Diabetes Metabolism and the Heart
Diabetes, Stoffwechsel und Herz

D&CVD

The 15th Annual International Conference of the

D&CVD Study Group

10–12 May 2023 | Tel-Aviv, Israel

ABSTRACTS

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Abstracts online auf diabetologie-online.de

Session I: Keynote Lectures

IS-01

Towards precision diabetes medicine based on individualized subtyping

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Defining the typology of diabetes mellitus goes back for less than 150 years and currently based on a classification into 2 major types according to insulin resistance or impaired ß-cell function. Some years ago, the German Diabetes Study (GDS) cohort already identified a broad variation of these key features among persons with recent-onset type 1 and type-2-diabetes. This cohort also allowed to validate the Scandinavian concept of phenotype-based clustering and even more detected that the five endotypes (subgroups) of diabetes differently associate with the prevalence and progression of diabetes-related comorbidities and complications. For example, the severe insulin-resistant subgroup (SIRD) features markedly higher liver fat content and surrogate indices of hepatic fibrosis at follow-up, but also a greater prevalence of nephropathy and erectile dysfunction. On the other hand, the severe insulin-deficient subgroup (SIID) shows a higher prevalence and progression of neuropathy. Of note, membership to one diabetes subgroup is not irreversible, but may change over time. More recently, independent approaches of genotype- and phenotype-based subclassification identified similar subgroups of diabetes as well as prediabetes, underlining the heterogenous pathogenesis of the metabolic diseases currently termed diabetes. Taken together, diabetes research is entering a new era of refined diagnosis, which may help to improve risk assessment, monitoring and to develop tailored management of people with diabetes in a novel concept of Precision Diabetology.

IS-02

Obesity and treatment challenges – a game changer for Diabetes & Cardiovascular disease?

John Wilding – University of Liverpool, UK

Obesity is a direct causative factor in the pathophysiology of both type-2-diabetes (T2D) and cardiovascular disease (CVD), yet until recently effective treatments for obesity have not been prioritised in the range of treatments that are widely used to treat these conditions. These have instead focussed on reduction of other risk factors such as LDL cholesterol, blood pressure and blood glucose. Whilst these interventions have been shown to be effective they do not target one of the root causes of T2D and CVD, and patients still have considerable residual risk even after optimum treatment of these risk factors.

Epidemiological and clinical trial evidence using various diet and lifestyle interventions has shown that modest weight loss (around 5 %) can reduce progression to diabetes in people with impaired glucose regulation, but greater weight loss of 10 – 15 % or more is needed to put diabetes into remission. In contrast, although some indirect evidence from epidemiological studies and observational data after bariatric surgery supports the concept that weight loss can reduce the incidence of cardiovascular disease, this has not yet been demonstrated in an RCT.

Pharmacotherapy may reduce T2D and CVD by mechanisms that are both due to weight loss and also have weight independent effects. For example SGLT2i reduce body weight by 2 – 3 % but are effective glucose lowering agents and reduce heart failure hospitalisations in people with and without diabetes, and some have shown reduced atherosclerotic related CV events in those at highest risk. GLP1 receptor agonists, and more recent medications that target other gut hormones such as GIP and amylin result in weight loss of 15 – 20 % or more, and have clinically relevant benefits on conventional risk factors. Some of these medications have been shown to reduce cardiovascular events in people with type-2-diabetes. Ongoing and planned trials, including the SELECT CVOT with the GLP1-RA semaglutide and trials with tirzepatide may soon give us the information we need to know if weight loss strategies can really be a game changer in the treatment of T2D and CVD.

IS-03

A world without diabetes

Prof. Peter E. H. Schwarz – Technical University of Dresden, Germany

Living in a world without diabetes would be a dream to be accomplished by the International Diabetes Federation. Of course, it is unrealistic to believe that there will be no diabetes in the world, but the vision that we are able to prevent any preventable case of diabetes can become realistic. The new vision of the International Diabetes Federation is to be enthusiastic and put activities in place to provide excess to affordable, quality diabetes care and education worldwide. This has been translated into a new mission – to improve the lives of people living with diabetes and prevent diabetes in those at risk. This vision and mission of the International Diabetes Federation is the road map to a world without diabetes – a world without any preventable case of diabetes.

Since a few months I have been elected as the new president-elect of the International Diabetes Federation. It is a great honour to serve people with diabetes worldwide but it also needs rethinking about strategies in a changing world with changing challenges globally. We have to listen to the need of people with diabetes. My passion is addressing the need of people with diabetes. Many needs are in common but many will vary between patients in Bangladesh, United States, Finland, Salomon Islands, Korea and Cameroon. Listening to the need of people will tell us successful strategies how to improve quality of diabetes care worldwide. Improving quality of care needs the knowledge about the current state of the art of diabetes care quality. The International Diabetes Federation will lounge an annual global diabetes survey to access the quality of diabetes care by asking patients and health care provider the

same question mirroring diabetes care reality and their environment. These data can be used to motivate political stake holder and policy developer every year around world diabetes day to act on behalf of people with diabetes. Prevention, prevention, prevention is the ultimate goal of the International Diabetes Federation. Educating health care providers and patients about preventive measures is the first step. Developing policies and national diabetes plans including diabetes prevention a second one. The third one is providing interventions to prevent diabetes from developing. Digitalisation gives us an enormous attractive tool to reach people at risk and those with diabetes. My dream would be that the International Diabetes Federation is in the pocket of every patient worldwide. We have never been so close to our patients than using a smartphone rethinking strategies of diabetes care by using digital biomarkers and digital interventions (digital diabetes therapeutics or digiceutical) can become a strategic alternative for people in low and middle income countries. The International Diabetes Federation is an organisation built up by its member organisations. Those organisations provide an enormous energetic engagement for people with diabetes in their environment. Listening to their needs and challenges and keeping an open heard for the needs of people with diabetes worldwide will be my strategy to fulfil the mission and vision of the International Diabetes Federation – to improve the lives of people living with diabetes and prevent diabetes in those at risk.

Session II

IS-04

Epigenetic changes, oxidative stress and CV damage in obesity and diabetes

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Obesity, insulin resistance and type-2-diabetes (T2D) are increasing health problems worldwide. Women with gestational diabetes (GD) are at risk of developing T2D later in life. Similarly, children born to mothers with GD are prone to the early development of metabolic phenotypes like obesity and T2D. The risk of cardiovascular disease is elevated despite improved lifestyle and novel treatments. Alltogether these conditions alter the expression of genes causing oxidative stress and inflammation that are responsible for endothelial dysfunction and, hence, the development of cardiovascular disease. However, the specific molecular mechanisms triggering inflammatory and oxidative changes and their mother-to-offspring transmission remain poorly elucidated. The use of integrative epigenetic/transcriptomic technologies provides, for the first time, a mapping of detrimental molecular changes underlying the activation of inflammatory and oxidative pathways and proof of their intergenerational transmission. A better understanding of these mechanisms and their transmission to the offspring may contribute to identify novel targets of pharmaceutical interventions to prevent early cardiovascular damage in this setting.

IS-05

How glucose lowering treatments interfere with the autonomic nervous system

Professor Paul Valensi – Polyclinique d'Aubervilliers, Aubervilliers, and Paris Nord University, Bobigny, France

Cardio-vascular vago-sympathetic balance is early impaired in diabetes history. This impairment consists of a defect in vagal activity and an excess in sympathetic activity. Sympathetic predominance contributes to peripheral vasoconstriction and artery stiffness, increase in renin–angiotensin–aldosterone system activity and sodium renal reabsorption, and may thus favor hypertension. It may alter heart rate (HR) variability and accelerate HR. High HR and reduced HR variability are predictive of worse cardio-vascular outcomes, and sympathetic overactivity is an important trigger for heart failure-related events. Reducing sympathetic activity should be regarded as a still neglected therapeutic target in diabetes.

Weight loss, lifestyle changes and glucose control may reverse cardiac autonomic disorders and prevent cardiac autonomic impairment. The knowledge about the impact of glucose lowering treatments on cardio-vascular autonomic function is rather limited.

One study performed in patients with type-2-diabetes (T2D) reported beneficial effects of metformin on sympathovagal balance, which might be explained by a decrease in free fatty acids and insulin resistance, and by a central sympatho-inhibitory effect.

In healthy individuals insulin per se acutely enhances sympathetic activity and depresses vagal control, which results in HR acceleration while blood pressure (BP) increase is dampered by concomitant peripheral vasodilation. Insulin-induced sympathetic activation was shown to result from a peripheral baroreflex-mediated mechanism, a central mechanism, and possibly chemoreflex augmentation with subsequent baroreflex impairment. However, sympathetic activation with insulin is lesser in obese individuals. In patients with poorly-controlled T2D, cardiac vago-sympathetic indexes were not significantly changed after long-term insulin treatment.

Similarly, GLP1-receptor agonists (GLP1-RAs) act towards some detrimental changes in autonomic function. In experimental studies central and peripheral administration of a GLP1-RA reduced HR variability by central inhibition of neurotransmission to preganglionic parasympathetic cardiac neurons and stimulation of sympathetic outflow while direct effects on the sinus node are not excluded. In human studies results are less consistent with some differences among GLP1-RAs and more marked HR acceleration with long-acting agents.

Despite sympathetic enhancement insulin and GLP1-RA treatment do not increase BP probably due to their favorable effects on peripheral blood flow and endothelial function.

Regarding DPP-4-inhibitors some experimental data indicate that they might activate the sympathetic nervous system. In patients with obesity and impaired glucose tolerance we showed that postprandial cardiac vagal activity

was further depressed after 12 weeks of treatment with saxagliptin compared with placebo, possibly due to a slight increase in plasma GLP1 levels.

SGLT2-inhibitors exert an inhibitory effect on sympathetic activity through various mechanisms including a reduction of intrarenal hypoxia and chemoreceptor-mediated activation of renal afferent sensory and efferent sympathetic fibres. In line with sympathetic depression, HR does not increase despite slight BP lowering as shown during long-term treatments by SGLT2-inhibitors. Thus, among the glucose lowering agents this class is unique in lowering sympathetic activity, and this effect might be one of the mechanisms accounting for their benefit on cardio-vascular outcomes.

In some patients the effects of GLP1-RAs on the autonomic nervous system activity may increase the arrhythmogenic risk while sympathetic inhibition with SGLT2is may lead to postural hypotension. Whether the occurrence of such adverse events depend on basal autonomic activity and the presence of cardio-vascular neuropathy needs to be clarified.

IS-06

Glucose lowering drugs with positive and negative impact on heart failure or HFpEF: Role of the diabetologist tackling a multidisciplinary problem

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Type-2-diabetes is one of the most relevant risk factors for heart failure, the prevalence of which is increasing worldwide. The aim of the presentation is to highlight the current perspectives of the pathophysiology of heart failure as it pertains to type-2-diabetes. This review summarizes the proposed mechanistic bases, explaining the myocardial damage induced by diabetes-related stressors and other risk factors, i.e., cardiomyopathy in type-2-diabetes. We highlight the complex pathology of individuals with type-2-diabetes, including the relationship with chronic kidney disease, metabolic alterations, and heart failure. We also discuss the current criteria used for heart failure diagnosis and the gold standard screening tools for individuals with type-2-diabetes. Currently approved pharmacological therapies with primary use in type-2-diabetes and heart failure, and the treatment-guiding role of NT-proBNP are also presented. Every physician looking after people with diabetes has to assure early diagnosis of heart failure and implementation of appropriate cardiometabolic therapy.

IS-07

Diabetes and Lipids: current drug therapy and future perspectives

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Diabetic dyslipidemia is characterized by elevated levels of triglycerides, decreased levels of high-density lipoprotein cholesterol (HDL-C) and increased number of small-dense low-density lipoprotein (LDL) particles, whereas levels of LDL-cholesterol may be normal or slightly elevated. This type of dyslipidemia, also known as "mixed atherogenic dyslipidemia", has been linked to atherosclerosis and cardiorenal disease. Therefore, it is of paramount importance to early diagnose and adequately treat lipid abnormalities in patients with diabetes. Both LDL and non-HDL targets should be achieved based on individual's cardiovascular (CV) risk category.

Several hypolipidemic drugs are currently available and have been proven to improve the lipid profile and reduce cardiometabolic risk in the presence of diabetes, including statins, ezetimibe, fibrates and PCSK9-inhibitors. More recently, inclisiran (a PCSK9-inhibitor) and bempedoic acid (as monotherapy or combined with ezetimibe) have been approved for clinical use, whereas eicosapentaenoic acid (EPA) was reported to significantly decrease cardiovascular risk. Pemafibrate was also shown to decrease triglycerides but failed to improve cardiovascular outcomes in patients with diabetes. Emerging nucleic acid-based therapies are being developed focusing on either lipoprotein (a) or hypertriglyceridemia.

IS-08

CVD Risk factors in the CVOTs

Antonio Ceriello – IRCCS MultiMedica, Milan, Italy

Several studies suggest that, together with glucose variability, the variability of other risk factors, as blood pressure, plasma lipids, heart rate, body weight, and serum uric acid, might play a role in the development of diabetes complications. Moreover, the variability of each risk factor, when contemporarily present, may have additive effects. However, the question is whether variability is causal or a marker. Evidence shows that the quality of care and the attainment of the target impact on the variability of all risk factors. On the other hand, for some of them causality may be considered. Although specific studies are still lacking, it should be useful checking the variability of a risk factor, together with its magnitude out of the normal range, in clinical practice. This can lead to an improvement of the quality of care, which, in turn, could further hesitate in an improvement of risk factors variability.

Session III

IS-09

GLP-1 RA-based treatments and cardiovascular effects – are all the same?

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GLP-1 receptor agonists (GLP-1 RA) have been shown to prevent acute myocardial infarction, stroke, and cardiovascular death (composite endpoint Major Adverse Cardiovascular Events, MACE. The class of GLP-1 RA is heterogeneous. Still, the reduction in MACE has been quite uniform for most GLP-1 RAs, with the exception of lixisenatide and exenatide once-weekly $p = 0.06$). Comparing effect sizes needs to take into consideration differences in study population (subjects with pre-existing CV damage vs. high-risk only), and, more importantly, sample size/duration of the studies (particularly for a look at individual

endpoints; myocardial infarction, stroke, CV death). Another question is, whether the cardiovascular benefit is somehow related to the ability to reduce HbA_{1c}. Indeed, there has been a significant correlation of the reduction in HbA_{1c} and MACE, with the strongest relation to the reduction in stroke. However, this may be an association indicating different degrees of target engagement for different agents. Another point to consider is the heterogeneity in providing meaningful data for certain patient groups (e.g., pre-existing CV disease, impaired renal function). It appears important to compare GLP-1 RA effects to those of SGLT-2 inhibitors, which have similar, but not identical CV effects (focusing on congestive heart failure). In summary, most GLP-1 RAs have significant cardioprotective effects of comparable effect size. In the absence of head-to-head comparisons, it appears difficult to conclude that clinically important difference exist between compounds belonging to the GLP-1 RA class. It will be of interest to determine cardio-protective effects of dual (GIP/GLP-1) receptor agonists like tirzepatide.

IS-10

The rule of Metformin in Diabetes treatment – is it still essential? PRO

Dr. Mahmoud Ibrahim – EDC Center for Diabetes Education, USA

Metformin is the most popular diabetes medication almost all over the world, it has been viewed as the main foundation for the management of type-2-diabetes. Metformin is considered as an effective medication with good glucose-lowering capacity, almost very safe especially for the lack of hypoglycemia and probably some cardio-protection, coupling this with its low cost resulted in a very wide use of this medication. Metformin may be used as a monotherapy or in combination with other glucose-lowering medications for type-2-diabetes.

The American Diabetes Association (ADA) standards of care 2003, indicated that the first-line therapy should depends on the existing comorbidities if any, the management of type-2-diabetes generally includes metformin and comprehensive lifestyle modification. Metformin should also be continued upon initiation of insulin therapy (unless contraindicated or not tolerated), however for those with type-2-diabetes and established/high risk of atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and/or chronic kidney disease (CKD), the treatment regimen should include agents that reduce cardio-renal risk.

The ADA also recommended metformin therapy for the prevention of type-2-diabetes which may be considered in adults at high risk of type-2-diabetes.

Similarly, the American Association of Clinical Endocrinology AACE management algorithm 2023 recommended the first step in the management of type-2-diabetes to be lifestyle intervention, and to start or continue metformin if appropriate

Despite this popularity, efficacy and safety, there still remains controversy about the starting point in the management of type-2-diabetes, should we remain with the metformin or replace it with the newer medications even in the absence of atherosclerotic cardiovascular disease (ASCVD), heart failure (HF), and/or chronic kidney disease (CKD).

Session IV

IS-12

New horizon about glycemic management and CVD: GLP-1 + GIP, GLP-1 + Glucagon, GLP-1+ GIP + Glucagon, GLP-1 + Amylin

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Glucagon-like peptide-1 (GLP-1) receptor agonists are currently considered as first or second-line treatments in the management of type-2-diabetes (T2D), due to their high glucose-lowering effect associated with weight loss, low risk of hypoglycemia and documented cardiovascular (CV) protection. Dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 agonists have been recently developed, of which tirzepatide is the most advanced, being currently approved by both the FDA and EMA. Tirzepatide has shown unprecedented efficacy on control of multiple CV risk factors and specifically greater effects on hyperglycemia, excess body fat, systolic blood pressure and lipids, as compared to the GLP-1 receptor agonist semaglutide. However, whether its action profile on CV risk factors will result in reduced incidence of major adverse cardiovascular events (MACE) is currently unknown and is being addressed by a dedicated trial (SURPASS-CVOT). Adding glucagon receptor agonism to GLP-1 receptor agonists or dual GLP-1/GIP agonists may enhance the extent of weight loss, further reduce hepatic fat, and potentially stimulate energy expenditure: while the impact of this on the CV system and atherosclerosis is not known, reducing hepatic fat could be particularly beneficial. Finally, the addition of amylin agonism to GLP-1 receptor agonists, as for cagrilintide, is expected to provide larger reductions in body weight and fat with potential for CV protection. In general, all these dual and triple peptide agonists could exert potential benefits on MACE and heart dysfunction by multiple mechanisms, including (i.) more effective lowering of HbA_{1c} without hypoglycemia, (ii.) reduction of body weight and other CV risk factors, and (iii.) direct effects on the vasculature and heart. However, unexpected and off-target drug effects, also deriving from the chemical nature of the dual/triple agonist cannot be ruled out, always demanding a dedicated CV outcome trial.

IS-13

New ESC Guidelines and 2022 ADA Consensus for the diagnosis and treatment of heart failure key points

Oliver Schnell – Forschergruppe Diabetes e. V., Helmholtz Center Munich, Germany

Heart failure remains a leading cause of morbidity and mortality worldwide. Heart failure guidelines are designed to improve the quality of care and reflect the interests of patients. Leading medical societies have recently updated their state-of-the-art recommendations for

the management of heart failure. The European Society of Cardiology (ESC) Heart Failure Guideline 2021 provides general recommendations for the diagnosis and management of heart failure. In addition, the American Diabetes Association (ADA), in collaboration with the American College of Cardiology (ACC), published a consensus report in 2022 that specifically addresses the role of diabetes in heart failure.

The particular focus on diabetes is driven by the fact that heart failure is one of the most common complications of diabetes. Conversely, the presence of diabetes is associated with increased hospitalisation and mortality in heart failure patients. The overwhelming evidence of the cardiovascular benefits of SGLT-2 inhibitors, independent of the presence of diabetes, resulted in both guidelines recommending the class of drugs as first-line therapy for heart failure. While this is one of the most significant updates, emphasising the need for multidisciplinary collaboration in the management of heart failure, other changes can be found in the nomenclature and specific advice for comorbid patients. Furthermore, the importance of early diagnosis, with a special focus on the measurement of natriuretic peptides, continues to be emphasised by both societies.

IS-14

New treatment approaches for CKD with a cardiovascular benefit-Key points

Prof. Christoph Wanner – Würzburg, Germany

Since the publication of the EMPA-REG OUTCOME trial, the first CVOT in the field of diabetes and CV disease, 3 more CVOTs, 5 trials in heart failure and 4 trials with the kidney in the primary endpoint have been published. On November 6, 2022 THE LANCET has published a comprehensive metaanalysis of all the 13 trials including more than 90.000 patients. The recently EMPA-KIDNEY trial, the largest trial testing the effects of empagliflozin in more than 6600 patients with diabetic and non-diabetic kidney disease has been published in parallel. For the first time people with normal albuminuria, but prominent reduction in kidney function (eGFR >20 up to 45 ml/min/1.73m^2), have been studied and the reduction in risk was consistent. All kidney trials have been terminated early because of overwhelming benefit. Taken all together, SGLT2 inhibitors reduce kidney outcomes (dialysis, kidney transplant, doubling of serum creatinine) by more than 40 % relative risk reduction, which is twice as much risk reduction the patients can expect from RAS inhibition. Thus, SGLT2 inhibitors, as a class, have received a class 1A recommendation by all major guidelines (KDIGO, ADA, ESC) and are becoming standard of care to reduce kidney disease progression and the rate of renal replacement therapy. Further kidney protective approaches with Finerenone, a non-steroidal Mineralocorticoidreceptor Antagonist in the context of KDIGO diabetes managment in CKD will be discussed.

IS-15

The fatty liver – a game changer in D&CVD?

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Non-alcoholic fatty liver disease (NAFLD) is defined as a chronic liver disease characterized by excessive fat accumulation in the liver. The leading cause of death among patients with NAFLD is cardiovascular disease (CVD), then extra-hepatic cancers and liver-related complications. NAFLD encompasses a disease continuum from steatosis with or without mild inflammation (non-alcoholic fatty liver), to non-alcoholic steatohepatitis, which is characterised by faster fibrosis progression than non-alcoholic fatty liver. The global prevalence of NAFLD is about 30 % and is often comorbid with other metabolic disorders including type-2-diabetes (T2D), hypertension, coronary artery disease, and metabolic syndrome. The current evidence describing the many ways that NAFLD itself increases CVD risk, both in obese and non-obese subjects. NAFLD may directly contribute to atherosclerotic CVD (ASCVD) through the hepatic secretion of atherogenic lipoproteins and procoagulant factors. Also, factors that may drive both NAFLD and ASCVD are insulin resistance, hypertension, and potentially chronic periodic hypoxia, intestinal dysbiosis and chronic low grade inflammation. That was the reason for the proposal of the novel nomenclature, metabolic-associated fatty liver disease (MAFLD) which better depict pathogenetic relationship between hepatic steatosis, metabolic dysregulation and important extra-hepatic complications, such as T2D and CVD. Moreover, T2D is often associated with NAFLD/MAFLD and is one of the most important risk factors for the development of this disease. Therefore, several studies are underway to demonstrate the efficacy of anti-diabetic drugs on fatty liver disease. Newer glucose-lowering drugs, GLP-1RAs, as well as SGLT2i may exert benefit on both hepatic fat content and CVD outcomes.

Session V

IS-16

The Diabetes-Cardio-Renal – Metabolic Concept

Yehuda Handelsman, MD – FACP, FNLA, FASPC, MACE

Cardiovascular disease is a ssignificant cause of mortality in patients with type-2-diabetes. [1] Risk for ccardiovascular Eeeents is greatest when both diabetes and CKD are present. [2] Increase risk of stroke in diabetes [3], heart failure (HF) is common in diabetes, prevalence of 20–40 % [4] Comprehensive management of diabetes rrequires ccontrol all CV risks [5]. Micro- macro-vascular disease may be parts of the same spectrum microvascular disease predicts macrovascular disease: nephropathy, (autonomic) neuropathy, retinopathy [6–10]

Recent CVOTs of SGLT2-i & GLP1-RA led to a paradigm shift in DM guidelines focusing first on preventing the next CV/CKD event; recommending these drugs to People – with T2D and established or high risk for ASCVD & CKD – independent of glucose control to prevent CVD, strokes, HF, CKD and

PAD. Still recommending continued long term glucose and traditional CV risks reduction to prevent future co-morbidities.

These CVOT transcended beyond the original medications' indications across multiple disciplines. This calls for new directions in developing practice recommendations which are not restrained by a single medical society discipline. To overcome these limitations in developing encompassing guidance, we assembled a task force with recognized leaders representing multiple medical disciplines: cardiologists, nephrologists, endocrinologists, and primary care.

The result is the DCRM Practice Recommendations- a multispecialty consensus on the comprehensive management of diabetes cardiorenal and metabolic diseases. [11] The recommendations address the whole patient, targeting the non-expert clinicians: specialists and primary care alike. To enhance acceptance, the DCRM was published in a peer reviewed journal.

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Session VI: Starting Injectable Therapy – What is the evidence?

IS-17

Long acting insulin preparations – getting better

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The discovery of physiological basal and prandial insulin secretion confirmed the need of both long-acting and short-acting insulin administration. Human long-acting insulins did not maintain stable insulin level in the blood whereas first insulin analogues could partly resolve this problem. First long-acting 100 U insulin analogues extended their activities during 24 hours and decreased the valves of basal insulin levels. However, no significant improvement of persisted hypoglycemic episodes was found in many patients and new preparations have been awaited. Seveal ways to create new molecules have been suggested. Firstly, the increased insulin concentration to 300 U (i.e. glargin) caused better sustained level of insulin. Similar was found with 200 units insulin degludec overhelming 24 hours and decreasing the valves of plasma glucose together with decreased number of hypoglycemic events. The use of glucose sensors brought the evidence on basal insulin effects. The level of glucose concentration during 24 hours apparent from continual glucose monitoring (CGM) could help in proper decision how much units of long-acting insulin is needed in the respective patient.

New development in basal insulin treatment has been started with once-weekly insulins. Both basal insulin FC (BIF LY3209590) and icodec (LAI 287) demonstrated non-inferiority compared to 100 U glargin with comparable hypoglycemic events. The studies ONWARDS 1–6 confirmed the safety of icodec administration in different combinations in Type 2 (ONWARDS 1–5) and Type 1 (ONWARDS 6) diabetic patients. The icodec administration was associated with increased time-in-range (TIR) and comparable or better glucose control compared to once-daily 100 U glargin or 200 U degludec in type-2-diabetic patients. On the other hand, more hypoglycemic events were registered with icodec compared to degludec insulin in type-1-diabetes. Higher single doses of icodec insulin covering seven days a week induces new schema of dose titration. Once-weekly compared to once-daily insulins increase the adherence of diabetic patients, especially of type 2, to insulin injections. New long-acting insulin analogues extend new possibilities for improvement of diabetes care. Their final consequences could be closer to basal insulin regulation in healthy persons although new questions remain to be answered.

IS-18

Fixed Ratio Combination insulin preparations - getting better

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Fixed Ratio Combination (FRC) insulin preparations have been used for treating type-2-diabetes for many years. They consist of a fixed combination of two or more different types of insulin, usually basal and prandial, mixed in a single injection. FRC insulin preparations are effective in controlling blood glucose levels in patients with type-2-diabetes who have failed to achieve glycemic control with monotherapy or dual therapy. Recent developments in FRC insulin preparations have led to improved formulations that offer better glycemic control and reduced hypoglycemia. The first improvement is the development of FRC insulin preparations with a higher basal-to-prandial insulin ratio. These new formulations have been shown to provide better fasting blood glucose control and reduced postprandial hyperglycemia compared to older formulations with lower basal-to-prandial insulin ratios. Secondly, FRC insulin preparations with ultra-long-acting basal insulin analogs have been developed. These formulations provide a more stable basal insulin profile and a longer duration of action, which may reduce the risk of hypoglycemia and improve glycemic control. Additionally, using ultra-long-acting basal insulin analogs in FRC insulin preparations may allow for once-daily dosing, which could improve patient adherence to therapy. Thirdly, the development of FRC insulin preparations with rapid-acting insulin analogs has also been shown to improve glycemic control and reduce hypoglycemia. These formulations have a faster onset of action and

a shorter duration, allowing for more precise postprandial insulin dosing and reducing the risk of hypoglycemia. Finally, the use of FRC insulin preparations in combination with newer glucose-lowering agents, such as GLP-1 receptor agonists and SGLT2 inhibitors, has been shown to further improve glycemic control and reduce the risk of hypoglycemia. In conclusion, recent developments in FRC insulin preparations have led to improved formulations that offer better glycemic control and reduced hypoglycemia. These improvements include higher ratios of basal to prandial insulin, ultra-long-acting basal insulin analogs, rapid-acting insulin analogs, and combinations with newer glucose-lowering agents. These advances have the potential to improve patient outcomes and quality of life and should be considered in the management of patients with type-2-diabetes.

IS-19

GLP-1 RA based treatments – getting better

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"Faster than a speeding bullet, more powerful than a locomotive…" the GLP-1 receptor agonists (RA) and co-agonists are evolving into the super-drugs of type-2-diabetes (T2DM). The newer generation of GLP-1 RA are currently the most potent antihyperglycemic medications available, exceeding any other medication including basal insulin (semaglutide and tirzepatide led to an HbA_{1c} lowering effect double that of insulin glargine in the Sustain 4 and Surpass 4 trials, tirzepatide treatment resulted in an HbA_{1c} <5.7 in >40 % of subjects across all phase III studies). Moreover, in the large subset of patients who suffer from T2DM and obesity, treatment with these medications may lead to significant weight loss (>10 % mean weight loss in all phase III tirzepatide trials) thus both controlling glycemia, preventing diabetes related complications and alleviating the immediate and long-term morbidity associated with obesity. This in turn translates into improvements in health-related quality of life patient-reported outcomes observed with multiple GLP-1 RAs. The added "cherry on the topping" is a cardioprotective/antiatherosclerotic effect- across all vascular beds. This has been observed in several cardiovascular outcome trials (CVOT) and in a meta-analysis incorporating all available GLP-1 RA CVOTs including over 60 000 patients. However, treatment with GLP-1 RA is associated with significant adverse events, mostly gastrointestinal and during the dose escalation phase. These may often lead to drug discontinuation and necessitate further study and better understanding to increase adherence. Taken together, GLP-1 RA should not only be the first injectable but the first line of treatment in most patients with T2DM.

Session VII – Closing Symposium on New Technologies

IS-20

Leveraging technology for better care of older people with diabetes

Prof. Tali Cukierman-Yaffe – Sheba Medical Center, Israel

Diabetes is a major public health burden associated with high mortality, morbidity, hospitalization, a reduction in quality of life and increased health care services utilization rates [1]. Healthy aging with diabetes is a challenge. It is a challenge for health care systems due to the high prevalence of the disease in older age (~25 % of the population over 65) [2] and a challenge for health care providers, patients, family and other care providers as it is a disease that requires elaborate self-care management capacities. Diabetes may be viewed as a disease of accelerated ageing as it is a risk factor for cognitive dysfunction [3], dementia [4–6], depression [7] physical disability, frailty & Sarcopenia [8,9]. [10–14] These impede self-care management capacities, such as insulin scheduling, the ability to alter treatment regimen according to differing life situation and dealing with hypoglycemia events (and prevention of deterioration to severe hypoglycemia) [2]. [15,16] These factors (cognitive dysfunction, dementia, physical disability and frailty) are now considered long term complications of the disease and treatment is targeted at slowing their progression. Current technology has an important role in glucose management and avoidance of hypoglycemia and may also have a role in reduction of diabetes-related complications and slowing of functional decline and enhancement of quality of life. Future technology may also play an important role in setting treatment targets according to functional/cognitive state, enhancement of self-care capacity, and alleviating functional and cognitive dysfunction in older adults. The talk will provide an overview of the challenges of treating diabetes in older age and the role technology may play in coping with these unique challenges.

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IS-21

Artificial intelligence-based decision support systems for health care professionals treating people with diabetes mellitus.

Prof. Moshe Phillip – Schneider Children's Medical Center, Petah Tikva, Israel

Despite the increasing adoption of new medications and technologies like insulin pumps and continuous glucose monitoring devices, most people with diabetes (PWD) do not achieve their glycemic goals. This may be related to the tremendous burden that diabetes has on PWD and their health care providers but also could be related to the lack of time and/or expertise of clinicians who have to integrate all the information related to each person at each visit or interaction and come-up with a personally tailored therapeutic plan if needed. We have shown that artificially based decision support system can help clinicians provide a safe and effective advice to PWD which was not-inferior to that given by expert physicians from specialized diabetic academic centers.

IS-22

Automated insulin delivery systems – where do we go?

Dr. Eytan Roitman – Clalit Health Care Services, Israel

Automated insulin delivery systems have revolutionized diabetes management, enabling tighter glycemic control and improved quality of life for people with diabetes. Despite significant advances in this technology, challenges remain, and the question of where we go from here is fascinating .

The current AID systems utilize continuous glucose monitoring devices and insulin pumps to automatically adjust insulin delivery based on glucose levels. These systems have shown significant benefits, improving overall glycemic control, reducing the risk of hypoglycemia and improving quality of life. However, challenges remain, including sensor accuracy, algorithms based mostly on glucose levels and insulin, the complexity of system operation and insulin PK/PD.

Future AID systems could address these challenges by incorporating advanced algorithms that can account for individual differences in insulin sensitivity and glucose variability. This could allow better control and potentially reduce the need for user input. Additionally, incorporating other technologies, such as artificial intelligence or machine learning, could enable more personalized and adaptive treatment strategies.

An additional area of possible advancement is the incorporation of AID systems with wearable devices or smart sensors, which could provide additional data streams for more accurate and personalized treatment. This integration could potentially improve real-time monitoring and analysis of physiological parameters beyond glucose levels, such as heart rate, physical activity, or stress levels, to further enhance diabetes management.

Overall, AID systems have transformed diabetes management and hold enormous potential for future development. Continued innovation and collaboration are critical to realizing this potential and improving the lives of those living with diabetes.

Oral presentations – Heart Disease

P-01

Effects Of Molecular Hydrogen In The Pathophysiology And Management Of Cardiovascular And Metabolic Diseases

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There is evidence that western-type diet and lifestyle may cause oxidative stress and inflammation, whereas Mediterranean type of diet rich in antioxidants, may be inversely associated, with risk of mortality due to cardiovascular diseases (CVDs) and type-2-diabetes mellitus (T2DM). This article aims to highlight the role of diet, with reference to molecular hydrogen generation in the gut, and the role of hydrogen in the pathophysiology and prevention of above diseases. It is possible that beneficial effects of diet may be due to increased content of fiber and flavonoids and probiotics that are known to produce liters of molecular hydrogen in the gut. Increase in hydrogen, acts as an antioxidant and may inhibit free radical generation and inflammation. In the last two decades, it has become increasingly clear that molecular hydrogen, either produced endogenously or administered exogenously via inhalation or hydrogen rich water (HRW) or via any releasing agents, acts as potential anti-inflammatory agent, in a wide range of biochemical and pathophysiological processes. Recent studies indicate that molecular hydrogen can inhibit hydroxyl and nitrosyl radicals and can directly act as antioxidant in the cells and tissues, which can cause marked decline in oxidative stress and inflammation, leading to significant decline in CVDs and metabolic diseases

as well as perspectives in mitochondrial diseases. Clinical and experimental studies indicate that hydrogen therapy such as HRW can be beneficial in the management of CVDs and metabolic diseases. Larger studies are necessary to verify the role of hydrogen administration in all the chronic diseases.

P-02

The valuable role of non-invasive coronary artery assessment in patients with diabetes mellitus (DM)

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Background: Knowing that increased velocities in coronary arteries (CA) at rest was proposed for diagnostics stenose, the aim of the study was to evaluate the prognostic role of coronary artery ultrasound assessment in patients with DM.

Methods: This is a prospective cohort study comprises 189 consecutive patients (105 females; age 64+11 years) referred to echocardiography with diagnosed DM. Echocardiography was performed with additional scans for coronary arteries. Their exams were performed for other reasons, primarily for arterial hypertension, and 74 patients had known CAD. Death and non-fatal myocardial infarction (MI) were defined as hard endpoints. Death, MI, acute coronary syndrome, severe heart failure with hospitalization and/or revascularization were defined as major adverse cardiac events (MACE).

Results: 180 patients were followed up with for a median of 27 months. Seventy-four MACE, including 13 deaths, 1 non-fatal myocardial infarctions occurred. With a ROC analysis, a coronary flow velocity in left anterior proximal part of 76 cm/s was the best indicator for risk prediction of death/MI (area under curve 0.72 [95 % CI 0.65–0.79]; sensitivity 69 %, specificity 76 %, p 0.0012). The cut-off value of 64 cm/s was a predictor of MACE (area under curve 0.78 [95 % CI 0.70–0.84]; sensitivity 73 %, specificity 78 %, p 0.0001). The maximal velocities in the proximal left-sided coronary arteries were independently associated with MACE (HR 1.02, 95 % CI 1.01; 1.02; p0.0001).

Conclusion: The non-invasive assessment of coronary artery velocities during routine echocardiography can predict a poor prognosis for patients with DM.

P-03

Longitudinal Observational Study on the Association of Peripheral Arterial Disease, Albuminuria, Dyslipidemia with HbA_{1c} in Patients with T2DM: Two-Year Follow-up Results

Ragini Rohatgi, Pooja Kudkar, Daisy Alfred – Diabetes, Rohit Diabetes Centre, India

This observational study aimed to investigate the utility of several markers, including ankle-brachial index (ABI), toe brachial index (TBI), Albumin Creatinine Ratio (ACR), and Low Density Lipoprotein Cholesterol (LDL-C) in the context of changes in HbA_{1c} among patients with type-2-diabetes mellitus (T2DM). The study followed 50 patients receiving standard care and was conducted in a real-world setting for two years. The results showed that during the follow-up period, there was an increase in the percentage of patients achieving the targeted glycemic control by 44 %, indicating a potential benefit of standard care for diabetes management. Modest improvements in other markers, such as LDL-C and ACR, and a slight increase in the proportion of patients with a TBI within the normal range were observed. However, there was a decrease in the proportion of patients with an ABI within the target range during the follow-up period. No significant correlation was found between the changes in HbA_{1c} and other markers, indicating that achieving glycemic control may not necessarily lead to improvements in other markers. The study suggests that standard care for patients with T2DM can lead to some improvements in glycemic control and cardiovascular risk factors, but further interventions may be needed to address other comorbidities such as kidney disease and peripheral artery disease.

P-04

The legacy effect of hyperglycemia is ameliorated by the early use of SGLT-2 inhibitors: a cohort study with newly-diagnosed people with type-2-diabetes

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Background: A delay in reaching HbA_{1c} targets in patients with newly-diagnosed type-2-diabetes (T2D) is associated with an increased long-term risk of developing cardiovascular diseases (CVD), a phenomenon referred to as legacy effect. Whether an early introduction of glucose-lowering drugs with proven benefit on CVD can attenuate this phenomenon is unknown.

Methods: Using data derived from a large Italian clinical registry, i.e. the AMD Annals, we identified 251,339 subjects with newly-diagnosed T2D and without CVD at baseline. Through Cox regressions adjusted for multiple risk factors, we examined the association between having a mean HbA_{1c} between 7.1 and 8 % or 8 %, compared with ≤ 7 %, for various periods of early exposure (0-1, 0-2, 0-3 years) and the development of later (mean subsequent follow-up 4.6±2.9 years) CVD, evaluated as a composite of myocardial infarction, stroke, coronary or peripheral revascularization, and coronary or peripheral bypass. We performed this analysis in the overall cohort and then splitting the population in two groups: those that introduced sodium-glucose transport protein 2 inhibitors (SGLT-2i) during the exposure phase and those never treated with these drugs.

Findings: Considering the whole cohort, subjects with both a mean HbA_{1c} between 7.1 and 8 % and 8 %, com-

pared with patients attaining a mean $HbA_{1c} \leq 7\,\%$, showed an increased risk of developing the outcome in all the three early exposure periods assessed, with the highest risk observed in patients with mean HbA_{1c} 8 % in the 3 years exposure period (hazard ratio 1.33; 95 % confidence interval 1.063–1.365). The introduction of SGLT-2i during the exposure periods of 0-1 and 0-2 years denied the association between poor glycemic control and the outcome (p for interaction 0.006 and 0.003, respectively, vs patients with the same glycemic control but not treated with these drugs).

Interpretation: Among patients with newly diagnosed T2D and free of CVD at baseline, a poor glycemic control in the first three years after diagnosis is associated with an increased subsequent risk of CVD. This association is no longer evident when SGLT-2i are introduced in the first two years, suggesting that these drugs attenuate the phenomenon of metabolic memory.

Oral presentations – Obesity

P-05

A Call for the Allometric Central Body Anthropometrics A Body Shape Index (ABSI) and Hip Index (HI) in Clinical Practice

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Background: The use of waist circumference (WC) and other indices based on WC and hip circumference (HC) to identify abdominal obesity is confounded by correlations with weight and height or BMI from ~0.4 for WC/HC to ~0.8 for WC. A decade ago power law formulas based on Cox regression were derived from population samples: ABSI for WC and HI for hip circumference. Subsequently, it has become apparent that BMI, ABSI and HI can be applied to populations worldwide.

Methods: We have categorized and posted on our websites, publications that evaluate ABSI (~500): Mortality; Metabolic Syndrome (MS) and MS components; Cardiovascular Disease (CVD) and CVD testing; Cancer; Body composition and genomics; Additional Studies including Hepatic, Pulmonary, Renal and Inflammation.

We further present power law equivalents of ABSI, HI and popular anthropometrics. We show how based on mutual independence an Anthropometric Risk Indicator (ARI) gives an overall risk estimate. Moving to our present call to conference attendees, we provide examples of cases showing clinical utility.

Results: Our presentation is to explain the nature of the allometric approach to central body measurements and the potential for clinical venues.

Conclusion: The present challenge is to evaluate use of allometric indices for health care and planning. BMI is the measure of body size. We suggest ABSI for waist shape and HI for hip shape. Reporting should be customized appropriately for users.

P-06

Correlation of Body Mass Index with Body Fat Indices, Skeletal Muscle Mass, neck circumference waist-hip ratio in people with type-2-diabetes

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Background and aims: BMI is an inaccurate measure of body fat content and does not consider muscle mass and overall body composition. Hence, we undertook this study to find out the correlation between the BMI, body fat indices (Percent Body Fat, Body Fat Mass of Trunk, Body Fat Mass % of Trunk, Visceral fat area and visceral fat level) Basal Metabolic Rate (BMR) Waist-Hip Ratio (WHR) and circumference of neck.

Materials and methods: We conducted a descriptive cross-sectional study on 365 people with T2DM over 18 months (August 2021 to January 2023). InBody 770, a multi-frequency bioelectrical impedance device was used to assess the body fat composition. GraphPad version 9.5 was used for statistical analysis.

Results: The mean age, BMI (Kg/m2), body weight (kg) was 46 years (±14, 95 % CI 44 to 47), 29 kg/m2 (±5.4, 95 % CI 28 to 30), 77 kg (±15, 95 % CI 75 to 78), respectively. 93.4 % (341/365) had body fat 25 %, whereas 35.8 % (131/365) had BMI 30kg/m². The mean visceral fat level (VFL) was 15 (±4.9, 95 % CI 14 to 15). There were 65.2 % (238/365) people who had VFL 12, which was the cut-off for healthy

Parameter	Age	BMI	Weight	Body Fat Mass	Skeletal Muscle Mass	Percent Body Fat	Body Fat Mass of Trunk	Body Fat Mass % of Trunk	Target Weight	Weight Control	BFM Control	Free Fat Mass Control	BMR (Basal Metabolic Rate)	WHR (Waist-Hip Ratio)	VFL (Visceral Fat Level)	VFA (Visceral Fat Area)	Circumference of Neck
Minimum	14	17	39	6,4	14	10	2,8	63	42	–61	–61	0	965	0,72	2	26	25
Median	46	28	77	30	25	41	16	362	59	–17	–20	1.2	1345	0.97	16	162	38
Maximum	80	58	137	78	41	57	28	751	85	13	4	13	1931	1.2	20	276	57
Range	66	40	98	72	26	47	25	688	43	74	65	13	966	0.5	18	250	32
Mean	46	29	77	31	25	40	16	363	59	–18	–20	2.4	1357	0.97	15	158	38
Std. Deviation	14	5.4	15	11	5.5	9.3	5.1	121	8.4	12	11	2.8	196	0.076	4.9	58	3.7
Std. Error of Mean	0.72	0.28	0.79	0.58	0.29	0.49	0.27	6.3	0.44	0.63	0.55	0.15	10	0.004	0.26	3	0.19
Lower 95 % CI of Mean	44	28	75	30	24	39	15	350	58	–19	–21	2.1	1337	0.96	14	152	37
Upper 95 % CI of Mean	47	30	78	32	26	41	16	375	60	–17	–19	2.7	1377	0.98	15	164	38

P-06, Fig. 1: Analysis of Body Composition Parameters (n = 365)

level of visceral fat. (Table). There was a significant correlation between the BMI and skeletal muscle mass (Pearson r 0.17, 95 % CI 0.07 to 0.27, p = 0.0007), BMI and percent body fat (Pearson r 0.73, 95 % CI 0.68 to 0.78, p 0.0001), BMI and body fat mass % of trunk (Pearson r 0.87, 95 % CI 0.84 to 0.89, p 0.0001), BMI and Basal Metabolic Rate (Pearson r 0.19, 95 % CI 0.09 to 0.28, p 0.0001, BMI and Waist-Hip Ratio (Pearson r 0.52, 95 % CI 0.44 to 0.59, p 0.0001), BMI and VFL (Pearson r 0.78, 95 % CI 0.74 to 0.82, p 0.0001), BMI and neck circumference (Pearson r 0.83, 95 % CI 0.79 to 0.86, p 0.0001, BMI and visceral fat area (Pearson r 0.84, 95 % CI 0.81 to 0.87, p 0.0001)

Conclusion: Assessing body fat composition using multiple measures, such as percent body fat, body fat mass of trunk, visceral fat area and level, basal metabolic rate, waist-hip ratio, and neck circumference, provides a more accurate picture of an individual's adiposity. A majority of individuals with T2DM in the study population had high levels of body fat, highlighting the importance of precise screening for adiposity in this patient population. Normalizing body fat levels should be a targeted therapeutic approach for individuals with T2DM to address chronic metabolic diseases associated with excess body fat. The use of bioelectrical impedance devices for assessing body fat composition is a valuable tool for healthcare professionals working with individuals with T2DM to provide more personalized care and improve patient outcomes.

Poster presentations – Heart Disease

P-07

Complications after one-year observation of patients with type-2-diabetes mellitus and various types of coronary heart disease

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Summary Aim: Evaluation of complications after one-year observation in patients with acute and chronic coronary heart disease (CHD) depending on the presence of type-2-diabetes mellitus (T2DM).

Material and methods: This comparative clinical study included 202 men and women with acute and chronic CHD. Patients were divided into four groups, depending on the presence of type-2-diabetes mellitus: acute CHD and T2DM; acute CHD without T2DM (control group); chronic CHD and T2DM; chronic CHD without T2DM (control group). Depending on the results of clinical status and coronary angiography data, patients underwent myocardial revascularization (balloon angioplasty without stenting, stenting, coronary bypass grafting, stenting + coronary bypass grafting) followed by pharmacological treatment. One-year composite endpoints included: recurrent myocardial infarction, acute cerebrovascular accident, readmission, and death.

Results: After admission, up to 80 % of patients, regardless of CHD type and glycemic status, underwent revascularization. Patients without T2DM underwent stenting significantly more often compared with patients with T2DM. Coronary artery bypass grafting, including in combination with stenting, was more frequent in patients with T2DM with acute and chronic CHD. One year after discharge, readmissions and reoperations were more prevalent among patients with acute and chronic CHD and T2DM. The groups did not differ by the number of non-fatal and fatal complications. The total number of endpoints in patients with T2DM, regardless of the CHD type, were 2 times higher compared with the control group (p 0.001).

Conclusion: Patients with acute and chronic CHD without T2DM, underwent stenting of one coronary artery more often, while patients with T2DM underwent coronary bypass surgery, including in combination with stenting. After one-year observation, the number of complications in patients with various CHD types and T2DM was higher compared with patients without T2DM. This once again indicates the need for comprehensive secondary prevention.

P-08

Left ventricular hypertrophy and inflammation in diabetic patients

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Introduction: The association between diabetes and adverse cardiovascular outcome may be partially explained by the strong independent association of type 2 diabetes with cardiovascular target organ damage, such as left ventricular hypertrophy (LVH), a well-known predictor of cardiovascular events independent of coronary artery disease. The aim of the present study is to evaluate the relation of LVH to fibrinogen and C-reactive protein (CRP) as markers of inflammation and susceptibility to atherothrombosis.

Methods and subjects: We selected 50 adults with type-2-diabetes. 32 were women and 18 were men, mean age 45 ± 14. Hypertension was defined by systolic blood pressure 135 mmHg and/or diastolic blood pressure 85 mmHg. Diabetes was defined by fasting plasma glucose levels 126 mg/dl or by specific treatment. BMI was calculated by the standard formula. The left ventricular mass index (LVMI) has been evaluated according to the method of Devereux and Reichek. Participant's laboratory data were examined in the morning after an overnight fast 12 h. The levels of CRP and fibrinogen have been measured.

Results: From 50 participants, 22 (44 %) presented LVH, which was associated with higher BMI and CRP, fibrinogen levels, left ventricular hypertrophy, markers of inflammation. We found relationships between fibrinogen and concentric LVH (p 0,001) and also between CRP with concentric hypertrophy (p 0,005).

Conclusions: 22 patients presented concentric LVH, 10 patients eccentric LVH, and 18 patients normal LV mass. Concentric LVH was associated with elevated markers of systemic inflammation and susceptibility to atherothrombosis (CRP and fibrinogen levels) independently of clinically overt cardiovascular disease and traditional cardiovascular risk factors. No correlation was found between CRP and fibrinogen and eccentric LVH.

P-09

Integration of chronic care model for non communicable diseases patient management at primary health care in Northern Uganda: protocol for outpatient quasi experimental study

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Background: In Uganda, the burden of noncommunicable diseases (NCDs), particularly cardiovascular disease and diabetes mellitus (DM), is rising rapidly in a fragmented health-care system. There is a lack of large-scale intervention studies on NCDs integration and context-specific clinical outcomes, cost-effectiveness data at lower health facilities (Health cente IVs) to inform policy and prioritization of NCDs care in government health facilities.

Study designs and Methods: Over a two-year period, the intervention sites (Health centre IVs) will implement chronic care model (CCM) interventions, while the control sites will continue with usual care practice. The interventions will include a hybrid of Wegner's and the World Health Organization's Innovative Care for Chronic Conditions framework (ICCCF) elements for chronic care such as routine use patients registry for diabetes and hypertension alongside HIV/AIDS care, planned outpatient visits, evidence-based clinical guidelines, self-management, linkages to formal community programs, and referral to tertiary facilities. The primary hypothesis is that after intervention, participants will have lower blood pressure and HbA_{1c} scores by the end of the follow-up periods than before intervention. The secondary hypotheses are that integrating diabetes and hypertension care at HCIVs will improve access to care, retention in care, adherence, continuity of care, quality of life, and cost of care when compared before intervention.

Conclusion: The evaluation will provide significant evidence for NCDS integration at lower level health facilities (Health IVs) at various timepoints (6, 12, and 18 months), the acceptability, effectiveness and efficiency of integrated service provision prior to scaling up.

P-10

Astaxanthin Improves Lipid Metabolism in Skeletal Muscle in an Experimental Model of Metabolic Syndrome

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Background: Metabolic Syndrome (MS) is a cluster of multiple metabolic abnormalities (dyslipidemia, hypertension, visceral adiposity, insulin resistance, oxidative stress, inflammation and prothrombotic state, among others) that increase the cardiovacular risk. Skeletal muscle play a key role in the glucose and lipid homeostasis. Evidence suggests that an enhanced lipogenic pathway in this tissue could be a potential mechanism involved in intramuscular lipid accretion and the impaired insulin action in MS.

Astaxanthin – AST – (freshwater crustaceans), is a powerful antioxidant that could exert preventive actions against MS via its potential to improve oxidative stress, inflammation, lipid and glucose metabolism.

Objective: The aim of this study was to evaluate the effects of astaxanthin on lipid metabolism in skeletal muscle in an experimental model of MS (rats fed a sucrose-rich diet for 90 days).

Methods: Wistar rats received one of the following 4 diets (90 days):

1. Reference Diet (RD): standard commercial diet
2. Sucrose rich diet (SRD)
3. RD lus 10 mg/kg body weight/day of AST (RD+AST)
4. SRD plus 10 mg/kg body weight/day of AST (SRD+AST)

We analized: Serum: triglycerides (Tg) and cholesterol. Skeletal muscle: Tg content. Lipogenic enzymes activities: Acetyl-CoA carboxylase (ACC), Fatty acid synthase (FAS), Glucose-6-phosphate dehydrogenase (G-6-P DH) and Malic Enzyme (ME).

Results: AST administration in the SRD improved the dyslipidemia, decreased triglyceride content, FAS and ME activities, although the values were still higher than RD. Moreover, AST restaured ACC and G-6-PDH activities (P0.05). No differences were observed between DR and DR+AST groups.

Conclusion: The results show that AST could be a potential target for treatment/prevention of MS disorders.

Poster presentation – CGM

P-11

Prevalence and Associated Factors of Prediabetes in Adult East African Population: A Systematic Review and Meta-Analysis

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Background: Diabetes mellitus is a major public health problem with serious consequences and over 3 in 4 adults with diabetes live in low- and middle-income countries. According to a recent study, pre-diabetic people are nearly six times more likely to develop diabetes than people with normal glucose levels. However, due to the presence of inconsistency and absence of representative data this study aimed at estimating the prevalence of prediabetes and its associated factors in adult East African population.

Methods: Articles published between January 1, 2013 and December 30, 2022 were systematically searched in databases. All observational community-based studies conducted in adult East African populations that reported the prevalence of prediabetes or associated factors were included. Three authors independently extracted all required data using the data extraction format and analyzed using Stata™ Version 11. The I2 test was used to determine whether there was significant heterogeneity or not. Finally, a random effects model was computed to fix overall prediabetes prevalence and its associated factors. The study registered with Prospero number CRD42023389745.

Results: The search strategy identified 267 articles. After screening for full text review, twenty-one articles were included for final analysis. The overall prevalence of prediabetes was 12.58 % (95 %CI: 10.30, 14.86 %) in adult East African population. Furthermore, the subgroup analysis revealed that prediabetes in the urban population 20 % (95 % CI: 1.60, 38.37) is twice higher than rural 10.0 % (95 % CI: 5.52, 14.48) populations. The prevalence of prediabetes by the ADA diagnostic criteria 21.45 % (95 % CI: 15.54, 27.35) was three times higher than the WHO 7.20 % (95 % CI: 5.70, 8.69). Moreover, prediabetes was significantly associated with older age (OR = 1.64, 95 %, CI: 1.07, 2.53), hypertension (OR = 2.43, 95 %, CI: 1.02–5.79), obesity and overweight (OR = 1.70, 95 %, CI: 1.09, 2.65).

Conclusion: This study showed that the population of east Africa had a high prevalence of prediabetes. Prediabetes was found to be significantly associated with older age, hypertension and BMI. This study recommended that health policy makers focus on the prevention and management of prediabetes in order to reduce the burden and complication of type-2-diabetes mellitus.

Keywords: Prevalence, associated factors, prediabetes, meta-analysis, systematic review, East Africa

Poster presentation – Insulin Treatments

P-12

Effect of Sports Activity on Metabolite Profile in Patients with Type 1 Diabetes

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Background: The remarkable performance of athletes with type-1-diabetes mellitus (T1DM) in competitive sports has prompted research into the unique physiology of people with this disease. Objectives: The aim of the study was to search for compensatory mechanisms that give a metabolic advantage in T1DM patients, active in sports compared to T1DM subjects not physically active, with respect to healthy volunteers active in cross-country running compared to people with a sedentary lifestyle.

Methods: For the study, 30 men with T1DM (15 trained and 15 inactive) at least 2 years from disease diagnosis and glycated haemoglobin percentage (HbA_{1c}) less than 8.0 %, and 37 healthy volunteers (15 trained and 22 sedentary), aged 18–48 years, with a BMI of less than 27 kg/m^2 was used. The level of physical activity was determined using the International Physical Activity Questionnaire (IPAQ) and a 10-item physical activity scale. Systemic NO bioavailability was assessed by nitrite and nitrate concentrations in plasma. To characterize profile of metabolites, LC-MS/MS-based targeted metabolomics was applied.

Results: 90 known metabolites belonging to 10 metabolic pathways involved in arginine metabolism, branched-chain amino acids, aromatic amines, glycolysis, tricarboxylic acid cycle, the pentose phosphate pathway, redox, methylation, hexosamine biosynthetic pathway remained altered in physically active T1DM patients. In a group of T1DM subjects active in sports, the increased concentration of plasma ATP, pyruvate, lactate, citrate/F-6-P ratio, 6-P-gluconate/F-6-P ratio, ethanolamine and hypoxanthine was evident.

Conclusion: Possible alterations in energy metabolism in response to sport activity in T1DM subjects were highlighted.

Funding statement: The study was financed by POB qLIFE Priority Research Area under the program 'Excellence Initiative – Research University' (no. U1C/P04/NO/02.09) at Jagiellonian University Collegium Medicum.

Poster presentations – Obesity

P-13

Association of socio-demographic factors and dietary patterns with biochemical blood profiles among High School students having normal and higher body mass index, in Mekelle, Northern Ethiopia

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Background: Higher Body mass index (BMI) associated with elevated levels of abnormal lipid profiles have been well established as an important risk factor for accelerated atherosclerosis and chronic NCDs. School-based BMI measurement programs are effective at reducing childhood obesity, stigma, and unsafe weight control behaviors in young adults. Therefore, this study aimed to investigate the association of socio-demographic factors and dietary patterns with biochemical blood profiles among high school students.

Methods: A comparative cross-sectional study design was conducted from March to July 2020 at Mekelle City High School. Data on socio-demographic factors and dietary patterns were collected using a structured pretested questionnaire and interviews. A random blood sample was collected from each participant for lipid profile analysis. Lipid profile concentration was analyzed using Cobas Integra 600 Plus. Data were analyzed by using the SPSS version 20. P-value 0.05 was considered statistically significant.

Results: Students who were consuming fruits more than 16 times per month had the chance of not having high serum TG levels by 87.5 % as compared to consumption of fruits less than 16 times per month. However, 21 (33.8 %) subjects with higher BMI and who consumed alcohol at least once per month were approximately 5 times more likely to have high serum TC levels as compared to those who had never taken alcohol.

Conclusion: Being male and consumption of fruits were negatively as-

sociated with high serum TC, TG, and LDL-C levels. However, consumption of alcohol and increasing age were positively associated with high serum TG, LDL-C & BGL.

P-14

Supplementary Steviol Glycosides Can Regulate Lipid Metabolism in Diabetes

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Background: A number of health-promoting properties of Stevia rebaudiana Bertoni and its glycosides, including the antihyperglycemic activity, have been found. The mechanisms of these effects have not been fully understood.

Objectives: Discussing the results of own in vitro and in vivo studies, especially the effect of steviol glycosides (stevioside, rebaudioside A) and steviol on lipid metabolism in diabetes.

Methods: In vitro studies: investigating the effects of steviol and steviol glycosides on adipogenesis, lipogenesis and glucose uptake in hypertrophied insulin-resistant 3T3-L1 adipocytes.

In vitro studies: investigating the effects of steviol glycosides on health condition of diabetic rats, particularly on glucose and lipid metabolism related parameters.

Results: It was found that the most active compound in modulating adipogenesis, lipogenesis and insulin resistance was steviol that significantly down-regulated the expression of adipogenic transcription factors (PPARγ, CEBPα, SREBP1) and lipogenic genes (FAS, aP2, LPL), which caused decreased lipid accumulation and triglyceride content in adipocytes. Treatment of insulin-resistant adipocytes with steviol and stevioside increased GLUT-4 transcript level and improved glucose uptake. Steviol also lowered resistin gene expression. It was found that steviol glycosides normalized hyperlipidemia that was associated with regulation of some gene ex-

pression in tissues (Fasn, Cebp-α, Glut4, Pparγ), as well as attenuated blood liver and kidney function indices, and reduced tissular damage in diabetic rats.

Conclusion: Steviol glycosides have appreciable lipid-regulating properties that could be used as supportive therapy in type-2-diabetes.

**The presented work is an integral part of the research project (National Science Centre, Poland, NCN 2017/27/B/NZ9/00677).*

P-15

Steviol Glycosides and Lipid Profile Regulation — is it the Type or the Dose that Really Matters?

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Background: Recently, the amount of research on the health-promoting effects of natural plant constituents has been increasing. Stevia Rebaudiana Bertoni and steviol glycosides (SG) have been recently studied for their anti-obesity, anti-hypertensive and anti-diabetic effects. However, it is not known exactly what mechanisms are responsible for the aforementioned effects, what the effective dose is, or which of the many glycosides is responsible for these properties of the plant.

Objectives: The aim of this study was to assess the effects of type and dose of SG on rats with induced type-2-diabetes, with a particular focus on lipid metabolism.

Methods: The experiment was carried out on 60 Wistar rats with type-2-diabetes (high-fat diet + streptozotocin injection) and 10 healthy rats (control). The intervention included dietary enrichment with SG, such as stevioside and rebaudioside A at 0.5 and 2.5 % of the diet. The results of the study were subjected to a range of statistical analyses, such as one-way analysis of variance, multivariate analysis of variance or post-hoc tests.

Results: It was found that supplementary SG normalized blood triacylglycerol and total cholesterol concentrations, as well as made a slight improvement in low-density lipoprotein levels in diabetic rats. Moreover, these effects for blood triacylglycerols concentrations were dose-dependent, regardless of the type of SG.

Conclusion: The results indicate that tested SG, have appreciable, dose-depended lipid metabolism regulating potential, however further studies are warranted to confirm these effects in patients with diabetes.

**The presented work is an integral part of the research project (National Science Centre, Poland, NCN 2017/27/B/NZ9/00677).*

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