
CEDA

# CEDA 2026

## 25 – 27 June 2026, Düsseldorf, Germany

**FINAL PROGRAMME**



Universitätsklinikum Düsseldorf, Unternehmenskommunikation

CEDA 2026 takes place at MNR Clinic at Heinrich Heine University Düsseldorf and University Hospital Düsseldorf.

## PROGRAMME AND ABSTRACTS OF CEDA 2026 IN DÜSSELDORF

From June 25 – 27, 2026, the Annual Congress of the Central European Diabetes Association (CEDA) takes place in Düsseldorf, Germany. Under the leadership of Professor Michael Roden, Scientific Executive Director and Spokesman for the Board of the German Diabetes Center (DDZ) as well as Director of the Department of Endocrinology and Diabetology at University Hospital Düsseldorf, the CEDA Board looks forward to three inspiring days featuring a high-level scientific programme.

The congress comprises 16 scientific sessions addressing topics of major clinical relevance, including among others cardio-diabetology, precision diabetology, diabetes-related comorbidities, and prevention through diet, exercise and lifestyle changes.

In addition, the programme includes two joint symposia organised in collaboration with the European Association for the Study of Diabetes (EASD) and the German Center for Diabetes Research (DZD), as well as five industry symposia hosted by renowned pharmaceutical companies. More than 50 submitted abstracts will be presented as posters, providing an excellent platform for scientific exchange. The organising team looks forward to engaging discussions, interdisciplinary dialogue and the strengthening of ties within the European diabetes community.

Deutsches Diabetes-Zentrum

CEDA 2026 is hosted by the German Diabetes Center (DDZ) in Düsseldorf. For more than 60 years, scientists here have been conducting research into diabetes with the aim of improving its prevention, early detection, diagnosis and treatment.

**11:00-12:00** **CEDA Board Meeting**

**12:00-13:00** **Arrival/Registration**

## HALL 1

### 13:00-14:00 Opening Ceremony

**Welcome**
*Michael Roden (Congress President, German Diabetes Center)*

**Greetings from Representatives**

### Jühling Prize Ceremony*

**Introduction and Laudatio**
*Michael Roden (Congress President, German Diabetes Center)*

**Jühling Prize and Jühling Lecture***
*Péter Kempler (Budapest, Hungary): A short journey to no man's land*

**Jühling Award 2025: Report***
*Georgia Xourafa, Rita Vesce (both Düsseldorf, Germany)*

**Jühling Award 2026***

**A Jühling Foundation event*

## HALL 2

### 14:00-15:00 Session 1: CEDA/EASD Symposium

**Chairs:** *Michael Roden (Düsseldorf, Germany), Anca Pantea-Stoian (Bucharest, Romania)*

**Francesco Giorgino** *(Bari, Italy)*
*Impact of obesity on development and progression of type 2 diabetes*

**Hindrik Mulder** *(Lund, Sweden)*
*Translating genetic signals into the pathophysiology of type 2 diabetes*

**Patrick Schrauwen** *(Düsseldorf, Germany)*
*Chronobiology and type 2 diabetes: does time matter?*

### Session 2: Diabetes Technology

**Chairs:** *Helmut Schatz (Bochum, Germany), Andrej Janez (Ljubljana, Slovenia)*

**Latife Bozkurt** *(Vienna, Austria)*
*Continuous glucose monitoring and hybrid closed-loop systems in pregnancy with type 1 diabetes*

**Julia Mader** *(Graz, Austria)*
*Beyond glucose: emerging biosensors for comprehensive metabolic monitoring*

**Tim Heise** *(Neuss, Germany)*
*New developments in insulin formulations*

**15:00-15:30 – COFFEE BREAK**

### 15:30-17:00 Session 3: Steatotic Liver Disease

**Chairs:** *Francesco Giorgino (Bari, Italy), Sabine Kahl (Düsseldorf, Germany)*

**Eckhard Lammert** *(Düsseldorf, Germany)*
*Novel pathophysiology: MASLD and angiokines*

**Michael Roden** *(Düsseldorf, Germany)*
*Detecting and phenotyping MASLD*

### Session 4: Type 1 Diabetes

**Chairs:** *Julia Mader (Graz, Austria), Adam Kretowski (Bialystok, Poland)*

**Clara Möser** *(Düsseldorf, Germany)*
*From physiology to algorithms: managing exercise in type 1 diabetes*

**Tomasz Klupa** *(Krakow, Poland)*
*Continuous glucose monitoring: does the quality of the device matter?*

**Maurizio Didac** *(Barcelona, Spain)*
*Multifactorial approach to MASH*

**Christos Mantzoros** *(Boston, USA)*
*Diabetes and MASLD: the central role of the diabetologist*

**Thomas Meissner** *(Düsseldorf, Germany)*
*Adherence in adolescents with type 1 diabetes: how to enhance engagement*

**Reinhard Holl** *(Ulm, Germany)*
*Heterogeneity of type 1 diabetes*

**17:00-18:00** **Industry Session 1: Novo Nordisk Pharma**

**18:00-19:00** **Industry Session 2: Lilly**

**19:30 – FACULTY DINNER**

FRIDAY, 26 JUNE 2026

## HALL 1

**08:00-09:00** **Industry Session 3: AstraZeneca**

### 09:00-10:30 Session 5: Cardio-Diabetes 1

**Chairs:** *Robert Wagner (Düsseldorf, Germany), Maria Grandoch (Düsseldorf, Germany)*

**Malte Kelm** *(Düsseldorf, Germany)*
*Myocardial infarction and type 2 diabetes*

**Eberhard Standl** *(Munich, Germany)*
*Heart failure in type 2 diabetes: diagnose early – treat preventively*

**Nikolaus Marx** *(Aachen, Germany)*
*CKM – cardio-kidney-metabolic syndrome – Update 2026*

**Manfredi Rizzo** *(Palermo, Italy)*
*Managing the cardiometabolic continuum: a consensus from Europe East and South*

## HALL 2

### Session 6: Young Investigator 1

**Chairs:** *Ilze Konrade (Riga, Latvia), Christian Herder (Düsseldorf, Germany)*

**Alba Sulaj** *(Heidelberg, Germany)*
*Targeting metabolism with fasting interventions to alleviate diabetic complications*

**Adrienn Menyhárt** *(Budapest, Hungary)*
*Weekly and seasonal blood glucose fluctuation based on a large database*

**Viviana Maggio** *(Palermo, Italy)*
*Cardiometabolic effects of dual GIP/GLP-1 RAs in people with obesity and diabetes*

**Djurdja Rafailovic** *(Belgrade, Serbia)*
*The role of glucose lowering vs weight reduction in prevention of CVD in type 2 diabetes*

**10:30-11:00 – COFFEE BREAK**

### 11:00-12:30 Session 7: Diabetic Neuropathy and Retinopathy

**Chairs:** *Péter Kempler (Budapest, Hungary), Alexander Strom (Düsseldorf, Germany)*

**Gidon Bönhof** *(Düsseldorf, Germany)*
*New approaches to screen and diagnose diabetic neuropathy*

**Zoltan Kender** *(Heidelberg, Germany)*
*Painful diabetic neuropathy: current management and future directions*

**Anna Körei** *(Budapest, Hungary)*
*Osteoporosis and diabetic neuropathy*

**Rainer Guthoff** *(Düsseldorf, Germany)*
*Diabetic retinopathy: predictor for diabetic neuropathy?*

### Session 8: Nutrition, Lifestyle and Prevention

**Chairs:** *Jan Skrha (Prague, Czechia), Tsvetalina Tankova (Sofia, Bulgaria)*

**Sabrina Schlesinger** *(Düsseldorf, Germany)*
*Plant-based diets for diabetes prevention and management*

**Georgia Xourafa** *(Düsseldorf, Germany)*
*The role of dietary fat in the prevention of diabetes*

**Ilze Konrade** *(Riga, Latvia)*
*Type 1 diabetes and celiac disease: clinical considerations*

**Dario Rahelic** *(Zagreb, Croatia)*
*Weight variability as a cardiovascular risk factor?*

**12:30-14:30 – LUNCH BREAK & POSTER SESSION**

## HALL 1

### 14:30-16:00 Session 9: Precision Diabetology

**Chairs:** *Erifili Hatziagelaki (Athens, Greece), Oliver Kuß (Düsseldorf, Germany)*

**Robert Wagner** *(Düsseldorf, Germany)*
*Precision medicine in prediabetes*

**Emma Ahlqvist** *(Lund, Sweden)*
*Early determinants and long-term outcomes of diabetes subtypes*

**Lukasz Szczerbinski** *(Bialystok, Poland; Boston, USA)*
*Pharmacogenetics of diabetes and obesity therapies*

**Julia Szendrödi** *(Heidelberg, Germany)*
*Sex-specific aspects of metabolic flexibility*

## HALL 2

### Session 10: Diabetic Kidney Disease

**Chairs:** *Jaroslawna Meister (Düsseldorf, Germany), Manfredi Rizzo (Palermo, Italy)*

**Nebojsa Lalic** *(Belgrade, Serbia)*
*Cardiorenal complications in type 1 diabetes: mechanisms, early markers and outcomes*

**Boris Mankovsky** *(Kyiv, Ukraine)*
*Association of diabetic kidney disease and cardiovascular diseases in type 2 diabetes*

**Karin Jandeleit-Dahm** *(Melbourne, Australia; Düsseldorf, Germany)*
*NOX5 as a novel biomarker in the CKM syndrome*

**Bogdan Timar** *(Timisoara, Romania)*
*The future of diabetic chronic kidney disease pharmacotherapy*

**16:00-16:30 – COFFEE BREAK**

### 16:30-17:00 Session 11: New Avenues in Diabetes Research

**Chairs:** *Nebojsa Lalic (Belgrade, Serbia)*

**Iuliana Popescu** *(Lexington, USA)*
*Endogenous pathways of beta-cell regeneration in diabetes*

**Nikolaos Papanas** *(Alexandroupolis, Greece)*
*Diabetic hand*

**Oana-Patricia Zaharia** *(Düsseldorf, Germany)*
*Early detection of complications in diabetes subtypes*

### Session 12: Cardio-Diabetes 2

**Chairs:** *Katarina Lalic (Belgrade, Serbia), Kálmán Bódis (Düsseldorf, Germany)*

**Maria Grandoch** *(Düsseldorf, Germany)*
*Bone marrow niche remodeling during prediabetes and diabetes progression*

**Norbert Gerdes** *(Düsseldorf, Germany)*
*Reversing cellular senescence to restore cardiovascular functionality in metabolic disease*

**Thomas Stulnig** *(Vienna, Austria)*
*Emerging lipid lowering drugs*

### 17:30-18:00 Evening Lecture

**Christos Mantzoros** *(Boston, USA)*
*Publishing with impact: lessons from the editor's desk*

**18:00-19:00 General Assembly**

**19:30 – CEDA DINNER FOR ALL PARTICIPANTS (INCLUDING POSTER PRIZES)**

## HALL 1

**08:00-09:00** **Industry Session 4: Madrigal Pharmaceuticals Deutschland**

**09:00-10:00** **Industry Session 5: Wörwag Pharma**

### 10:00-11:30 Session 13: DZD Symposium – Innovation in Diabetology

**Chairs:** *Michael Roden (Düsseldorf, Germany), Georgia Xourafa (Düsseldorf, Germany)*

**Meriem Ouni** *(Nuthetal, Germany)*
*Discovery of epigenetic classifiers and predictors of obesity and type 2 diabetes*

**Michele Solimena** *(Dresden, Germany)*
*Coxsackie virus and SARS-CoV-2-driven beta cell demise in type 1 diabetes*

**Andreas Birkenfeld** *(Tübingen, Germany)*
*Pathways to prevention of type 2 diabetes*

**Panel Discussion**

## HALL 2

### Session 14: Psychosocial Aspects and Health Outcomes Research

**Chairs:** *Tomasz Klupa (Krakow, Poland), Tatjana Milenkovic (Skopje, North Macedonia)*

**Katarzyna Cyranka** *(Krakow, Poland)*
*Emotional and cognitive factors shaping health outcomes in chronic disease*

**Andrea Icks** *(Düsseldorf, Germany)*
*Psychosocial outcomes in diabetes subtypes: results from the German Diabetes Study*

**Katarina Lalic** *(Belgrade, Serbia)*
*A holistic approach to diabetes care: linking psychosocial and clinical factors*

**Christian Herder** *(Düsseldorf, Germany)*
*Inflammation and depression in diabetes*

**11:30-12:00 – COFFEE BREAK**

### 12:00-13:30 Session 15: Obesity

**Chairs:** *José Silva-Nunes (Lisbon, Portugal), Emmanuel Van Obberghen (Nice, France)*

**Alexandra Chadt** *(Düsseldorf, Germany)*
*Obesity in motion: preclinical insights into genes, signals and lifestyle*

**Mustafa Cesur** *(Ankara, Turkey)*
*A Turkish nationwide study: a real-world comparison of semaglutide and tirzepatide*

**Gyula Petrányi** *(Limassol, Cyprus)*
*Polycystic ovary syndrome*

**Nanette Schloot** *(Bad Homburg, Germany)*
*New data on retatrutide for treatment of obesity*

### Session 16: Young Investigator 2

**Chairs:** *Nikolaos Papanas (Alexandroupolis, Greece), Kalliopi Pafili (Düsseldorf, Germany)*

**Theresa Körbel** *(Vienna, Austria)*
*Once-weekly semaglutide in type 1 diabetes managed with automated insulin delivery*

**Roxana Adriana Stoica** *(Bucharest, Romania)*
*Modulation of inflammatory pathways by SGLT2 inhibitors*

**Martin Schön** *(Düsseldorf, Germany)*
*Unraveling diabetes heterogeneity: from mechanisms to clinical application*

**Michał Kania** *(Krakow, Poland)*
*Oral microbiota in people with diabetes – does it matter?*

**Stella Papachristou** *(London, UK; Alexandroupolis, Greece)*
*AGEs and diabetic neuropathy*

**13:30-14:00 – CLOSING CEREMONY & FAREWELL**

# Abstracts

**The abstracts will be presented as posters during the CEDA 2026.**

## A01

### Mitochondrial DNA copy number and its association with prior ischemic myocardial injury in patients with coronary artery disease and type 2 diabetes

Dzhun, Yana; D. F. Chebotarev Institute Of Gerontology Of The National Academy Of The Medical Sciences Of Ukraine; Kyiv

Co-Authors: Saienko, Yanina; Rebrova, Yanina; Varbanets, Daria; Mankovsky, Borys

**Aim:** To assess the association between prior myocardial infarction (MI) and mitochondrial DNA (mtDNA) copy number in patients with coronary artery disease (CAD) and type 2 diabetes (T2D), and the potential modifying role of the ACE I/D polymorphism.

**Methods:** Sixty-seven patients with CAD and T2D were stratified by MI history (MI+ vs MI−). Relative telomere length (T/S ratio) and mtDNA copy number were quantified in peripheral blood leukocytes by real-time PCR. ACE I/D polymorphism was analysed using an additive model. Between-group differences were assessed with the Mann-Whitney U test; multivariable linear regression adjusted for age, diabetes duration, $HbA_{1c}$, and eGFR.

**Results:** Patients with prior MI were older, had longer diabetes duration, and lower eGFR (all $p < 0.05$). $HbA_{1c}$ levels, T/S ratio, and ACE genotype distribution did not differ between groups ($p > 0.05$). MtDNA copy number showed a trend toward lower values in the MI+ group compared with MI− (1.030 [0.826 – 1.322] vs 1.312 [0.967 – 1.614]; $p = 0.053$). In multivariable analysis, prior MI was independently associated with reduced mtDNA copy number ($\beta = -0.323$; $p = 0.025$). Higher $HbA_{1c}$ was also independently associated with lower mtDNA levels ($\beta = -0.078$; $p = 0.010$). ACE I/D polymorphism was not associated with mtDNA copy number ($\beta = 0.025$; $p = 0.798$) and showed no interaction with MI status.

**Conclusions:** Although unadjusted analysis showed only a trend toward lower mtDNA in MI+ patients, multivariable regression confirmed an independent association between prior myocardial infarction and reduced mtDNA levels. ACE I/D polymorphism showed no association and did not modify this relationship, supporting a link between prior ischemic injury and mitochondrial dysfunction in T2D.

## A02

### Treatment with a mitochondrial complex I ROS modulator shows dose-dependent improvements of albuminuria and glomerular morphology in db/db mice

Aboolian, Ara; German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf; Germany

Co-Authors: Urner, Sofia; Jeruschke, Kay; Strauch, Martin Tobias; Roden, Michael; Boor, Peter; Jandeleit-Dahm, Karin; Meister, Jaroslawna

**Aims:** Excessive formation of reactive oxygen species (ROS) is one of the pathomechanisms in diabetic kidney disease (DKD) and contributes to renal injury and disease progression. This injury can manifest clinically as albuminuria and is accompanied by morphological alterations in the renal cortex. The aim of this study was to investigate the effects of a mitochondrial complex I ROS modulator (CIM) on albuminuria and glomerular and tubular morphology.

**Methods:** The effects of CIM were evaluated in a 10-week intervention study using db/db mice as a model of type 2 diabetes. Mice received chow containing 0, 20, or 60 mg/kg CIM, while db/+ mice served as non-diabetic controls. Kidney function was evaluated by plasma cystatin C levels, and albuminuria was assessed by determining the urinary-albumin-to-creatinine ratio (UACR). Period acid-Schiff-stained kidney sections were subjected to next-generation morphometric analyses to identify glomerular and tubular structural alterations. Glomerular basement membrane (GBM) thickness was assessed using transmission electron microscopy images of glomeruli.

**Results:** Vehicle-treated db/db mice showed lower plasma cystatin C levels compared to db/+ controls, which remained unaffected by CIM treatment. Db/db mice exhibited elevated UACR, and treatment with 20 mg/kg CIM, but not 60 mg/kg CIM, reduced UACR by 34 %. Morphometric analyses revealed increased glomerular tuft size and reduced tuft elongation in db/db mice, whereas glomerular density remained unchanged. Tubular size and diameter were increased in db/db mice without changes in tubular density. Treatment with 20 mg/kg CIM reduced glomerular tuft size. GBM thickness increased in db/db mice and was reduced by both CIM dosages.

**Conclusion:** CIM attenuated albuminuria and structural hallmarks of DKD in a dose-dependent manner, highlighting the importance of optimal dosing for therapeutic efficacy.

## A03

### When type 2 diabetes is not type 2: delayed diagnosis of latent autoimmune diabetes following empirical sulfonylurea therapy

Khvedelidze, Khatia; Caucasus Medical Center; Tbilisi, Georgia

Co-Authors: Nutsubidze, Teona

**Aims/Hypothesis:** Correct classification of diabetes is essential for optimal treatment. However, young adults presenting with hyperglycaemia are frequently classified as having type 2 diabetes and treated empirically with oral antidiabetic agents. This approach may delay recognition of autoimmune diabetes and expose patients to ineffective therapies. We present a case of latent autoimmune diabetes in adults initially misdiagnosed as type 2 diabetes and treated with sulfonylureas, illustrating the consequences of delayed diagnosis.

**Methods:** We describe the clinical course of a young adult male in Georgia initially treated as having type 2 diabetes. Clinical characteristics, treatment history, and laboratory findings including pancreatic autoantibodies and C-peptide levels were evaluated to reassess the diabetes classification.

**Results:** A 25-year-old man was referred for persistent hyperglycaemia despite oral therapy. Diabetes had been diagnosed at age 20 during routine laboratory testing. At diagnosis, the patient had a normal body mass index and lacked features of metabolic syndrome. Nevertheless, he was classified as having type 2 diabetes and treated with metformin. Due

to inadequate glycaemic control, sulfonylurea therapy was subsequently added. Over the following years, glycaemic control progressively worsened despite adherence to therapy. Considering the young age at onset, lean phenotype, and rapid failure of oral therapy, further evaluation for atypical diabetes was performed. Laboratory testing revealed positive pancreatic autoantibodies and low C-peptide levels, confirming latent autoimmune diabetes in adults. Oral therapy was discontinued and insulin therapy was initiated, resulting in improved glycaemic control.

**Conclusions:** This case highlights the risk of misclassification of autoimmune diabetes as type 2 diabetes in young adults. Early antibody testing in atypical presentations may prevent delayed diagnosis and avoid inappropriate use of sulfonylureas, enabling timely insulin therapy and improved metabolic outcomes.

## A04

### Changes in information needs of people with diabetes over the course of the disease – insights from the German Diabetes Study

Wasser, Anne-Catherine; German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf; Germany

Co-Authors: Borgmann, Sandra Olivia; Gontscharuk, Veronika; Chernyak, Nadja; Mendez, Dania; Wagner, Robert; Schlesinger, Sabrina; Roden, Michael; Icks, Andrea

**Aims/Hypothesis:** Information needs of individuals with diabetes may change over the disease course and differ by diabetes type and participant characteristics. This study examined (I) changes in diabetes-related information needs from the first year after diagnosis to five-year follow-up; (II) changes in the top three topics with highest information need; and (III) differences by diabetes type and participant characteristics.

**Methods:** This prospective longitudinal study included 261 respondents with newly diagnosed diabetes mellitus participating in the German Diabetes Study (GDS). Participants completed standardised questionnaires at baseline and follow-up (2014 – 2025, Düsseldorf, Germany; 63 % men, mean age 47.5, 68 % type 2 diabetes). Information needs were assessed across 11 predefined topics, and participants selected up to three topics with the highest current need. Changes over time were analysed descriptively, stratified by diabetes type and participant characteristics.

**Results:** Information needs declined across all topics over five years but remained moderate to high. At follow-up, at least half of the participants still wanted more information on diabetes research (62 % vs. 83 % at baseline), lifestyle adjustment, health promotion and prevention (51 % vs. 78 %), and treatment/therapy (50 % vs. 74 %), which all ranked among the top three topics at both times. Information needs on mental strain increased in relevance, rising from 8 % to 20 % among top three topics overall, and from 14 % to 32 % in type 1 diabetes. Social and legal aspects also increased in type 1 diabetes (9 % to 19 %) but remained low in type 2 diabetes (~5 %). Information needs on disease course increased in type 2 diabetes (25 % vs. 19 %), while remaining stable in type 1 diabetes (11 %).

**Conclusions:** Information needs remain substantial five years after diagnosis and vary over time and by patient characteristics, underscoring the need for tailored, continuous patient information and education to support patient empowerment, informed decision-making, and long-term outcomes.

## A05

### A 3 month course of multispecies probiotic supplementation enhances insulin sensitivity, lipid profile, inflammation and symptoms in young adults with early metabolic risk

Elrayess, Mohamed; Qatar University; Doha, Qatar

Co-Authors: Yassin, Esraa; Elashi, Asma; Almuraikhy, Shamma

**Aims/Hypothesis:** We investigated whether a high-dose, multispecies Lactobacillus/Bifidobacterium probiotic could improve insulin sensitivity, lipid profile, systemic inflammation and symptom burden in apparently healthy young adults with early features of metabolic syndrome, and whether these effects were maintained after discontinuation.

**Methods:** In a double-blind, randomised, placebo-controlled study, 71 adults aged 18 – 40 years were assigned in a 2:1 ratio to receive a daily capsule containing Lactobacillus/Bifidobacterium strains plus fructooligosaccharides or a matching placebo for 3 months. Clinical and biochemical assessments at baseline and 3 months included HOMA-IR, fasting lipid profile, renal and hepatic function tests, inflammatory cytokines, and standardised gastrointestinal and global physical symptom scores. Participants then completed a further 3-month washout without study product and were reassessed at 6 months to evaluate durability of probiotic-related changes.

**Results:** Relative to placebo, the probiotic group showed a mean reduction in HOMA-IR of 0.8 units and a 27 percent increase in HDL-cholesterol, consistent with improved insulin sensitivity and a more favourable lipid profile. Probiotic supplementation shifted the cytokine milieu towards a less inflammatory state, with significant decreases in IL-1β, TNF-α, IL-8, MCP-1 and IL-6, alongside higher concentrations of the anti-inflammatory mediators IL-10 and IL-1RA. These biochemical benefits were paralleled by substantial reductions in gastrointestinal complaints and overall physical symptom scores. Improvements in insulin sensitivity, HDL-cholesterol and inflammatory cytokine profiles remained evident at 6 months despite the 3-month washout period.

**Conclusions:** A 3-month course of multispecies probiotic supplementation induced clinically meaningful, weight-independent improvements in insulin sensitivity, HDL-cholesterol, systemic inflammatory cytokines and gastrointestinal and physical symptom burden in young adults at elevated metabolic risk. The persistence of these effects after washout supports targeted probiotic use as a practical adjunct to strengthen metabolic resilience and reduce early dysmetabolic risk before overt metabolic syndrome develops.

**Acknowledgement:** QU Health is gratefully acknowledged for sponsoring this participation.

## A06

### Orthostatic hypertension as an unusual manifestation of cardiovascular autonomic neuropathy in long-standing type 2 diabetes: a case report

Balogh, Dóra Marietta; Semmelweis University; Budapest, Hungary

Co-Authors: Menyhárt, Adrienn; Körei, Anna Erzsébet; Vági, Orsolya Erzsébet; Zsigrai, Sára; Kempler, Péter

**Aims/Hypothesis:** Cardiovascular autonomic neuropathy (CAN) is a severe and frequently underdiagnosed form of diabetic neuropathy. Resting tachycardia, hypertension and orthostatic hypotension are well-recognised manifestations. We present a case of orthostatic hypertension highlighting the clinical relevance and diagnostic challenges of CAN.

**Methods:** The 82-year-old female patient with type 2 diabetes mellitus was admitted to our department due to recurrent falls and progressive functional decline. Clinical assessment included laboratory testing, chest X-ray, echocardiography, 24-hour ambulatory blood pressure monitoring (ABPM), Holter monitoring and comprehensive neuropathy assessment including evaluation for CAN.

**Results:** The patient had obesity, osteoporosis, atrial fibrillation, long-standing hypertension and type 2 diabetes mellitus. Her medical history included subtotal bilateral strumectomy due to nodular goiter-related hyperthyroidism requiring hormone replacement therapy, long-standing diabetic neuropathy (18 years) and chronic kidney disease. $HbA_{1c}$ values ranged between 36 – 45 mmol/mol (5.5 – 6.5 %). She had previously been hospitalised twice due to heart failure. During the preceding two years, recurrent collaptiform falls occurred without loss of consciousness. Brain CT excluded acute cerebrovascular events. Twenty-four-hour ABPM demonstrated nocturnal hypertension with a reverse dipping pattern. Holter monitoring ruled out clinically significant arrhythmias. Echocardiography revealed dilated cardiac chambers, an atherosclerotic aortic valve and mild mitral regurgitation with preserved left ventricular ejection fraction. Neuropathy assessment confirmed severe sensory hypoaesthesia, definite parasympathetic autonomic neuropathy and orthostatic hypertension as a rare manifestation of CAN, with an increase of systolic blood pressure by 28 mmHg after standing up. Doxazosin was added to the antihypertensive treatment and alpha-lipoic acid infusions were administered for ten days.

**Conclusions:** Cardiovascular autonomic neuropathy including relevant orthostatic hypertension, as well as severe sensory hypoaesthesia were considered as the most likely causes behind recurrent falls. This patient's case highlights the importance of screening for diabetic neuropathy including CAN in patients with long-standing diabetes.

## A07

### Non-invasive monitoring of hepatic glycogen dynamics using sensitivity-corrected $^{13}$C-MRS

Jonuscheit, Marc; German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf; Germany

Co-Authors: Mevenkamp, Julian; Wierichs, Stefan; Korzekwa, Benedict; Roden, Michael; Schrauwen-Hinderling, Vera B.

**Aims/Hypothesis:** In type 2 diabetes (T2D), glycogen metabolism is impaired with lower postprandial glycogen synthesis and blunted glycogen dynamics over 24 hours. Accurate, dynamic quantification of hepatic glycogen is crucial for further investigation and evaluating interventions to normalise glycogen dynamics. Carbon-13 magnetic resonance spectroscopy ($^{13}$C-MRS) enables dynamic non-invasive assessment but remains technically challenging. Absolute quantification requires correction for the distance between coil and liver. In obese individuals, large surface coils are often required, but their extended sensitive volume introduces bias, as non-liver tissue contributes to the signal. This study compared the classical distance-based approach with a method incorporating sensitivity mapping and liver segmentation. Additionally, reproducibility and feasibility of repeated $^{13}$C-MRS for monitoring intra-day glycogen dynamics were assessed.

**Methods:** Six volunteers (30.7 ± 7.1 years, BMI 26.8 ± 3.1 kg/m²) were examined after an overnight fast at 3T using a dual-tuned $^{1}$H/$^{13}$C surface coil. Glycogen quantification was performed using (1) classical distance correction and (2) a sensitivity-corrected approach with volunteer-specific liver masks derived from anatomical imaging. For dynamic assessment, six volunteers (25.3 ± 2.1 years, BMI 26.8 ± 2.5 kg/m²) were measured at 08:00 h (fasted baseline) and every 2 hours following a standardised 680 kcal meal (five scans in total). Additionally, reproducibility was assessed by two consecutive scans.

**Results:** Using distance correction alone, mean hepatic glycogen concentration was underestimated (93 ± 13 mM), falling below the expected physiological range. Incorporating sensitivity maps and liver segmentation yielded values consistent with literature using smaller coils (168 ± 32 mM). In the dynamic study, glycogen decreased with prolonged fasting. Mean signal intensity decreased to 77.5 ± 4.4 % of baseline after 8 hours. Reproducibility showed a CV of 7.0 %.

**Conclusions:** Accounting for the spatial sensitivity profile of large surface coils substantially improves the accuracy of hepatic glycogen quantification by $^{13}$C-MRS. Repeated measurements further demonstrate the method's potential to monitor glycogen dynamics, enabling future studies on hepatic glycogen metabolism in T2D.

## A08

### TRIM21 is a novel interactor of PKC epsilon and associates with hepatic insulin resistance

Heilmann, Geronimo; German Diabetes Center, Leibniz Center for Diabetes Research at Heinrich Heine University Düsseldorf; Germany

Co-Authors: Piribauer, Marlene; Lipaeva, Polina; Lehr, Stefan; Hartwig, Sonja; Mastrototaro, Lucia; Dewidar, Bedair; Gancheva, Sofiya; Kahl, Sabine; Al-Hasani, Hadi; Schrauwen, Patrick; Belgardt, Bengt-Frederik; Trenkamp, Sandra; Roden, Michael

**Aims/Hypothesis:** Interactors of protein kinase C epsilon (PKCε) may mediate insulin resistance, a central feature of metabolic dysfunction-associated steatotic liver disease (MASLD). We identified novel PKCε interactors in hepatocytes and examined whether their hepatic abundance associates with insulin resistance in humans.

**Methods:** In a hepatic cellular model of insulin resistance, PKCε interactors were identified using mass spectrometry-based interactomics. Hepatic protein abundances of these interactors were quantified by unbiased proteomics in lean people (n = 4), people with class 3 obesity without MASLD (n = 8), and people with class 3 obesity and histology-proven MASLD (n = 8). Metabolic parameters were assessed using hyperinsulinaemic-euglycaemic clamp and routine laboratory variables. Associations between interactors and metabolic parameters were calculated using linear regression before and after BMI adjustment.

**Results:** Three novel PKCε interactors were identified: E3 ubiquitin-protein ligase TRIM21 (TRIM21) as well as propionyl-CoA carboxylase alpha-chain (PCCA) and testis-expressed protein (TEX2). In human liver, the abundance of TRIM21 and PCCA did not differ between the groups, whereas TEX2 was reduced in people with obesity ($p = 0.020$) but not in those with obesity and MASLD compared with lean people. Across the whole cohort, TRIM21 showed a negative association with the M-value ($r = -0.825$, $p = 0.003$) and DEGP ($r = -0.556$, $p = 0.031$), whereas it was positively related to Adipo-IR ($r = 0.730$, $p = 0.001$) and fasting glucose ($r = 0.637$, $p = 0.007$), both before and after BMI adjustment. PCCA was negatively associated with fasting insulin ($r = -0.501$, $p = 0.040$), whereas TEX2 was positively associated with circulating high-density lipoprotein ($r = 0.522$, $p = 0.032$), both associations did not remain after BMI adjustment.

**Conclusions:** The identified PKCε interactor TRIM21 associated with insulin resistance and metabolic variables in humans, independent of BMI. In line with previous reports that suggest TRIM21 as mediator of metabolic dysfunction-associated steatohepatitis, these findings identify TRIM21 as a therapeutic candidate already in MASLD.

## A09

### An animal-based, low-plant-food dietary pattern is associated with higher fasting C-peptide independent of whole-body insulin resistance in recent-onset type 2 diabetes

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**Aims and Hypothesis:** Hyperinsulinemia is commonly interpreted as a compensatory response to insulin resistance (IR). However, evidence suggests that primary hypersecretion may precede and potentially contribute to the development of IR. The potential role of diet in this context remains unclear. We defined fasting C-peptide levels independent of whole-body IR as discordant hyperinsulinemia (DH) and investigated whether dietary patterns are associated with DH.

**Methods:** Data from 266 participants with recent-onset type 2 diabetes (T2D) (<12 months after diagnosis) in the German Diabetes Study (GDS) who completed food-frequency questionnaires were analysed. Whole-body insulin sensitivity (IS) was assessed using euglycaemic-hyperinsulinaemic clamp. DH was defined as residuals of fasting C-peptide after regression on IS. Partial least squares (PLS) regression was applied to identify a dietary pattern related to DH. Associations between the derived dietary pattern score and DH were examined using linear regression models adjusted for sex, age, socioeconomic status, physical activity, smoking status, alcohol intake and BMI. Estimates represent the change in DH per SD increase in the dietary pattern score.

**Results:** Mean IS was 6.0 mg/kg/min (SD 2.5 mg/kg/min) and mean fasting C-peptide levels were 3.3 ng/ml (SD 1.5 ng/ml). The derived dietary pattern included higher intake of processed meat, sweets and potatoes and lower intake of vegetables, legumes, nuts/seeds, cereals, tea and plant fats. Higher adherence to this pattern was associated with higher DH both before ($\beta = 0.24$, 95 % CI 0.10; 0.38; $p < 0.001$) and after additional adjustment for BMI ($\beta = 0.19$, 95 % CI 0.06; 0.32; $p < 0.05$).

**Conclusions:** In individuals with recent-onset T2D, greater adherence to a diet high in processed meat, sweets and potatoes and low in plant-based, fiber-rich food groups was associated with higher DH. These findings suggest that dietary habits may relate to variation in fasting C-peptide independent of whole-body IR in early T2D.

## A10

### Long term exposure to air pollution and diabetes-related comorbidities in adults with recent-onset type 1 and type 2 diabetes

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**Aims/Hypothesis:** Air pollutants such as inhalable particulate matter (PM2.5, PM10) and nitrogen dioxide ($NO_2$) have been linked to increased risk of diabetes-related comorbidities. However, whether such exposures contribute to the early development of comorbidities remains unknown. This study aims to determine whether long-term exposure to PM2.5, PM10 and $NO_2$ is associated with diabetes-related comorbidities in individuals with recent-onset type 1 (T1D) and type 2 diabetes (T2D) and diabetes subtypes.

**Methods:** Data are based on 985 adults from the German Diabetes Study (GDS; 358 with T1D, 627 with T2D, time since diagnosis <1 year). Diabetes-related risk factors and comorbidities included 10-year cardiovascular disease (CVD) risk (SCORE2-Diabetes), urinary albumin as an indicator of impaired kidney function and clinical diagnosis of distal sensorimotor polyneuropathy (DSPN). Air pollution exposures were derived from daily data provided by the German Federal Environment Agency. Long-term exposures to PM2.5, PM10 and $NO_2$ were calculated as average of exposures during the 5 years preceding study enrolment.

Associations between each exposure-outcome pair were estimated using regression adjusted for age, sex, smoking, socioeconomic status, season and physical activity.

**Results:** In participants with T2D, exposure to higher PM2.5 per interquartile range increase was associated with higher CVD risk (exp(β) = 1.12 (95 % CI 1.03 – 1.22)), higher urinary albumin (exp(β) = 1.78 (1.49 – 2.13)) and higher odds of DSPN (OR = 1.46 (1.01 – 2.10)). Similar associations were observed for PM10, and $NO_2$. Among individuals with T1D, higher exposures to PM2.5 and PM10 were also associated with higher urinary albumin (exp(β) = 1.52 (1.20 – 1.93) and 1.32 (1.05 – 1.65), respectively). Exploratory analyses suggested differences in associations across diabetes subtypes.

**Conclusion:** Long-term exposure to air pollution was consistently associated with an increased burden of diabetes-related risk factors and comorbidities already in recent-onset T2D, while associations were less consistent in T1D.

## A11

### Practical use of artificial iIntelligence in the management of patients with type 1 diabetes mellitus

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**Background and Objectives:** A cornerstone of managing patients with type 1 diabetes mellitus (T1DM) is accurate carbohydrate estimation and appropriate adjustment of insulin dosing and timing, both of which often present significant challenges. Artificial intelligence (AI) may estimate carbohydrate content in meals and, based on clinician-recommended carbohydrate-to-insulin ratios, calculate the required insulin dose for a given meal.

**Methods:** The Hungarian-developed Vivvy application – among its many functions – estimates carbohydrate content from food images and calculates the recommended insulin dose based on a predefined carbohydrate-to-insulin ratio. Fifty sensor-using patients with T1DM tested the application. Its effectiveness was assessed through changes in continuous glucose monitoring (CGM) metrics and validated questionnaires (Diabetes Treatment Satisfaction Questionnaire [DTSQ], Differential Emotions Scale [DES], and the abbreviated Summary of Diabetes Self-Care Activities [SDSCA]).

**Results:** Significant improvements were observed in CGM-derived metrics: time in range (TIR 3.9 – 10 mmol/l) increased from 68 % to 74 %, time in tight range (TITR 3.9 – 7.8 mmol/l) from 45 % to 51 %, and glucose management indicator (GMI) decreased from 6.9 % to 6.7 %. Time above range (TAR > 13.9 mmol/l) decreased from 6.9 % to 3.6 % ($p < 0.001$ for all), while TAR 10 – 13.9 mmol/l decreased from 23 % to 19 % ($p = 0.01$). Patient satisfaction with treatment, autonomy, and self-management abilities also improved significantly ($p < 0.05$). The overall usefulness of the application was rated 4.2 on a 5-point scale.

**Conclusions:** By applying artificial intelligence, the Vivvy app can be considered an intelligent healthcare assistant that provides immediate support to patients and translates clinician-defined therapeutic goals into everyday practice. Based on patient feedback, the application is useful, and its effectiveness is objectively supported by improvements in CGM metrics.

## A12

### Cognitive impairment in normoglycaemic patients: the potential role of cerebral insulin resistance

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**Aims:** Central insulin resistance represents an important link between metabolic dysfunction and cognitive impairment. Impaired brain insulin signaling may contribute to reduced neuronal function and progressive decline in memory and cognition. Nevertheless, its precise role in the development and progression of neurodegenerative disorders remains insufficiently clarified.

**Methods:** In this study, we included 120 normoglycaemic, non-obese participants divided into three groups: 40 patients with Alzheimer's disease (AD; group A, BMI 23.56 ± 0.86 kg/m², mean age 70.24 ± 8.63 years), 40 patients with mild cognitive impairment (MCI; group B, BMI 24.45 ± 0.56 kg/m², mean age 68.47 ± 8.25 years), and 40 age- and BMI-matched healthy controls (group C, BMI 24.41 ± 0.69 kg/m², mean age 68.53 ± 7.85 years). Insulin sensitivity (IS) was assessed using the euglycaemic hyperinsulinaemic clamp technique, while insulin secretory capacity (ISC) was evaluated by first-phase insulin response. Plasma and cerebrospinal fluid (CSF) insulin concentrations were measured by radioimmunoassay.

**Results:** IS was significantly lower in the AD group compared with both the MCI and control groups (6.51 ± 0.60 vs 7.81 ± 0.41 vs 8.26 ± 0.37 mg/min/kg, $p < 0.01$). Similarly, ISC was significantly reduced in patients with AD (67.81 ± 3.42 vs 111.42 ± 7.25 vs 146.32 ± 8.75 mU/l, $p < 0.01$). In contrast, basal plasma insulin concentrations were significantly higher in the AD group (15.48 ± 2.02 vs 13.65 ± 1.07 vs 7.49 ± 1.14 mU/l, $p < 0.01$). CSF insulin levels were lower in the AD group, although this difference did not reach statistical significance. However, linear regression analysis demonstrated a significant association between IS and CSF insulin concentrations ($R^2 = 0.795$, $p < 0.001$).

**Conclusions:** These findings support the concept of cerebral insulin resistance in AD and suggest that altered insulin homeostasis may contribute to its pathogenesis, at least in part through reduced central insulin availability.

## A13

### Renal intra-parenchymal fat is linked to renal function decline in people with diabetes

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**Introduction:** People with diabetes have an increased risk to develop chronic

kidney disease (CKD). How the ectopic accumulation of lipids in the renal compartments is related to nephropathy is not yet clear. In this study, we investigated the relationship between renal intra-parenchymal fat (RIPF), based on the analysis of fat- and water-reconstructed images, and kidney function as assessed by glomerular filtration rate (eGFR).

**Methods:** Participants (n = 221) from the German Diabetes Study (GDS), including people with type 1 (n = 66), type 2 diabetes (n = 55) and participants with normoglycaemia (n = 26) underwent abdominal MRI examination (3T Achieva X-series, Philips Healthcare, The Netherlands). To this end, dual-echo (repetition time (TR)/minimum echo time (TE) = 3.76 ms, TE1/2 = 1.32/2.40 ms, flip angle = 10 °, reconstructed voxel dimension = 0.78 × 0.78 × 2 $mm^2$) and multi-echo Dixon sequences were acquired (repetition time (TR/TE = 5.78.00/1.00 ms, TE interval = 0.70 ms, reconstructed voxel dimension = 1.95 × 1.95 × 3 $mm^3$). Quantification of RIPF content was performed by automatic segmentation of kidney structures, following by clustering of fat fraction signal to exclude the surrounding adipose tissue. The association of RIPF with renal function was tested by multiple linear regression (n = 145), adjusting for sex, age, BMI, mean arterial pressure (MAP), subcutaneous (SAT) and visceral adipose tissue (VAT). Further, the association of the RIPF with the eGFR slope over follow-up (7.0 ± 4.0 years) was tested (n = 121).

**Results:** An increase of 1 % in RIPF was inversely associated with a 3.95 ± 1.21 ml/min/1.73 $m^2$ lower eGFR, independently of sex, age, BMI, MAP, VAT and SAT. Further, RIPF content was associated with a faster decline of eGFR (β = -0.57, *p = 0.001) over a mean follow-up duration of 7.5 years, independent from all the included confounders.

**Conclusion:** Renal intra-parenchymal fat content was found to be negatively associated with eGFR and with eGFR decline over time. Our results highlight the potential of RIPF as a predictive marker of CKD in people with diabetes.

## A14

### Health economic evaluation of the risk-stratified Prediabetes Lifestyle Intervention Study (PLIS) for prediabetes remission in Germany

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**Background:** Lifestyle interventions can promote remission of prediabetes, but their cost-effectiveness is not well established. This study evaluated both within-trial and lifetime cost-effectiveness of intensive and standard lifestyle interventions in individuals with prediabetes, stratified by risk level.

**Methods:** A health economic evaluation was conducted alongside the 12-month, multicentre PLIS study (n = 908). High-risk participants were randomised to either intensive (HR-INT) or conventional (HR-CONV) intervention, while low-risk participants received either conventional intervention (LR-CONV) or a control (LR-CTRL). Risk stratification was based on insulin secretion, insulin sensitivity, and liver fat content. Within-trial analyses estimated incremental costs per additional remission to normoglycaemia and per quality-adjusted life year (QALY). Long-term cost-effectiveness was assessed using a four-state Markov model.

**Findings:** At 12 months, HR-INT and LR-CONV increased remission rates compared with their respective comparators. The incremental cost per additional remission was € 7,081.48 (95 % CI: dominated to 47,276.62) for HR-INT and € 4,278.36 (95 % CI: 1,312.21 to 11,793.41) for LR-CONV from the statutory health insurance perspective. A willingness-to-pay threshold of € 22,000 for HR-INT and € 7,500 for LR-CONV corresponded to a 90 % probability of cost-effectiveness. Neither intervention was cost-effective in terms of QALYs within the trial period. However, lifetime modelling suggested that both HR-INT and LR-CONV could be cost-saving compared with HR-CONV and LR-CTRL, respectively, among individuals at increased risk of type 2 diabetes. Probabilistic sensitivity analyses largely indicated dominance.

**Interpretation:** Short-term cost-utility analyses did not demonstrate cost-effectiveness for any intervention. However, long-term modelling suggests potential cost savings. Targeting individuals with prediabetes using lifestyle interventions to achieve remission may offer good value for money over the long term.

## A15

### Correlation between diabetic peripheral neuropathy and renal function in patients with long-standing type 2 diabetes mellitus

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**Background and Aims:** Diabetic peripheral neuropathy and diabetic nephropathy are common microvascular complications of type 2 diabetes mellitus (T2DM). Both share similar pathophysiological mechanisms; however, their clinical correlation remains variable across populations. This study aimed to determine the frequency and association between diabetic peripheral neuropathy and reduced glomerular filtration rate (GFR), and to evaluate the correlation between neuropathy severity and renal function in patients with long-standing T2DM.

**Materials and Methods:** This descriptive cross-sectional study was conducted at a tertiary care hospital over six months. A total of 140 patients with T2DM of ≥ 10 years duration were enrolled using consecutive sampling. Neuropathy was assessed using vibration perception threshold (VPT) measured by biothesiometer. A VPT > 15 volts in both feet was considered diagnostic of neuropathy. Estimated GFR (eGFR) was calculated using the MDRD equation, and reduced renal function was defined as eGFR < 60 ml/min/1.73 $m^2$. Statistical analysis was performed using SPSS version 23. Chi-square test was used to assess association, and Spearman correlation was

used to evaluate the relationship between mean VPT and eGFR.

**Results:** Among 140 participants, 75 (53.6 %) had diabetic peripheral neuropathy, and 88 (62.9 %) had impaired GFR. The association between neuropathy and reduced GFR was borderline but not statistically significant ($\chi^2 = 3.53$, $p = 0.060$). However, a statistically significant weak negative correlation was observed between mean VPT and eGFR ($r = -0.211$, $p = 0.0125$).

**Conclusion:** Diabetic peripheral neuropathy and renal dysfunction are highly prevalent among patients with long-standing T2DM. Although categorical association was not statistically significant, neuropathy severity demonstrated a significant inverse correlation with renal function. These findings suggest parallel progression of diabetic microvascular complications and support the use of biothesiometry in routine clinical screening.

## A16

### Telomere length as a marker of cellular aging in type 2 diabetes mellitus patients with and without chronic kidney disease

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**Introduction:** Chronic kidney disease (CKD) in type 2 diabetes mellitus (T2DM) is a major contributor to morbidity and mortality, particularly due to cardiovascular complications. Beyond traditional risk factors, CKD is increasingly recognised as a state of accelerated biological aging. Telomere shortening reflects cellular senescence and may serve as an early biomarker of disease progression and systemic damage.

**Aim:** To assess the relationship between telomere length and clinical characteristics in patients with T2DM with and without CKD.

**Methods:** A cross-sectional study included 100 patients with T2DM, divided into two groups: 50 with CKD and 50 without. CKD was defined as estimated glomerular filtration rate < 60 ml/min/1.73 m² and/or albumin-to-creatinine ratio ≥ 30 mg/g. Leukocyte telomere length was measured by quantitative real-time polymerase chain reaction and expressed as T/S ratio. Age-adjusted telomere length (ΔT/S) was calculated using regression residuals. Statistical analysis included Mann-Whitney U test, $\chi^2$ test, and regression analysis.

**Results:** Patients with CKD were older and had a longer duration of diabetes ($p < 0.05$). Cardiovascular disease was more frequent in CKD patients (60 % vs 34 %, $p = 0.009$). Median telomere length was lower in CKD patients (0.56 [0.38 – 0.74]) compared with non-CKD (0.89 [0.60 – 1.40]), without statistical significance ($p = 0.21$). However, after adjustment for age, telomere length was significantly shorter in CKD patients ($p = 0.035$). Pathologically short telomeres ($Z < -1$) were more prevalent in CKD patients (20.8 % vs 2.1 %, $p = 0.0076$).

**Conclusions:** T2DM patients with CKD demonstrate accelerated cellular aging, reflected by shorter age-adjusted telomere length and a higher prevalence of critically short telomeres. Telomere length assessment may serve as a potential biomarker for biological aging and risk stratification in CKD.

## A17

### Beyond the algorithm: patient-driven behaviour drives optimal glycaemic outcomes in older adults using automated insulin delivery

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**Aims:** Diabetes self-management in older adults with type 1 diabetes (T1D) presents a unique clinical challenge, where the goals of maintaining tight glycaemic control must be carefully weighed against age-related vulnerabilities. This study aimed to analyse glycaemic control and the effects of customised algorithm settings in a cohort of AID users aged 60 years and above.

**Methods:** This retrospective analysis included users of the MiniMed™ 780G AID system (aged ≥ 60 years), who shared their device data via cloud-based connectivity. Continuous glucose monitoring (CGM) metrics, including Time in Range (TIR, 3.9 – 10.0 mmol/l), Time in Tight Range (TITR, 3.9 – 7.8 mmol/l), Time Below Range (TBR < 3.9 mmol/l), were analysed alongside daily insulin distribution (manual bolus and auto-correction proportions) and algorithm settings. Statistical significance was assessed using Welch's t-test and Mann-Whitney U test.

**Results:** The cohort comprised 97 AID users (68.5 % female; mean age 67.9 ± 6.7, range 60 – 90 years) with excellent overall glycaemic control, with a mean TIR of 76.4 %, TBR of 1.2 %. Utilising the most aggressive algorithm settings (glucose target 5.5 mmol/l and active insulin time of 2 hours; n = 13) did not exhibit a statistically significant difference in TIR (73.9 % vs. 76.5 %, $p = 0.396$) or TBR (0.9 % vs. 1.2 %, $p = 0.322$). Stratification of older adults based on TITR revealed that the high-performing group, achieving a TITR > 50 % (n = 50), utilised a significantly higher proportion of manual boluses (60.9 % vs. 56.1 %, $p = 0.003$) and required fewer algorithm-driven auto-corrections (23.7 % vs. 37.4 %, $p < 0.001$). The adoption of aggressive algorithm settings did not differ between the high and low TITR groups (14.0 % vs. 13.0 %, $p = 1.000$).

**Conclusion:** While the Minimed™ 780G AID system provides safe and highly effective glycaemic control, consistently preventing hypoglycaemia regardless of customised settings, the true driver of optimal glycaemic success remains proactive patient-driven bolus behavior. The algorithm supports, but cannot replace, patient engagement.

## A18

### Beta-cell function influences the relationship between visceral adiposity and insulin sensitivity

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**Aims/Hypothesis:** Visceral adipose tissue (VAT) is a key determinant of insulin

resistance (IR). Whether insulin secretion modifies this relationship and whether early ("primary") hyperinsulinaemia contributes to IR development remain debated. Clarifying this link is essential for understanding early metabolic deterioration across the glycaemic spectrum.

**Methods:** We analysed 1,641 individuals with normal glucose tolerance (NGT), type 1 (T1D) and type 2 diabetes (T2D) from the German Diabetes Study (GDS). VAT and subcutaneous adipose tissue volumes were quantified by MRI. Insulin sensitivity (M-value derived from Botnia clamps) and insulin secretion (glucagon-stimulated 6-minute C-peptide) were assessed by gold-standard measures. Repeated measurements across the 5-year follow-up intervals were available in 640 individuals. Multivariable regression models including interaction terms were applied cross-sectionally and longitudinally. Longitudinal models predicted M-value change (ΔM) from baseline VAT, ΔVAT, baseline BCF and interactions.

**Results:** Adjusted for sex, BMI and diabetes type, higher VAT was strongly associated with lower insulin sensitivity (per SD VAT: $\beta = -0.54$ SD log-M, $p < 0.001$), whereas subcutaneous fat showed weaker associations ($\beta = -0.14$, $p = 0.012$). Higher beta-cell function was associated with higher insulin sensitivity ($\beta = 0.13$, $p = 0.018$) but strengthened the inverse association between VAT and M-value (VAT × beta-cell function: $\beta = -0.19$, $p < 0.001$). In line with this interaction, the association of VAT with beta-cell function was pronounced in NGT ($\beta = -1.22$, $p < 0.001$) and T2D ($\beta = -1.41$, $p < 0.001$), but attenuated in T1D ($\beta = -0.57$, $p = 0.054$). Longitudinally, ΔVAT predicted declining M-value only with higher baseline beta-cell function ($\beta = -6.53 \times 10^{-4}$, $p = 0.018$).

**Conclusions:** Beta-cell function modifies VAT-associated insulin resistance, supporting a contributory role of primary hyperinsulinaemia in IR development and progression.

## A19

### A cautionary tale of seemingly „good" metabolic control in a patient with immune mediated inflammatory diseases and diabetes

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Periodic measurement of the proportion of glycated haemoglobin in the blood has long been an essential part of everyday diabetes care. However, in addition to the current blood sugar level, in certain special situations, the measured values can be significantly influenced by the abnormal lifespan of red blood cells. Even in cases of subclinical haemolysis, which does not show up at all in routine laboratory parameters, the results may be significantly lower than expected. Premature breakdown of erythrocytes can sometimes occur as a side effect of certain medications. Our 42-year-old female patient received high doses of a conventional antirheumatic drug (sulfasalazine) in addition to biological therapy due to her cumulative immune-mediated inflammatory diseases (seropositive rheumatoid arthritis, ankylosing spondylitis, and ulcerative colitis). Her type 2 diabetes required basal-bolus insulin treatment. Despite deceptively low $HbA_{1c}$ values (which could even indicate recurrent hypoglycaemia), her blood glucose levels measured at home and in the laboratory were consistently above the target range. Her routine laboratory tests showed no other abnormal findings, including CBC, ESR, CRP, bilirubin, albumin and LDH. However, after special tests (haptoglobin, direct antiglobulin test) and fructosamine determination, the clinical scenario and treatment direction changed fundamentally. In accordance with international guidelines sulfasalazine is a very commonly used antirheumatic drug. However, it can cause haemolysis, which even if it is subclinical in appearance, may considerably interfere with laboratory tests such as $HbA_{1c}$. In diabetic patients this can lead to suboptimal treatment and even serious long term complications. Therefore among sulfasalazine treated diabetic patients fructosamine measurement should be used to properly assess long term glycaemic status.

## A20

### Re-analysis of existing $^1$H-MRS data for quantification of hepatic lipid composition

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**Aims:** High hepatic lipid (HL) content is strongly associated with whole-body and hepatic insulin resistance and enhances the risk of developing type 2 diabetes. $^1$H magnetic resonance spectroscopy ($^1$H-MRS) is used to investigate HL content, but using optimised protocols can also provide information on fatty acid composition. While these optimised methods can be implemented for prospective studies, here we investigated whether retrospective post-processing of $^1$H-MRS data, acquired for HL quantification, can also be utilised for estimating hepatic saturated, (mono)- and (poly)-unsaturated fatty acid (SFA, (M)UFA and (P)UFA) fractions.

**Methods:** 311 $^1$H-MRS data sets (3 T Philips Archieva dStream, 25 × 25 × 25 mm STEAM localization, CHESS water suppression, TR/TE 4000/10 ms) of the German Diabetes Study were analysed with a custom MATLAB script. Only data from individuals with type 2 diabetes and controls were considered and in case of multiple visits, the first visit was analysed. Fit quality was evaluated for single resonances (methyl, methylene, α-carbonyl, allylic and diallylic).

**Results:** From 311 datasets, 139 spectra (44.7 %) were successfully fitted with good quality for the α-carbonyl and allylic resonances, which are required to calculate SFA and UFA fractions. We found that with increasing total HL content, lipid composition shifted toward higher SFA fraction ($r = 0.52$, 95 % CI [0.39, 0.63]).

**Conclusion:** In this study, we investigated whether routinely acquired $^1$H-MRS data for HL quantification can also provide information on fatty acid composition. Our findings demonstrate the feasibility of extracting lipid composition parameters from standard acquisitions and motivate further work to examine the link between these measures and metabolic

dysfunction. The relationship between saturated fat accumulation and markers of insulin sensitivity or inflammation is currently under investigation.

## A21

### Participative conception of a clinical study on transverse tibial bone transfer (TTT) for the treatment of diabetic foot ulcers (DFU)

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**Aims:** This study explores how structured and continuous patient and stakeholder engagement (PSE) can contribute to the conceptualization of a clinical study on transverse tibial bone transport (TTT) for the treatment of diabetic foot ulcers (DFU) and support a patient-centered, methodologically sound study planning.

**Methods:** The TTDO-DFU-CoCo project applied a participatory research approach that systematically involved patients and relatives in the conceptual phase of a randomised controlled trial. Three co-researchers, including a patient with personal experience of TTT treatment, were continuously involved throughout the project. In addition, three workshops were conducted over twelve months with patients with and without DFU, relatives and clinical researchers. A patient network was established to provide advisory input to the main clinical study. The German Diabetes Aid ("Deutsche Diabetes-Hilfe") was involved from the start to ensure links with patient representative structures. Methods included moderated group discussions, PhotoVoice, co-design elements and iterative feedback loops. A further participatory work package addressed health economic evaluation, identifying patient-relevant cost domains and decision attributes for a discrete choice experiment.

**Results:** The participatory formats enabled a differentiated assessment of patient-relevant perspectives on TTT treatment. Perceived burdens, expectations, information needs and outcome dimensions beyond classic clinical endpoints were incorporated. Continuous involvement of the co-researchers supported the design phase, including iterative reflection on workshop results. For the health economic evaluation, key cost components and patient-relevant endpoints for a discrete choice experiment were identified, providing a basis for further study planning. Based on these experiences, the main clinical study will also follow a participatory approach.

**Conclusions:** Early, structured and continuous participatory involvement of patients and stakeholders can substantially contribute to the conceptual preparation of clinical trials on TTT in diabetic foot syndrome. The PSE approach supports patient-centered study planning and provides a robust basis for the application and implementation of a main clinical trial.

## A22

### Monocyte function exhibits subtype-specific variation in diabetes, notably with increased IL-1β responsiveness in mild obesity-related diabetes subtype

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**Aim:** Circulating leukocyte profiles, specifically leukocyte numbers and T cell frequencies, differ between novel subtypes of diabetes – with SIRD (severe insulin-resistant diabetes) and MOD (mild obesity-related diabetes) showing pro-inflammatory phenotypes. Although the frequency and pro-inflammatory cytokine production of monocytes has been associated with type 2 diabetes and associated complications, it is currently unknown, whether differences in monocyte frequency or function exist between diabetes subtypes.

**Methods:** We quantified the frequency of circulating monocyte subsets (classical, intermediate, non-classical) and assessed their capacity to produce IL-1β (interleukin-1 beta), IL-6 (interleukin-6) and TNF-α (tumor necrosis factor-alpha) upon LPS (lipopolysaccharide) stimulation. These analyses were performed by flow cytometry in participants with type 2 diabetes from the German Diabetes Study, focusing on the two most prevalent diabetes subtypes: MOD (mild obesity-related diabetes; n = 11; time since diabetes diagnosis 10.4 ± 4.0) and MARD (mild age-related diabetes; n = 10; time since diabetes diagnosis 10.5 ± 4.1).

**Results:** Despite no differences in overall monocyte frequency or subset composition between MOD and MARD ($p > 0.05$), LPS stimulation revealed a significantly greater upregulation of IL-1β in MOD compared with MARD ($p = 0.022$), whereas no significant differences were observed for IL-6 or TNF-α responses ($p > 0.05$).

**Conclusion:** Our data suggest that monocyte function differs between diabetes subtypes, which may have relevant application of therapeutic strategies targeting inflammation in type 2 diabetes.

## A23

### Provider preferences for alternative payment models for a new integrated type 2 diabetes and periodontitis care model

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**Aims/Hypothesis:** Payment models play a crucial role in the successful implementation of interprofessional care models. We investigated providers' payment preferences promoting mutual screening for type 2 diabetes and periodontitis. We considered a baseline € 30 capitation payment as well as an alternative payment model with optional bonus payments for providers and patients based on a quality indicator.

**Methods:** We conducted a discrete choice experiment to measure payment preferences of general practitioners and dentists. Payment options included a baseline € 30 capitation and payment models with a performance-related bonus payment for a successful referral uptake. Three attributes were: the share of capitation paid as a performance bonus, the premium applied to this bonus, and the share of the bonus allocated to the patient. Participants received six choice sets with

alternative payment models and a standard capitation option and an opt-out option. We recruited providers participating in the DigIn2Perio randomised controlled trial and intervention-naïve providers.

**Results:** 191 participants answered the questionnaire. 79.6 % of participants always chose to participate in the new care model. Preferences for alternative payment models were heterogeneous: 37.2 % always preferred them, 39.8 % opted out in at least one choice and 23 % always preferred a capitation payment. The most important attribute was the patient payment fraction with a positive coefficient for the 50 % split and a negative coefficient when 100 % was allocated to the patient.

**Conclusion:** Most providers stated a general intention to implement the new care model into standard care, and an alternative payment model was preferred by a substantial number of providers. An alternative payment model incorporating a performance-based quality indicator appears acceptable to providers when it ensures an adequate performance payment for providers and allows a part of the performance payment to be shared with patients as an incentive.

## A24

### The role of glucose lowering vs weight reduction in prevention of CVD in type 2 diabetes

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**Aim:** This study aimed to assess the relationship between the impact of glucose lowering and weight reduction regarding cardiovascular outcomes in patients with type 2 diabetes (T2D) across different glucose-lowering strategies, including lifestyle interventions and pharmacological treatments.

**Methods:** A systematic search of electronic databases was conducted to identify cardiovascular outcome trials (CVOTs), observational cohort studies, and post hoc analyses of clinical trials involving adults with T2D. We examined the association between glucose lowering, body weight loss (BWL) and cardiovascular outcomes.

**Results:** A total of 25 studies were included: 19 RCTs of novel glucose-lowering agents (GLP-1 receptor agonists, DPP-4 inhibitors, and SGLT2 inhibitors) accompanied by structured lifestyle intervention and 6 RCTs or observational studies using other treatment strategies, with a total of 379,904 patients with T2D. The BWL during treatment with GLP-1 receptor agonists was associated with a more pronounced reduction in the risk of major adverse cardiovascular events (MACE) than when SGLT2 inhibitors were used, whereas no such association was observed with DPP-4 inhibitors. Among studies assessing other strategies, unstructured substantial BWL could be associated with an increased risk of MACE and all-cause mortality.

**Conclusions:** In CVOTs, glucose-lowering therapies in patients with T2D were associated with modest weight reduction that correlated with improved cardiovascular outcomes. This relationship was evident with GLP-1 receptor agonists and SGLT2 inhibitors. In contrast, evidence from non-CVOTs suggests that substantial BWL in the absence of structured behavioural interventions and appropriate pharmacotherapy may be associated with increased risks of cardiovascular events and all-cause mortality.

## A25

### Efficacy of cardio-protective molecules based on achieving $HbA_{1c}$ and weight reduction targets

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**Aims:** The aim of the study is to evaluate the efficacy of antidiabetic molecules GLP-1 Ra, iSGLT2 and metformin, by the target of $HbA_{1c}$ < 7 % and body weight reduction (BWR) of 5 % in patients with type 2 diabetes mellitus (DM).

**Methods:** Retrospective analysis of consecutively inpatients from a tertiary DM center in Bucharest, with 261 patients evaluated at baseline, 3 and 6 months. Group characteristics consisted of mean age 58 ± 9.96 years, mean $HbA_{1c}$ 7.2 ± 1.7 %, mean LDL-C 91.5 ± 34.1 mg/dl and 39 % females.

**Results:** iSGLT2 with a 22.7 % combined target rate at 12 months, $p < 0.001$, proved superior to GLP-1 Ra and metformin. Both $HbA_{1c}$ and serum glucose (SG) reductions were more consistent at the 12-month visit: 6.58 % for metformin, 22.68 % for iSGLT2 and 5.88 % for GLP-1 Ra, compared to the baseline visit, while at 12 months as compared to 6-month visit were as follows: 4.79 % for metformin, 5.04 % for iSGLT2 and 5.88 % for GLP-1 Ra. Despite the fact that the $HbA_{1c}$ target < 7 % at baseline was achieved at 38.92 % for metformin, 17.64 % for iSGLT2 and 41.17 % for GLP-1 Ra, SG was lower, probably influenced by insulin treatment. When adjusting for $HbA_{1c}$, DM duration, insulin treatment, age, BMI, eGFR no significant differences were obtained for each type of treatment.

**Conclusions:** This real-world study from Romania of type 2 DM patients evaluated for targets of $HbA_{1c}$ < 7 % and SG of 5 %, shows iSGLT2 outperforming metformin and GLP-1 Ra.

## A26

### Sex-specific amputation rate in Germany in people with and without diabetes – trend between 2013 and 2021 including the impact of the COVID-19 pandemic

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**Aims/Hypothesis:** This study aimed to analyse the time trend of sex-specific amputation rate (AR) among people with and without diabetes 2013 – 2021 considering the COVID-19 pandemic.

**Methods:** We used data from the BARMER statutory health insurance company, covering roughly 11 % of the German population. We identified all people with a first lower extremity amputation in 2013 – 2021 and differentiated between major and minor amputation. People with diabetes were identified using an established algorithm based on quarterly diabetes diagnoses and prescriptions of

anti-hyperglycaemic medications. We analysed sex-specific age-standardised AR in the population with and without diabetes. Time trend was examined using Poisson regression. Moreover, we predicted rate for the pandemic years 2020 – 2021 based on age-sex standardised rate from 2013 – 2019 in comparison with observed rate (relative risk observed/expected (RR O/E)).

**Results:** Between 2013 and 2019, major AR significantly decreased in women with diabetes by 3 % per year and 4 % in those without diabetes (p-value < 0.05 respectively) with no changes in men. Minor AR decreased in women with diabetes by 2% per year, but increased among men with diabetes by 1 % (p-value < 0.05 respectively) per year. In the population without diabetes minor AR remained stable in both sexes. During the pandemic period, we found significant changes only in women with diabetes in 2020 (RR O/E: 0.71 [95 % CI: 0.55 – 0.91]). Regarding minor AR a significant change was identified only in men with diabetes (RR O/E: 2020 0.93 [0.86 – 1.008]; 2021 0.90 [0.83 – 0.98]) and in women without diabetes (RR O/E: 2020 0.86 [0.74 – 0.995]).

**Conclusions:** The significant differences observed between men and women with diabetes underscore the necessity for sex-specific diabetes care strategies as well as continuous monitoring of amputation rates as part of diabetes surveillance. In view of the COVID-19 pandemic's impact, further studies based on German nationwide data are required.

## A27

### Familial hypercholesterolemia and cardiovascular risk: analysis of traditional risk factors and proinflammatory markers over 15 years of follow-up

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**Aim:** Despite lowering LDL-C, many patients with familial hypercholesterolemia (FH) remain in high residual cardiovascular (CV) risk. The aim of this study was to explore the relationship between proinflammatory markers, Lp(a), and lipid parameters in statin-treated FH patients, and to assess their association with cardiovascular events over a 15-year follow-up period.

**Methods:** Study included 145 FH patients, all treated with statins. Total cholesterol, LDL-C, HDL-C, and triglycerides were measured at baseline and annually throughout the follow-up period (spectrophotometry). Apolipoproteins were also assessed (nephelometry). High-sensitivity C-reactive protein (hsCRP) and interleukin-6 (IL-6) were measured in all patients (immunoturbidimetry). Cardiovascular events were identified based on relevant medical records.

**Results:** 24.4 % patients experienced a new cardiovascular event during the 15-year follow-up. The use of high-intensity statins increased markedly, from 37 % at baseline to 70.2 % at the end of the study. Although baseline lipid levels were similar between groups, patients who experienced cardiovascular events had significantly lower total cholesterol and LDL-C levels at the end of follow-up (4.51 mmol/l vs. 5.1 mmol/l; p < 0.05; 2.38 mmol/l vs. 3.09 mmol/l; p < 0.01). Interestingly, they also tended to have higher HDL-C levels (1.69 mmol/l vs. 1.32 mmol/l; p = 0.08). There were no significant differences in hsCRP (0.8 mg/l vs. 1.3 mg/l patients without new CVD), as well as and IL-6 (2.5 pg/l vs. 2.7 pg/l patients without new CVD; p = 0.68). However, elevated Lp(a) levels (> 50 mg/dl) were considerably more common among patients who experienced cardiovascular events, suggesting a strong association with increased risk (OR = 2.5; 95 % CI: 0.38 – 0.91, p < 0.05).

**Conclusion:** Even with substantial LDL-C reduction, patients with FH remain at high cardiovascular risk. These findings highlight the importance of additional risk factors, particularly Lp(a) in our population. The lack of differences in inflammatory markers may be explained by the widespread use of high-intensity statin therapy.

## A28

### Impact of pecan nut consumption on glycaemic outcomes: a systematic review and meta-analysis of randomised controlled trials

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**Aims:** Tree nuts are generally recommended as part of healthy dietary patterns; however, the effects of pecan-specific interventions on markers of glycaemic control have not yet been comprehensively synthesised. This systematic review with meta-analysis aimed to quantify the effects of pecan consumption on markers of glycaemic control.

**Methods:** CENTRAL, PubMed, and Scopus were searched up to March 3, 2026 for randomised controlled trials (RCTs) investigating pecan intake for at least two weeks on glycaemic outcomes in healthy adults or at increased cardiometabolic risk. Random-effects meta-analyses were conducted using mean differences (MDs) with 95 % CIs, risk of bias was assessed using the Rob 2.0 tool, while the certainty of evidence was evaluated using the GRADE approach.

**Results:** Five RCTs involving 411 participants were included. Pecan interventions ranged from 30 to 68 g/day and lasted 4 to 12 weeks. Pecan consumption did not affect most glycaemic outcomes, including fasting blood glucose, glycated haemoglobin, or insulin resistance; however, it reduced fasting insulin levels (MD -1.0 µIU/ml; 95 % CI -1.9, -0.2; moderate certainty of evidence).

**Conclusions:** Although pecan consumption did not affect most glycaemic outcomes, it improved fasting insulin levels, suggesting a potential beneficial effect on insulin regulation. However, the currently available trials are limited by small sample sizes, and further well-designed RCTs with larger populations are needed to clarify the effects of pecan consumption on glycaemic outcomes, particularly over longer follow-up periods and in individuals with impaired glucose metabolism.

## A29

### Sex-specific acylcarnitine and amino acid responses to acute lipid loading indicate reduced metabolic flexibility in prediabetes

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**Aims/Hypothesis:** Elevated plasma free fatty acids drive insulin resistance. We investigated whether acute lipid loading alters metabolites of lipid oxidation and amino-acid metabolism in individuals with normal glucose tolerance (NGT) and prediabetes (PRED), with attention to sex.

**Methods:** In a randomised crossover design, 12 individuals with NGT (7 male/5 female, BMI 22.46 ± 1.52 kg/m², age 21.50 ± 2.24 years) and 4 with PRED (3 male/1 female, BMI 32.12 ± 7.99 kg/m², age 57.75 ± 3.50 years, $HbA_{1c}$ 5.35 ± 0.26 %) received glycerol and lipid infusions followed by a hyperinsulinaemic-euglycaemic clamp. Circulating acylcarnitines and amino acids were determined by mass spectrometry. Acetylcarnitine/carnitine (C2/C0) and glutamine/glutamate (Gln/Glu) ratios were calculated and linear mixed-effects models included sex.

**Results:** PRED showed lower basal levels of short-chain acylcarnitines (SCACs) than NGT females (0.90 vs. 1.39 µM; p = 0.0030) and NGT males (1.34 µM; p = 0.0057). Under lipid loading, NGT females showed the strongest adaptive response, with a 47 % decrease in SCACs (p < 0.0001) and a 40 % decrease in C2/C0 (p = 0.0081), whereas NGT males showed smaller reductions in SCACs (41 %, p < 0.0001) and C2/C0 (37 %, p = 0.0056). No significant change in C2/C0 was observed in PRED under either condition. In the glycerol arm, NGT females also showed a 20 % decrease in Gln/Glu from baseline to steady state (82.3 vs. 66.2; p = 0.0387), whereas no significant temporal change was observed in PRED. Branched-chain amino acids decreased in both NGT groups across the protocol, but remained higher in PRED at clamp steady state (p ≤ 0.0275).

**Conclusion:** The observed changes indicate greater metabolic flexibility in NGT, strongest in females, weaker but preserved in males, and reduced in PRED. These findings support reduced metabolic flexibility in prediabetes, although age and BMI differences warrant confirmation in larger, matched cohorts.

## A30

### Analysis of mitochondrial function in blood cells and circulating mitokines in gestational diabetes

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**Aims:** Decline in mitochondrial function was found in placental and skeletal tissues in gestational diabetes (GD), the most prevalent pregnancy complication. Circulating mitokines: fibroblast growth factor 21 (FGF21) and growth differentiation factor 15 (GDF15) levels in GD showed, so far, an inconsistent result. This study aimed to examine the mitochondrial function of peripheral blood mononuclear cells (PBMCs) and serum GDF15 and FGF21, in both healthy pregnant women and women diagnosed with GD.

**Materials and Methods:** This study included 21 patients diagnosed with GD, and 21 healthy pregnant women as a control group, between 24 and 28 weeks of gestation. After obtaining informed consent, body weight and height measurements, a 2-hour oral glucose tolerance test (OGTT), and venous blood sampling were conducted. PBMCs were isolated using Lymphoprep density gradient medium. The mitochondrial function of fresh isolated PBMCs was measured by high-resolution respirometry. Serum concentrations of GDF15 and FGF21 were measured by ELISA assay.

**Results:** Mitochondrial respiration was lower in PBMCs of women with GD, compared to healthy controls in respiration of intact cells (5.65 ± 1,01 amol $O_2$/(s × cell) in control, n = 18 and 4.28 ± 0.99 in GD group, n = 16, p < 0.01) and complex I linked oxidative phosphorylation capacity (7.75 ± 2,17 amol $O_2$/(s × cell) in control n = 18 and 5.67 ± 2,11 n = 16 in GD group, p < 0.01). FGF21 levels were below the detection limit. No difference was found in serum GDF15 level (58,53 ± 14,37 pg/ml in control and 72,52 ± 31 in GD group, n = 21 for both groups, p = 0.075).

**Conclusion:** PBMCs from GD-affected women had decreased mitochondrial respiration compared to healthy pregnant women. GDF15 levels should be further studied, as the results are variable in the GD group. Monitoring these parameters in gestational diabetes could provide better insight into the molecular mechanisms underlying the pathogenesis of this condition. This would be crucial for further development of diagnostic tools and therapeutic approaches.

## A31

### Dynamic epigenetic imprints of metabolic control in adolescents with type 1 diabetes

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**Aims/Hypothesis:** Early glycaemic control in paediatric type 1 diabetes (T1D) creates a "metabolic memory" that influences the risk of long-term complications. We hypothesised that short-term changes in glycaemia drive prospective epigenetic remodelling in newly diagnosed youth with T1D, and that improving glycaemic control may partially reverse these changes.

**Methods:** We conducted a 12-month pilot study in youth with newly diagnosed T1D aged 6 – 18 years. DNA methylation in whole blood and glycaemic control were assessed at 3 and 12 months after diagnosis. Glycaemic control was classified as on-target vs off-target ($HbA_{1c}$ < 7.0 %; time-in-range [TIR] > 70 %). Differentially methylated CpG sites were identified between groups and correlated with within-individual changes in glycaemia. Effect sizes were contextualised against a meta-analysis of landmark methylation-metabolic memory cohorts (~2,300 participants).

**Results:** Eight participants (median age 12 years; 75 % male) were enrolled; 50 % met glycaemic targets at 3 months. Suboptimal glycaemic control was associated with differential methylation at 68 CpG sites after multiplicity

correction, with directions concordant with landmark cohorts. Improvement at 12 months (mean -0.7 percentage points) was associated with partial rescue of methylation changes, suggesting early "reversibility" of epigenetic imprinting. The subgroup with worsening of glycaemic control (mean $HbA_{1c}$ +1.6 percentage points; TIR -28.4 percentage points) further exacerbated the observed methylation changes.

**Conclusions:** Despite the small sample size, these preliminary data demonstrate early epigenetic plasticity in the formation of metabolic memory and support a dynamic relationship between glycaemic control and DNA methylation, hinting at a potential for partial epigenetic rescue through early therapeutic intervention.

## A32

### An integrated cumulative score for diabetic sensorimotor polyneuropathy including quantitative sensory testing

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**Aims/Hypothesis:** Current classifications of diabetic sensorimotor polyneuropathy (DSPN) are mainly based on neurological symptoms and deficits (Neuropathy Symptom Score, NSS; Neuropathy Deficit Score, NDS) and nerve conduction studies according to Toronto criteria. However, sensory phenotypes and small-fiber function are not adequately captured. We therefore aimed to develop an integrated DSPN classification incorporating small- and large-fiber function together with sensory phenotypes.

**Methods:** Neurological phenotyping was performed in 522 participants of the HEIST-DiC study, including 67 with normal glucose tolerance, 107 with prediabetes, 83 with type 1 diabetes, and 265 with type 2 diabetes. Assessments included neurological symptoms and deficits (NSS, NDS), nerve conduction studies of the sural, peroneal and tibial nerves, and quantitative sensory testing (QST). Nerve conduction findings were considered abnormal if at least one parameter of the respective nerve fell below the 2.5th percentile. All components were normalised and combined into a cumulative score ranging from 0 to 4. Descriptive statistics, non-parametric tests, and ROC-analyses were applied.

**Results:** The cumulative score clearly discriminated between individuals with and without DSPN. Median scores were higher in individuals with DSPN defined by NDS/NSS than in those without DSPN (2.25 [1.80 – 2.77] vs 0.60 [0.20 – 1.00]; $p < 0.0001$), and similarly higher in individuals with DSPN defined by Toronto criteria (2.73 [2.40 – 3.23] vs 0.70 [0.43 – 1.30]; $p < 0.0001$). ROC analyses showed excellent discrimination for DSPN according to NDS/NSS (AUC 0.97; $p < 0.0001$) and Toronto criteria (AUC 0.97; $p < 0.0001$). Optimal cut-offs were > 1.38 for NDS/NSS-defined DSPN (sensitivity 93.1 %, specificity 89.5 %; Youden index 0.83) and > 2.07 for Toronto-defined DPSN (sensitivity 89.7 %, specificity 93.3 %; Youden index 0.83).

**Conclusions:** This cumulative score expands DSPN classification by integrating small- and large-fiber function with sensory phenotypes. It broadens phenotypic stratification and may identify neuropathic changes not captured by symptom- and nerve conduction-based criteria.

## A33

### Proteomic profiling of the contraction-induced secretome in insulin-resistant TBC1D4-deficient skeletal muscle

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**Aims/Hypothesis:** Insulin resistance is a hallmark of type 2 diabetes (T2D), and exercise improves metabolic health. TBC1D4 is a key regulator of insulin- and contraction-stimulated glucose uptake, and carriers of loss-of-function mutations exhibit postprandial hyperglycaemia and increased T2D risk. Physical activity can fully rescue these glycaemic impairments, and studies in Tbc1d4-deficient (D4KO) mice show improved adipose tissue insulin sensitivity. We hypothesised that contraction-induced changes in phosphorylation and the secretome of skeletal muscle modulate adipose insulin sensitivity. This study aimed to identify candidate factors linking TBC1D4-dependent muscle contraction to insulin sensitivity in adipocytes.

**Methods:** Glycolytic extensor digitorum longus (EDL) and oxidative soleus muscles from D4KO and wild-type mice were subjected to ex vivo contraction using a DMT myograph system. Muscle tissue and corresponding supernatants were analysed by mass spectrometry to characterise the secretome and phosphoproteome.

**Results:** Secretome analysis identified 1265 and 1373 proteins in soleus and EDL muscles, with over 100 proteins significantly regulated by contraction. In soleus from D4KO mice, contraction reduced proteasomal proteins (e. g. Psmb8) and increased vesicle transport–related proteins (e. g. Cdc42). In contrast, EDL muscles showed the opposite pattern, with higher abundance of protein degradation–associated proteins (e. g. Psmb10) and reduced vesicle transport proteins. These patterns highlight muscle-type–specific responses to contraction in the context of TBC1D4 deficiency.

**Conclusion:** Candidate mediators linking contraction in insulin-resistant skeletal muscle to peripheral insulin sensitivity include Cdc42 and proteasomal components. This study provides proteomic insights into the contraction-induced secretome of Tbc1d4-deficient muscle and identifies potential signaling factors for further functional validation in peripheral tissues.

## A34

### Phenotype-based assignment reveals distinct hepatic, renal and vascular involvement patterns in type 2 diabetes

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**Aims/Hypothesis:** Metabolic dysfunction-associated steatotic liver disease (MASLD) and type 2 diabetes (T2D) are heterogeneous metabolic states. We

examined whether cardiometabolic-like MASLD phenotype assignment in T2D identifies a subgroup with convergent multi-organ burden and differential hepatic, renal and vascular relationships.

**Methods:** Retrospective nearest-medoid assignment was performed in 243 individuals with T2D from the Heidelberg Study on Diabetes and Complications using age, BMI, $HbA_{1c}$, alanine aminotransferase, triglycerides and LDL-cholesterol. Individuals were assigned to the published cardiometabolic (CM; cluster 2) and liver-specific (LS; cluster 5) MASLD clusters, while remaining clusters were pooled into a comparator category. Hepatic steatosis, renal involvement, vascular dysfunction, multi-domain burden and phenotype-specific trait relationships were assessed.

**Results:** Assigned groups comprised 174 individuals in the comparator category, 60 in CM and 9 in LS. Given the small LS subgroup, analyses focused on CM versus comparator. CM differed in expected defining and hepatic traits (all $p \leq 0.004$), but also showed higher pulse wave velocity, urine albumin-to-creatinine ratio, and albuminuria prevalence (all $p \leq 0.014$). CM was enriched for at least 2 affected domains (56.7 % vs 24.7 %) and all 3 domains (25.0 % vs 1.7 %), and remained associated with at least 2-domain burden after adjustment (OR 3.6, 95 % CI 1.5 – 9.1; $p = 0.006$), including sensitivity analysis (OR 3.0, 95 % CI 1.2 – 7.6; $p = 0.021$). Importantly, albuminuria was more strongly associated with pulse wave velocity in CM than in the comparator (rho 0.4 vs 0.1; interaction $p = 0.010$), suggesting coordinated renal–vascular dysfunction beyond isolated trait differences. No significant sex interaction was detected.

**Conclusions:** In T2D, assignment to a cardiometabolic-like MASLD phenotype identifies a subgroup with convergent multi-organ burden. While hepatic differences partly reflect defining variables, stronger coupling of albuminuria with vascular stiffness suggests a distinct renal–vascular interaction pattern rather than greater metabolic severity.

## A35

### Ketogenic diet increases insulin clearance independently of insulin secretion with partial reversal after short-term carbohydrate refeeding in women with obesity

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**Background:** Ketogenic diets are highly effective in reducing insulin resistance and improving glycaemic control, making them a relevant intervention in metabolic diseases including obesity and type 2 diabetes. However, the mechanisms underlying reduced circulating insulin remain unclear. The reversibility of these effects with short-term carbohydrate refeeding is also not well characterised.

**Methods:** We studied 22 women with obesity undergoing a 28-day isocaloric ketogenic diet followed by 2 days of high carbohydrate refeeding. At baseline (V1), after ketogenic diet (V2), and after refeeding (V3), participants underwent a standardised oral glucose tolerance test with measurements of glucose, insulin, and C-peptide. Insulin secretion rate (ISR) was derived by C-peptide deconvolution. Insulin clearance was estimated as the ratio of total insulin secretion to circulating insulin (AUC ISR/AUC insulin). Insulin sensitivity was assessed using the Matsuda index.

**Results:** Ketogenic diet significantly increased insulin clearance (V1: 1.19 vs V2: 1.44 l/min, $p < 0.001$) and reduced circulating insulin (AUC insulin: 12,275 vs 9,456 mU × min/l), while insulin secretion remained unchanged (AUC ISR: $p = 0.34$; AUC C-peptide: $p = 0.11$). Insulin sensitivity improved (Matsuda: 3.03 vs 4.62, $p < 0.001$). Short-term carbohydrate refeeding partially reversed these effects. Insulin clearance decreased compared to the ketogenic phase (V2: 1.44 vs V3: 1.30 l/min, $p = 0.002$), while circulating insulin increased (AUC insulin: 9,456 vs 10,817 mU × min/l), again without significant changes in insulin secretion. Changes in insulin clearance were positively associated with changes in insulin sensitivity ($r = 0.45$, $p = 0.037$) and inversely with circulating insulin ($r = -0.50$, $p = 0.018$).

**Conclusion:** Ketogenic diet lowers circulating insulin primarily through increased insulin clearance rather than reduced insulin secretion. This effect is partially reversible with short-term carbohydrate refeeding, suggesting that insulin clearance is a dynamic regulator of systemic insulin exposure in response to dietary carbohydrate availability.

## A36

### Distinct MASLD subtype trajectories after bariatric surgery: findings from the ChARMeD study

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**Aims:** Bariatric surgery causes major weight loss in severe obesity, yet improvement in MASLD varies between individuals. We examined 12-month phenotype trajectories after bariatric surgery, focusing on whether transitions reflect stable heterogeneity or mainly weight-loss-driven changes in the defining variables.

**Methods:** Participants from ChARMeD ($n = 92$; 77 % female; 25 % type 2 diabetes) were assessed at baseline, 1, 6 and 12 months after bariatric surgery. A subgroup ($n = 17$) underwent paired baseline/12-month euglycaemic-hyperinsulinaemic clamps to quantify insulin sensitivity. HOMA-IR and Adipo-IR were analysed longitudinally. Baseline histology was scored using SAF criteria, and CAP was available in 88 participants. MASLD clusters were assigned at each visit and grouped as cardiometabolic (CM), liver-specific (LS) or control-like (CON).

**Results:** Twelve-month weight loss was 30.8 ± 9.2 %. Insulin sensitivity improved: M increased from 2.30 [1.48 – 3.45] to 5.57 (3.20 – 7.94) mg/kg/min ($p = 1.53 \times 10^{-5}$); HOMA-IR decreased from 4.68 [3.26 – 6.72] to 1.61 [1.07 – 2.24] ($p = 2.78 \times 10^{-15}$), and Adipo-IR from 96.61 [60.57 – 130.36] to 27.98 [21.13 – 39.39] ($p = 1.2 \times 10^{-12}$). Baseline CM/LS prevalence was 14/91 (15.4 %; CM 3, LS 11). Given the small CM subgroup, CM and LS were pooled for trajectory analyses. No participant remained CM/LS at 12 months, indicating that cluster shifts largely tracked

weight-loss-driven changes in the defining variables. Resolution kinetics varied: 43 % exited CM/LS by 1 month and 50 % by 6 months. Baseline HOMA-IR and Adipo-IR did not distinguish earlier from later exit, including after adjustment for early ΔBMI. LS showed higher steatosis grade than CON, whereas MASH and F2+ fibrosis prevalence did not differ. Earlier exit was associated with higher baseline CAP (p = 0.022).

**Conclusions:** In this bariatric setting, postoperative CM/LS transitions primarily reflect weight-loss-driven changes in the defining cluster variables, limiting interpretation as stable biologic endotypes. However, heterogeneity in resolution timing, together with higher baseline CAP in earlier responders, suggests that hepatic fat burden may influence transition timing.

## A37

### Short-term nutraceutical efficacy of Glucoerb® and Epavin® in overweight and obese adults: a 3-month observational study

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**Aims/Hypothesis:** Nutraceutical interventions may complement dietary strategies to improve body composition and reduce adiposity in adults with overweight or obesity. Glucoerb® and Epavin® contain plant-derived bioactives designed to support metabolic homeostasis and modulate fat and lean mass.This study aimed to evaluate the short-term effects of Glucoerb®, Epavin®, and their combination on antropometric and bioimpedance-derived body composition parameters.

**Methods:**Thirty adults with overweight or obesity (BMI ≥ 27 kg/m²) were assigned to receive Glucoerb® (Group 1, n = 10), Epavin® (Group 2, n = 10), or their combination (Group 3, n = 10) for three months. All participants received individualised Mediterranean dietary counseling and lifestyle support. Assessments at baseline and follow-up included weight, BMI,waist circumference, fat mass, fat-free mass, and skeletal muscle mass, measured via bioimpedance analysis.Within-group changes were analysed using paired t-tests or Wilcoxon signed-rank tests.

**Results:** All groups showed improvements in anthropometric and body composition parameters. In Group 1, waist circumference decreased from 96 ± 15 cm to 93 ± 15 cm (-2.5 %, p = 0.035), and fat mass from 29 ± 8 kg to 26 ± 8 kg (-12.3 %, p = 0.042). In Group 2, body weight decreased from 88 ± 15 kg to 86 ± 15 kg (-2.61 %, p = 0.006), waist circumference from 103 ± 10 cm to 98 ± 11 cm (-5.0 %, p = 0.007), and fat mass from 29 ± 12 kg to 26 ± 14 kg (-9.1 %, p = 0.011). In Group 3, body weight decreased from 97 ± 14 kg to 93 ± 14 kg (-3.5 %, p = 0.049), waist circumference from 112 ± 10 cm to 100 ± 13 cm (-11 %, p = 0.015), and fat mass from 38 ± 7 kg to 32 ± 9 kg (-15.4 %, p = 0.019).Fat-free mass and skeletal muscle mass were preserved across all groups.

**Conclusions:** Short-term supplementation with Glucoerb®, Epavin®, or their combination, alongside a combined Mediterranean dietary and lifestyle approach, improves anthropometric and bioimpedance-derived body composition in adults with overweight or obesity.

## A38

### Real-world effectiveness of 6-month tirzepatide therapy on body weight and composition in adults with overweight or obesity

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**Aims/Hypothesis:** Obesity drives cardiometabolic dysfunction and increases cardiovascular risk, with excess fat mass and impaired body composition playing a key role in metabolic outcomes; this study aimed to evaluate the real-world effectiveness (RWE) of tirzepatide on body weight, body composition, and metabolic parameters in adults with obesity or overweight and at least one obesity-associated comorbidities.

**Methods:** A 24-week retrospective observational analysis included 122 adults (80 % women; mean age 44 ± 15 years) with overweight or obesity, excluding patients with diabetes. Participants received tirzepatide (5 mg weekly) in combination with a standardised low-carbohydrate diet and tailored physical activity. Anthropometric measurements, bioelectrical impedance analysis and metabolic parameters were assessed at baseline and after 24 weeks.

**Results:** At 24 weeks, mean body weight reduced from 95 ± 20 to 80 ± 22 kg (-16 %, p < 0.001). BMI decreased from 35 ± 6 to 29 ± 7 kg/m², along with reductions in waist circumference (109 ± 16 to 92 ± 12 cm) and waist-to-height ratio (0.66 ± 0.1 to 0.56 ± 0.1) (all p < 0.001). Fat mass largely reduced from 42 ± 13 to 27 ± 11 kg (-35 %, p < 0.001), while fat-free mass slightly decreased from 53 ± 9 to 50 ± 7 kg (-5.1 %, p < 0.001). By contrast, skeletal muscle mass was preserved (from 31 ± 8 to 31 ± 7 kg, p = 0.151). Metabolic parameters were also improved, including $HbA_{1c}$ (from 5.5 ± 0.4 % to 5.2 ± 0.1 %, p = 0.007), fasting plasma glucose (from 93 ± 12 to 84 ± 9 mg/dl, p < 0.001), fasting insulin (from 17 ± 15 to 12 ± 9 µIU/ml, p = 0.002) and HOMA-IR (from 4.2 ± 4.7 to 2.5 ± 2.1, p = 0.001). Lowering body weight and BMI was both positively correlated with the reduction in fat mass (r = 0.762 and r = 0.738, respectively, p < 0.001 for both) and with the improvements in both insulin (r = 0.527, p < 0.01) and HOMA-IR (r = 0.465, p < 0.05).

**Conclusions:** In a RWE study, 24 weeks of tirzepatide treatment led to significant improvement on body weight, BMI and fat mass, together with preservation of lean skeletal muscle mass, and improved glycaemic control and insulin sensitivity.

## A39

### Metabolic heterogeneity in gestational diabetes: a focus on insulin sensitivity and secretory capacity

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**Background:** Identifying metabolic heterogeneity in gestational diabetes (GD)

is an important step toward precision diabetology, as uniform diagnostic criteria often mask distinct pathophysiological subtypes.The aim of this study was to identify distinct metabolic sub-phenotypes in GD based on insulin sensitivity and beta-cell secretory capacity.

**Methods:** Study included 90 pregnant women who underwent 75 g 2-hour OGTT between 24 – 28 weeks of gestation. Based on the results, participants were divided into groups: Group A (GD, n = 50) and B (NGT, n = 40). We analysed maternal age, pre-conception BMI, and family history of type 2 diabetes (T2D). To evaluate metabolic profiles, the Matsuda Index (MI) and Strumvoll 2 Index (S2I) were used as markers of insulin sensitivity and secretion.

**Results:** Age did not differ significantly between the study groups (Group A: 34.78 ± 0.82 vs. B: 31.36 ± 0.79 years; p = 0.396). However, group A showed a significantly higher pre-conception BMI (26.47 ± 0.82 vs. 22.48 ± 0.25 kg/m²; p < 0.01) and higher prevalence of family history of T2D (64.7 % vs. 30 %; p < 0.001). Metabolic assessment showed Group A had significantly lower MI: 3.25 ± 0.34 vs. 6.55 ± 0.67; p = 0.01 and reduced S2I: 289.93 ± 3.29 vs.806.47 ± 4.54; p < 0.01. To explore heterogeneity, Group A was stratified into clusters using the 25th percentile thresholds for MI and S2I within the GD cohort. Cluster 1 (resistant, 13.2 %) was defined by MI £ 2.0, Cluster 2 (Secretory Deficit) by S2I < 275.0 and 3 as mixed phenotype (29.7 %). Differences were observed across clusters in pre-conception BMI (Cluster 1: 26.8 vs. 2: 24.1 vs. 3: 25.4 kg/m²; p = 0.009) and insulin sensitivity (MI: 1.81 vs. 4.98 vs. 3.01; p < 0.001). Structural differences via S2I approached significance (Cluster 1: 296.7 vs. 2: 274.0 vs. 3: 288.4; p = 0.054).

**Conclusion:** Our study confirms GD is highly heterogeneous condition, characterised by distinct metabolic sub-phenotypes driven by varying degrees of insulin resistance and secretory failure. In line with this, recognising these clusters particularly high-BMI resistant phenotype represents vital step toward precision medicine and more personalised treatment in GD.

## A40

### Artificial intelligence-based retinal screening for cardiometabolic prevention: a 3-month real-world evidence study

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**Aims/Hypothesis:** Overweight, obesity, and type 2 diabetes (T2DM) increase the risk of microvascular complications, including diabetic retinopathy (DR). AI-based retinal screening may enable early detection of retinal damage and support cardiometabolic prevention. This study aimed to assess the prevalence of positive AI-based retinal screening and its association with glycaemic and vascular parameters in a real-world prevention setting.

**Methods:** During a 3-month period, 301 consecutive adults with overweight, obesity, or T2DM were recruited. All participants underwent comprehensive cardiometabolic assessment including anthropometric measures, fasting glucose, $HbA_{1c}$, carotid intima-media thickness (cIMT), carotid stenosis, and flow-mediated dilation (FMD). Retinal screening was performed using the Aireen AI system. Statistical analyses included ANOVA and multivariate logistic regression.

**Results:** Only 42 patients (the 14 %) resulted positive at the retinal screening (RS+), and a subsequent visit with the ophtalmologist confirmed the retinal alteration in all. RS+ prevalence increased progressively with worsening glycaemic status: from 21 % (fasting glucose < 100 mg/dl) to 29 % (between 100 and 125 mg/dl) to 50 % (≥ 126 mg/dl), and from 10.3 % ($HbA_{1c}$ < 5.7 %) to 20 % (between 5.7 % and 6.5 %) to 69 % ($HbA_{1c}$ > 6.5 %), p < 0.001 for both. Significant trends were also observed across vascular and endothelial parameters, with RS+ rates increasing across cIMT categories, from 26.8 % (< 0.75 mm) to 34.1 % (0.75 – 0.85 mm) to 39.1 % (> 0.85 mm) (p < 0.001), and decreasing across FMD categories, from 52.8 % (< 20 %) to 27.8 % (20 – 30 %) to 19.4 % (> 30 %) (p < 0.001). At multivariate logistic regression, RS+ was independently associated with $HbA_{1c}$ (OR 2.29; 95 % CI 1.65 – 3.17; p < 0.001), carotid stenosis (OR 1.06; 95 % CI 1.03 – 1.09; p < 0.001), and fasting glucose (OR 1.02; 95 % CI 1.01 – 1.03; p < 0.001).

**Conclusions:** Retinal positivity strongly reflects glycaemic burden and systemic vascular dysfunction. Integrating AI retinal assessment into cardiometabolic prevention programmes may enable timely interventions and support comprehensive cardiovascular risk management.

## A41

### Association between intake of food groups and all-cause mortality in diabetes subgroups: a prospective cohort study from the UK Biobank

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**Background and Objective:** Individuals with type 2 diabetes (T2D) are at increased risk for all-cause mortality, and risk may differ by diabetes subgroups. Therefore, this study aims to investigate the association between the intake of preselected food groups and all-cause mortality in people with diabetes and in diabetes subgroups.

**Methods:** We included 4290 participants with T2D from the UK Biobank with at least 2 available 24-h dietary recalls. Pre-selected food groups included vegetables and fresh fruit, potatoes, nuts, whole grains, dairy, and red meat. Hazard Ratios (HRs) with 95 % confidence intervals (95 % CIs) were estimated per serving size/day using multivariable Cox proportional hazard models. Separate analyses were performed for diabetes subgroups defined by $HbA_{1c}$ (≥ 48 vs. < 48 mmol/mol), waist circumference (≥ 102 vs. < 102 cm for men and ≥ 88 vs. < 88 cm for women), and diabetes duration (≥ 10 years vs. < 10 years).

**Results:** During a mean follow-up of 11.4 years, 602 deaths occurred. An increase of 1 serving/d of vegetables and fresh fruit (HR 0.96, 95 % CI 0.92; 1.00), nuts (HR 0.92, 95 % CI 0.86; 0.97), and whole grains (HR 0.97, 95 % CI 0.94; 1.00) was inversely associated with all-

cause mortality. Dairy showed a similar association, though the estimate was imprecise (HR 0.92, 95 % CI 0.81; 1.05). Higher potato intake was positively associated with all-cause mortality (HR 1.11, 95 % CI 1.01; 1.24), and the HR for red meat was 1.08 (95 % CI 0.99; 1.19). There was an indication for effect modification by diabetes subgroups, with some associations more pronounced in individuals with elevated waist circumference and higher $HbA_{1c}$ values.

**Conclusions:** In individuals with T2D, higher consumption of vegetables and fresh fruit, nuts, and whole grains was associated with lower all-cause mortality, while potato and red meat intake showed positive associations. There is an indication that associations differed across diabetes subgroups.

## A42

### Anti-obesity innovative therapies improve atherogenic lipoproteins and inflammatory biomarkers in adults with overweight or obesity: a 3-month prospective study

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**Aims/Hypothesis:** Obesity is strongly associated with atherogenic dyslipidemia and chronic low-grade inflammation, both key drivers of cardiovascular risk. Innovative anti-obesity therapies, including glucagon-like peptide-1 (GLP1) receptor agonists and dual glucose-dependent insulinotropic polypeptide (GIP)/GLP1 receptor agonists, may improve lipoprotein profile and exert early anti-inflammatory effects beyond weight reduction, particularly when combined with dietary interventions. This study evaluated the early effects of GLP1- and GLP1/GIP–based therapies combined with an anti-inflammatory Mediterranean diet on atherogenic lipoproteins, including small dense low-density lipoproteins (sdLDL), as well as inflammatory biomarkers and anthropometric parameters in adults with overweight or obesity with at least one obesity-related comorbidity.

**Methods:** In a prospective observational study 40 overweight or obese adults were evaluated over 3 months. Participants were stratified into traditional care (Group 1, n = 20), with very large use of metformin (90 %), and innovative therapy (Group 2, n = 20), with the use of semaglutide or tirzepatide (100 %). All participants received individualised nutritional counseling based on an anti-inflammatory Mediterranean diet. Anthropometric parameters, lipoprotein subfractions assessed by nuclear magnetic resonance spectroscopy, and circulating inflammatory biomarkers, including interleukin-6 (IL-6) and C-reactive protein (CPR), were measured at baseline and after 3 months of therapy.

**Results:** After 3 months, in relation to Group 1, patients in Group 2 showed a greater reduction in body weight (-13.1 % vs -0.5 %), BMI (-12.1 % vs -1.7 %), and waist circumference (-8.5 % vs -0.1 %), with $p < 0.001$ for all. Lipoprotein analysis revealed a significant reduction in atherogenic sdLDL, which was more pronounced in Group 2 than Group 1 (-75 % vs -54 %, $p = 0.032$). Group 2 further showed a significant decrease in both IL-6 (-36 %, $p = 0.004$) and CRP (-40 %, $p = 0.008$) levels.

**Conclusions:** Innovative anti-obesity therapies, combined with an anti-inflammatory dietary intervention, induced significant improvements in anthropometric parameters and favorable modulation of both atherogenic lipoproteins and inflammatory biomarkers during a 3-month follow-up.

## A43

### Artificial intelligence-based retinal screening and ocular parameters in cardiometabolic disease: an ophthalmologist-confirmed RWE study

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**Aims/Hypothesis:** AI-based retinal screening can detect retinal alterations requiring specialist confirmation and further characterisation through optical coherence tomography (OCT). This study evaluated the distribution of OCT-derived ocular parameters, including central retinal thickness (CRT) and intraocular pressure (IOP), in relation to glycaemic and vascular parameters among AI screened-positive patients.

**Methods:** 301 consecutive adults with overweight, obesity, or T2DM were recruited and underwent comprehensive cardiometabolic assessment including fasting glucose, $HbA_{1c}$, carotid intima-media thickness (cIMT), carotid stenosis, and flow-mediated dilation (FMD). Retinal screening was performed using the Aireen AI system. The 42 patients (14 %) who tested positive at AI-based retinal screening (RS+) underwent ophthalmologist-confirmed evaluation including OCT assessment of CRT and IOP. Statistical analyses included ANOVA, multivariate logistic regression, and Spearman rank correlation.

**Results:** In RS+ patients significant trends were observed across CRT and IOP categories in relation to glycaemic burden. CRT > 280 µm, indicative of early retinal thickening or diabetic macular edema, was significantly associated with $HbA_{1c}$ ($p = 0.035$) and fasting glucose ($p = 0.049$). Notably, 91.7 % of patients with CRT > 280 µm had $HbA_{1c}$ > 6.5 %, suggesting that worsening glycaemic control is strongly linked to structural retinal deterioration. IOP also showed a significant overall trend ($p < 0.001$), with 52.8 % of RS+ patients exhibiting high-normal values (> 16 mmHg). Spearman rank correlation analyses further supported these findings with CRT showing a significant positive correlation with $HbA_{1c}$ ($\rho = 0.444$, $p = 0.045$).

**Conclusions:** Among AI screen-positive patients, OCT-derived retinal structural parameters, particularly CRT, demonstrated meaningful associations with glycaemic burden, reinforcing the role of glycaemic control in microvascular and retinal damage. These findings suggest that retinal alterations detected by OCT may serve as an accessible window into systemic cardiometabolic dysregulation. Integrating AI-based screening with specialist OCT evaluation and glycaemic profiling may enhance early identification of high-risk individuals, supporting a more comprehensive and metabolically-informed approach to cardiovascular and microvascular risk management.

## A44

### Sciatic nerve microstructure predicts future sensory loss in diabetes: a prospective MR neurography study

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**Aims/Hypothesis:** Distal symmetric polyneuropathy is a heterogeneous complication of diabetes, and early identification of individuals at risk of sensory loss remains challenging. Quantitative sensory testing (QST) enables sensory phenotyping, while magnetic resonance neurography (MRN) allows non-invasive assessment of nerve microstructure structure. We hypothesised that microstructural alterations of the sciatic nerve, assessed by fractional anisotropy (FA) predict incident sensory loss (SL) in individuals with diabetes.

**Materials and Methods:** In this prospective observational study, 64 individuals with diabetes (type 2: n = 51; type 1: n = 13; age 61.6 ± 12.6 years; diabetes duration 10.0 [5.0 – 17.8] years) without SL at baseline underwent QST-based phenotyping and MRN of the sciatic nerve. Participants were classified as healthy, thermal hyperalgesia, or mechanical hyperalgesia. Median follow-up was 6.3 years. Incident SL was the primary endpoint. Cox regression adjusted for age, diabetes duration, renal function, and baseline phenotype was used to assess the predictive value of FA.

**Results:** At baseline, 26.6 % were classified as healthy, 39.1 % as thermal hyperalgesia, and 34.4 % as mechanical hyperalgesia. FA showed a decreasing trend across phenotypes. During follow-up, 17 participants developed SL, corresponding to an incidence 4.21 per 100 person-years. Lower baseline FA independently predicted incident SL (HR 1.014 per 0.01 decrease; 95 % CI 1.006 – 1.022; $p < 0.001$). ROC analysis identified an optimal FA cut-off of < 0.405 (AUC 0.718). Participants below this threshold had a markedly increased risk of SL (HR 7.986; 95 % CI 2.800 – 22.782; $p < 0.001$).

**Conclusions:** Structural alterations of the sciatic nerve precede clinically overt sensory loss in diabetes, indicating early proximal involvement. These findings provide mechanistic insight into the early structural progression of diabetic neuropathy, rather than immediate clinical risk stratification.

## A45

### Unmasking a rare complication: metformin-associated lactic acidosis in the setting of alcohol consumption

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Metformin-associated lactic acidosis (MALA) is a rare, but potentially life-threatening complication with a mortality rate up to 30 – 50 %. Metformin is a biguanide antidiabetic drug that lowers blood glucose primarily by inhibiting hepatic gluconeogenesis and mitochondrial complex I, thereby reducing ATP production. This shifts metabolism toward anaerobic glycolysis, increasing lactate production. Lactic acidosis has become relatively uncommon in clinical practice, therefore it is often overlooked in the initial evaluation. Risk factors primarily include renal impairment, along with conditions that further disrupt lactate elimination such as sepsis, cirrhosis, as well as chronic alcohol consumption (1). A 69-year-old female patient with a history of chronic alcohol abuse and type 2 diabetes mellitus treated with metformin was found unresponsive at her home. Prehospital evaluation showed hypoglycaemia; administration of parenteral glucose led to improvement in her mental status. Heteroanamnesis later revealed that days prior to her episode of unconsciousness, she had experienced nausea, dizziness and loss of appetite, whilst her medication compliance was unreliable. Laboratory findings demonstrated moderate renal impairment (GFR 49 ml/min), elevated liver enzymes (AST: 96 U/l, ALT: 47 U/l), elevated plasma ethanol concentration (92.0 mg/dl), and ketonuria (3.9 mmol/l). Arterial blood gas analysis revealed severe metabolic acidosis (pH: 7.068, $cHCO_3$(st): 8.4 mmol/l, $pCO_2$: 23.0 mmHg) with markedly elevated lactate levels (cLac: 17 mmol/l) and a highly increased anion gap (17.5 mmol/l). Considering the patient's history and clinical findings, high anion gap metabolic acidosis was likely due to metformin-associated lactic acidosis, precipitated by acute alcohol consumption and renal impairment as a contributing factor. MALA remains a diagnosis of exclusion. Conditions leading to high lactate metabolic acidosis – e. g. toxicological and non-toxicological etiologies – should be ruled out. The patient received supportive care aimed at restoring metabolic and electrolyte disturbances, with full recovery. Thorough evaluation, prompt recognition and early treatment are essential for optimal outcome measures.

## A46

### Cardiovascular risk in patients with familial hypercholesterolemia and type 2 diabetes: beyond lipoprotein (a)

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**Introduction and Aim:** Lipoprotein(a) [Lp(a)] is a genetically determined, independent cardiovascular risk factor and an important contributor to residual cardiovascular risk despite contemporary lipid-lowering therapy. Patients with familial hypercholesterolemia (FH) represent a high-risk population, and the coexistence of type 2 diabetes mellitus (T2DM) may further increase this risk. However, the contribution of Lp(a) in this setting remains insufficiently defined. This study aimed to assess the impact of T2DM on incident cardiovascular events in patients with FH and to evaluate the role of elevated Lp(a) in this context.

**Material and Methods:** A retrospective cohort study included 246 patients treated at a Department for Lipid disorders of Clinic for Endocrinology, diabetes and metabolic diseases University Clinical Center of Serbia with a three-year follow-up on statin therapy. FH was defined by a Dutch Lipid Clinic Network (DLCN) score ≥ 3. Patients with FH were stratified according to the presence of T2DM into two groups. Lipid parameters, including Lp(a), were measured using standard laboratory methods. Elevated Lp(a) was defined as > 0.3 g/l. Incident cardiovascular events were identified

from medical records. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate.

**Results:** Among patients with FH, those with T2DM had a significantly higher incidence of cardiovascular events compared with those without diabetes (21.8 % vs. 5.6 %, p = 0.01). Elevated Lp(a) levels did not differ significantly between groups (25.5 % vs. 33.5 %, p > 0.05). In FH patients with T2DM who developed incident cardiovascular events only a minority had elevated Lp(a) (17.2 %).

**Conclusion:** In patients with FH, coexistence of T2DM was associated with a markedly higher risk of incident cardiovascular events. These findings suggest that the increased cardiovascular risk observed in FH patients with T2DM is not primarily driven by elevated Lp(a), supporting a more intensive approach to traditional cardiovascular risk factor management.

## A47

### Peripheral neuropathy and heart failure in patients with type 2 diabetes mellitus

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**Background:** Heart failure (HF) and diabetic peripheral neuropathy (DPN) are common complications of type 2 diabetes mellitus (T2DM). However, the relationship between these conditions and the potential influence of sex and age remain insufficiently studied.

**Aim:** To evaluate the association between diabetic peripheral neuropathy and heart failure with preserved ejection fraction (HFpEF) in patients with T2DM.

**Materials and Methods:** A total of 340 patients with T2DM were included (median age 63.5 years; 221 men and 119 women). Median $HbA_{1c}$ was 7.2 % [6.4 – 8.6], and median diabetes duration was 6.0 [2.0 – 12.0] years. HFpEF (EF > 50 %) was diagnosed based on clinical and echocardiographic data. DPN was diagnosed according to clinical symptoms and standardised assessments of tactile, pain, and temperature sensitivity, as well as Sudoscan and electroneuromyography. Statistical analysis included Fisher's exact test, odds ratios (OR) with 95 % confidence intervals, multiple logistic regression with interaction analysis, and the Mann-Whitney U test with Bonferroni correction.

**Results:** DPN was detected in 208 patients (61.2 %), while 132 patients (38.8 %) had no neuropathy. HF was present in 180 of 208 patients with DPN (86.5 %) and in 100 of 132 patients without DPN (75.8 %). A significant association between DPN and HF was observed in the overall cohort (OR = 2.06; 95 % CI: 1.17 – 3.61; p = 0.013). Patients with DPN had longer diabetes duration (8.0 vs 3.5 years; p < 0.001) and higher $HbA_{1c}$ levels (7.55 % vs 6.9 %; p = 0.003). Sex-stratified analysis showed a significant association in men (OR = 3.05; 95 % CI: 1.55 – 6.00; p = 0.001) but not in women. In multivariable regression, female sex was an independent protective factor for DPN (aOR = 0.44; p < 0.001), whereas older age increased risk (aOR = 1.03 per year; p = 0.016).

**Conclusions:** DPN is significantly associated with HFpEF in patients with T2DM. This relationship demonstrates a pronounced sex-specific pattern, being present in men but not in women.

## A48

### Modulation of inflammatory pathways by SGLT2 inhibitors: a new frontier in cardiorenometabolic research

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Previous studies and meta-analyses have shown that sodium–glucose cotransporter-2 inhibitors (SGLT2i) suppress pro-inflammatory M1 macrophage activation, promote anti-inflammatory M2 phenotypes, and reduce the release of cytokines – including interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) – through multiple mechanistic pathways. This prospective observational study aimed to evaluate the effect of SGLT2i therapy on serum inflammatory markers in patients with type 2 diabetes mellitus (T2DM) complicated by heart failure and chronic kidney disease (CKD), compared with standard of care. We consecutively enrolled 110 patients over 12 months. Fifty-nine participants were initiated on SGLT2 inhibitor therapy. Results are expressed as mean ± standard deviation or median (interquartile range [IQR]). A p-value of 0.05 was considered significant. At baseline (n = 110), the mean age was 69.63 ± 8.97 years, median diabetes duration was 6 years. Median concentrations of inflammatory and metabolic biomarkers were as follows: IL-6, 29.7 pg/ml (IQR 343.25); TNF-α, 14.0 pg/ml (IQR 102.3); VCAM-1 (vascular adhesion molecule-1), 180.2 ng/ml (IQR 60.25); RANTES (Regulated upon Activation, Normal T cell Expressed and Secreted), 2424.5 pg/ml (IQR 1497.85); hsCRP, 2.71 mg/l (IQR 4.17); and ferritin, 107.06 ng/ml (IQR 151.82). In univariate analysis, N-terminal pro-B-type natriuretic peptide (NT-proBNP) was inversely correlated with estimated glomerular filtration rate (eGFR; Spearman's ρ = -0.328, p = 0.01) and positively correlated with urinary albumin-to-creatinine ratio (UACR; Spearman's ρ = 0.225, p = 0.028). Additionally, eGFR demonstrated significant inverse correlations with both VCAM-1 (Spearman's ρ = -0.207, p = 0.039) and hsCRP (Spearman's ρ = -0.210, p = 0.037). The significant inverse correlations between eGFR and both VCAM-1and hsCRP align with established evidence linking declining renal function to heightened systemic inflammation and endothelial activation. These findings reinforce the concept that declining renal function is intimately associated with endothelial activation and systemic inflammation.

## A49

### Longitudinal dynamics of quantitative sensory testing phenotypes and C-fiber function in diabetic sensorimotor polyneuropathy

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**Aims/Hypothesis:** Diabetic sensorimotor polyneuropathy (DSPN) is characterised

by heterogeneous sensory dysfunction, but the temporal stability of quantitative sensory testing (QST) phenotypes and their relationship to early C-fiber dysfunction remain incompletely understood. We hypothesised that longitudinal assessment of QST and C-fiber excitability can identify early functional changes in DSPN progression.

**Methods:** In a longitudinal observational study, 39 participants (6 with normal glucose tolerance, 33 with diabetes) were re-evaluated after 1 – 2 years. Assessments included clinical neuropathy scores (NDS/NSS), QST-based sensory phenotyping (healthy, thermal hyperalgesia [TH], mechanical hyperalgesia [MH], sensory loss [SL]), and slowly depolarising transcutaneous electrical stimulation to assess C-fiber excitability. Longitudinal changes in thermal and mechanical detection thresholds, pain thresholds, and electrically evoked pain responses were analysed. Subgroup analyses were performed to identify early functional abnormalities and their evolution over time.

**Results:** Overall, 48 % of participants with diabetes (n = 16) retained their baseline QST phenotype. MH and SL phenotypes remained stable, whereas healthy and TH phenotypes showed bidirectional transitions. At baseline, the SL group exhibited elevated detection and pain thresholds compared with all other phenotypes. Participants with normal glucose tolerance showed no significant changes in C-fiber parameters during follow-up. Among participants with diabetes, a subgroup (n = 11) showed reduced heat pain sensitivity (HPT $z < -0.5$) despite preserved electrically evoked pain responses (NRS ≥ 6), suggesting early impairment of peripheral nociceptive signalling. Longitudinally, this subgroup showed decreasing electrically evoked pain responses while HPT remained low, consistent with progressive C-fiber dysfunction.

**Conclusions:** QST phenotypes in DSPN show variable longitudinal stability, with greater instability in healthy and thermal hyperalgesia phenotypes than in mechanical hyperalgesia and sensory loss. Combined assessment of QST and C-fiber excitability may help detect early functional deterioration not captured by phenotype classification alone.

## A50

### Productivity-adjusted life years lost due to type 2 diabetes by socioeconomic position in Germany in 2022 and 2060

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**Aims:** To estimate age- and sex-specific productivity-adjusted life years (PALYs) lost due to type 2 diabetes (T2D) by socioeconomic position (SEP) in 2022 and 2060.

**Methods:** We used an established projection model to estimate age- and sex-specific productivity losses associated with T2D by SEP in working-age (20 – 69 years) while accounting for future trends in mortality and T2D incidence, using nationally representative and publicly available data for Germany. Depending on the data source, individual and area-level indices were used to define three SEP groups: low, medium, and high. PALY lost were calculated as the sum of years of life lost (YLL), defined as the difference in remaining life expectancy between individuals with and without T2D, and years of productivity lost (YPL) due to reduced labour force participation, presenteeism, and absenteeism, based on SEP-specific inputs from representative studies.

**Results:** Productivity losses were highest among persons with low SEP, followed by medium and high SEP. In 2022, 20-year-old men with T2D and low SEP are expected to lose 11.4 PALYs (9.9 YPL, 1.5 YLL) up to age 69, whereas PALYs lost with high SEP were 3.8 (2.7 YPL, 1.1 YLL) compared with those without T2D. A similar socioeconomic gradient was observed among women and remained largely unchanged until 2060. On the population level, T2D resulted in 9.5 million PALYs lost in 2022, most of which occurred in persons with low SEP (5.6 million), compared with 0.8 million with high SEP. These estimates combine both sexes and include YPL and YLL, and are projected to increase to 13.6 million by 2060, mainly due to an increase in the number of persons with T2D.

**Conclusions:** T2D-related productivity losses were higher in persons with low than high SEP, with no evidence for differences by sex. PALYs lost declined with age and were predominantly driven by YPL.

## A51

### Fat-free mass index and fat mass index in recently diagnosed diabetes

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**Aims/Hypothesis:** To investigate the combined effect of fat-free mass index (FFMI, $kg/m^2$) and fat mass index (FMI, $kg/m^2$) on hepatic lipid content (HLC) and insulin sensitivity in individuals with recently diagnosed diabetes.

**Methods:** Participants from the German Diabetes Study (GDS) with available FMI and FFMI measured by bioimpedance analysis were included. Multivariable linear regression models with interaction terms were used to determine sex-specific associations of FMI and FFMI as well as their associations with HLC measured by $^1H$ magnetic resonance spectroscopy, and insulin sensitivity, examined by hyperinsulinaemic–euglycaemic clamp, in glucose-tolerant individuals (controls; n = 200), participants with type 1 (n = 364) and type 2 diabetes (n = 555).

**Results:** FMI was positively associated with FFMI in women and men with and without diabetes (all $p < 0.001$), with the association being more pronounced in women than in men (controls: $\beta = 1.44$; type 1 diabetes: $\beta = 0.89$; type 2 diabetes: $\beta = 0.95$; all $p < 0.001$). Next, in type 2 but not in type 1 diabetes (all $p > 0.05$), interactions between FMI and FFMI were observed for HLC ($\beta = -0.05$, $p < 0.001$ in men; $\beta = -0.02$, $p = 0.044$ in women) and insulin sensitivity ($\beta = 0.01$, $p = 0.002$ in both sexes). In controls, men but not women showed an interaction between FMI and FFMI for insulin sensitivity ($\beta = 0.005$; $p = 0.027$; $\beta = 0.003$, $p = 0.782$) but not for HLC (men: $\beta = -0.01$, $p = 0.441$; women: $\beta = -0.02$, $p = 0.551$).

**Conclusions:** Our findings demonstrate that fat-free mass modifies the metabolic impact of adiposity, with higher

FFMI mitigating the detrimental associations of FM with hepatic lipid accumulation and insulin resistance in people with type 2 diabetes.

## A52

### Mitochondrial remodeling and secretome signaling mediate improved insulin signaling upon electrical-pulse stimulation in insulin-resistant skeletal muscle

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Exercising improves insulin sensitivity, mitochondrial oxidative capacity and lipid repartitioning in skeletal muscle (SkM), but the role of mitochondrial remodeling upon exercising remains unclear. In addition, exercising results in the release of myokines, which might contribute to improved insulin sensitivity. We therefore investigated whether muscle contraction, mimicked by electrical pulse stimulation (EPS), mitigates impairment of insulin signaling in lipid-stressed muscle cells and explored potential roles of mitochondrial remodeling and contraction-derived secreted factors. Differentiated C2C12 myotubes were exposed to palmitate (0.3 mM) to induce lipid-mediated insulin resistance and stimulated with EPS (1 Hz, 11.5 V) for 24 hours. Insulin signaling pathways and proteins involved in mitochondrial dynamics were evaluated using Western blotting, respiratory capacity by high-resolution respirometry, and lipotoxins by liquid chromatography–tandem mass spectrometry. The influence of contraction-derived factors was examined using conditioned media from EPS-treated myotubes. Palmitate reduced insulin-stimulated AKT phosphorylation at Ser473 and Thr308 by 41 % and 54 %, respectively vs untreated (CON) cells (both $p < 0.01$). EPS partially restored this response with increased AKT phosphorylation compared to palmitate alone (Ser473, $p < 0.01$; Thr308, $p < 0.05$) and reductions of 22 % (Ser473) and 37 % (Thr308) versus CON, EPS also reduced the fusion proteins mitofusin 1 and 2 by 20 % ($p < 0.01$) and 15 % ($p = 0.05$) respectively, while increasing the fission marker dynamin-related protein 1 (+23 %; $p < 0.01$) and decreasing the mitophagy protein PINK1 (-23 %; $p = 0.05$) in palmitate-treated cells, suggesting a shift in mitochondrial dynamics toward a more fragmented phenotype. These changes occurred without alterations in mitochondrial respiratory function or lipotoxins. Interestingly, conditioned media from EPS-stimulated cells increased AKT(Ser473) phosphorylation in palmitate-treated myotubes by 50 % compared to palmitate alone. In conclusion, EPS-induced contractile activity partially reverses lipid-induced insulin resistance in muscle cells. However, despite changes in markers of mitochondrial dynamics, EPS did not alter mitochondrial respiration but rather exercise-induced secreted factors might mediate improvements in insulin sensitivity.

## A53

### Optimised unbiased morphological analysis identifies lower mitochondrial size and content in metabolic dysfunction-associated steatotic liver disease

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**Background and Aims:** Impaired mitochondrial plasticity contributes to metabolic dysfunction-associated steatotic liver disease/steatohepatitis (MASLD/MASH) and recently developed as relevant therapeutical target. This abnormality results from changes in intrinsic mitochondrial activity or content/morphology. The gold-standard for assessing mitochondrial content/morphology is transmission electron microscopy (TEM), but manual analysis is time-consuming and potentially biased. We developed an AI-based automated TEM-based approach to quantify hepatic mitochondrial features and evaluated the accuracy of surrogate biomarkers of mitochondrial content.

**Methods:** Dedicated 2D U-shaped neural network (U-Net) models were trained to assess mitochondrial density and morphology from TEM of liver samples from mice and humans with and without MASLD/MASH. Results were compared with conventional biomarkers (citrate synthase activity, mtDNA copy number, cardiolipin level and OXPHOS complexes protein content) and the proteomic-based mitochondrial enrichment factor (MEF).

**Results:** U-Net models showed excellent agreement with manual annotations for quantifying hepatic mitochondrial density (intraclass correlation coefficient in mice: 0.977 and humans: 0.986). TEM analysis revealed reduced mitochondrial number, but increased size in murine MASH (all $p < 0.05$ vs control). In humans with MASLD, mitochondrial area and density tended to be lower ($p = 0.06$ and 0.07), while size was decreased by 22 % as compared to controls ($p < 0.05$). While conventional biomarkers showed no associations with TEM-derived mitochondrial features ($r = -0.46 – 0.40$, all $p > 0.05$), MEF correlated with mitochondrial area ($r = 0.68$ in mice and $r = 0.42$ in humans, both $p < 0.05$).

**Conclusion:** Automated U-Net-driven segmentation and analysis enables rapid, robust and unbiased quantification of mitochondrial content from TEM images. Its application showed a reduction of features of mitochondrial mass in humans with MASLD and identified the MEF as a valid surrogate index of hepatic mitochondrial content.

## A54

### Isolation of extracellular fluids reveals novel secreted bioactive proteins from muscle and fat tissues

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Proteins secreted by cells transmit information between neighboring cells and distant tissues, playing a central role in inter-organ communication. The development of insulin resistance is not solely attributable to intracellular changes but is strongly influenced by this cross-talk, particularly involving myokines released from skeletal

muscle and adipokines from adipose tissue. The secretome underlying these interactions is modulated by physical activity, obesity, and diabetes, and secreted proteins can exert both beneficial and detrimental effects depending on tissue, concentration, and context. Systematic identification and functional characterisation of myokines and adipokines are therefore essential to understand their roles in systemic metabolic regulation. Studying myokines and adipokines by proteomics is challenging because serum and plasma contain highly abundant proteins that limit detection of low-abundance factors. To overcome this, we developed a method to analyse the proteome of extracellular fluids (EF) from mouse muscle and adipose tissue. Unlike tissue lysates or plasma, the EF proteome provides a more specific view of proteins actually secreted into the interstitial space. Mass spectrometry analysis of EFs from mice subjected to physiological perturbations, such as exercise or cold exposure, enabled quantification of many candidate myokines and adipokines. Using this approach, we identified prosaposin (PSAP) as a secreted product of both muscle and adipose tissue. PSAP expression and secretion stimulate thermogenic gene expression, increase mitochondrial respiration, and elevate whole-body energy expenditure. Together, these findings demonstrate the utility of EF isolation as a discovery platform for adipokines and myokines and identify prosaposin as a potential regulator of whole-body energy metabolism.

## A55

### Blunted postprandial acylcarnitine suppression reflects metabolic inflexibility in prediabetes and type 2 diabetes

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**Background and Aims:** Acylcarnitines (AcylCarn), intermediates of fatty acid metabolism, reflect mitochondrial substrate handling and may serve as sensitive markers of early metabolic dysfunction. However, dynamic changes in postprandial AcylCarn profiles remain insufficiently explored in prediabetes and type 2 diabetes mellitus (DM).

**Materials and Methods:** The study involved 45 participants: 13 healthy controls, 17 with prediabetes and 15 with type 2 DM. Ages ranged from 28 to 76 years. The mixed meal tolerance test MMTT meal consisted of yoghurt and a granola bar. Plasma samples were collected in the fasting state and at 30, 60 and 120 minutes postprandially to assess serum glucose, C-peptide and AcylCarn profiles (short-chain AcylCarn (SCAC, C2-C4), medium-chain AcylCarn (MCAC, C5-C10) and long-chain AcylCarn (LCAC, C12-C18)). Statistical analysis was performed using the Kruskal-Wallis test.

**Results:** AcylCarn concentrations changed significantly during the MMTT. At 30 minutes, SCAC concentrations decreased more in the control group than in the prediabetes group ($p = 0.008$), but not in the DM group. Similarly, MCAC decreased more in the control group compared to prediabetes ($p = 0.0004$) and DM groups ($p = 0.017$). LCAC also decreased more in the control group than in the prediabetes group at 30 minutes, but not in the DM group. At 60 minutes, SCAC decreased by 33.6 % from baseline in the control group (IQR 28.6 – 37.2), significantly more than in the prediabetes group (5.1 %, IQR -1.6 – 20.3, $p = 0.004$) and the DM group (15.9 %, IQR 0 – 23.1, $p = 0.045$). MCAC decreased by 42.1 % (IQR 38.5 – 54.7) in the control group, compared with prediabetes (27.8 %, IQR 4.1 – 34.9, $p = 0.002$) and DM (13.9 %, IQR 5.4 – 41.9, $p = 0.008$). LCAC decreased by 39.5 % (IQR 54.4 – 78.3) in the control group, more than the prediabetes group (19.6 %, IQR 6.4 – 27.1, $p = 0.011$), but not the DM group.

**Conclusion:** Healthy individuals demonstrate pronounced postprandial suppression of acylcarnitines, whereas this response is attenuated in prediabetes and type 2 DM, indicating impaired metabolic flexibility.

## A56

### Gut microbiome alterations and dietary effects in Georgian T2DM patients

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**Aims:** This study aimed to evaluate the gut microbiome composition in Georgian individuals using faecal microbiological methods and to assess how its modification, including the use of traditional fermented products such as Matsoni, affects metabolic parameters in patients with type 2 diabetes mellitus (T2DM).

**Methods:** A total of 134 Georgian adults were enrolled, including 67 patients with T2DM and 67 healthy controls matched for age and sex. Baseline laboratory investigations included fasting plasma glucose (FPG), glycated haemoglobin ($HbA_{1c}$), lipid profile and C-reactive protein (CRP). Gut microbiota composition was assessed through conventional faecal microbiological analysis using stool culture techniques to quantify major bacterial groups such as Lactobacillus, Bifidobacterium, Escherichia coli and opportunistic pathogens. The T2DM group underwent a 12-week intervention consisting of a high-fiber traditional Georgian diet, daily consumption of Matsoni (200 – 250 g), reduced intake of processed foods and probiotic supplementation. Post-intervention laboratory and faecal microbiology assessments were performed. Matsoni was included due to its richness in lactic acid bacteria, which support beneficial gut microbiota and metabolic regulation.

**Results:** At baseline, T2DM participants demonstrated elevated FPG ($8.9 \pm 1.7$ mmol/l) and $HbA_{1c}$ ($7.8\ \% \pm 1.2$) compared to controls ($5.2 \pm 0.6$ mmol/l and $5.4\ \% \pm 0.4$). CRP levels were also higher ($4.2 \pm 1.5$ mg/l). Faecal microbiological analysis revealed reduced counts of beneficial bacteria (Lactobacillus, Bifidobacterium) and increased levels of opportunistic microorganisms such as Clostridium spp. and Candida spp. Following the intervention, $HbA_{1c}$ decreased to $6.9\ \% \pm 0.9$, FPG to $7.1 \pm 1.3$ mmol/l, and CRP levels declined by 28 %. Regular Matsoni intake was associated with increased Lactobacillus counts and improved microbial balance.

**Conclusion:** Gut microbiome dysbiosis, assessed via faecal microbiology, is strongly associated with T2DM in Georgian individuals. Dietary interventions incorporating traditional fermented foods like Matsoni significantly improve both microbial composition and metabolic outcomes, supporting culturally adapted strategies for T2DM management and prevention.