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## Abstract Book

# **Oral Presentations**

## THE DEVELOPMENT AND IMPLEMENTATION OF AN INTEGRATED MULTI-MORBIDITY MODEL OF CARDIOVASCULAR-RENAL (KIDNEY)-METABOLIC CARE IN LONDON, UK

### LUNCH, NETWORKING & ORAL PRESENTATIONS

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**Background and Aims:** Our local population is ethnically diverse (47.2% non-white) with high levels of socioeconomic deprivation. One third are living with a long-term condition (LTC) and 26,583 people are living with two or more cardiorenal metabolic LTCs (chronic kidney disease (CKD), cardiovascular disease, diabetes). People with multiple LTCs often experience a lack of personalisation and co-ordination in care with multiple appointments in different settings. Our aim is to build a person-centred, holistic, horizontally and vertically integrated model of care for people with multiple LTCs across the interface, improve early identification of LTCs and optimise modifiable risk factors.

**Methods:** To develop an integrated model of care, six project sites were identified, one within each borough, across 4 acute hospitals and 72 GP practices. A validated risk stratification tool was embedded into electronic health records to detect patients at risk of developing CKD, ensure appropriate coding in primary care and ensure early optimisation of evidence-based treatments including ACE inhibitors, SGLT2-inhibitors and statins. Furthermore, a smaller cohort of patients were identified for complex and holistic case management. To support this and ensure rapid access to specialist advice, integrated multidisciplinary team meetings (MDTs) were implemented consisting of primary care clinicians and non-clinical staff including care co-ordinators and social prescribers, consultant diabetologist, nephrologist, cardiologist, geriatrician and two multi-specialist pharmacists.

**Results:** Primary care teams have identified 15,448 patients with potential uncoded CKD, of which, 2,412 (16%) patients have been reviewed, coded and optimised on evidence-based treatments. In addition, 747/1,748 (43%) high-risk patients have been reviewed for complex case management. MDTs have successfully improved communication and timely access to specialist advice, whilst reducing referrals to secondary care.

**Conclusions:** An integrated, multidisciplinary and multi-specialty model of care can facilitate early identification of modifiable risk factors for cardiorenal metabolic LTCs and deliver high quality person-centred, holistic care for patients closer to home.

## THE ROLE OF INTEGRATED MULTI-SPECIALIST PHARMACISTS IN THE DELIVERY OF A MULTI-MORBIDITY CARDIOVASCULAR-RENAL (KIDNEY)-METABOLIC MODEL OF CARE IN LONDON, UK

### LUNCH, NETWORKING & ORAL PRESENTATIONS

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**Background and Aims:** Significant health inequalities exist in our local population with a high burden of cardiorenal metabolic (CRM) diseases from an earlier age, associated with premature mortality. Pharmacists are integral in delivering holistic, person-centred care through medicines optimisation, addressing polypharmacy and improving adherence. Our aim is to embed multi-specialist pharmacists (MSPs) into an integrated model of care to transform horizontal and vertical communication across the interface, improve health outcomes by optimisation of evidence-based treatments and promote medicines safety.

**Methods:** This model is driven by two MSPs working as the primary and secondary care interface to streamline care across the CRM specialities in three hospital trusts, provide specialist education and training (E&T) to colleagues in primary care, support rapid medicines optimisation through point of care testing clinics and support complex case management through integrated multidisciplinary team meetings (MDTs). The MSPs are developing a novel pathway to identify patients with stable chronic kidney disease (CKD) stage 3 and/or type 2 diabetes (T2D) in secondary care to be safely managed in primary care and promoting medicines safety in patients with eGFR less than 20 ml/min at high risk of hypoglycaemia (HbA1c less than 58 mmol/mol and taking insulin and/or sulfonylureas).

**Results:** MSPs are successfully delivering E&T to primary care teams and discussed over 50 patient cases in MDTs to date. A total of 83 patients in trust A identified with stable CKD stage 3, which 17/29 (59%) patients and 9/22 (41%) patients with T2D and CKD stage 3 in trust B reviewed to date, are suitable for repatriation to primary care. Trust A has identified 14 out of 41 patients at high risk of hypoglycaemia. Interventions include de-prescribing of sulfonylureas and patient education focusing on hypoglycaemia.

**Conclusions:** MSPs have a transformative role in providing integrated and comprehensive care to patients with CRM diseases across all health sectors.

## **SOCIAL ATTITUDES, FAMILY SUPPORT, AND SELF-STIGMA IN ADULT POLISH WOMEN USING ANTI-OBESITY MEDICATIONS**

### **LUNCH, NETWORKING & ORAL PRESENTATIONS**

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**Background and Aims:** Obesity and its consequences go beyond metabolic health. Individuals living with obesity face not only stigma, negative attitudes or prejudice but also social discrimination. This is especially important since family support can significantly influence treatment outcomes and adherence. The aim of this study was to evaluate social attitudes towards obesity, anti-obesity medications (AOMs) and patients' self-stigmatization. Additionally, we explored the role of family support and willingness to disclose treatment to others.

**Methods:** The study involved 829 adult women. Data was collected via a Computer-Assisted Web Interview (CAWI) method, using an original questionnaire.

**Results:** Current users of anti-obesity medications showed significantly lower self-stigma levels compared to non-users across all three assessed dimensions. Furthermore, women actively taking AOMs were more likely to openly discuss their treatment with close family members, which might have influenced treatment adherence.

**Conclusions:** Patients actively using AOMs reported lower self-stigma and fewer concerns about medication safety. Additionally, openness about treatment within their close family circle was associated with improved adherence. Promoting an environment where patients feel comfortable discussing their treatment with family members may positively impact the effectiveness of obesity management.

## STRATEGIES TO IMPROVE THERAPEUTIC COMPLIANCE OF CAREMELO PATIENTS

### LUNCH, NETWORKING & ORAL PRESENTATIONS

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**Background and Aims:** Background Therapeutic compliance has been defined as “the extent to which a person’s behaviour – taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider”. It was estimated by the researchers, that compliance rate of chronically ill patients is only 30-60%, depending on the settings. CaReMeLo patients are at high risk of non-compliance that is associated not only with poor treatment outcomes and higher mortality rates but also higher economic costs. That is why, it is crucial to implement strategies to improve therapeutic compliance in this group of patients.

**Methods:** Presented strategies are built on three main pillars: patient-centered consultation, therapeutic alliance and shared-decision making based on literature review and author’s experience.

**Results:** 1. Exploring patient perspectives (about the disease, medical history, life situation) 2. Addressing patient’s concerns (non-judgmental manner, empathy) 3. Explaining the diagnosis and treatment - anchoring diagnosis - using decision aids - using “pros and cons” technique 4. Setting SMART goal (specific, measurable, attainable, relevant, time) 5. Simplifying the therapeutic regimen (reducing the number of medications, administering in a single pill, replacing in case of side effects) 6. Self-monitoring (diaries, applications) 7. Motivational Interviewing (reflection statements, appreciation, summary)

**Conclusions:** The strategies to improve therapeutic compliance of CaReMeLo patients presented in the abstract are useful and worth implementing. They not only enable achieving better therapy goals in a primary care setting but also improve doctor-patient relationship.

**USING THE CONSTRAINED-DISORDER-PRINCIPLE-BASED SECOND-GENERATION ARTIFICIAL INTELLIGENCE SYSTEM FOR IMPROVING THE RESPONSE TO THERAPIES FOR CARDIOMETABOLIC DISORDERS.**

**LUNCH, NETWORKING & ORAL PRESENTATIONS**

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**Background and Aims:** Variability in metabolic parameters refers to the fluctuations in body mass index, systolic blood pressure, fasting glucose, and total cholesterol that occur within an individual during multiple health examination visits. These parameters have been extensively studied about various health outcomes. Biological variability and the emergence of resistance mechanisms to chronic therapies highlight the need for personalized treatment approaches. Inter-individual and intra-individual variability significantly affect how patients respond to chronic therapies, making it challenging to provide a single therapeutic regimen that consistently works for everyone. The dynamic nature of this variability further complicates the process of personalizing treatment. Although the mechanisms behind poor responsiveness to chronic medications are not yet well understood and can vary from one individual to another, current methods for addressing the loss of response are inadequate.

**Methods:** The Constrained Disorder Principle (CDP) offers a framework for understanding biological systems based on their inherent variability. This principle suggests that biological systems operate within dynamic boundaries that shift in response to both internal and external changes. An artificial intelligence system based on the CDP is an outcome-focused dynamic platform incorporating personalized variability signatures into therapeutic regimens. This system provides strategies to enhance treatment responses and mitigate the loss of effectiveness over time.

**Results:** By integrating variability into drug administration, this approach aims to develop more effective and personalized therapeutic strategies. Additionally, signatures of metabolic variability may help identify new biomarkers for early diagnosis, monitor immune-related disorders, and evaluate responses to immunotherapies. Using this system in patients with congestive heart failure has improved clinical and laboratory parameters, resulting in fewer emergency room visits and hospitalizations. Similar beneficial effects were observed in patients with cancer, chronic pain, and immune disorders.

**Conclusions:** In summary, employing platforms focusing on biological variability may offer a novel approach to developing personalized therapies for patients with cardiometabolic disorders.

## PREVALENCE AND IMPACT OF COMORBIDITIES IN PRIMARY SJÖGREN'S SYNDROME: A RETROSPECTIVE STUD

### LUNCH, NETWORKING & ORAL PRESENTATIONS

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**Background and Aims:** Patients with autoimmune diseases, such as primary Sjögren's syndrome (pSS), have a higher risk of developing comorbidities compared to the general population, particularly among women. Screening for these comorbidities is essential, as it impacts both the patient's quality of life and therapeutic decisions. However, epidemiological data on pSS-related comorbidities remain inconsistent, and no studies have been conducted in Castelo Branco, Portugal. This study aimed to assess the prevalence and relationship between the clinical expression of pSS and associated comorbidities in 47 patients from the Rheumatology Unit of the Local Health Unit of Castelo Branco (ULSCB), Portugal.

**Methods:** An observational, cross-sectional, and retrospective study was conducted, analyzing clinical, laboratory, demographic, and therapeutic data from patients' medical records. All participants met the 2016 classification criteria for pSS established by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). Disease activity and comorbidities were assessed using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and the Newcastle Sjögren's Stratification Tool (NSST).

**Results:** The mean age of participants was 65.3 years, with 43 out of 47 being women. The study revealed a high prevalence of comorbidities, including dyslipidemia (48.94%), hypertension (46.81%), obesity (38.30%), depression (27.66%), fibromyalgia (23.40%), and overweight (23.40%). Other conditions, such as secondary autoimmune diseases, hematological disorders, and cardiovascular complications, were also identified, highlighting the complexity of pSS.

**Conclusions:** The findings suggest that pSS patients are at risk of developing metabolic syndrome and further reinforce that pSS is a complex and multifaceted disease that requires a personalized therapeutic approach and integrated clinical follow-up involving multiple medical specialties. These patients would benefit from regular cardiovascular risk screening. Implementing early screening protocols and targeted interventions could improve prognosis and enhance patients' quality of life. Future research is essential to better understand the underlying mechanisms driving the interaction between pSS and its associated comorbidities.



## AN APPLICATION OF URINARY PEPTIDOMICS AND IN SILICO METHODS TO GUIDE MULTIFACTORIAL INTERVENTION IN CHRONIC KIDNEY DISEASE

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Chronic kidney disease (CKD) significantly contributes to global morbidity and mortality. Early, targeted intervention offers an ideal strategy for mitigating this burden. Peptidomic changes inform CKD onset, progression, and treatment strategies. We investigated the molecular effects of six therapeutic interventions in silico, alone and in combinations, on the urine peptidome to identify the most beneficial treatment for individual patients.

**Methods:** This study predicted major adverse kidney events (MAKE), defined as a  $\geq 40\%$  decline in estimated glomerular filtration rate (eGFR) or kidney failure (median follow up: 1.50 (95%CI 0.35, 5.0)), using the urinary peptidomic classifier CKD273 in a retrospective cohort of 935 participants. Treatment effects were assessed from previous studies of four drug-based interventions (MRA, SGLT2i, GLP1-RA and ARB), one dietary intervention (olive oil), and exercise. Fold changes in peptide abundance after treatment were recalibrated to align with randomized controlled trial outcomes and applied to patient-specific urinary profiles, simulating intervention effects and recalculating CKD273 scores. For combination treatments, the effects of multiple interventions were combined to model their cumulative impact.

**Results:** Simulated interventions demonstrated a significant reduction in median CKD273 scores, from 0.57 (IQR: 0.19–0.81) before to 0.039 (IQR: -0.192–0.363) after intervention ( $P < 0.0001$ ), when the most beneficial treatment or combination of treatments was applied individually. The combination of all available treatments was found optimal only for 17.6% of the patients and not the most frequently predicted optimal intervention. Patients with higher baseline CKD273 scores required more complex intervention combinations to achieve the greatest reduction in scores. The findings present potential individualized treatment strategies in CKD management.

**Conclusions:** This study supports the feasibility of in silico predicting effects of therapeutic interventions on CKD progression. By identifying the most beneficial treatment combinations for individual patients, this approach paves the way for precision medicine in CKD.

## TELOMERE LENGTH AS A BIOMARKER IN DIABETIC KIDNEY DISEASE

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Telomeres are DNA-protein structures at chromosome ends, ensuring genomic stability. In most somatic tissues, telomeres shorten with cell division, triggering apoptosis or senescence. However, data on telomere length in type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) remain limited. This study aimed to assess telomere length in patients with T2DM with and without CKD.

**Methods:** We examined 105 subjects divided into three groups. The first group included 65 patients with T2DM and CKD (age  $70.9 \pm 8.0$  years, diabetes duration  $5.9 \pm 2.5$  years, HbA1c  $7.1 \pm 1.7\%$ , creatinine  $145.0 \pm 87.0$   $\mu\text{mol/L}$ , eGFR  $44.0 \pm 11.0$  ml/min/1.73m<sup>2</sup>, ACR  $36.0 \pm 74.0$  mg/g). The second group included 25 patients with T2DM without CKD (age  $53.2 \pm 6.8$  years, diabetes duration  $3.7 \pm 2.2$  years, HbA1c  $7.6 \pm 2.2\%$ , creatinine  $89.6 \pm 14.9$   $\mu\text{mol/L}$ , eGFR  $81.3 \pm 12.2$  ml/min/1.73m<sup>2</sup>, ACR  $18.0 \pm 9.7$  mg/g). The third group included 15 controls (age  $50.3 \pm 3.8$  years, HbA1c  $5.45 \pm 0.3\%$ , creatinine  $100.7 \pm 22.5$   $\mu\text{mol/L}$ , eGFR  $83.0 \pm 22.8$  ml/min/1.73m<sup>2</sup>, ACR  $11.0 \pm 4.4$  mg/g). Telomere length was measured in whole blood using monochrome multiplex qPCR (T/S ratio). Statistical analysis included Student's t-test and correlation analysis.

**Results:** T/S ratio was higher in patients with T2DM and CKD ( $0.989 \pm 0.767$ ) and those with T2DM without CKD ( $1.11 \pm 0.789$ ) than in controls ( $0.535 \pm 0.341$ ,  $p < 0.05$ ). No difference was observed between T2DM groups. No correlation was found between telomere length and eGFR or ACR.

**Conclusions:** Telomere length is longer in T2DM patients. CKD does not contribute to telomere shortening. Further research is needed to determine the pathogenic and prognostic role of telomere changes in T2DM.

## TLT-1 AS A POTENTIAL INTERVENTIONAL TARGET IN CARDIOVASCULAR DISEASE.

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Platelets play a critical role in cardiovascular disease (CVD) progression. The triggering receptor expressed in myeloid cells-like transcript-1 (TLT-1), stored in platelet  $\alpha$ -granules, is released as a soluble fragment (sTLT-1) upon activation. Elevated sTLT-1 levels have been linked to coronary artery disease, acute coronary syndrome, left ventricular dysfunction, and heart failure. Here we aim to assess TLT-1's role in CVD progression and its potential as an interventional target.

**Methods:** We examined TLT-1 expression in human atherosclerotic lesions at various stages and induced atherosclerosis in genetic mouse models to assess its role in disease progression.

**Results:** High sTLT-1 levels were detected in CVD patients, prompting the analysis of human coronary artery specimens. TLT-1 was expressed in all stages of lesion development but was absent in non-diseased arteries. To evaluate its role in atherosclerosis, we crossed TLT-1-deficient mice onto an ApoE<sup>-/-</sup> background (DKO). DKO mice exhibited a twofold reduction in aortic lesion size after 4 and 12 weeks on a Western diet ( $p \leq 0.05$ ), independent of cholesterol and lesion macrophage content. However, they showed a >5% reduction in platelet activation ( $p < 0.05$ ). Intravital microscopy revealed a ninefold decrease in initial clot size after FeCl<sub>3</sub> injury ( $p < 0.01$ ), supporting TLT-1's role in platelet-endothelial interactions. Blocking TLT-1 in wild-type mice reduced aortic lesions after 8 weeks on a Western diet. Additionally, treatment with a human anti-TLT-1 single-chain antibody reduced platelet adhesion to collagen under flow conditions.

**Conclusions:** TLT-1 enhances platelet activation and adhesion to the endothelium, contributing to atherosclerosis progression. Its inhibition presents a potential therapeutic strategy to mitigate CVD.

## THE DUAL IMPACT OF CHOLESTEROL AND PULSE PRESSURE ON CHRONIC KIDNEY DISEASE OUTCOMES

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Chronic kidney disease (CKD), is a significant global health burn, that often is influenced by a complex interplay of cardiovascular and metabolic factors, including elevated cholesterol levels and high pulse pressure (PP). These factors have been identified as crucial drivers of chronic kidney disease (CKD) progression. This study aimed to evaluate the association between cholesterol levels, pulse pressure, and CKD outcome.

**Methods:** Materials and Methods: We conducted a prospective cohort study involving 139 adult patients with an estimated glomerular filtration rate (eGFR) greater than 30 ml/min/1.73m<sup>2</sup>. The mean follow-up period was two years. Comprehensive medical histories and detailed clinical data were collected for each participant. Levels of serum creatinine, eGFR, cholesterol, uricemia, and hemoglobin were measured at baseline and throughout the follow-up period. Appropriate statistical methods were employed to analyze the data. A p-value of less than 0.05 was considered statistically significant.

**Results:** RESULTS: 84 were male patients. The mean age of patients with elevated cholesterol levels was 55 ± 13.5 years. The mean creatinine and eGFR were 2.35±1.1 mg/dL and 54.5±13.2 mL/min/1.73 m<sup>2</sup>, respectively. 100 patients had hypercholesterolemia, and 75 patients had PP ≥ 60mmHg. We found a significant positive correlation between PP and high cholesterol levels p=0.014, and a significant correlation between eGFR and hypercholesterolemia p=0.06. By using the ANOVA test, we found a strong relation between CKD outcome (progression and mortality) and elevated PP, p ≤0.001.

**Conclusions:** Conclusion: Hypercholesterolemia emerged as a robust predictor of arterial stiffness and harmful CKD outcomes. Elevated cholesterol and pulse pressure were found to play a pivotal role in CKD progression. Therefore, early interventions targeting dyslipidemia and arterial stiffness are crucial for improving CKD outcomes. Healthcare providers should prioritize the management of these modifiable risk factors to enhance patient outcomes and slow the progression of CKD.

## THE ROLE OF SGLT2 INHIBITORS IN THE COMPLEX TREATMENT OF PATIENTS WITH CHRONIC KIDNEY DISEASE – THE RESULTS OF ONE TERTIARY CENTER

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Background: SGLT2-inhibitors have central role in the complex treatment of patients with chronic kidney disease (CKD) of different etiology. The aim of our study was to evaluate the effects of SGLT2-inhibitors on renal parameters at the background of standard treatment in a real-life observational study.

**Methods:** Materials and methods: in 2024 we observed 54 CKD patients treated with SGLT2-inhibitors (empagliflozin in 16 and dapagliflozin in 38), at the background of standard treatment, for a period of 6 months. Our cohort consisted of 33 males and 21 females, aged 19-85 years, 38 received dapagliflozine and 16 – empagliflozine; 20 had type 2 diabetes, 20 had biopsy-proven glomerular diseases (6 with IgA glomerulonephritis (GN), 5 with focal and segmental glomerulosclerosis, 5 with lupus nephritis, 2 with mesangioproliferative GN, 1 with primary membranous GN and 1 with polyangiitis with granulomatosis) – 3 of them had concomitant type 2 diabetes, 4 had systemic amyloidosis (3 with AL amyloidosis in multiple myeloma with biopsy-proven renal involvement, and 3 with AF amyloidosis and heart failure), and 10 had hypertensive renal disease. Written informed consent was obtained from all patients prior to any medical procedures.

**Results:** on months 3 and 6 in all patients we observed decrease in serum creatinine, proteinuria and uric acid levels and increase in glomerular filtration rate, only 3 patients developed lower-urinary-tract infections, we observed no cases of hypoglycemia, ketoacidosis or significant worsening of renal function, and in none of the patients we discontinued treatment.

**Conclusions:** Conclusion: given at the background of standard treatment, SGLT2 inhibitors have beneficial effect in patients with CKD of different etiology.

## LOW-FREQUENCY ULTRASOUND AS A THERAPEUTIC ENHANCER OF RENIN-ANGIOTENSIN SYSTEM INHIBITOR EFFECTS IN ENDOTHELIAL, RENAL, AND HEPATIC CELLS: FOCUS ON CELLULAR FUNCTION AND INFLAMMATION MARKERS

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** Endothelial dysfunction plays a central role in CMD, and while angiotensin-converting enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) help restore vascular function, their efficacy varies. Emerging research suggests that low-frequency ultrasound (LFU) may enhance drug delivery and endothelial responses. This study explored the combined effects of LFU and pharmacological treatments on endothelial, renal, and hepatic cells, as well as redox state and inflammation markers.

**Methods:** Human umbilical vein endothelial cells (HUVECs), renal proximal tubular epithelial cell line (RPTEC/TERT1), and hepatic cell line (HepG2) were treated with captopril, losartan, or dexamethasone alone or combined with LFU. Cell viability, wound healing, nitric oxide (NO), and reactive oxygen species (ROS) assays evaluated cellular responses. qPCR was used to analyze gene expression related to inflammation, vascular, and renal function.

**Results:** Captopril and losartan, when combined with LFU, improved HUVECs viability, wound healing, and NO production ( $p = 0.029$ , respectively), whereas only losartan with LFU enhanced these functions in RPTEC/TERT1 cells. In HepG2 cells, LFU with dexamethasone increased ROS levels while reducing viability and wound healing ( $p = 0.029$ , respectively), whereas losartan with LFU decreased ROS production ( $p = 0.029$ ). LFU also downregulated VCAM-1, ICAM-1, and PTGS2 in captopril-treated HUVECs and CYP4F2 in losartan-treated HUVECs ( $p = 0.029$ , respectively). In RPTEC/TERT1 cells, captopril with LFU suppressed GGT1 expression, while dexamethasone with LFU upregulated SGLT2 at higher concentrations ( $p = 0.029$ ).

**Conclusions:** LFU may enhance drug efficacy through anti-inflammatory effects, offering a non-invasive approach to vascular protection and CMD management.

## GUT MICROBIOME DYSBIOSIS AND CARDIOVASCULAR-KIDNEY-METABOLIC (CKM) SYNDROME: IS THERE A LINK?

### WELCOME RECEPTION, ORAL PRESENTATIONS & NETWORKING

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**Background and Aims:** In recent years, awareness of the gut microbiome and its impact on the development of chronic diseases has increased. Small intestinal bacterial overgrowth (SIBO) is defined as a manifestation of gut microbiome dysbiosis, resulting in a range of clinical manifestations, including both gastroenterological and systemic symptoms. According to the literature, there may be a link between CKM syndrome and SIBO, which could lead to new approaches in nutritional treatment and the management of certain systemic symptoms

**Methods:** A literature review was conducted using the PubMed database. Publications from the last five years were considered, focusing on the prevalence of SIBO in cardiovascular diseases, metabolic disorders, and kidney failure. After applying the exclusion criteria, 10 publications were taken into consideration, including five meta-analyses.

**Results:** Systematic reviews and meta-analyses confirm the relationship between SIBO and obesity, diabetes, chronic kidney disease, non-alcoholic fatty liver disease, and heart failure. Impaired gastrointestinal motility, delayed transit, and increased absorption in the proximal intestine may contribute to the development of SIBO in obese patients. Some of the data presented remain inconclusive and warrant further investigation in this field. Treatment of SIBO in heart failure may improve prognosis in this group of patients. A confirmed diagnosis of SIBO is associated with a higher rate of rehospitalization in patients with HFrEF and an increased risk of death in patients with HFpEF. Patients with renal failure present a range of gastrointestinal symptoms and are more susceptible to SIBO due to changes occurring in the intestinal wall.

**Conclusions:** This literature review highlights the prevalence of SIBO in the cardiovascular, kidney, and metabolic components of CKM syndrome. The aim of the research is to raise diagnostic awareness and expand therapeutic options for SIBO symptoms, ultimately improving the quality of life in this patient group

## MACHINE LEARNING IDENTIFIES PATTERNS IN MICROBIOME COMPOSITION IN TYPE 2 DIABETES PATIENTS

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** Type 2 diabetes mellitus (T2DM) remains a substantial global health concern. As its already high prevalence constantly increases, early diagnosis and better management are of the highest importance. T2DM is associated with underlying insulin resistance, excess adiposity and sarcopenia. Usually, T2DM patients also follow a “Western diet”, rich in saturated fats and low in fibre. This results in little gut microbiome diversity, perhaps with specific predominant bacterial strains. In this study, we compared gut microbiome compositions of T2DM versus non-T2DM adults. We focused on the most abundant strains to gain insight into the (dys)functionality of the T2DM gut.

**Methods:** We combined the Recursive Ensemble Feature Selection (REFS) with a DADA2-based pipeline to analyse 16s rRNA sequences extracted from stool samples of 112 T2DM and non-T2DM adults (BioProject PRJNA325931). This taxonomy-based methodology can deal with established limitations in the biomarker discovery state-of-the-art, providing robust results.

**Results:** 9 best-defining bacterial strains, members of Erysipelotrichales, Monoglobales, Oscillospirales, Lachnospirales, Bacteroidales, and Coriobacteriales orders, were selected using REFS. After REFS performance validation, we obtained an area under the Receiver Operating Characteristic (ROC) curve (AUC) of 0.79, which is considered a “good” diagnostic accuracy. When validated in two independent datasets (BioProjects PRJNA554535 and PRJEB53017), 5 out of 9 features were shared across all, with “good” and “sufficient” diagnostic accuracies, respectively. Considering the general variability of human gut microbiome composition, we find these results sufficient to deserve further investigation, especially as the selected bacterial strains have already been linked to metabolic syndromes, insulin resistance, obesity, and T2DM itself.

**Conclusions:** We propose 9 bacterial strains, with specific genetic signatures, as potential (prognostic) biomarkers of T2DM. We highlight the importance of further investigation as these findings may help in better T2DM prediction and diagnosis. They can also contribute to T2DM treatment and maintenance through therapeutic modulation with diet or probiotic supplementation.



## SIGNS OF MYOCARDIAL FIBROSIS IN PATIENTS WITH OBESITY WITHOUT CARDIOVASCULAR DISEASE

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** Obesity is a global health problem associated with a 30-50% increased risk of heart failure for every 5-unit increase in body mass index (BMI). Obesity-associated cardiomyopathy, characterized by structural and functional changes in the heart, often leads to cardiac dysfunction and heart failure. This study aimed to evaluate left ventricular systolic function and extracellular volume (ECV) in obese individuals without cardiovascular disease to better understand the early effects of obesity on the heart.

**Methods:** The study included 39 obese patients (16 men, 23 women; mean age  $57.31 \pm 9.43$  years; BMI  $34.78 \pm 4.52$  kg/m<sup>2</sup>) and 33 healthy controls (19 men, 14 women; mean age  $57.33 \pm 5.74$  years; BMI  $25.85 \pm 3.18$  kg/m<sup>2</sup>). ECV was measured using cardiac MRI on a 3T scanner, and segmental myocardial contractility was assessed using global longitudinal strain (GLS) via echocardiography.

**Results:** Left ventricular ejection fraction (LVEF) did not differ between groups ( $56.85 \pm 9.26\%$  in obese patients vs.  $59.45 \pm 5.74\%$  in controls,  $p > 0.05$ ). NT-proBNP levels in obese patients ( $84.67 \pm 40.87$  pg/ml) were within the normal range, ruling out heart failure. However, ECV was significantly higher in obese patients ( $36.59 \pm 4.94\%$  vs.  $27.58 \pm 3.18\%$ ,  $p < 0.001$ ), indicating myocardial fibrosis. GLS was also impaired in obese patients ( $-13.30 \pm 5.63\%$  vs.  $-20.02 \pm 1.81\%$  in controls,  $p < 0.01$ ), reflecting reduced myocardial contractility. A moderate positive correlation was found between BMI and ECV ( $r = 0.45$ ,  $p < 0.05$ ), and a moderate inverse correlation was observed between BMI and GLS ( $r = -0.45$ ,  $p < 0.05$ ).

**Conclusions:** Obese individuals without cardiovascular disease exhibited increased ECV and impaired myocardial contractility, as measured by GLS. These findings suggest early structural and functional changes in the heart, consistent with obesity-associated cardiomyopathy. Such alterations may predispose obese individuals to heart failure, highlighting the need for early intervention and monitoring in this population.

## REAL-WORLD DATA FOR TIRZEPATIDE TREATMENT IN TYPE 2 DIABETES MELLITUS (T2DM) TO ADDRESS HBA1C AND OBESITY WITH CONSIDERATION OF ATHEROSCLEROTIC CARDIOVASCULAR DISEASE (ASCVD)

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** Individuals with T2DM face a considerably elevated risk of ASCVD, which impacts morbidity and mortality rates. Studies suggest that the early initiation of comprehensive glucose-lowering therapy, particularly those with cardiometabolic advantages, can mitigate this risk. Tirzepatide, a dual GIP/GLP-1 receptor agonist, has shown efficacy in glycaemic control and weight reduction and is postulated to reduce ASCVD risk. This evaluates the impact of tirzepatide on HbA1c and BMI while assessing holistic ASCVD risk reduction in patients with T2DM.

**Methods:** Primary care patients were reviewed in a rural clinic, which employs a holistic best-practice care philosophy embracing lipidology, diabetology, and cardiology. Baseline data for medications, patient observations, T2DM management, and weight were collected from the electronic patient record and, where possible, re-measured after 3 months. Descriptive statistics were performed, and where required, paired t-tests were employed.

**Results:** Fifty-six patients (19F:28M) with a mean age of 62.5 years (SD=11.2) were reviewed. Mean LDL-C was recorded at baseline 1.49mmol/L (SD0.92), and TGs 2.0mmol/L (SD1.0). One patient declined LLT; of the others, 61% have been prescribed a statin, 30% a bempedoic acid compound, 7% ezetimibe, and 2% inclisiran. One patient stopped tirzepatide due to side effects, and two chose to convert to semaglutide. All but 4 had their tirzepatide dose increased from 2.5 to 5mg after one month. Their BP was 129/77mmHg pre-treatment and 126/73mmHg three months post-treatment. The mean HbA1c was reduced from 67.5mmol/L (SD20.2) to 55.1mmol/L (SD13.1;  $p<0.05$ ), and the mean BMI from 38.36 (SD6.78) to 34.7 (SD6.98;  $p<0.05$ ).

**Conclusions:** Tirzepatide offers a strategy to reduce HbA1c and BMI. This real-world data shows significant improvements in both, reinforcing clinical trial results. This is encouraging for healthcare professionals, especially in rural areas. While more long-term research is needed, tirzepatide has the potential to reduce morbidity and mortality, easing healthcare and socioeconomic burdens.

## REAL WORLD STUDY OF TIRZEPATIDE IN A SECONDARY CARE SPECIALIST DIABETES SERVICE IN THE UNITED KINGDOM (UK)

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** Tirzepatide is a novel dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist commonly used in the treatment of type 2 diabetes (T2DM). It was licensed by NICE in the UK in December 2024 (Technology Appraisal 1026). In this study, we aimed to assess its use in our secondary care diabetes service in Ipswich in relation to both conformity with NICE guidelines as well as assessing its efficacy and safety in the management of T2DM.

**Methods:** In this real-world, retrospective, open-labelled, single centre study, patients who were started on tirzepatide between March to December 2024 were assessed via electronic patient records. Anthropometry, glycaemic and weight changes, changes in total daily insulin dose requirement, and retinopathy changes (if any) were recorded at baseline as well as at every dose escalation which was done as per the summary of product characteristics (SmPC). Changes from baseline were statistically calculated.

**Results:** A total of 169 patients (106 males; 63 females; mean age ( $\pm$ SD) was  $57.86 \pm 11.80$  years) were studied. Of these, 105 patients (65 males; 40 females) were on a combination of insulin and oral hypoglycaemic agents (OHA) whilst the rest (64) were on OHA alone. HbA1c improved from the baseline  $9.48 \pm 1.76\%$  to  $7.2 \pm 0.44\%$  ( $p < 0.001$ ) after the 4<sup>th</sup> dose escalation. Similarly, weight reduction was observed from  $109.66 \pm 3.70$  kg at baseline to  $88.11 \pm 5.86$  kg after 4<sup>th</sup> dose escalation ( $p < 0.001$ ). Total daily insulin requirement reduced from  $82.86 \pm 45.47$  units to  $28.18 \pm 25.53$  units ( $p < 0.01$ ). No worsening of retinopathy was noted. A total of 3 patients (1.7%) did not continue the drug beyond the first escalation.

**Conclusions:** Our real world study shows that tirzepatide is a well-tolerated and efficacious drug for T2DM with clinically significant improvements of all glycaemic parameters. When patients are appropriately selected as per NICE guidelines, this can lead to improvement of long-term diabetes outcomes.

## TREATMENT WITH A NOVEL ZINC-SIDEROPHORE COMPLEX MINIMIZES (UP TO COMPLETE ELIMINATION) OF THE INSULIN RESISTANCE) IN TYPE 2 DIABETIC ANIMAL MODELS

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** We obtained evidence and proof of concept for many-fold lowering of insulin resistance, by treatment with Zygosid-50 of diabetic Sand Rats, a model of nutritionally-induced Type 2 Diabetes (T2D).

**Methods:** To examine the anti-T2D therapeutic efficacy of Zygosid-50 of our novel and safe drug-candidate, using the db/db genetically modified mouse, and (ii) start clinical trials evaluating its safety/efficacy in Man. db/db (male, 10-week old) mice, were treated (i.p. injection) with Zygosid-50 (6mg/kg, 3x/week) starting on Day 1.

**Results:** Under the Ministry of Health in Israel, as the Regulatory entity, we have completed the requirements for an initial PILOT TYPE clinical study. This abstract describes the pre-clinical activities that serve as the foundation for the requested Study. Diabetic Sand Rats (*Psammomys obesus*) and db/db mice were used. Following transfer of the rats to high energy diet they became diabetic (BGL > 300 mg/dl) within 10-12 days. Treatment with Zygosid-50 2 mg/Kg resulted in the lowering the insulin resistance (IR). In addition' In addition lowering body weight, by 20%, was observed for the Zygosid-50 treated animals. Similar results were observed for the db/db mice. The treatment also caused a marked improvement of the GTT curves, as compared to non-treated animals.

**Conclusions:** Zygosid-50, as well as other zinc complexes, demonstrated robust therapeutic efficacy in the treatment of T2D, in 2 animal models: the Sand Rat and the db/db mouse. In particular the return to the normal range of IR could prove a novel mode of treatment of diabetes type 2. Importantly, no adverse effects could be detected, in all the experiments, indicating high safety profile of this drug-candidate. We are confident that Zygosid-50 and its analogs will provide relief for millions of T2D patients.

## TRAINING PROGRAM FOCUSED AT IMPROVING MUSCULOSKELETAL PAIN AND WEIGHT LOSS IN PATIENTS WITH OBESITY

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** Obesity is a concerning non-communicable chronic disease (NCD) because it is a risk factor for other NCDs, including chronic musculoskeletal pain (1–5). In patients with obesity and chronic pain, it is crucial to address lifestyle factors such as physical inactivity, which is a risk factor for increased pain intensity and disability, in addition to contributing to weight gain (6,7).

**Methods:** This study is a quasi-experimental trial in which the patient serves as their own control, before and after intervention with a training program, including up to 5 consultations within 18 months. Anthropometric measurements, physical-functional, medical, nutritional, and psychological assessments were conducted at three time points. The Physical Activity Laboratory (LAF), based on this information, evaluates, prescribes, and monitors a training program focused on reducing body weight, musculoskeletal pain intensity and interference in activities due to pain. Statistical analysis: Anthropometric data - weight, body mass index (BMI), neck, abdominal and waist circumferences, waist-hip ratio - and body fat (fat and lean mass in kilograms and percentages) were compared, along with pain intensity and interference scale, at three consultations within 18 months using the Friedman test with correction for multiple comparisons by the Bonferroni test.

**Results:** Of those who completed 18 months of follow up (n=40), 31 were women (75.6%) with a median age of 54 years (SD: 10.9). In the main analyses, differences were found in the following parameters (values expressed as medians): from the 1st to the 3rd consultation, weight: 94 kg to 89 kg ( $p<0.0001$ ), fat mass: 39.8 kg to 33.2 kg ( $p<0.001$ ), BMI: 37.1 to 35.2 ( $p<0.0001$ ), and abdominal circumference: 115.5 cm to 108.5 cm ( $p<0.001$ ). No significant difference was found in other parameters.

**Conclusions:** The training program was effective in reducing anthropometric measurements, but not in reducing musculoskeletal pain intensity and interference in activities due to pain.

## STRATEGY FOR SCREENING AND MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD) IN PRIMARY CARE

### LUNCH AND ABSTRACT PRESENTATIONS

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**Background and Aims:** NAFLD is a prevalent condition associated with obesity, type 2 diabetes, and metabolic syndrome. Early detection and management in primary care can prevent progression to non-alcoholic steatohepatitis (NASH) and cirrhosis. This protocol provides a structured, evidence-based approach for Family Medicine Doctors/ General Practitioners (GPs) to screen, diagnose, and manage NAFLD effectively.

**Methods:** The proposed protocol consists of five key steps: Screening and Identification: Target adults with risk factors such as obesity (BMI  $\geq 30$ ), type 2 diabetes, metabolic syndrome, or persistently elevated liver enzymes (ALT/AST). Screening includes liver function tests, metabolic assessment, and ultrasound if indicated. Diagnostic Evaluation: Rule out alternative causes (e.g., excessive alcohol intake, viral hepatitis, autoimmune disorders). Utilize non-invasive fibrosis risk scoring tools (FIB-4 Index, NAFLD Fibrosis Score) and imaging to assess disease severity. Management: Implement lifestyle interventions as first-line treatment, focusing on 7-10% weight loss, a Mediterranean diet, and physical activity. Address comorbidities such as diabetes, dyslipidemia, and hypertension. Consider pharmacologic options (e.g., GLP-1 agonists, SGLT2 inhibitors, aGLP1-/GIP) in patients with metabolic risk factors. Referral Criteria: High-risk patients (FIB-4  $> 3.25$ , NAFLD Fibrosis Score  $> 0.676$ , persistent LFT elevation, signs of cirrhosis) require specialist evaluation. Patient Education and Follow-Up: Emphasize lifestyle modifications and schedule regular follow-ups (annual for low-risk, biannual for intermediate-risk). Integrate electronic medical record prompts and multidisciplinary collaboration to enhance implementation.

**Results:** This protocol is aligned with current guidelines (AASLD, NICE) and adaptable for primary care settings. It facilitates early NAFLD detection, optimizes management, and reduces disease progression risk.

**Conclusions:** Implementation in general practice can improve patient outcomes and reduce healthcare burden. Future research should assess its real-world impact.

# **E-Poster Viewings**

## NSAID- INDUCED ACUTE KIDNEY INJURY AND MALA (METFORMIN ASSOCIATED LACTIC ACIDOSIS).

### CASE STUDIES HIGHLIGHTING SUCCESSES AND CHALLENGES

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**Background and Aims:** Background Metformin is the most frequent drug used to treat diabetes and is well tolerated. Metformin associated lactic acidosis (MALA) is a rarely well-known serious side effect of biguanides. MALA can occur gradually in patients with renal dysfunction due to decreased excretion.

**Methods:** Case Presentation In the last 10 years, two cases have been present in our hospital with MALA. The first case a 56 -year-old female, who was admitted in our hospital with acute confusional state, extreme fatigue, nausea, vomiting and anuria. She was in treatment with indomethacin for leg pains for more than one week. She was in treatment for high blood pressure and diabetes with Metformine 2550 g/day. The second patient, 73, was after a contrast CT scan and use of treatment with diclofenac for a few days. She had also type 2 diabetes in treatment with Metformin 2000 g/day and high blood pressure

**Results:** Laboratory data: ABG showed severe lactic acidosis. pH = 6.9; lactate 21 mmol/L; K = 6.5 mmol/l (3.7-5.5), creatinine = 9.6 mg/dl (0.6-1.2) and BUN = 130 mg/dl (18-35). They had been diagnosed with NSAID- induced acute injury and MALA and were admitted to the ICU and treated with intravenous fluid, diuretics, sodium bicarbonate and insulin to manage profound metabolic acidosis. The urgent hemodialysis session was done. Since the first case continues to be with altered mental status and acidosis state an additional session of continue renal replacement therapy to remove metformin as done. In both cases progressive recovery was observed, and patients were discharged from the ICU to the ward on the fourth and fifth day.

**Conclusions:** Conclusion Both cases had NSAID- induced acute kidney injury and MALA. Although rare condition, lactic acidosis should be considered in patients with acute kidney failure in treatment with metformin when lactate exceeds 5 mmol/L.



## TAMOXIFEN INDUCED QTC PROLONGATION IN A YOUNG FEMALE PATIENT

### CASE STUDIES HIGHLIGHTING SUCCESSES AND CHALLENGES

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**Background and Aims:** Tamoxifen is a widely used drug in the treatment of breast cancer patients. Considering the high prevalence of this type of malignancy, the side effects of Tamoxifen should be recognized early. Cardiovascular side effects include: increased risk of thromboembolism particularly during periods of immobility, mild increase risk of deep vein thrombosis, pulmonary embolism, stroke, lipid metabolism changes. There are very few case reports of Tamoxifen effects on QTc interval as recorded on an ECG. QTc prolongation followed by ventricular arrhythmias could be life threatening

**Methods:** A 29y.o female presented as an outpatient for a routine check-up. She had no complaints, was in good physical condition, but was diagnosed with left breast invasive ductal carcinoma grade II 2 years ago, treated with neoadjuvant chemotherapy, surgery and radiation. Because cancer cells were HER-positive, Tamoxifen as an estrogen receptor antagonist was the chosen hormonal therapy drug, started a year ago at 20mg/day. The ECG showed normal sinus rhythm 66/minute, but a prolonged QT (QT/QTc 466/488 ms). All the other parameters were within normal ranges including a 24 hour holter monitor.

**Results:** The ECG before surgery was normal. Because the patient was only on Tamoxifen therapy and no other factors could be implicated, it was deduced that the QTc interval prolongation was a side effect. According to the ESC Guidelines on Oncocardiology our pt had a QTc of 488 ms and it was decided to continue with Tamoxifen and to perform an ECG every week if asymptomatic.

**Conclusions:** QTc prolongation as a side effect of chemotherapy is widely recognized. However, Tamoxifen is considered a hormonal therapy and QTc prolongation is not yet generally recognized as a possible side effect. This medication is prescribed more than any other drug in women with breast cancer for at least 5 - up to 10 years. It is important that even patients on Tamoxifen be routinely screened for QTc prolongation. The ECG is a readily available and cheap examination that could detect possible life threatening but preventable complications.

## PRIMARY CARE CASE SERIES OF 4-PILLAR TREATMENT FOR DIABETIC KIDNEY DISEASE (DKD) ASSESSING HBA1C, EGFR AND BMI WITH AN ASSESSMENT OF ASCVD

### CASE STUDIES HIGHLIGHTING SUCCESSES AND CHALLENGES

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**Background and Aims:** The use of RAAS inhibitors, SGLT2 inhibitors, and non-steroidal MRA has become central to managing DKD. GLP-1 receptor agonists also offer renal protection beyond glycaemic control and are emerging as a new fourth pillar of treatment for DKD. DKD is common in primary care patients, and embedding best-practice four-pillar care in general practice can enhance patient outcomes. This case series evaluates semaglutide use in patients with DKD, specifically assessing HbA1c, BMI, and renal function while considering ASCVD risk reduction in these patients.

**Methods:** Primary care patients were reviewed for patients receiving four-pillar treatment with semaglutide. Baseline data for medications, patient observations, T2DM management, and weight were collected from the electronic patient record and, where possible, re-measured at varying intervals. Descriptive statistics and trend analysis were performed for BMI.

**Results:** Five patients (1F:4M) with an average age of 55 were reviewed over one year. All were prescribed semaglutide; four used oral formulations, and one patient used injectable but temporarily converted to oral semaglutide during shortages of the injectables. All increased their dose after one month. The average HbA1c was reduced from 53mmol/L to 37mmol/L. The mean BMI was reduced from 35.6(SD8.35) to 30.9(SD6.2), with the trend analysis suggesting the average BMI would be 28 after a further six months. DKD remained KDIGO G3b throughout. Mean LDL-C was recorded at baseline 0.65mmol/L(SD0.69), falling to 0.6mmol/L(SD0.35), an ≈8% reduction. Five patients were prescribed a statin, three a bempedoic acid compound, one ezetimibe, one inclisiran and one icosapent ethyl.

**Conclusions:** Integrating GLP1-RAs into the treatment protocols for DKD presents a more comprehensive and practical approach to disease management with positive real-world results. This improves patient outcomes and potential savings for healthcare systems. By employing simple strategies, HCPs and patients can see benefits even in the short

**PUNE DIABETES PREVENTION LOGIQUE : APPLICATION OF FINNISH DIABETES PREVENTION PROGRAM WITH INDIANISATION FOR SCREENING OF FIRST-CLASS RELATIVES OF PERSON WITH TYPE 2 DIABETES MELLITUS**

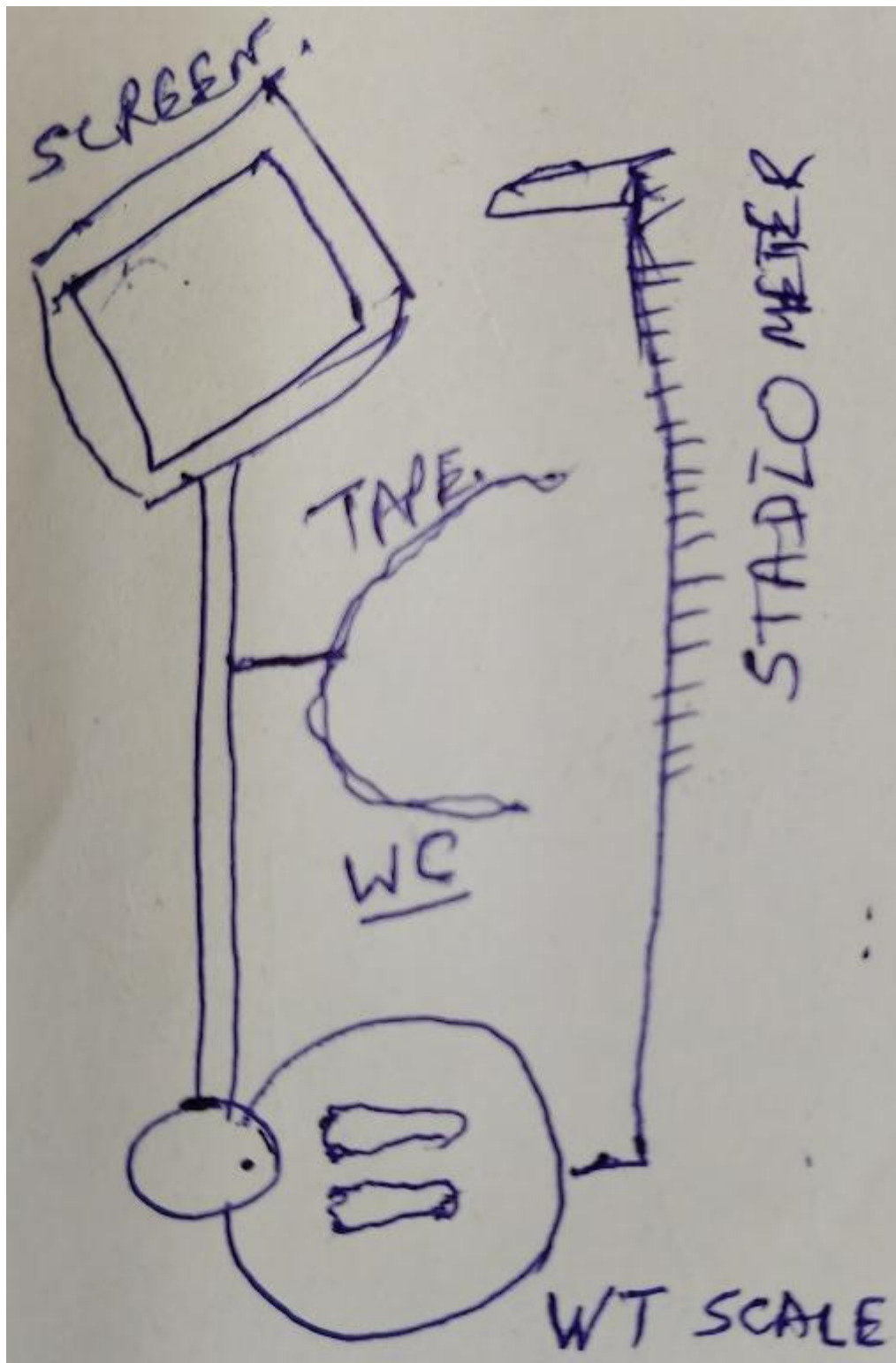
**EARLY DETECTION AND INTERVENTION STRATEGIES**

Dr Sanjay Gandhi

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**Background and Aims:** RISING PREVALANCE OF DIABETES MELLITUS TYPE 2 IN INDIA THE UNDIAGNOSED T2DM AND THE PREDIABETES. WE HAVE DEVELOPED - COMMON MAN FRIENDLY KIOSK TYPE PREVENTION SCREENING AT AIRPORT & MALLS AND THEATRES ALL OVER THE WORLD. WE HAVE STUDIED AND PRAISED THE FINNISH DIABETES PREVENTION PROGRAM. WE, THE HEALTHCARE PROFESSIONAL AND CO WORKERS ARE UNABLE TO DO MORE DUE TO LACK OF TIME AND RESOURCES. THERE FORE, WE DEVELOPED A QUESTIONNARE BASED ON SIMPLE POINTS AS F.D.P.P WITH INDIAN TADKA OF GENETIC PREPONDERANCE AND THE AGE QUENTILES. ABOUT 500 FIRST DEGREE RELATIVES OF T2DM PERSONS VISITING OUR CLINIC WERE SCREENED USING THIS QUESTIONNARE SINCE 2007. FEW OF THEM WERE FOLLOWED UP OVER ABOUT TWO DECADES - FREE OF COST. THE RESULTS ARE VERY ENCOURAGING TO SEE THAT QUITE A FEW TURNED OUT TO BE DIABETICS LATER. THE CHANGES IN TERMS OF AGE GROUPS AND THE GENETIC BACKGROUND CHECK WAS PROBABLY MORE CORRECTLY APPLIED TO INDIAN POPULATION AS COMPARED TO EUROPEAN POPUTION. THE LEADERS OF THE WORLD IN PREVENTION OF NCDS WOULD AGREE THAT THE PREVENTION IS THE ONLY POSSIBLE WAY TO SAVE INDIAN ECONOMY FROM EXPLOSION OF THIS DISASTER IN FUTURE. THIS CAN BE APPLIED TO THE ALL OF SOUTH EAST ASIAN POPULATION ALL OVER THE WORLD. PDPlogiQ : A platform of 3 ft by 3ft is made with the steel hollow pipes on which a weighing machine is installed. A standing kiosk having a notepad / ipad in the front and the person would stand on the weighting machine. A movable and adjustable measuring tape holder would be on the posterior stand of stadiometer for measuring the Waist Circumference .

**Methods:** KIOSK DESIGN:



**Results:** EASE OF SCREENING FOR OBESITY. IDENTITY OF THE PERSON NOT PUBLICLY DISCLOSED. EASE OF DATA ANALYSIS NATIONWIDE.

**Conclusions:** VERY USEFUL FOR SE ASIA.

## INDEPENDENT EXTERNAL VALIDATION AND COMPARISON OF AN EXISTING METABOLIC SYNDROME RISK SCORE (CHINESE METS RISK SCORE): A COHORT STUDY.

### EARLY DETECTION AND INTERVENTION STRATEGIES

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**Background and Aims:** Many risk models are developed for predicting Metabolic syndrome (MetS). Yet, they are hardly validated on an external sample. The purpose of this study is to conduct independent external validation of an existing MetS risk prediction model (Chinese MetS risk score) using a large prospective cohort data.

**Methods:** The study participants were 7626 members of the 1958 British birth cohort who participated in the biomedical survey at age 45 and have complete information on MetS. The variables utilised were obtained prospectively at birth, 7, 16, 23 and 45 years. The original model equation formula of the Chinese MetS risk score was retrieved and used to calculate the risk of MetS. The predictive performance of the Chinese MetS risk score was evaluated using measures of discrimination and calibration. Finally, a comparison was made between the model developed using the local data and the Chinese MetS risk score.

**Results:** The Chinese MetS risk score has overall good discriminative ability with AUROC of 0.87 (95% CI [0.86, 0.88]) but became poorly calibrated when applied to the 1958 British birth cohort (Hosmer-Lemeshow 6.40 P 0.0407). Furthermore, when compared with the model developed using the local data, the developed model outperforms the Chinese MetS risk score (AUROC 0.91 (95% CI [0.90, 0.92]) vs 0.87 (95% CI [0.86, 0.88])) and calibration (Hosmer-Lemeshow (6.47 P 0.595 vs 6.40 P 0.0407)).

**Conclusions:** There is scope to utilise the Chinese MetS risk score, however, it may not be suitable to directly apply the Chinese MetS risk score in its current form to an external population data without adjustment/ updating.

## IDENTIFICATION OF KEY MARKERS ASSOCIATED WITH MYOCARDIAL INFARCTION IN TYPE 2 DIABETES MELLITUS USING EXPLAINABLE MACHINE LEARNING

### EARLY DETECTION AND INTERVENTION STRATEGIES

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**Background and Aims:** Type 2 diabetes mellitus (T2DM) is a major risk factor for cardiovascular diseases, including myocardial infarction (MI). Dyslipidemia, chronic hyperglycemia and endothelial dysfunction significantly contribute to cardiovascular complications. Traditional risk models often overlook complex interactions between predictors. Machine learning (ML) with SHapley Additive exPlanations (SHAP) and permutation importance can identify key markers associated with myocardial infarction (MI) in their interaction. Aim: To identify key features associated with MI in patients with T2DM using an interpretable ML.

**Methods:** SHAP and permutation importance analysis were used to determine significance of the different variables in MI prediction. For the top 10 models out of 50 examined, the average AUC was 0.76. Data from 355 patients with T2DM (230 men, 125 women) were analyzed. Mean age was  $62 \pm 11.1$  years, diabetes duration  $7.8 \pm 7.6$  years, fasting glucose  $8.2 \pm 3.3$  mmol/L, HbA1c  $6.8 \pm 1.8\%$ , total cholesterol  $5.1 \pm 1.5$  mmol/L and LDL cholesterol  $3.1 \pm 1.1$  mmol/L. A total of 147 patients had ischemic heart disease (IHD).

**Results:** Used explainable ML identified IHD as the strongest predictor for MI. Elevated LDL and decreased HDL cholesterol were linked to an increased probability of MI, highlighting the role of dyslipidemia in atherosclerosis. Older age and longer diabetes duration also contributed to a higher MI probability, reflecting the impact of chronic hyperglycemia and vascular damage. While anthropometric measurements had a lower impact on model performance, they remained an important source of information.

**Conclusions:** Cardiometabolic factors, particularly dyslipidemia, diabetes duration and age are key markers associated with MI history in T2DM. Early lipid and glycemic control are essential for cardiovascular prevention. Explainable ML provides valuable insights for personalized risk assessment.

## LIPOPROTEIN (A) , A NOVEL RISK FACTOR FOR PREMATURE CORONARY ARTERY DISEASE

### EARLY DETECTION AND INTERVENTION STRATEGIES

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**Background and Aims:** Premature Coronary Artery Disease (CAD) has devastating consequences. Although the number of new coronary atherosclerosis events has decreased in older adults, the same cannot be stated for the younger population. CAD in a younger population means a worse long term prognosis (4-10% of myocardial infarctions happen in this age group), therefore it is crucial to be aware and identify conventional and special risk factors in order to avoid primary and secondary cardiovascular risk events.

**Methods:** Premature CAD is defined as a first clinical event diagnosed in males < 50y.o and females <55y.o. Ischemic heart disease is one of the main reasons for increased morbidity and mortality. An unhealthy lifestyle combined with an early presence of major risk factors are considered nowadays the main causes of premature CAD. However, apart from traditional risk factors causing CAD (smoking, hypercholesterolemia, hypertension, diabetes), recently novel risk factors have come into the spotlight such as Lipoprotein (a). Lp(a) is a genetic risk factor with a high prevalence in CAD. A 2018 study estimated that approximately 1.4 billion people worldwide had a high Lp(a) level (> 50 mg/dl), 3 times more than diabetes, with a prevalence 10-30% or more in patients with CAD, calcified aortic stenosis or chronic kidney disease. Circulating levels of Lp(a) can be measured only once and are not influenced by age, gender, physical activity, diet or statin therapy. At whatever LDL-cholesterol level, if Lp(a) is elevated, the risk for CAD increases 2-3 times and atherogenicity starts from birth.

**Results:** In many countries, including Albania, there is still a gap in the recognition of novel risk factors in patients with premature CAD and the Lipoprotein (a) test is not an exception. Very few clinicians request this relatively simple assay resulting in an underestimation of the Atherosclerotic Cardiovascular Disease risk in patients that have a high circulating level.

**Conclusions:** Early identification can lead to prompt intervention and therapy providing primary and secondary prevention and overall decreased mortality and morbidity in this age group.

## THE POTENTIAL ROLE OF NT-PROBNP IN EARLY HEART FAILURE DIAGNOSIS IN PATIENT WITH T1DM

### EARLY DETECTION AND INTERVENTION STRATEGIES

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**Background and Aims:** Diabetes mellitus (DM) is a major risk factor for heart failure (HF), particularly HF with preserved ejection fraction (HFpEF), due to metabolic dysfunction, inflammation, and myocardial stiffness. Early HFpEF diagnosis in DM remains challenging due to symptom overlap and limitations of conventional tools like echocardiography and NT-proBNP measurement.

**Methods:** Plasma NT-proBNP levels were measured in patients with type 1 (T1DM) and type 2 diabetes mellitus (T2DM). A total of 87 patients (mean age:  $57 \pm 9$  years) were examined. Echocardiographic assessment confirmed preserved left ventricular ejection fraction (LVEF  $\geq 50\%$ ) in all cases. The impact of T1DM duration on NT-proBNP levels was analyzed.

**Results:** A total of 87 patients with DM were enrolled (T1DM:  $n=30$ ; T2DM:  $n=57$ ). The mean diabetes duration was 16 years. NT-proBNP  $> 125$  pg/ml was detected in 76% of T1DM patients ( $n=23$ ) and  $< 125$  pg/ml in 14% ( $n=7$ ). In the T2DM group, 80.7% ( $n=46$ ) had NT-proBNP  $> 125$  pg/ml, while 19.3% ( $n=11$ ) had levels  $< 125$  pg/ml. Further analysis revealed a correlation with T1DM duration: all patients ( $n=23$ ) with elevated NT-proBNP had diabetes for  $>10$  years, whereas those with lower levels had a duration of 7-10 years.

**Conclusions:** NT-proBNP levels can serve as an early diagnostic marker for heart failure in patients with long-standing type 1 diabetes mellitus. Regular monitoring may enable the timely detection of subclinical cardiac dysfunction, facilitating early intervention and improved outcomes. Further studies are needed to explore additional factor relationships and their impact on NT-proBNP levels.



## CYTOKERATIN-18 IN OBESE CHILDREN WITH METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER FIBROSIS

### EARLY DETECTION AND INTERVENTION STRATEGIES

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**Background and Aims:** Early diagnosis of metabolic dysfunction-associated steatotic liver fibrosis is necessary because of the reversibility of liver changes at early stages. Despite the variety of available diagnostic scales, validation of new non-invasive tests is needed. So, the aim of our study was to investigate the diagnostic accuracy of cytokeratin-18 (CK18) in the diagnosis of liver fibrosis in children with metabolic dysfunction-associated steatotic liver disease (MASLD).

**Methods:** 94 patients (average age  $12.15 \pm 2.51$  years) were divided into groups according to body mass index, transient elastography (Fibroscan®502 touch, Echosens, France) data: 1 group consisted of 27 obese patients with MASLD and liver fibrosis  $\geq F1$ , 2 group - 35 obese patients with MASLD without fibrosis, 3 group - 18 obese patients without MASLD, 4 group (control) - 14 patients with normal weight without liver steatosis and fibrosis. Serum CK18 levels were determined by the enzyme-linked immunoassay (IDL Biotech AB, Sweden). Correlations with liver fibrosis and steatosis grade were investigated. ROC analysis for CK18 cut-off value evaluation was conducted.

**Results:** The mean value of CK18 in 1 group children increased 2.2 times ( $p < 0.05$ ) compared to the control group. The median CK18 level in 1 group patients was 1.4 times ( $p < 0.05$ ) and 1.8 times ( $p < 0.05$ ) higher than in 2 and 3 groups, respectively. A positive correlation between CK18 level and liver fibrosis ( $r = 0.468$ ;  $p = 0.008$ ), and liver steatosis ( $r = 0.357$ ;  $p = 0.048$ ) was found. The threshold level of CK18 for the diagnosis of fibrosis was 96.5 U / l (sensitivity 75.0%, specificity 77.0%, AUC 0.743, 95% CI 0,736-0,950,  $p < 0.05$ ).

**Conclusions:** Thus, in children with metabolic dysfunction-associated steatotic liver fibrosis, a significant increase in the CK18 level correlated with liver fibrosis and steatosis grade. The cut-off CK18 value of 96.5 U/l might be helpful for steatotic liver fibrosis diagnosis and selection of patients for early intervention.

## THE EFFECTS OF ESCULIN TREATMENT ON MITOCHONDRIAL DYNAMICS IN THE EARLY STAGE OF EXPERIMENTAL DIABETIC NEPHROPATHY

### INNOVATIONS IN MANAGING CARDIORENAL, METABOLIC, OR OBESITY-RELATED CHALLENGES

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**Background and Aims:** Diabetes mellitus (DM) is a chronic disease associated with mitochondrial dysfunction caused by hyperglycemia. Previous study in our Laboratory showed that esculin treatment improved mitochondrial function and reduced the deleterious effects of hyperglycemia in the kidneys of diabetic Wistar rats. The objective of this study is to evaluate whether the improvement in mitochondrial function observed after treatment with esculin is attributed to modulations in mitochondrial dynamics.

**Methods:** Diabetes was induced in male Wistar rats at 8 weeks of age by administering streptozotocin (60 mg/kg; IV). Control and diabetic animals received daily doses of esculin hydrate (50 mg/kg; p.o.) for 8 weeks. At the end of the protocol, the animals were euthanized, and the remaining kidneys were collected for evaluating mitochondrial dynamics using immunohistochemistry and transmission electron microscopy techniques.

**Results:** Immunohistochemistry analysis revealed alterations in the protein content of mitochondrial fission markers, such as FIS and DRP1, in diabetic animals, indicating increased susceptibility to mitochondrial fission. Esculin treatment reversed this condition by increasing the protein content of mitochondrial fusion markers, including MFN1 and OPA1. Corroborating the expression of these markers, morphometric analyses revealed that diabetic animals had mitochondria with smaller area and perimeter, a higher compaction and sphericity index, and lower elongation—a characteristic fission profile. Diabetic animals treated with esculin showed an increase in perimeter and elongation, as well as a reduction in compaction and sphericity—a characteristic fusion profile.

**Conclusions:** In addition to reducing degenerative processes in the kidneys, such as loss of tubular microvilli, mesangial expansion, and lymphomononuclear infiltrates, esculin treatment appears to modulate mitochondrial dynamics. Esculin promoted mitochondrial fusion, suggesting increased ATP production and reduced oxygen consumption for reactive species generation.

## EVALUATION OF INFLAMMATORY BIOMARKERS AND OXIDATIVE/ NITROSATIVE STRESS IN ADULT OR ELDERLY DIABETIC PATIENTS SUPPLEMENTED WITH ACAI JUICE

### INNOVATIONS IN MANAGING CARDIORENAL, METABOLIC, OR OBESITY-RELATED CHALLENGES

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**Background and Aims:** Aging is known as one of the risk factors for Type-2 diabetes mellitus (DM2), along with a sedentary lifestyle and inadequate nutrition. To evaluate inflammatory biomarkers, oxidative/ nitrosative stress in adult or elderly diabetic patients supplemented with acaijjuice.

**Methods:** Blood samples were collected pre and after 30 days of açai juice in DM2 patients (elderly N=18 vs. adults N=17) for evaluation of: glycated hemoglobin (HbA1c), lipid profile, renal function, pro-inflammatory markers, oxidative/ nitrosative stress and antioxidants; anthropometry and food consumption were evaluated. Results were described as mean  $\pm$  SE;  $p < 0.05$  or not significant (NS).

**Results:** There was a reduction in HbA1c, triglycerides and urea in post vs. pre in adults; no difference was observed in the elderly except for urea. Regarding inflammatory parameters, there was no difference, except for VCAM-1 which was reduced in post vs. pre. In oxidative stress, there was a reduction in TBARS in the adults and elderly, post vs. pre. The nitric oxide was reduced in adults post vs. pre ( $p < 0.05$ ) and in the elderly (NS). Regarding antioxidants, there was no difference in superoxide dismutase; there was an increase in catalase and a reduction in glutathione, in adults post vs. pre ( $p < 0.05$ ) and in the elderly (NS). In anthropometry, there was no difference in the parameters except for increased visceral fat index, in the elderly post vs. pre.

**Conclusions:** In this study acai resulted in the improvement of some parameters in adult and elderly population. Perhaps the dose consumed and/ or the intervention time were insufficient to produce a greater effect, mainly in the elderly, because the damage to the organs resulting from more advanced age and time of diabetes. We believe that the ingestion of acai as soon as diabetes is diagnosed could be useful as an adjuvant therapy to prevent the complications of this disease.

## NON-TRADITIONAL CARDIAC RISK FACTORS IN CHRONIC KIDNEY DISEASE: INNOVATIONS IN THE MANAGEMENT OF CARDIO-RENAL-METABOLIC SYNDROME

### INNOVATIONS IN MANAGING CARDIORENAL, METABOLIC, OR OBESITY-RELATED CHALLENGES

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**Background and Aims:** Cardiovascular disease (CVD) remains the leading cause of mortality in patients with chronic kidney disease (CKD), yet traditional risk factors fail to fully explain this increased burden. Non-traditional factors such as asymmetric dimethylarginine (ADMA) and hyperhomocysteinemia contribute significantly to endothelial dysfunction, vascular stiffness, and atherogenesis in CKD. Addressing these factors through innovative therapeutic strategies is essential for improving outcomes in cardio-renal-metabolic (CRM) syndrome.

**Methods:** A theoretical approach is proposed, emphasizing the pathophysiological role of ADMA and hyperhomocysteinemia in CVD progression in CKD patients. Emerging therapeutic interventions, including SGLT2 inhibitors, GLP-1 receptor agonists, mineralocorticoid receptor antagonists (MRAs), and novel anti-inflammatory agents, are evaluated for their potential to mitigate these risks. Additionally, targeted nutritional and pharmacologic strategies for homocysteine-lowering therapy are explored.

**Results:** ADMA, an endogenous inhibitor of nitric oxide synthase, contributes to endothelial dysfunction and arterial stiffness, while hyperhomocysteinemia accelerates oxidative stress and vascular injury. Traditional lipid-lowering and antihypertensive therapies alone are insufficient in CKD patients with these metabolic disturbances. Studies suggest that SGLT2 inhibitors and GLP-1 receptor agonists not only improve glycemic control but also reduce oxidative stress and inflammation, indirectly benefiting vascular function. MRAs provide additional reno-cardiovascular protection by reducing fibrosis and vascular remodeling. Homocysteine-lowering strategies, including folate and vitamin B12 supplementation, have shown potential in reducing cardiovascular risk in selected CKD populations.

**Conclusions:** Recognizing ADMA and hyperhomocysteinemia as key non-traditional cardiovascular risk factors in CKD highlights the need for innovative management strategies. Emerging therapies, particularly SGLT2 inhibitors, GLP-1 receptor agonists, MRAs, and targeted metabolic interventions, offer promising avenues to address CRM syndrome. Future studies should focus on integrating these approaches into routine clinical practice to optimize cardiovascular outcomes in CKD.

## ADVANCEMENTS IN DEVICE-BASED THERAPIES FOR CARDIO-RENAL SYNDROME

### INNOVATIONS IN MANAGING CARDIORENAL, METABOLIC, OR OBESITY-RELATED CHALLENGES

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**Background and Aims:** Cardio-renal syndrome (CRS) encompasses disorders where acute or chronic dysfunction in the heart or kidneys precipitates dysfunction in the other organ. Traditional pharmacologic treatments often fall short in addressing the complex hemodynamic and neurohormonal disturbances inherent in CRS, particularly in patients unresponsive to standard therapies. This has spurred interest in device-based interventions targeting specific pathophysiological mechanisms of CRS.

**Methods:** A comprehensive review of clinical trials and observational studies was conducted to evaluate the efficacy and safety of various device-based therapies in CRS management. The analysis focused on devices such as splanchnic denervation systems (dilators), central and pulmonary pressure reduction devices (reducers), and systems targeting interstitial fluid mobilization (fluid shifters). Key endpoints included hemodynamic parameters, renal and cardiac function, symptom relief, and adverse events.

**Results:** Splanchnic nerve modulation devices demonstrated potential in reducing central venous pressure and enhancing diuretic responsiveness in acute CRS cases, with stabilization or improvement in renal function. Devices aimed at central and pulmonary pressure reduction showed promise in decreasing heart failure hospitalizations and renal adverse events, alongside improved quality of life scores. Fluid shifters effectively reduced tissue congestion, offering symptom relief. However, certain devices presented challenges, including procedure-related complications and a learning curve for optimal implantation.

**Conclusions:** Device-based therapies represent a valuable addition to the CRS treatment landscape, especially for patients unresponsive to conventional pharmacologic interventions. By targeting specific pathophysiological aspects of CRS, these devices have the potential to improve clinical outcomes. Nonetheless, further large-scale, long-term studies are necessary to establish their roles in standard care and to refine patient selection criteria. An enhanced understanding of device mechanisms and the development of comprehensive trial endpoints will be crucial in maximizing the therapeutic impact on quality of life and clinical outcomes for CRS patients.

## SERUM FIBROSIS MARKERS IN METABOLIC DYSFUNCTION-ASSOCIATED STEATOTIC LIVER FIBROSIS IN OBESE CHILDREN

### INNOVATIONS IN MANAGING CARDIORENAL, METABOLIC, OR OBESITY-RELATED CHALLENGES

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**Background and Aims:** The main problem in the field of pediatric metabolic dysfunction-associated steatotic liver disease (MASLD) is the lack of effective diagnostic tools that allow the selection of patients with advanced disease. Therefore, the aim of our study was to investigate serum fibrosis markers in obese children with MASLD depending on the presence of liver fibrosis.

**Methods:** 94 children aged 9 to 17 years were included in the study. According to the transient elastography data (FibroScan®502touch, Echosence, France) and body mass index, children were divided into 4 groups: I - 27 obese children with MASLD with fibrosis  $\geq$ F1, II - 35 obese children with MASLD without fibrosis, III - 18 obese children without MASLD and fibrosis. Control group IV consisted of 14 children with normal weight without MASLD and liver fibrosis. The levels of serum vascular endothelial growth factor (VEGF), transforming growth factor beta 1 (TGF- $\beta$ 1), hydroxyproline protein-bound (HPp/b), hydroxyproline free (HPf), and glycosaminoglycans (GAG) were examined.

**Results:** Significant increase in the median level of VEGF (2.4 times,  $p < 0.05$ ) and TGF- $\beta$ 1 (2.7 times,  $p < 0.05$ ) was found in I group compared to the control group. An increase in the content of serum HPp/b was found: in group I in 1.2 times ( $p < 0.05$ ), in group II – in 1.2 times ( $p < 0.05$ ), in group III – in 1.3 times ( $p < 0.05$ ) compared to the control group. Simultaneously with the increase in the level of HPp/b in group I children, an increased content of GAG was observed in 1.3 times ( $p < 0.001$ ). HPp/b/HPf ratio increased in all groups: 1.4 times ( $p < 0.01$ ) in groups I and II, 1.3 times ( $p < 0.01$ ) in group III. Correlations between HPf/CAP ( $r = -0.408$ ;  $p < 0.01$ ) and VEGF/liver stiffness ( $r = 0.372$ ,  $p = 0.036$ ) were found.

**Conclusions:** Children with MASLD-associated fibrosis are characterized by elevated serum VEGF, TGF- $\beta$ 1, HPp/b, and GAG levels. Assessment of these parameters may be useful for diagnosis of MASLD-fibrosis.

## **BARRIERS AND FACILITATORS FOR PROMOTING HEALTHY WEIGHT: A QUALITATIVE STUDY BASED ON FOCUS GROUP DISCUSSIONS WITH OBESE PATIENTS**

### **OPTIMIZING MULTIDISCIPLINARY CARE MODELS**

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**Background and Aims:** Obesity is a chronic metabolic condition associated with multiple comorbidities that, besides mortality, impacts on quality of life <sup>1</sup>. In Brazil, the prevalence of obesity continues to rise, reaching 24% in 2023<sup>2</sup>. The literature indicates that, although awareness of the need for weight management is widespread among patients, several obstacles such as adherence to healthy diets, regular exercise practices, issues of self-esteem, and social support significantly impact the effectiveness of these programs<sup>3</sup>. Previous qualitative studies highlight the prevalence of significant barriers rather than facilitators, especially in low- and middle-income populations, and reveal a need for more personalized and culturally sensitive approaches <sup>4,5,6</sup>.

**Methods:** In 2022, the Multidisciplinary Study Group for Promoting Healthy Weight (GEMPPS) was initiated, a multidisciplinary weight management program held at the Hospital Universitário - Universidade de São Paulo (HU-USP). To be included in the program, patients must have BMI  $\geq 30$  kg/m<sup>2</sup> and can be self-referral or medical referral from one of the outpatient clinics of HU-USP. These patients undergo continuous monitoring throughout the program by teams from medicine, nursing, nutrition, physiotherapy, psychology, and physical education at the initial time and 3, 6, 9, and 12 months. This study used qualitative methodologies through pre-scripted focus group discussions (FGDs) to capture in-depth insights into the perceptions of obese individuals enrolled.

**Results:** In preliminary results, we found high rates of anxiety (90%)

**Conclusions:** Anxiety is a main barrier in obesity treatment management

## METABOLIC NEUTRALITY AND ORGANOPROTECTIVE EFFECTS OF ANTIHYPERTENSIVE THERAPY

### OPTIMIZING MULTIDISCIPLINARY CARE MODELS

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**Background and Aims:** Objective. To evaluate the metabolic and nephroprotective effects of antihypertensive therapy (AHT) including nitrendipine and amlodipine in patients with arterial hypertension (AH).

**Methods:** Materials and Methods. The study included 111 male and female patients with grade I–III arterial hypertension (AH) according to the ESC/ESH 2018 classification. The average age of the patients was  $56.2 \pm 12.3$  years, and the average duration of AH was  $9.73 \pm 6.67$  years. All patients were divided into two groups: Group 1 – patients receiving combination AHT including nitrendipine ( $n=58$ ), Group 2 – patients receiving AHT including amlodipine ( $n=53$ ). Serum uric acid and creatinine levels were measured using an enzymatic method on the Daytona TM biochemical analyzer (Rendox, UK). The results are presented as  $M \pm SD$ .

**Results:** . Over the 12-month period of antihypertensive therapy, no negative impact was observed on lipid profile, glucose levels, uric acid, or creatinine levels in either group, indicating the metabolic neutrality of the applied treatment. In the nitrendipine group, a tendency toward a decrease in creatinine levels was noted, accompanied by a significant increase in glomerular filtration rate ( $77.6 \pm 18.5$  ml/min/ $1.73$  m<sup>2</sup>  $\rightarrow$   $79.3 \pm 21.1$  ml/min/ $1.73$  m<sup>2</sup>,  $p < 0.02$ ), suggesting a pronounced nephroprotective effect of nitrendipine-based therapy. In the amlodipine group, a tendency toward a reduction in uric acid levels was observed ( $6.6 \pm 1.64$  mg/dL  $\rightarrow$   $6.27 \pm 1.69$  mg/dL,  $p = 0.059$ ), which may indicate a potential uricosuric effect of the drug.

**Conclusions:** Conclusion. The findings highlight the safety and additional benefits of antihypertensive therapy with nitrendipine and amlodipine, particularly in terms of renal protection and metabolic profile maintenance in hypertensive patients.



## PRO-INFLAMMATORY MEDIATORS SEQUESTERED IN AORTIC VALVE DISEASE PLAQUE AND THEIR RELATIONSHIP WITH ADIPOSITY AND INFLAMMATORY RESPONSE

### OTHER

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**Background and Aims:** Cardiovascular diseases (CVD) are prevalent worldwide and are associated with high morbidity and mortality. Valve lesions and vascular atherogenesis negatively impact the prognosis of CVD. Some studies highlight the importance of valvular tissue components and their ability to sequester bioactive molecules. Additionally, experimental models have shown that the sequestration of inflammatory interleukins in extracellular matrix structures similar to cardiac valves, such as atheromatous plaques, may be related to the progression of vascular aging.

**Methods:** This was a cross-sectional, observational, analytical, and correlational study. The population included patients with valvular disease and CVD undergoing valve replacement. During surgery, a sample of the plaque adhered to the damaged valve was obtained, where the tissue concentration of IL-1 $\beta$  and nitric oxide was determined using an in vitro secretome assay in the presence of different concentrations of collagenase, verified by MMP activity. Mediator levels in the supernatant were measured using ELISA immunoassay. The results were compared with epidemiological and cardiometabolic data.

**Results:** The study population consisted of 15 patients undergoing cardiothoracic surgery, either for valve replacement (11 patients, 73.3%) or coronary revascularization (4 patients, 26.6%). The median age was 72 years (66.7, 80.0), with 12 (80%) being male, and diabetes mellitus (53.3%) being the most common comorbidity. The median plasma LDL cholesterol level was 151.5 mg/dL (121.0, 182.3), and HDL cholesterol was 39.8 mg/dL (27.0, 52.7). Gelatinolytic activity was evidenced by gel zymography. After collagenase treatment, IL-1 $\beta$  and nitric oxide levels sequestered in the atheromatous plaque showed a correlation of  $\rho = 0.05$  and  $0.62$ , respectively, with BMI.

**Conclusions:** The results suggest that pro-inflammatory mediators sequestered in valvular plaque may be related to factors such as adiposity and inflammatory response in patients with valvular heart disease undergoing cardiovascular surgery.

## YOUTHFUL GUT MICROBIOME IMPROVES LIVER FUNCTION AND SUPPRESSES HCC IN OLDER MICE

### OTHER

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**Background and Aims:** Hepatocellular carcinoma (HCC) is projected to affect 22 million individuals by 2032. Limited treatment options and challenges in early detection highlight the urgent need for safe, preventive strategies against HCC. This study investigates the impact of youthful microbiomes (YMs) on HCC development in aging mice.

**Methods:** Fecal pellets were collected at 4 months and monthly autologous fecal microbiota transplantation (autoFMT) started at 12 months. Heart/liver functions and molecular changes in the liver were evaluated.

**Results:** Microbiome profiling revealed that autoFMT mitigated age-associated dysbiosis and significantly enhanced alpha diversity. Differential abundance analysis showed a 213-fold decrease in *Ileibacterium* and a 27-fold increase in *Lachnospiraceae* FCS020 in YM-treated mice compared to controls. Echocardiography demonstrated significant improvements in ejection fraction, stroke volume, and fractional shortening in YM-treated mice, indicating improved cardiac function. Remarkably, multiple HCCs were detected in 20% of 22-month-old control mice but none in YM-treated mice, suggesting that YM suppressed age-induced HCC. Serum ALT and AST were elevated in older mice but attenuated by YM treatment. YM also mitigated age-induced telomere shortening and reduced mononuclear cell infiltration in the liver. Inflammation and fibrosis markers, including IL6 and fibronectin, were elevated in older mice but ameliorated with YM intervention. YM restored mitochondrial function by significantly mitigating the decline in oxygen consumption rate. DNA damage was observed in aged mice but were markedly reduced after YM treatment, as confirmed by LA-qPCR. Notably, aging-induced activation of MDM2, an oncogene associated with HCC, was suppressed by YM.

**Conclusions:** YMs improve heart function, prevent HCC development, and reverse age-related liver dysfunction, inflammation, fibrosis, telomere shortening, mitochondrial decline, and DNA damage. These findings highlight YM autoFMT as a novel approach to mitigate aging-related functional decline and cancer risk, providing a scientific basis for developing YM-based microbial therapeutics to promote healthy aging and prevent malignancies.

## DOES PULSE PRESSURE CORRELATE WITH CARDIOVASCULAR CALCIFICATIONS IN MODERATE TO SEVERE CHRONIC KIDNEY DISEASE PATIENTS?

### OTHER

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**Background and Aims:** Cardiovascular calcifications are an important risk factor for cardiovascular events in patients with chronic kidney disease (CKD). This study aimed to assess the relationship of the pulse pressure parameter with aortic and mitral valve calcification and abdominal aortic calcification in patients with CKD of stages 3B and 4.

**Methods:** A cross-sectional study was conducted on fifty-one patients (29 men and 22 women) with CKD stages 3B and 4 (eGFR 15- 45 ml/min). The mean age was  $61.5 \pm 12.3$  years, and 19 were diabetics. Plain X-ray images of the lateral lumbar spine from all subjects were studied to calculate semiquantitative vascular calcification scores, described by Kauppila. The severity of the anterior and posterior aortic wall calcification was graded individually on a 0-3 scale for each lumbar segment, and the results were summarized to develop a score (range 0-24). Echocardiograms were examined for the absence or presence of calcifications of the mitral and aortic valves. Blood pressure was measured, and the mean of three readings was recorded.

**Results:** The mean pulse pressure of the study population was  $55.31 \pm 13.86$  mmHg. Twenty-one patients were identified with aortic abdominal calcification; the mean Kauppila score was  $3.01 \pm 3.46$ . Fourteen patients had at least one valve calcified, while six had both valves. In univariate analysis, every 1 mmHg increase in pulse pressure was not associated with a significantly increased risk for cardiovascular calcifications OR 1.01 (0.98-1.02),  $p=0.152$ . Also, there was no association in multivariate analysis, where every increase of 1 mm Hg in pulse pressure was not associated with a significantly increased risk for cardiovascular calcifications OR 1.02 (0.99-1.04),  $p=0.119$ .

**Conclusions:** In our study, pulse pressure did not correlate with cardiovascular calcifications in patients with moderate to severe CKD, despite the theoretical support of this hypothesis and our previous positive results in hemodialysis patients.

## VITAMIN B12 DEFICIENCY IN DIABETES MELLITUS TYPE 2 PATIENTS IN TREATMENT WITH METFORMIN

### OTHER

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**Background and Aims:** Background: Metformin is the first line of treatment in Diabetes Mellitus type 2, but now it is reported that about 6-30% of patients who are under treatment with metformin can have a vitamin B12 deficiency.

Aims: The aim of our study is to describe the prevalence of vitamin B12 deficiency in adults with DM type 2 who were under treatment with metformin compared to patients without diabetes.

**Methods:** Patients and Methods: The study included 150 patients aged 16-84 years with an average age of  $54.2 \pm 16.4$  years. Females were 56.6% (85 patients) and males 43.3% (65 patients). Serum B12 concentrations were quantified by chemiluminescent enzyme immunoassay. Vitamin B12 deficiency was considered if the blood level was below 200pg/ml and borderline-low B12 ( $\leq 300$ pg/ml) and if they were on metformin treatment for more than a year.

**Results:** The average level of Vitamin B12 in all patients was  $337.1 \pm 155.5$ pg/ ml. About 16.1% (24 patients) had vitamin B12 deficiency with an average level of  $145.3 \pm 30.4$  pg/m; and 48.4% (73 patients) had a borderline-low level with an average level of  $214 \pm 56.9$ pg/ ml. In the group of patients with DM type 2 who were under treatment with metformin, the average levels of vitamin b12 were lower (264pg/ml) compared to the group without metformin (409pg/ml) ( $p=0.06$ ). 21.5% of patients with diabetes under treatment with metformin were deficient in vitamins B12 ( $< 200$ pg/ml) compared to 4% of patients without diabetes.

**Conclusions:** Conclusion: Metformin could be a major risk factor for Vitamin B12 deficiency. Routine testing of Vitamin B12 levels should be taken into consideration by clinicians.

## SUBCLINICAL HYPOTHYROIDISM IN OLD AGE. WHEN SHOULD IT BE TREATED?

### PRACTICAL IMPLEMENTATION OF GUIDELINES IN PRIMARY CARE

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**Background and Aims:** Background: The life expectancy of the general population is growing time by time. This increase in life has also been accompanied by the increase in chronic diseases. In Europe the prevalence of hypothyroidism varies from 0.2-5.3%. According to the National Health and Nutrition Survey (NHANES III), the global prevalence of hypothyroidism is 4.6%.

**Methods:** We use literature review and last guidelines regarding the treatment of subclinical hypothyroidism in older adules -

**Results:** The incidence of thyroid diseases is more prevalent in women compare to males. In several studies, nowadays we believe that values TSH in serum are probably age – dependent; so, for people more than 70 years old, the normal range of TSH could be 5.28-5.9 mIU/l. In subclinical hypothyroidism the values of TSH are high and FT3 and FT are in normal range. We know that in overt hypothyroidism the treatment often continued lifelong. Many research supports the idea that levothyroxine treatment should be started when TSH values are more than 10 mIU/ml. Especially individuals of young age and with cardiovascular risk factors benefit greatly from treatment with levothyroxine, but caution is necessary when treating older adults with levothyroxine. In many studies the values of TSH in subclinical hypothyroidism are decreased in the second measurement of TSH, and second TSH is in range without treatment. Based on a high number of cases with subclinical hypothyroidism, a third measurement should be repeated, so we can decrease overtreatment with levothyroxine.

**Conclusions:** Hypothyroidism, overt or subclinical, is a very frequent chronic disease among the older population; however, TSH circulating levels have been demonstrated to increase with aging, regardless of the existence of an actual thyroid disease. In subclinical hypothyroidism with TSH >10 mIU/L, treatment is indicated, but therapy of subclinical hypothyroidism should be made with caution.