of clinical management. Such surveys should help focus future educational activities, quality assurance audits, research and patients' advocacy with significant national, Africa-wide and international implications.

PPC9. A Critical review of whether goals for treatment in Type 2 Diabetes Mellitus as set out by the 2012 Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) guidelines are being achieved in patients attending the Diabetic clinic

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Background: The risk of complications from T2DM is high. Complications reduce quality of life and place a large burden on our health system and economy. Achieving targets in our diabetic patients significantly reduces the morbidity and mortality of the disease. This study aims to assess whether patients at the Helen Joseph Academic Hospital Diabetic Clinic are meeting the 2012 SEMDSA targets for diabetes with the current hospital treatment protocols.

Methods: A retrospective clinical audit was carried out at the Helen Joseph Hospital diabetic clinic. The files of 321 patients with T2DM for a duration of longer than five years and who were on insulin were reviewed. The following information was assessed: glycated haemoglobin (HbA_{1C}), blood pressure, abdominal circumference and lipogram.

Results: The study population of 321 patients comprised majority black (44.6%) and coloured (34%) patients. The mean age amongst these patients was 59.4 years. This sample was predominantly female (62.3%). A large proportion of patients had concomitant hypertension (89.1%) and dyslipidaemia (82.2%); with 91.2% fulfilling criteria for the diagnosis of metabolic syndrome. The majority of patients 56.3% did not exercise. A small amount participated in recreational activities that increase cardiovascular risk (smoking 12.5% and alcohol use 10.6%). Target HbA_{1C} used for the purpose of this study was 7% or lower. The mean HbA_{1C} in this study population was 9.5% (range 3.9 - 16.9%). Only 15.3% achieved the 7% target. The number of patients who achieved the target blood pressure of < 140/90 was 72 (25%) (95% CI 20.2-30.5). LDL target was achieved in 22.6% and abdominal circumference 11%.

Conclusions: Only a very small percentage of patients at the diabetic clinic are achieving proposed targets. When compared to studies carried out at the same clinic in 1996 and 2006 there is little change in this percentage in the last 20 years. Further analysis and critique is necessary to assess the reasons for this and how the situation can be improved.

PPC10. The Spectrum of Patients with Disorders of Sexual Development at Tygerberg Hospital: An audit

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Background: The diagnosis of disorders of sexual development (DSD) is challenging to all clinicians. Incomplete investigations may result in incorrect diagnosis, inappropriate sex of rearing and profound psychological complications. At Tygerberg Children's Hospital (TCH) Paediatric Endocrinology has been coordinating management of all intersex cases over the last 10 years. Due to resource constraints, required procedures could often not be performed when requested. The spectrum of DSD presenting at the hospital is also unknown. The objectives of this case series are to describe the spectrum of DSD patients presenting at TCH, document their sex of rearing and serve as an audit to establish whether these children are completely investigated and appropriately followed up.

Methods: All cases of intersex seen at the Paediatric Endocrine Outpatient Department at TCH between 2007 and 2016 were identified by reviewing outpatient records. The following information was extracted: diagnosis, sex of rearing, ethnic group, age at initial referral, completeness of investigations and appropriate follow-up.

Results: A total of 138 children diagnosed with DSD were seen at the Paediatric Endocrine Unit between 2007 and 2016. Seventy-three were classified as under-masculinised males. Of these, 71 (51%) cases had androgen insensitivity syndrome (AIS) and three (2.1%) had Leidig cell hypoplasia (LCH). Thirty (21.7%) were undetermined cases of 46XY DSD. Seventeen cases (12.3%) were diagnosed to have ovo-testicular DSD (OTDSD). 9 cases (6,5%) were virilised females [all with congenital adrenal hyperplasia (CAH)] and 2 cases (1,4%) of partial gonadal dysgenesis (GD). Of the total cohort, 69(50%) patients were black, 68(49%) patients of mixed race and 1(0.7%) patient was unclassified. In the OTDSD group, 12(61%) of the 17 patients were black and 5(38%) were mixed race. Sixty-eight of the 69 patients with partial AIS were raised as male and one patient with complete AIS was raised as female. Nine of the 17 patients with OTDSD were 46XX, of which four were raised as male and 5 as female. Age of presentation to the endocrine unit varied amongst the different groups as follows: 50 (72%) of patients with AIS, 14(77%) of patients with OTDSD and 7 (77%) of patients with CAH presented before the age of 6 months. In the undetermined group, 11 (36%) presented between the age of 1 and 5 years and 11(36%) presented between the ages of 5 and 12 years. Only 88 (63.7%) of all patients were completely investigated. Ninety-four (68%) were lost to follow up, while 4 (2.8%) were discharged/transferred.

Conclusions: The spectrum of DSD corresponds to the disease profile seen at other units. A large proportion of patients seen at this unit were not referred at birth. More than a third of the patients were incompletely investigated with even more being lost to follow up. Maternity centres need to be encouraged to refer intersex cases early. Co-operation among the various disciplines investigating and managing these cases needs to be improved.

PPC11. Achievement of therapeutic targets in South African patients with diabetes mellitus

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Background: The incidence of diabetes mellitus, particularly type 2 diabetes is increasing dramatically across the world because of increasing obesity, sedentary lifestyle and population aging, and is the cause of substantial morbidity and mortality. The International Diabetes Federation(IDF) predicts an increase in the diabetes incidence in Africa by 108% by the year 2040. This alarming rate of increase in incidence together with the potential complications of disease renders this disease to be a great challenge facing the healthcare system. The major goal of treatment of diabetic patients is to achieve good (near normal) metabolic control, thus preventing long term complications. Despite all recommendations, a large number of patients are not well-controlled, and do not reach the target of HbA_{1C} value below 7%, indicating a need to better assess the current practices in diabetes management. The aim of the International Diabetes Management Practices Study (IDMPS) study was to describe the characteristics of management and achievement of therapeutic targets in patients with diabetes mellitus. This abstract will focus on the South African cohort of the multinational study.

Methods: A total of 7165 patients was recruited globally in the sixth wave of the IDMPS study and 7122 were included in the eligible population for analysis. Data was analysed from 97 patients with type 1 (T1D, n = 31, 32%) and type 2 diabetes (T2D, n = 66, 68%) included in the South African cohort.

Results: Of the T2D patients, 50% were treated with oral glycaemia lowering drug (OGLD) alone, 15.2% were treated with insulin alone, 33.3% were treated with OGLD plus insulin and 1.5% treated with diet and exercise alone. A large proportion of T1D patients, 74.2%, were prescribed a basal plus a prandial insulin regimen whereas a lower proportion, 16.1% were treated using a premix regimen. After comparison with the international recommendations (EASD, ADA and IDF), it was shown that 16.7% of T1D patients and 33.9% of T2D patients reached the recommended target value of HbA_{1c} < 7%. The global target of HbA_{1c} < 7%, blood pressure < 130/80 mmHg and low-density lipoprotein cholesterol < 2.59 mmol/L was achieved by only 3.3% of the T1D patients and 6.3% of T2D patients. T1D and T2D patients showed a similar proportion of macrovascular complications, 3.2% and 3.1% respectively; however, T1D patients had more (32.3%) microvascular complications compared to T2D patients (16.9 %).

Conclusions: This small South Africa subset analysis of the IDMPS wave 6 study demonstrated that a large number of eligible patients did not achieve the global glycaemic targets. The study also demonstrates that few patients reach targets based on the holistic cardio-metabolic profile, which included combined blood pressure, HbA_{1c} and low-density lipoprotein cholesterol targets.

PPC12. A tough case to crack

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Background: Low bone mineral density (BMD) is an almost invariable finding in patients with increased fracture risk and skeletal fragility; however, one may infrequently encounter a high bone mineral density in this setting. True inherent skeletal diseases as a cause of increased bone mass (osteoscleroses) are rare and skeletal strength in this setting is variable. The sclerosteoses entities are associated with intact bone strength and excessive bone formation, whereas the heterogeneous group of osteopetroses [an adult onset form (ADO II), a malignant infantile form (ARO), and an intermediate form (IAO)] are characterized generally by skeletal fragility despite an abnormally high BMD. The shared genetic defect, in most cases, has been ascribed to a mutation in the chloride channel 7 gene (CLCN7). This mutation leads to ineffective bone resorption.

Methods: In this, we describe two cases of osteopetroses recently encountered in our department.

Results: The first case is a 36 year-old woman whose clinical course has been characterised by multiple fractures in childhood and severe bone marrow infiltration with a pancytopenia, requiring regular blood transfusions. We encountered her for the first time in adulthood following her most recent low-trauma, long-bone fractures (left humerus and left femur). Radiographs of her spine, skull base, chest and pelvis demonstrated marked osteosclerosis with sandwich vertebrae, a thickened skull base, ribs and pelvic bones. DXA measured BMD exceeded +5 SD compared to age and gender matched controls (Z-score). Genetic testing identified a pathogenic variant in CLCN7, establishing the diagnosis; probably a variant of the ADO II osteopetrosis (or Albers Schonberg disease). This was done at Michael Whyte's laboratory in Pennsylvania. Her current treatment is symptomatic only.

The second case centers around a 47-year old woman with non-specific backache, no fracture history and an incidental finding of typical sandwich-shaped vertebra and a very high DXA measured BMD. A full radiological assessment revealed, in addition to the sandwich vertebra, osteosclerosis of the skull base and rib cage. These radiological findings in an asymptomatic patient are very suggestive of Albers Schonberg disease. Her full blood count and biochemistry was normal. The outcomes of her genetic testing is still pending.

Conclusion: We have described two cases of a relatively rare metabolic bone disease, with two different expressions of a shared underlying pathology.

PPC13. Evolution of the management of type 2 diabetes mellitus in the South African population: a comparison of observational studies

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Background: According to the International Diabetes Federation (IDF) the incidence of diabetes in Africa is predicted to increase by 108% by the year 2040. To mitigate the risk for developing diabetes and enhance treatment success, the IDF developed risk scoring algorithms based on local epidemiological data. However, as diabetes disease registries do not currently exist in South Africa, the collection of local epidemiological data is limited. The International Diabetes Management Practices Study (IDMPS) is an international, observational study of the management of patients diagnosed with type 1 or type 2 diabetes mellitus. This study was conducted in waves spanning more than a decade. Here the data recorded for patients participating in the South African cohorts in 2006 (Wave 2) and 2013-2014 (Wave 6) are compared to evaluate evolution in diabetes management.

Methods: During the IDMPS study, data of patients diagnosed with type 1 or type 2 diabetes mellitus was collected over a period of two weeks. Data collected included patient demographics, treatment exposure and glycaemic status.

Results: Of the 899 patients who participated in the Wave 2 study, 701 (78%) were diagnosed with type 2 diabetes mellitus in comparison to 66 (68%) of the Wave 6 study. Patient demographics between the cohorts were similar with regards to age, BMI and

urbanization. Reported duration of diabetes of less than ten years were 90.6% in the Wave 2 cohort compared to 84.9% in the Wave 6 cohort. Proportion of type 2 patients treated with oral anti-diabetic agents only was similar in Wave 2 and 6 (47% vs 45%). However, an evolution in the insulin treatment was observed. Both studies indicate that the majority of insulin-treated patients were treated with premix insulin; however the recorded use of premix insulin decreased from 57.3% in the Wave 2 cohort to 46.8% in the Wave 6 cohort. Treatment with basal and prandial insulin increased from 21.1% in Wave 2 to 28.1% in Wave 6. Increased insulin utilization in terms of units was also observed: the mean insulin dose in the Wave 6 cohort exceeded that of the Wave 2 cohort for patients using basal insulin alone (42.94 vs 28.04 IU/day), basal bolus regimes (78.00 vs 64.05 IU/day) and premix insulin (77.53 vs 49.66 IU/day). Data indicate that 30.4% of patients in the Wave 2 cohort achieved an HbA_{1c} < 7%, while 28.3% of patients in the Wave 6 cohort reported HbA_{1c} values below 7%. The limitations of this report must be considered, such as inclusion of patients from the private sector only and the limited sample size of the South African cohort of Wave 6 (98 patients).

Conclusions: A comparison of the South African subset of two observational studies conducted 8 years apart reveal an evolution in the treatment of diabetes: the proportion of patients treated with oral anti-diabetic agents remains comparable between cohorts, while insulin utilisation as indicated by mean units/dose/day has increased. The small percentage of patients reaching glycaemic target in Wave 2 and Wave 6 of this study suggests that further optimisation of diabetes management may be required

PPC14. A Successful Pregnancy in Glycogen Storage Disease Type1b

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Background: Glycogen storage disease type 1 (GSD1) is an inherited disorder of carbohydrate metabolism caused by a defect in glucose-6-phosphatase activity. Typical features include severe fasting hypoglycaemia, hyperlipidaemia, hyperuricaemia and hyperlactataemia, along with growth failure and marked hepatomegaly. GSD type 1b carries the additional complication of neutropaenia. The mainstay of treatment is nutritional.

Life expectancy has improved dramatically, changing GSD from a previously purely paediatric illness to one which now requires the input of adult physicians. However, the rarity of the disease implies that long-term experience is limited. Pregnancy challenges metabolic stability with particular risks including hypoglycaemia, increase in hepatic adenomas and worsening renal function. Good metabolic control pre-conception and throughout pregnancy are directly related to successful outcome.

This case reports the first known successful pregnancy outcome in South Africa.

Case Presentation: We present the case of a 22 year old female patient with GSD1b, diagnosed on liver biopsy at 3 months of age. She had been managed by the paediatric endocrine unit and had maintained excellent metabolic control throughout her life with a regimen of uncooked corn starch (UCCS) and continuous nocturnal nasogastric feeds. She informed the unit of her pregnancy early in the first trimester and teratogenic drugs (allopurinol and tranexamic acid) were stopped immediately. A multi-disciplinary team was assembled including paediatric endocrinologists, dieticians, obstetricians, infectious diseases, haematologists and neonatologists.

During the first and second trimesters she maintained good glycaemic control and normal lactate levels with no changes in her dietary regimen. She was neutropaenic, but remained well on daily penicillin prophylaxis. During the third trimester her lactate levels rose, this responded well to increasing her doses of UCCS and nocturnal feeds. She presented with pneumonia at 32 weeks gestation, prompting concerns of neutropaenic sepsis and the risk of preterm labour. This was effectively treated with intravenous (IV) ceftriaxone; granulocyte-colony-stimulating-factor was not required.

Regular ultrasounds were performed. The patient developed a hepatic adenoma during the second trimester and unilateral hydronephrosis in the third trimester. Both of these findings remained stable during the remainder of the pregnancy. The foetus maintained good growth parameters.

She underwent elective Caesarean section at 37 weeks under general anaesthetic with perioperative antibiotic cover. Her blood glucose (BG) was maintained with IV 10% dextrose infusion with hourly monitoring of BG and lactate levels, until she was able to tolerate UCCS and meals postoperatively. A 2.5 kg male infant was delivered. He was managed in the neonatal ICU for respiratory distress and required a 12.5% dextrose concentration to maintain his BG.

The patient chose to breastfeed, despite being advised against this. Breastfeeding was initiated in the ward with daily measurement of her lactate levels, with no elevations observed. She was discharged on day 8 post-delivery.

Conclusions: In conclusion, as life expectancy for metabolic diseases improves, physicians need to be aware of long-term complications in these patients. This case demonstrates that successful pregnancy is possible within the South African context, but requires tight metabolic control and multi-disciplinary input.

PPC15. Metastatic multifocal paragangliomas

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Case Study: 23 year old male patient was referred to the Endocrine department at Steve Biko Academic Hospital (SBAH) from surgery with a mass protruding into the oral cavity, originating from the maxillary sinus, and an abdominal mass. He had symptoms of headaches, palpitations, sweating and abdominal pains and swelling of the left side of his face since June 2014.

On examination he had an ulcerating lesion in the oral cavity protruding from the left maxilla and a large firm mass palpable in his abdomen.

On the CT scan a large retroperitoneal mass as well as a left maxillary sinus mass were detected. The abdominal mass was 172 by 110

mm. Mixed sclerotic/lytic bone lesions were also seen. The 68Ga Dotatate/PET showed a locally destructive left maxillary sinus and an abdominal mass. On biochemistry he had raised normetanephrine and raised chromogranin levels. Histology of the mass in the maxillary sinus confirmed a paraganglioma of the head and neck. On his DNA studies the succinate dehydrogenase subunit B (SDHB) pathogenic mutation was confirmed.

The patient received 131 I MIBG therapy and five cycles of radiotherapy.

Our final diagnosis was that of metastatic multifocal paragangliomas, in keeping with paraganglioma type 4 syndrome, most likely of sympathetic origin.

On follow up visits the mass in the oral cavity resolved and the patient's symptoms have improved.

PPC16. Patient knowledge of self-management of hypoglycaemia

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Background: Diabetic patients on insulin and sulphonylureas are at risk of developing hypoglycaemia. Many patients do not respond appropriately because of poor knowledge and understanding of the symptoms of hypoglycaemia, which if not promptly treated can lead to permanent neurological and renal damage. Hypoglycaemic complications can be avoided if patients have a good knowledge of the early symptoms of hypoglycaemia and know how to respond appropriately. This study evaluated the efficacy of current patient education on hypoglycaemia and self-management.

Methods: This was a cross-sectional, descriptive study involving 200 diabetic patients attending a public hospital in KZN. Demographic data and details of current medication, knowledge of hypoglycaemia and how patients responded to the symptoms were collected using a validated questionnaire.

Results: The majority of the patients had fair to good knowledge of hypoglycaemia; however, less than 25% knew what action to take when they experienced symptoms suggestive of hypoglycaemia.

Conclusion: There is a need to improve the education given to diabetic patients on stepwise measures to take to avoid life-threatening complications associated with hypoglycaemia.

PPC17. Awareness of diabetic foot disease amongst patients with type 2 diabetes mellitus attending the chronic outpatients department at a regional hospital in Durban, South Africa

T Goie

Background: Diabetic foot disease (DFD) is a major challenge for the healthcare system, with enormous economic consequences for people living with diabetes, their families, and society, affecting both quality of life and quality of care. The study aim was to assess the level of awareness of DFD amongst patients with type 2 diabetes mellitus (T2DM).

Methods: An observational descriptive cross-sectional study was conducted at the chronic outpatients department of a regional hospital in Durban, South Africa.

Results: Two hundred participants with T2DM participated in the study. Ninety-one per cent of participants were either overweight or obese. Ninety-two per cent of participants had concomitant hypertension (57.5%), dyslipidaemia (26.7%) and eye disease (7.2%). Seventy-six per cent reported altered sensation in their lower limbs, and 90% reported having no previous DFD education. Only 22.2% of participants reported having examined their feet, but only when they experienced a problem. Participants achieved mediocre scores for knowledge (mean 4.45, standard deviation (SD) 2.201, confidence interval (CI) 4.2-4.7) and practice (mean 11.09, SD 2.233, CI 10.8-11.5) on diabetic foot care (DFC). Those who had a higher level of education and who were less than 65 years old had a significantly better score for previous foot care education ($p < 0.05$).

Conclusion: The study demonstrated that awareness of DFD was suboptimal, based on current DFC guidelines. To minimise the burden of DFD, improved screening and prevention programs as well as patient education should be provided to T2DM patients, whilst maintaining an aggressive approach to risk factor modifications, footwear and identifying the at-risk foot.

PPC19. The willingness to lose weight among predominantly overweight black African adults is dependent on body image and not perceived threat of obesity

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Background: The high rates of obesity and its associated health complications in populations undergoing rapid urbanisation and nutrition transition requires setting-specific behaviour change interventions. This study explored the effect of body image and perceived threat of obesity (PTO) on the willingness to lose weight (WTL) and weight change/year among adults in resource-poor communities.

Methods: This is a longitudinal survey and a qualitative inquiry with black African adults aged 35-78 years in the PURE (Prospective Urban and Rural Epidemiology) Study, Cape Town. A sub-sample of 963 original study participants from the rural (n=406) and urban (n=557) communities were randomly selected and interviewed at year four follow-up. Weight and height measurements were taken at baseline and at follow-up. Data on body size and body weight perceptions, PTO, and the WTL were collected at follow-up using a validated structured questionnaire. Narrative and pictorial constructs were used to describe body image dissatisfaction Feel Ideal Size Difference (FID) and body weight dissatisfaction Feel Actual Weight Difference (FAD) indexes. PTO and WTL constructs were each based on three different Likert-scale measures. The study hypothesised that readiness to lose weight is dependent on perceived obesity risk which would in turn impact on weight change. Structural equation modelling (SEM) was performed with SPSS version 24 and AMOS software to verify the hypothesis. Standard SEM model fit and model modifications were adhered to during the analysis. In addition, 13 focus group discussions were conducted with purposively selected separate groups of obese and non-obese men and women in the PURE study communities to further establish the SEM findings. Participants were asked to weight their perceptions of obesity threat, body image, and the willingness to lose excess body weight.

Qualitative data was analysed using a thematic analysis approach, and both qualitative and SEM results were triangulated.

Results: Of the predominantly (82%) overweight/obese adults, 341 (35%) were willing to lose weight, and 237 (25%) had positive annual weight change. Based on SEM, body size dissatisfaction (FID), weight dissatisfaction, and body mass index (BMI) had significant positive effects on WTL, with FID contributing comparatively highest variability of 20% (at p=0.001) of WTL. Participants' perception of threat and their age did not predict WTL. Although BMI had a strong correlation with weight change, WTL unexpectedly, had no significant effect on annual weight change. Qualitative findings, however, indicated that participants who had experienced chronic disease conditions indicated strongly that obesity can lead to chronic diseases such as stroke, hypertension, heart disease and diabetes. Overweight women were generally unwilling to lose weight. The belief that overweight size is 'normal' and not a disease, subjective norms, attitude towards vulnerability, and physical inactivity can be the mediating factors between the willingness to lose weight and actual weight change.

Conclusion: In a predominantly black overweight population with low perception of the threat of obesity, body size dissatisfaction index predicted the willingness to lose weight. Prevention of obesity should, therefore, include community-based health promotion interventions that target appropriate body image evaluation in adults.