Diabetes Self-care did not have an effect quality of life in people with type 2 diabetes followed in primary health care.

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This study investigated the relationship between adherence to self-care and quality of life (QoL) in people with type 2 diabetes (PwT2D) treated in primary health care (PHC). We included 199 participants aged ≥40 years, diagnosed with diabetes for at least two years and using oral antidiabetics and/or insulin. Participants completed the Diabetes Self-Care Activities Summary Questionnaire (SDSCA) and the Diabetes Quality of Life Measure (DQOL-Brazil), while clinical and laboratory data were collected from medical records. The average values were: age (63.1±10.4 years), duration of diabetes (10.2±8.8 years) and glycated hemoglobin (A1c) (8.2±2.1%). The total SDSCA and DQOL-Brazil scores were 45.8±16.5 and 93.6±10.5, respectively, with Cronbach's alpha coefficients of 0.61 and 0.8. Correlation analysis showed a weak relationship between SDSCA scores and diabetes duration (r=0.172; p=0.019) and no correlation with A1c (p=0.548). A similar pattern was observed for the DQOL-Brazil scores. No correlation was found between the SDSCA and DQOL-Brazil domains, regardless of glycemic control. Conclusion: Adherence to self-care did not have a significant impact on the QOL of PwT2D treated at the APS.

A sugars-sweetened beverages reduction strategy using non-nutritive-sweetened beverages or water for cardiometabolic risk reduction: The Strategies to Oppose Sugars with Non-Nutritive Sweeteners or Water (STOP Sugars NOW) randomized trial

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Background: Health authorities recommend against the use of non-nutritive sweeteners (NNS) and beverages (NSBs) as a replacement for sugars-sweetened beverages (SSBs) over metabolic and gut health concerns.

Aims: To assesses the effect of NSB versus water for SSB reduction on gut microbiota diversity, glucose tolerance, and cardiometabolic risk factors.

Methods: We conducted a pragmatic, open-label, crossover, randomized trial in adult consumers of SSB (≥1 serving/day) with obesity (NCT03543644). Participants were randomized to three 4-week interventions (SSBs, NSBs, water) with ≥4-week washouts. We prespecified three substitutions: NSBs for SSBs (intended), water for SSBs (standard of care), and NSBs for water (reference), and analyses: intention-to-treat (ITT; primary), completers (C), and per-protocol (PP). Primary outcomes were gut microbiota ß-diversity (weighted UniFrac distance) and glucose tolerance (incremental area under the curve (iAUC)). Other outcomes included markers

of adiposity, glucose-insulin regulation, lipids, and blood pressure (BP). Urinary biomarkers assessed adherence.

Results: Of 80 randomized participants (51% female; mean ± SD age, 42±13 y; BMI, 33.7±6.8 kg/m2; WC, 109±13.5cm; SSBs intake, 1.8 servings/d [range, 1-5]), 66 (83%) completed and 52 (65%) adhered to the protocol. There were no differences in primary outcomes across prespecified analyses. Substituting NSBs for SSBs improved WC (PP), triglycerides (ITT, C, PP), and high-density lipoprotein-cholesterol (HDL-C) (C), while water for SSBs improved insulin sensitivity (C, PP), insulin total and iAUC (C, PP), fasting C-peptide (PP), triglycerides (ITT, C, PP), HDL-C (C, PP), and diastolic BP (ITT, C, PP) (p<0.05). NSBs and water showed no differences for any outcomes. Urinary biomarkers confirmed intervention adherence based on group mean patterns, with 52/80 participants categorized as per protocol based on individual responses. There were no serious adverse events, and total adverse events were low with no differences across interventions.

Conclusions: In SSBs consumers living with obesity, the intended substitution of NSBs for SSBs did not affect glucose tolerance or gut microbiota ß-diversity with improvements for other cardiometabolic risk factors similar to the standard of care, water. These findings reinforce SSBs reduction by non-caloric approaches that may include NSBs.

Update on Soy Protein and Established Blood Lipid Targets: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Background: Current Health Canada and U.S. FDA approved health claims for soy protein and heart health are based on the ability of isolated soy protein (ISP)_to lower LDL-cholesterol (LDL-C) and total-C with an evidence census that extends only through 2013. There is a need to update these estimates and assess the ability of soy protein to lower other established blood lipid targets.
Aims: To update the evidence for ongoing development and re-evaluation of health claims for soy protein and heart health, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) of the effect of ISP on an expanded the set of established blood lipid targets in adults with and without diabetes.

Methods: We searched MEDLINE, Embase, and The Cochrane Central Register of Controlled Trials through March 25, 2024 for relevant randomized controlled trials (RCTs) of ≥3 weeks. Two independent reviewers extracted data and assessed risk of bias. The primary outcome was LDL-C and secondary outcomes were total-C and other established lipid targets (non-HDL-C, apo-B, HDL-C, and TG) . Data were pooled using the inverse variance method and expressed as a mean difference (MD) with 95% confidence intervals (95% CI). Heterogeneity was assessed by X2 and quantified by I2. Certainty of evidence was assessed using GRADE.

Results: We included 89 RCTs (138 trial comparisons) in 5,521 participants with various health statuses including people with and without diabetes. The median ISP dose was 30 g/d with non-ISP comparators that included animal protein, mixed macronutrients, carbohydrate, meal replacements and placebo over a median follow-up of 8 weeks. ISP reduced LDL-C (MD -0.13mmol/L [-0.17, -0.10 mmol/L]); total-C (-0.14mmol/L [-0.18, -0.10 mmol/L]); non-HDL-C (-0.16mmol/L [-0.21, -0.12 mmol/L]); and apo-B (-0.05g/L [-0.07, -0.04 g/L]); and triglycerides (-0.08mmol/L [-0.12, -0.05 mmol/L]) and increased HDL-C (0.03 mmol/L [0.04, 0.01mmol/L]), compared with a non-ISP comparator. No dose response (linear and non-linear) was seen for any

outcome. The certainty of evidence was assessed as moderate for LDL-C, total-C, non-HDL-C, apo-B, and HDL-C (single downgrade for imprecision or inconsistency) and low for triglycerides (downgrades for imprecision and inconsistency).

Conclusions: Updated evidence for LDL-C, total-C and an expanded set of established lipid targets reinforces the existing health claims for soy protein and heart health. There is a good indication that ISP at a median dose of 30g/d results in small important reductions in LDL-C and total-C as well as non-HDL-C and apo-B and trivial improvements in HDL-C in participants with varying health conditions including people with and without diabetes. There is some indication for trivial reductions in TG.

Registration: ClinicalTrials.gov identifier, NCT04861545.

Relation of Multiple Low Risk Lifestyle Behaviours with Cardiovascular Disease and All-Cause Mortality: A Systematic Review and Dose Response Meta-Analysis of Prospective Cohort Studies [Preliminary Results]

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Introduction: The association of combined low-risk lifestyle behaviours (LRLBs) with cardiovascular disease (CVD) and all-cause mortality has not been systematically quantified.

Objective: We undertook a systematic review and dose-response meta-analysis to assess the association of combined LRLBs with CVD and all-cause mortality.

Methods: MEDLINE, EMBASE and Cochrane were searched up to December 29, 2021. Prospective cohort studies reporting the association between a minimum of 3 combined LRLBs (including healthy diet) with CVD, coronary heart disease (CHD) and stroke incidence and mortality were included. Independent reviewers extracted data and assessed study quality. Highest vs. lowest LRLB score was pooled using random effects. Heterogeneity was assessed (Cochran Q) and quantified ($I2$). Global dose response meta-analysis (DRM) for maximum adherence was estimated using one-stage linear mixed model. The certainty of the evidence was assessed using GRADE.

Preliminary Results: 116 cohort comparisons (n=9,775,191) involving 382,922 cases were included. Comparing highest with lowest adherence LRLBs were associated with lower risk of CHD incidence (RR, 0.29 [95% CI, 0.21, 0.42]), stroke incidence (0.56 [0.50, 0.62]), CVD incidence (0.47 [0.37, 0.58]), CHD mortality (0.32 [0.25, 0.41]), stroke mortality (0.37 [0.30, 0.46]), CVD mortality (0.41 [0.34, 0.49]) and all-cause mortality (0.46 [0.41 to 0.52]). DRM analysis showed a linear association between LRLBs and all outcomes reaching a global DRM between 59-76% protection. LRLBs were defined with variable ranges as a healthy body weight

(body mass index <30kg/m2), healthy diet (healthy diet score >median), regular physical activity (1/week to >30 minutes/day), smoking cessation (never smoked or smoking cessation), light alcohol intake (≤30g/day) and adequate sleep (5.5-9 hours). The certainty of the evidence was graded as moderate to high owing to downgrades for inconsistency and/or upgrades for a large magnitude of effect and significant dose-response gradient.

Conclusions: Pooled analyses show that the combination of LRLBs was associated with a substantial lower risk of CVD outcomes and all-cause mortality. The available evidence provides a very good indication of the benefit of combined LRLBs.

Protocol Registration: ClinicalTrials.gov identifier, NCT03234101"

Low-GI Mediterranean diet reduces insulin secretion in adults at risk for type 2 diabetes: the MEDGICarb Trial

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Introduction: A Low- versus High-Glycaemic Index (GI) Mediterranean Diet (MedDiet) reduces postprandial glycemic and insulin responses in overweight/obese individuals at high risk of developing type 2 diabetes. However, the underlying mechanisms remain unclear.

Objectives: To assess if improved postprandial glycaemic and insulin responses to a low-GI MedDiet are mediated by changes in insulin secretion and gastrointestinal hormones, we evaluated the effects of low- versus high-GI MedDiet on postprandial C-peptide, free fatty acids (FFA), glucagon-like peptide 1 (GLP-1) in MedGiCarb study participants.

Methods: Fifty-four participants ((32M/22 F), aged 30-69 years, with a BMI of 25-37 kg/m², high waist circumference plus another component of metabolic syndrome, were enrolled in a randomized, controlled, parallel-group study. Participants were assigned to a low-GI (<55) or high-GI (>70) Mediterranean diet for 12 weeks. The diets were isocaloric and matched for macronutrient and fiber content. Blood samples were collected at baseline and after 12 weeks, both fasting and at 8-hour postprandial intervals following breakfast and lunch, which reflected the assigned diet. Postprandial responses of C-peptide and gastrointestinal hormones were assessed by ELISA methods and FFA by enzymatic method.

Results: Postprandial plasma C-peptide was significantly lower after low-GI meals compared to high-GI meals, both at baseline (p=0.004) and after 12 weeks (p=0.0001). The effect was most pronounced after lunch, with C-Peptide postprandial response (iAUC) 23% and 30% lower after low-GI lunch, at baseline and 12 weeks, respectively. GLP-1 postprandial response did not change at baseline, while it was 57% lower after low-GI meals compared to high-GI meals after 12 weeks (p=0.031). No significant changes were observed for FFA.

Conclusions: This study shows that a low- versus high- GI Mediterranean diet reduces insulin secretion, as shown by lower C-peptide levels. This effect helps preserve beta-cell function over time, thereby reducing the risk of developing type 2 diabetes in individuals at high cardiometabolic risk. Further analysis of gastrointestinal hormone responses, beyond GLP-1, will clarify their role in response to dietary glycemic index modifications.

MOCA-1 Study: Metabolic Impact of Different Milk vs Plant Protein in Type 2 Diabetes and Healthy Participants

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Background: High-protein diets influence metabolic responses, including glucagon and insulin secretion, depending on the protein type. This effect may be linked to differences in amino acid (AA) composition and absorption. AAs stimulate glucagon release, which promotes liver fat oxidation and insulin secretion.

Aims: We want to characterize the response of glucagon, insulin, C-peptide and AAs in different protein types. Specifically, we investigate the effect of slow and fast digesting milk proteins as well as a pea protein.

Methods: This RCT included ten participants with T2D and then without. Participants conducted seven investigation days at random. Each participant underwent mixed-meal-tests with double-blinded drinks containing one of the six different whey-to-casein protein ratios or a pea protein drink, all containing 30g protein.

Results: 20 participants (50% female, mean age 59 years, BMI of 32kg/m²)were included. Fasted and postprandial glucose and C-peptide levels of T2D participants were significantly higher than controls, with no basal insulin differences. Glucose, insulin and C-peptide did not differ between drinks. In the control group, postprandial glucagon was significantly higher after consumption of protein drinks with 80% casein and 20% whey and significantly lower with 10% casein and 90% whey, when compared to the pure casein or pea protein drinks. No differences were observed in the T2D group. Amino acid analysis showed differences in arginine AUC for 100% whey and alanine iAUC after 90% whey and 10% casein, and methionine iAUC containing pure casein. Comparing drinks across the control group, we found significant differences in the AUC of phenylalanine, proline, and tryptophan. In the diabetes group, significant differences between drinks were only observed for tryptophan.

Conclusions: Protein type impacts glucagon secretion and postprandial glucose regulation. In controls, we observed differences in glucagon response while in T2D no, indicating a dysregulation. Selecting appropriate protein types could modulate glucagon secretion and improve metabolic outcomes.

Towards a non-invasive glucose monitoring approach using wearables and AI

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Introduction: Non-invasive glucose monitoring for diabetes is an emerging area of research due to its potential to improve patient long-term disease management and compliance. Current invasive methods, often cause discomfort and poor compliance. These limitations motivate the search for non-invasive alternatives that can provide accurate real-time measurements.
This project is part of a larger EU-funded initiative, involving a consortium of European partners developing advanced technological pipelines, one of which will focus on using wearables to collect photoplethysmography (PPG) data for non-invasive glucose monitoring.

Aim: The aim of this study is to develop a machine learning (ML) algorithm that can accurately estimate glucose levels from PPG signals collected through wearables.

Methods: In this study, adults with and without T2D will undergo metabolic tests while wearing wearables (smartwatches and finger clips) to collect PPG data. This data will be used to develop a ML algorithm that integrates not only glucose values but also physiological insights to filter noise and enhance glucose prediction accuracy. A human-in-the-loop approach is ensured with explainable AI and the AI-Dapt platform that makes the algorithm capable of adapting to new data and information. The study will proceed in two phases: 1) development, during which we will collect PPG and glucose data to train the predictive algorithm, and 2) validation, where the algorithm's performance will be tested to improve accuracy and reliability.

Results and conclusion: It is an ongoing project. We expect to develop a non-invasive approach to estimate blood glucose levels using PPG from 600 samples to further refine the algorithm and improve its predictive accuracy. As more data is integrated, we will provide a robust solution for glucose monitoring. The application of AI and ML in this context holds the potential to revolutionize continuous, real-time glucose monitoring, a field that currently lacks accessible and accurate non-invasive alternatives.

The possible effects of low income on glycemic control in elderly patients with type 2 diabetes

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Background-Aims: Type 2 diabetes mellitus (T2DM) is common in high rates among the elderly, resulting in significantly higher rates of morbidity, mortality and cost. The aim of this study was to evaluate the level of glycemic control in these patients in relation to their dietary habits and income.

Methods: A total of 453 patients, aged 65-75 years, with T2DM participated in the study. These were outpatients of the general diabetes clinic of the General Hospital of the National Institute of Diabetes and Digestive and Kidney Diseases in collaboration with the scientific medical team of the National Institute of Diabetes and Digestive and Kidney Diseases. The value of glycosylated hemoglobin was measured, among other things.

Results: The mean age was 71 ± 2.8 years. The prevalence of dietary diversion in relation to dietary guidelines given in our sample was 36%. Participants with dietary diversion were significantly more likely than participants with dietary discipline to have poorer glycemic control, as defined by hemoglobin A1c $\geq 8.5\%$ (42 vs. 33%, adjusted odds ratio 1.48 [95% CI 1.07–2.04]). Participants with dietary diversion were more likely to report difficulty affording more for a typical diet for diabetes (64 vs. 49%, $P < 0.001$). They also reported lower diabetes self-efficacy ($P < 0.001$) and higher diabetes-related emotional distress ($P < 0.001$). Difficulty following a healthy diet and emotional distress partially mediated the association between dietary diversion and glycemic control.

Conclusions: Dietary diversion is an independent risk factor for poor glycemic control. This risk may be partly attributed to increased difficulty in implementing dietary guidelines and to economic conditions that do not favor dietary adherence to these guidelines.

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Investigation of dietary intake in individuals with type 2 diabetes and comparison with the dietary recommendations of the DNSG

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Introduction-Objective: Diet plays a crucial role in the management of Type 2 Diabetes (T2D), improving clinical markers and the quality of life of patients. The aim of this study is to assess the dietary intake of energy and macronutrients in individuals with T2D and compare it with the recent evidence-based dietary recommendations of the European Association for the Study of Diabetes (DNSG: Diabetes and Nutrition Study Group) (Aas et al., 2023).

Materials-Methods: This is a cross-sectional study involving 100 adults with T2D, diagnosed at least 1 month before enrolling in the study. For each participant, social, anthropometric, and medical data were collected, and a semi-quantitative food frequency questionnaire (FFQ) was used to assess dietary intake (Bountziouka et al., 2012). FFQ were analyzed according to Greek food composition tables.

Results: 51% of the study participants are obese, and 39% are overweight. The average energy intake was 2.336 kcal. Carbohydrates accounted for 33.3% of total energy intake, proteins for 14.6%, and fats for 52.4%. The average % energy intake of the sample in saturated fats and sugars differed significantly ($p < 0.01$) from the recommendations (<10%), with the average intake of saturated fats being higher (12.9%) and sugars being lower (4.9%). Finally, the average intake in grams of dietary fiber differed significantly ($p < 0.01$) from the recommendation (35g), being lower (24.2g).

Conclusions: Study participants have focused on reducing carbohydrates and seem to have adhered to the restriction of sugars. However, the reduction in carbohydrates may have led to an increase in the consumption of foods high in saturated fatty acids and low in fiber. Therefore, it is of utmost importance for individuals with T2D to receive dietary guidance, so that any recommendations are communicated in a way that ensures the adoption of an overall quality diet."

Approaches for Sustaining Diabetes Prevention Program Practices Post-Graduation: A Narrative Review

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Background: Diabetes Prevention Programs (DPP), year-long group-based lifestyle interventions, have been shown to reduce the incidence of type 2 diabetes (T2DM) by 58% and improve cardiometabolic risk factors for the 537 million adults with prediabetes worldwide. However, the sustainability of these benefits in DPP graduates and the effectiveness of booster intervention programs designed to support long-term cardiometabolic health remain unclear. Aims: The objective of this narrative review was to examine the availability, structure, and effectiveness of post-DPP booster programs for graduates.

Methods: Searches were conducted for intervention studies published before February 2025 using electronic databases PubMed, CINAHL, and Cochrane Clinical Trials. Potential studies were screened for inclusion by two independent reviewers. Due to the small number of studies and reporting heterogeneity, a meta-analysis was not performed, and findings were synthesized narratively.

Results: Of 1,613 articles screened, nine publications representing four unique studies were eligible for inclusion. Post-DPP booster interventions significantly reduced long-term T2DM incidence ($p \leq 0.001$), but changes in blood glucose and hemoglobin A1c were inconsistent across studies. Significant improvements were observed in key anthropometric risk factors, including body mass index ($p < 0.05$), weight ($p < 0.05$), weight change ($p \leq 0.03$), and waist circumference ($p \leq 0.008$). Although longer intervention durations were commonly associated with greater effectiveness, variations in program structure, intensity, and participant adherence likely contributed to the inconsistencies in review findings.

Conclusions: Booster programs for DPP graduates may help reduce long-term T2DM risk and improve cardiometabolic risk factors. This review highlights strategies to sustain DPP benefits after graduation and can be used to inform the design of cost-effective, scalable interventions to address the growing global prediabetes burden."

Impact of morning vs. evening intake of high-protein meals on metabolic state of individuals with prediabetes or type 2 diabetes: pilot results of the PROTIME trial

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Background: High-protein diets have been shown to positively impact glucose metabolism, but the role of protein intake timing is unclear. We conduct a clinical trial comparing two isocaloric and normoproteic diets with different protein distributions in individuals with prediabetes and type 2 diabetes (T2D).

Aims: To investigate feasibility and preliminary efficacy of tested diets for improving glucose metabolism and cardiometabolic parameters.

Methods: For the ongoing trial (NCT06382480), 30 individuals (BMI 25-40 kg/m2) with prediabetes (n=15) and non-insulin-treated T2D (n=15) are being recruited. The trial employs a randomized cross-over design comparing two 4-week dietary interventions: high-protein (HP) breakfast / high-carbohydrate (HC) dinner (HP/HC) and HC breakfast / HP dinner (HC/HP) compared to baseline. Participants receive personalized nutritional plans, report food intake and undergo continuous glucose monitoring (FreeStyle Libre Pro iQ). Anthropometry, metabolic parameters, SF-36, PSQI, satiety and hunger questionnaires were analyzed.

Results: In the preliminary results within HP/HC intervention, morning meals were 35.9±4.5 EN% carbohydrate (CHO), 31.0±3.1 EN% fat (F) and 34.4±2.7 EN% protein (P), evening meals included 55.8±6.7 EN% CHO, 29.6±5.1 EN% F and 10.9±2.1 EN% P. In the HC/HP intervention, morning meals were 60.3±3.2 EN% CHO, 29.2±3.2 EN% F and 10.8±0.6 EN% P, evening meals included 34.5±5.6 EN% CHO, 33.3±7.1 EN% F and 32.9±5.7 EN% P. Body weight reduced in both interventions (HP/HC: p=0.02; HC/HP: p=0.01). Mean absolute glucose (MAG) decreased in HC/HP (p=0.03), indicating increased glucose fluctuations, but other glycemic indices remained unchanged. HDL cholesterol reduced in HC/HP (p=0.004). AST decreased in HP/HC (p=0.04). Emotional well-being improved in HC/HP (p=0.002). No changes were found in other metabolic parameters, anthropometry, PSQI, satiety and hunger scores.

Conclusion: The preliminary findings of the PROTIME trial show high adherence and feasibility of both dietary interventions. Cardiometabolic effects of protein distribution need to be investigated in the larger cohort.

The Integration and Evaluation of Behaviour Change Theory in a Plant-based Intensive Lifestyle Intervention for Diabetes Remission

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Background: With type 2 diabetes rates continuing to rise, there is a need to identify sustainable strategies to alleviate both the public health and economic burden of this disease. Successful diabetes remission trials using intensive lifestyle interventions (ILI) have targeted weight loss through dietary and physical activity approaches. These interventions have limited evidence of integration of behavioural change theory (BCT), which could better support sustainable behaviour change, weight loss, and diabetes remission.

Aim: To design and assess a sustainable plant-based ILI that integrates BCT for weight loss and diabetes remission.

Methods: Following the REAIM and Quadruple Aim frameworks, the implementation of our plant-based ILI will be evaluated in the REPAIR (REmission of diabetes using a PlAnt-based weight loss InteRvention) trial. The REPAIR trial is a 12-month, parallel, 2-arm randomized trial in 160 adults living with early type 2 diabetes (<6 years) and obesity. Participants will be randomized to either standard of care or the plant-based ILI targeting 15% weight loss. The ILI will include: 1. a plant-based dietary intervention (consisting of a weight-loss phase with a high plant protein total diet meal replacement [0-12 weeks] and a weight maintenance phase with a stepped-food [12-28 weeks] and full-food [28-52 weeks] reintroduction using the Portfolio Diet Program [mobile app, kickstart package, text messages], 2. structured physical activity program (16-weeks [during 12-28 weeks], followed by self-monitoring), and 3. a sustainable behaviour curriculum (over 52-weeks). The sustainable behaviour curriculum, consisting of 19 modules, implemented behaviour change strategies mapped onto the COM-B model (3 elements: Capability, Opportunity and Motivation) and the Theoretical Domain Framework (TDF, 14 domains of behaviour change). Self-reported behavioural change will be assessed using a questionnaire with TDF mapped to intervention features and behavioural adherence to the intervention (e.g. energy, diet and exercise adherence, objective biomarkers of diet intake, curriculum completion, visit attendance, etc.) at 12-, 28- and 52-weeks. Focus groups will be held at 12-, 28- and 52-weeks to identify barriers and facilitators and inform adaptive design. Healthcare economic analyses will be evaluated using the EQ5D-5L and hospital administrative databases (ICES). Correlations will be calculated to assess the relationship between self-perceived behaviour change and behavioural adherence. Multiple logistic regression models will be used to identify the key behavioural adherence that predict weight loss (achieving ≥15% weight loss) at 12-, 28- and 52-weeks and diabetes remission at 28- and 52-weeks. Qualitative data from focus groups will be analyzed thematically. Subgroup analyses will assess effect modification by sex, gender, and social determinants of health.

Conclusions: By integrating and evaluating BCT and assessing behavioural adherence, this research will provide a sustainable health behaviour intervention with direct evidence of the healthcare economic benefits to inform healthcare program development and address the pressing diabetes epidemic in Canada.

Effect of a sugars-sweetened beverages reduction strategy using soymilk versus cow's milk on liver fat: The Soy Treatment Evaluation for Metabolic health (STEM) randomized trial

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Background: Liver fat represents an early metabolic lesion in the development of diabetes and its cardiometabolic complications. Diets high in free sugars, particularly from sugars-sweetened beverages (SSBs), are associated with abdominal obesity and increased cardiometabolic risk, prompting global guidelines to limit SSBs as a major public health strategy. Low-fat cow's milk is promoted as the preferred caloric replacement strategy for SSBs due to its high nutritional value and cardiometabolic advantages. Fortified soymilk is a plant-based alternative that offers an equivalent nutritional value with approved health claims for cholesterol and coronary heart disease risk reduction. With concerns regarding its classification as an ultra-processed food (UPF), it is unclear whether soymilk has comparable metabolic health benefits to milk as part of clinical and public health strategies for SSBs reduction.

Aims: To assess the effect of SSBs reduction using fortified soymilk versus low-fat cow's milk as the standard of care on intrahepatocellular lipid (IHCL) in at-risk SSBs consumers living with obesity.

Methods: The STEM trial was a 24-week, pragmatic, 3-arm, parallel, randomized trial. We recruited adults living with obesity (high BMI plus high waist circumference) consuming ≥1 SSBs/day. Participants were randomized to one of 3 groups based on their usual intake (servings/day) of SSBs at baseline: SSBs (355 mL can); fortified, sweetened 2% soymilk (250mL Tetra Pak); or 2% cow's milk (250mL Tetra Pak). The primary outcome was change in IHCL (measured by ¹H-MRS) at 24-weeks. Hierarchical testing was done to reduce the familywise error rate. The superiority of the cow's milk to SSBs were assessed first to establish assay sensitivity. If superiority was established, then the non-inferiority of the soymilk to the cow's milk was assessed using a pre-specified noninferiority margin of 1.5% IHCL units (assessed by difference of means using a 90% confidence interval [CI]). Analyses were

performed by the intention-to-treat (ITT) principle, using ANCOVA with inverse probability weighting (IPW), adjusted for age, sex, background medications, dose (usual SSBs intake at baseline), and baseline IHCL.

Results: We randomized a total of 186 participants (57% male; mean [SD] age, 39.9 [11.8] years; BMI, 34.6 [6.1] kg/m², waist circumference, 112.6 [13.8] cm; IHCL, 10.0% [8.2%] with 64.1% meeting the criteria for non-alcoholic fatty liver disease [≥5% IHCL]; SSBs intake, 2.3 [1.3] servings/day). Both cow's milk (mean change difference [95% CI], −1.58% [−3.39 to -0.23]) and soymilk (−2.27% [−4.33 to −0.20]) reduced IHCL, demonstrating superiority to SSBs at 24-weeks. With superiority established, soymilk was found to be non-inferior to cow's milk with the upper 90% CI falling below the prespecified 1.5% noninferiority margin (difference of means [90% CI], -0.69% [−2.60 to 1.19]).

Conclusions: In at-risk SSBs consumers living with obesity, SSBs reduction using fortified, sweetened soymilk is non-inferior to the standard of care, cow's milk in reducing liver fat. Soymilk represents an effective clinical and public health SBBs reduction strategy for improving metabolic health.

Trial registration: ClinicalTrials.gov identifier, NCT05191160

Metabolomics profiles associated with type 2 diabetes and their associations with mortality

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Background: Type 2 Diabetes has been associated with increased mortality risk. Metabolomics offers a comprehensive approach to identifying metabolic alterations associated with type 2 diabetes, potentially improving risk stratification for all-cause mortality and longevity.

Aims: This study aimed to identify metabolomic profiles of type 2 diabetes and assess their association with the risk of all-cause mortality and longevity.

Methods: The study was conducted in a subset of participants at high risk of cardiovascular disease from a plasma metabolomics diabetes case-cohort study (mean age 66.5, 62% women; 176 with incident type 2 diabetes and 523 without diabetes) in the context of the Prevención con Dieta Mediterranea (PREDIMED) trial. Plasma metabolites were analyzed using LC-MS/MS methods at baseline (discovery sample) and 1 year of follow-up (validation sample). Metabolomic signature for type 2 diabetes was derived using elastic net regression. Cox proportional hazards models and conditional logistic regression assessed the association of metabolomic profiles with all-cause mortality and longevity (>84 years old).

Results: A total of 31 metabolites were associated with type 2 diabetes. Type 2 diabetes metabolomic profile was significantly associated with a higher risk of mortality (HR = 1.55, 95% CI: 1.04–2.33) and lower odds of longevity (OR = 0.52, 95% CI: 0.34–0.91)

Conclusion: In an older population at high cardiometabolic risk, we identified a metabolomic signature of type 2 diabetes associated with all-cause mortality risk and longevity, potentially explaining some mechanisms behind the increased risk of mortality observed in epidemiological studies for individuals with glycemic dysregulations.

The effect of food sources of soy protein on blood pressure: A systematic review and meta-analysis of randomized controlled feeding trials

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Background: Soy protein's approved health claim for coronary heart disease risk reduction is based on its ability to lower cholesterol. The evidence for its ability to lower blood pressure, a leading modifiable risk factor for coronary heart disease, remains unclear.

Objective: To clarify the effects of soy protein on reducing blood pressure, we conducted a systematic review and meta-analysis of randomized controlled trials (RCTs).

Methods: MEDLINE, Embase, and The Cochrane Central Register of Controlled Trials were searched through September 29, 2024. We included RCTs of >3-weeks. Two independent reviewers extracted data and assessed risk of bias. Outcomes included systolic blood pressure (SBP) and diastolic blood pressure (DBP). Data were pooled using the inverse variance method and expressed as a mean difference (MD) with 95% confidence intervals (95% CI). Certainty of evidence was assessed using GRADE.

Results: We included 57 RCTs with 77 trial comparisons in 4043 participants across various health conditions. Food sources of soy protein included mixed soy foods, soy protein beverages, soymilk, soy nuts, soy yogurt, soybeans, and soy baked goods, with a median dose of 25g of soy protein. Comparators included whole food animal proteins, whey, casein, milk protein, cow's milk, carbohydrate, placebo or usual diet, with a median dose of 15g of protein. Total soy protein sources reduced SBP (MD -1.37mmHg [95% CI, -2.32 to -0.43mmHg]) and DBP (-0.93 [-1.64 to -0.22]). There was effect modification by food source (P<0.001) for SBP and DBP, with soymilk showing reductions in SBP and DBP (-4.98 [-9.08 to -0.88], -3.63 [-6.60 to -0.65] respectively), soy nuts in SBP and DBP (-3.78 [-6.16 to -1.40], -1.79 [-3.49 to -0.08] respectively) and soy baked goods in DBP (-2.52 [-4.81 to -0.23]). The certainty of evidence was low-to-moderate for these food sources.

Conclusion: The effect of soy protein on blood pressure is dependent on food source. The available evidence provides an indication that soymilk results in a moderate reduction and soy

nuts a small important reduction in SBP and DBP, and soy baked goods a moderate reduction in DBP, in participants with varying health conditions.

Registration: ClinicalTrials.gov identifier, NCT05638061.

Postprandial Glucose Dynamics Reveal Pathophysiological Subtypes of Type 2 Diabetes: Implications for Precision Nutrition

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Background: Reducing postprandial glucose response (PPGR) is essential for glycemic control and the prevention of complications in type 2 diabetes (T2D). However, individuals with T2D show heterogeneous responses to the same meal, suggesting distinct underlying pathophysiological mechanisms.

Objective: To characterize the shape of the PPGR using dynamic modeling and identify subtypes of T2D that may benefit from tailored nutritional interventions.

Methods: Fifty individuals with T2D underwent continuous glucose monitoring (CGM) during a standardized breakfast test. A dynamic model was applied to describe the 4-hour PPGR through three parameters: amplitude (magnitude of glucose excursion), frequency (rate of glucose rise), damping (rate of glucose decline). Subjects were clustered based on these parameters, and clinical/metabolic variables were compared across groups using one-way ANOVA.

Results: Three distinct PPGR patterns were identified: Pattern 1 (n=18): high amplitude; Pattern 2 (n=21): low damping and frequency (delayed and prolonged response); Pattern 3 (n=11):high frequency (rapid glucose rise). No differences were observed in age, BMI, waist circumference, HbA1c, or diabetes duration. However, Pattern 2 showed higher fasting insulin, HOMA-IR, GGT, and triglycerides (features of metabolic syndrome) compared to Pattern 1 ($p<0.05$). Pattern 3 exhibited lower C-peptide levels compared to Pattern 2 ($p=0.044$), suggesting reduced insulin secretion.

Conclusions: Modeling PPGR dynamics revealed distinct T2D subtypes with specific metabolic profiles, independent of traditional glycemic and anthropometric measures. These findings support the use of CGM-derived PPGR patterns as a tool to guide precision nutrition strategies in T2D management.

Vegetable Intake and Coronary Heart Disease Risk: Discovery, Replication, and Application of Food Biomarkers in Free-Living Individuals

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Background: Objective biomarkers for assessing vegetable intake are sparse.

Aims: To identify urinary biomarkers of vegetable intake and examine their prospective associations with coronary heart disease (CHD) risk.

Methods: Food biomarker discovery was conducted within the Lifestyle Validation Study, using urinary 1H nuclear magnetic resonance (1H-NMR) metabolomic features and 7-day diet record assessments. Two-part models were used to identify NMR features sensitively and specifically responsive to individual food items. The Least Absolute Shrinkage and Selection Operator (LASSO) was applied to derive multi-feature indices for total and subgroup vegetable intake. Feature replication was conducted in the Hispanic Community Health Study/Study of Latinos (SOL). Associations with CHD risk were examined in nested case-control studies in the Nurses' Health Study (NHS), NHSII, and SOL.

Results: LASSO identified >=20 features for total, dark-green, and red/orange vegetables, and legumes, and multi-feature indices showed Pearson correlations of 0.32-0.56 in the discovery cohort. Indices for total and dark-green vegetables and legumes, but not red/orange vegetables, were replicated in SOL (de-attenuated Pearson correlations = 0.40-0.48). Multivariable-adjusted ORs (95% CIs; highest vs. lowest quartile) of CHD risk were 0.76 (0.54-1.06) for total vegetables (P-trend=0.07), 0.67 (0.47-0.94) for dark-green vegetables, and 0.61 (0.44-0.85) for legumes (both P-trend<0.05). As a specific example, NMR features responsive to Brussels sprout intake were identified and confirmed to be S-methyl cysteine sulfoxide and levulinate, with Pearson correlations of 0.49 and 0.39 with intake, respectively.

Conclusions: Using untargeted metabolomics and diet records-assessed diet, we identified urinary biomarkers of Brussels sprout intake in an observational study setting. Additionally, developed multi-feature indices of the intake of dark-green vegetables and legumes were inversely associated with CHD risk. Overall, this study demonstrated the feasibility of food biomarker discovery through this cost-effective approach, as well as the use of NMR data to aid in nutritional epidemiological investigations with disease outcomes.

Replacement of Animal with Plant Protein Foods Reduces Blood Pressure in Individuals with Prehypertension or Hypertension: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Background: Hypertension is the top modifiable risk factor of cardiovascular disease, the leading cause of global mortality. Over one billion individuals are living with hypertension worldwide, with prevalence twice as high in those with type 2 diabetes (T2D). The hypertension-T2D comorbidity increases the risk of cardiovascular diseases by 2-4-fold, highlighting the importance of hypertension management in the prevention and management of T2D. While dietary modifications are the cornerstone of hypertension management, with T2D guidelines emphasizing the integration of plant-based dietary components, the specific role of replacing animal with plant protein foods on blood pressure (BP) in those with prehypertension or hypertension is unclear.

Objective: To assess the effect of replacing animal with plant protein foods on BP in individuals with prehypertension or hypertension in a systematic review and meta-analysis of randomized controlled trials (RCTs).

Methods: MEDLINE, Embase, and Cochrane Library were searched through March 2024 for RCTs ≥ 3 weeks. Systolic BP (primary outcome) and diastolic BP data were extracted by two independent reviewers. Random-effect models were used to estimate pooled mean differences and 95% confidence intervals (CI). Heterogeneity was assessed and quantified using Cochran Q and I^2 statistics. The certainty of evidence was evaluated using GRADE.

Results: The analysis included 7 RCTs, comprising 8 trial comparisons in prehypertension or hypertension (n=635). Intervention arms featured soy protein powders (n=4) and soy-based foods (n=4) as substitutes for milk protein powder (n=4), animal meat (n=2), and dairy products (n=2). Replacing animal with plant protein foods reduced systolic BP by 4.33 mmHg (95% CI -8.41 to -0.26 mmHg) and diastolic BP by 2.35 mmHg (95% CI -4.50 to -0.21 mmHg), with substantial heterogeneity (I^2=88.94% and 83.75%, respectively, PQ<0.001). Subgroup analyses showed influence by food matrix in both systolic and diastolic BP (P=0.004 and P=0.029, respectively), with the replacement of whole foods showing greater reductions in systolic BP

(-9.54 mmHg, 95% CI -16.82 to -2.26) and diastolic BP (-4.75 mmHg, 95% CI -8.90 to -0.60). GRADE was moderate owing to downgrades for inconsistency.

Conclusion: Available evidence suggests that replacing animal with plant protein foods, especially soy-based products, leads to moderate BP reductions in people with prehypertension or hypertension. This reduction appears to be restricted to the displacement of whole foods. These findings support T2D clinical practice guidelines recommending plant-based dietary patterns for hypertension prevention and management (ClinicalTrials.gov identifier, NCT02037321).

Correlations between VeggieMeter and self-reported carotenoid, fruit and vegetable intake among older adults: Results from BRinging the Diabetes prevention program to Geriatric populations

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Background: Fruit and vegetable intake (FVI) among older adults remains below recommended levels for disease prevention. Subjective dietary assessment can be burdensome and costly. Reflection spectroscopy (RS) offers a non-invasive method to assess skin carotenoids as a biomarker of FVI but remains underexplored in older adults.

Aim: To test the hypothesis that VeggieMeter® (VM) scores will be positively correlated with self-reported vegetable and carotenoid intake among older adults.

Methods: This is a secondary analysis of data from an ongoing NIH-funded randomized, controlled trial where participants were counseled to make healthy changes including increased FVI. Participants were n=151 older adults (>=65 years) with prediabetes and had their skin carotenoids levels (scored 0-800) measured by VM using RS technology. We performed univariate descriptive analyses of population characteristics, Spearman correlations, and linear regression models to examine the association between VM scores and self-reported FVI and carotenoid intake measured by food records (mean days=5.5 (sd=1.0)), adjusted for participant characteristics.

Results: Participants were 72.0 (sd=5.3) years old, 65.6% female, 60.9% White, 10.6% Hispanic/Latinx, with an average BMI of 31.9 (sd=4.3) kg/m2. 72.2% reported dietary supplement use. Average FVI was 3.5 (sd=2.9) servings per day, reported carotenoid intake was 9,182 (sd=7,090) mcg, and mean VM score was 267.5 (sd=104.2). VM score was not correlated with self-reported FVI, or vegetable or fruit intake alone (all $p>0.05$). VM scores were correlated with carotenoid intake (R=0.25, $p<0.05$), but this correlation was no longer significant after adjustment for age, sex, race, ethnicity, BMI, smoking status, and reported supplement use.

Conclusions: This study supports the hypothesis that VM score is correlated with self-reported carotenoid intake, suggesting potential utility of VM as an objective assessment measure of carotenoid status among older adults with prediabetes. Future work will examine sensitivity to change after participation in a Diabetes Prevention Program adapted for older adults."

Nutraceutical Improvement of glucose Metabolism, NAFLD and insulin Resistance by Oat-fiber supplementation in type 2 Diabetes mellitus patients – The randomised-controlled NIMROD study

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Background: Epidemiological studies suggest, that increased intake of insoluble cereal fiber is associated with lower risk for type 2 diabetes (T2D), NAFLD, cardiovascular disease and certain cancers. Contrary to that, previous RCTs found only small effects on glycemia and liver fat. However, these effects seemed to be pronounced in persons with NAFLD.

Aims: The NIMROD study investigates, whether insoluble oat fiber may reduce liver fat content, glycemia and inflammation in patients with T2D and NAFLD.

Methods: We recruited patients (18-75 years) with insulin-resistant T2D and NAFLD. Participants underwent a 12-week drinking powder supplementation providing 15 grams of insoluble oat fiber per day or placebo (maltodextrin). Patients should maintain overall diet and physical activity, which was monitored with pedometers, food and supplement records. Routine blood analyses, a mixed-meal tolerance test, anthropometry (including body composition) as well as magnetic-resonance tomography and spectroscopy were done at baseline and follow-up. Statistical analysis for primary (liver fat) and secondary outcomes was done by ANCOVA following ITT- and as-treated-principles (alpha<0,05).

Results: 94 participants (age 63±10 years; BMI 31,3±4,9 kg/m²; 48 % women) were randomized, 11 persons dropped out prematurely. After 12 weeks of intervention, there was no significant group difference for change in liver fat content (-0,2±2,5 % vs. 0,2±3,0 %; p=0,533) as well as for fasting and 2-h glucose, HOMA-IR, Matsuda-ISI, visceral fat, inflammatory and lipid outcomes. HbA1c showed a trendwise benefit for fiber (-0,1±0,3 % vs. 0,1±0,4 %; p=0,052). Body weight, food intake and physical activity remained constant in both groups.

Conclusions: Our data do not show a significant benefit by a 12-week supplementation with insoluble oat fiber in patients with T2D and NAFLD for any major metabolic outcome. The relatively short intervention period, limited assessment of insulin resistance or actual ineffectiveness in this group of patients could be reasons. Further research is needed.

Comparative Associations of the DASH, Mediterranean, and Portfolio Dietary Patterns with Cardiovascular Mortality in US Adults

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Background: Cardiovascular disease (CVD) persists as the main cause of death in the United States (US), despite effective pharmacotherapies. With nearly half of US adults consuming poor-quality diets, there is an opportunity to enhance public health. As dietary modification is a leading strategy for CVD prevention, evaluating the associations of established dietary patterns with CVD mortality in a nationally representative sample will inform clinical guidelines.

Aim: To evaluate the associations of adherence to the DASH, Mediterranean, and Portfolio dietary patterns with CVD mortality.

Methods: We included 13,586 nonpregnant adults without prior CVD from NHANES (1988-1994). Diet was assessed at baseline using a 24-hour dietary recall supplemented with a food frequency questionnaire to calculate three scores: the DASH-style diet adherence score (DASH score), the alternative Mediterranean diet score (aMED), and the Portfolio Diet Score (PDS). Mortality outcomes were ascertained through the National Death Index through December 31, 2019. Weighted Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs). The primary outcome was CVD-mortality. Other mortality outcomes included coronary heart disease (CHD), stroke, and all-cause mortality.

Results: Over 23-years of follow-up (311,826 person-years), 1,751 CVD deaths, including 1,416 CHD, 335 stroke deaths, and 5,202 all-cause deaths occurred. Comparing highest vs. lowest tertiles of adherence in multivariable-adjusted models: DASH was associated with lower risks of CVD (HR: 0.76; 95% CI: 0.61, 0.94), CHD (0.75; 0.60, 0.95), and all-cause mortality (0.82; 0.71, 0.94); aMED was associated with lower CVD (0.82; 0.73, 0.99) and all-cause mortality (0.80; 0.71, 0.90), while the estimate for CHD included the null (0.84; 0.70, 1.01); PDS was associated with lower CVD (0.84; 0.73, 0.98), CHD (0.82; 0.72, 0.95), and all-cause mortality (0.86; 0.78, 0.96). Associations with stroke mortality were uncertain for all three patterns: DASH (0.80; 0.48, 1.38), aMED (0.73; 0.46, 1.15), and PDS (1.03; 0.75, 1.44). When scores were

modeled continuously results were consistent and a higher score of aMED (by 3-points, range 0-9) was associated with a lower risk of CHD no longer including the null (0.86; 0.75, 0.99).

Conclusions: For all three dietary patterns higher adherence was associated with lower risk of CVD and all-cause mortality in US adults. These findings support the use of these dietary patterns in clinical and public health approaches to CVD prevention.

Ultra-processed foods consumption and cardiometabolic risk factors in children from the CORALS cohort

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Introduction: High ultraprocessed food (UPF) intake has been associated with cardiometabolic risk in adults, but evidence in children is limited. This study investigates the association between UPF consumption and cardiometabolic risk factors in preschool children from the Childhood Obesity Risk Assessment Longitudinal Study (CORALS).

Methods: This cross-sectional analysis included 1426 children aged 3-6 years recruited from seven Spanish cities (2019–2022). Inclusion required parental consent and completed questionnaires on prenatal history. UPF consumption was estimated using food frequency questionnaires and the NOVA classification. Associations between energy-adjusted UPF consumption and z scores of adiposity parameters (BMI, fat mass index, waist circumference,

waist-to-height ratio) and cardiometabolic parameters (blood pressure, fasting plasma glucose, insulin resistance, lipid profile) were analyzed using adjusted linear regression models.

Results: Children with higher UPF intake had younger mothers with higher BMI, lower education, and employment rates. Compared to the lowest UPF tertile, those in the highest tertile had increased BMI z scores (β=0.20, 95%CI: 0.05-0.35), waist circumference (β=0.20, 95%CI: 0.05-0.35), fat mass index (β=0.17, 95%CI: 0.00-0.32), and fasting plasma glucose (β=0.22, 95%CI: 0.06-0.37), and lower HDL cholesterol z scores (β=−0.19, 95%CI: −0.36 to −0.02). Replacing 100 g of UPFs with unprocessed or minimally processed foods was associated with lower BMI, fat mass index, and fasting plasma glucose z scores.

Conclusions: High UPF consumption in preschool children is associated with adiposity and cardiometabolic risk factors. Public health initiatives should promote replacing UPFs with healthier alternatives to improve early childhood health outcomes.

Changes in dietary intake and eating behavior traits during a 3-year lifestyle intervention (T2D-GENE study).

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Background: The burden of type 2 diabetes (T2D) demands new resource-effective solutions for its prevention. Not all high-risk individuals can receive individual counseling for lifestyle changes; therefore, group and internet-based solutions are needed.

Aims: We aimed to investigate whether group and internet-based counseling is effective in changing diet and eating behavior in people at high risk of T2D.

Methods: T2D-GENE trial involved 973 pre-diabetic men (fasting plasma glucose ≥5.6 mmol/l) from the Metabolic Syndrome in Men (METSIM) cohort, with either high or low genetic risk for T2D. Participants were assigned to either intervention or control group for three years. Participants in the intervention group received group-based intervention with 5-7 group sessions and had access to a web portal focused on healthy diet and physical activity. They had four laboratory visits and five 4-day food records, for which they received individual feedback. The Three-Factor Eating Behavior questionnaire-R18 was used to assess three eating behavior traits (cognitive restraint, uncontrolled eating and emotional eating). Participants in the control group had two laboratory visits and they got general health advice as a part of their METSIM cohort protocol. All participants also filled out food frequency questionnaires.

Results: The intervention lowered the risk of T2D by 52%. There were statistically significant changes towards more recommended food consumption (higher frequency of whole-grain products and non-tropical vegetable oils and increased consumption of fruits, vegetables and berries) in the intervention group. Participants in the intervention group decreased dietary intake of saturated fatty acids and increased intakes of monounsaturated fatty acids, polyunsaturated fatty acids and fiber. During the intervention, cognitive restraint increased while uncontrolled eating and emotional eating decreased statistically significantly.

Conclusions: The T2D-GENE intervention demonstrated that a group and interned-based lifestyle intervention can effectively improve diet quality and eating behavior, as well as decrease the risk of T2D.

Urinary sodium and potassium excretions, gut microbiome, circulating metabolites, and cardiometabolic risk

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Background: A high-sodium, low-potassium diet promotes hypertension and cardiovascular disease (CVD). The role of the gut microbiome in this association is not well-characterized.

Aim: To understand the impact of salt intake on the gut microbiome and investigate the identified microbial features in relation to metabolomic profiles and cardiometabolic incidence.

Design: In 264 men from the Men's Lifestyle Validation Study, we examined the gut taxonomic and functional compositions in response to 24-hour urinary sodium and potassium excretion. We further assessed plasma metabolomic profiles responsive to the identified gut microbial features and their associations with coronary heart disease (CHD), CVD, and type 2 diabetes (T2D) among 12,225 participants from Nurses' Health Study (NHS), NHSII, and the Health Professionals Follow-up Study.

Results: We identified 25 sodium-responsive species, including Collinsella, Desulfovibrio, and Roseburia species, along with 4 potassium- and 4 sodium-to-potassium ratio-responsive species. Microbial scores correlated strongly with urinary sodium, potassium, and their ratio (Pearson r = 0.37–0.57). High-sodium and low-potassium microbiome scores were linked to a favorable plasma metabolomic profile, characterized by higher imidazole propionate, and lower hippuric acid and 3-indolepropionic acid levels. These metabolomic alterations were associated with an increased risk of developing CHD (Quintile5 vs. Quintile1: HR=2.14 [95%CI: 1.53, 2.99]; p-trend < 0.0001), CVD (HR=1.56 [1.34, 1.83]; p-trend < 0.0001), and T2D (HR=3.03 [2.56, 3.60]; p-trend < 0.0001).

Conclusions: Our findings linked high sodium and low potassium intake to a specific gut microbial pattern that predicted an adverse metabolomic profile precipitating an elevated risk of developing cardiometabolic conditions. Overall, these data suggest that the human gut microbiome can actively participate in the etiological processes linking high salt intake with adverse health outcomes.

From Research to Results: New Evidence for Diabetes-Specific Formulas to Manage Individuals with Type 2 Diabetes. Impact on Acute and Long-Term Glycemic and Metabolic Control

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Background: There is a lack of large-scale, well-designed randomized controlled trials (RCTs) examining the acute and long-term effects of diabetes-specific formulas (DSFs) in individuals with type 2 diabetes (T2D) in Asia.

Aims: This research comprises three RCTs aimed at investigating the effects of DSFs on a wide range of outcomes.

Methods: Two randomized, crossover studies compared the effects of DSFs on postprandial glucose, insulin, glucagon-like peptide-1 (GLP-1), and satiety with commonly consumed breakfasts (rice porridge, bread with jam, noodle soup, glutinous rice) in 156 individuals with T2D. Additionally, a randomized, controlled, parallel study investigated the long-term effects of DSF as a meal replacement or partial meal replacement with standard of care (DSF group) versus standard of care alone (control group) in 235 overweight and obese adults with T2D. All three RCTs were conducted in Asia between 2020 and 2024, using DSFs with similar nutrient profiles.

Results: The crossover studies showed that the incremental area under the curve (iAUC) for glucose and insulin were significantly lower, while insulin sensitivity (Insulin Secretion Sensitivity Index-2, Insulinogenic Index) was significantly higher for DSF, compared to rice porridge, bread with jam, and glutinous rice (all P≤0.042). The GLP-1 iAUC for DSF was significantly higher than bread with jam (P<0.001). Ad libitum lunch intake was significantly lower with DSF compared to rice porridge (P=0.030). No significant differences were found in subjective appetite between any of the breakfasts (all P≥0.331). The parallel study showed that at day 90, the DSF group had more pronounced reductions in glycated hemoglobin, fasting blood glucose, body weight, visceral adipose tissue, and body fat percentage, and an increase in percent fat-free mass (all P=0.047) compared to the control group. The DSF group also showed significant improvements in blood pressure, waist and hip circumferences compared to the control group (all P≤0.045).

Conclusions: These findings demonstrate the efficacy of DSFs in improving both acute and long-term glycemic and metabolic control in individuals with T2D.

Children's perception of snacks with reduced sugar content

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Developing snacks and beverages with reduced sugar content contributes to the strategies aimed at decreasing sugar intake. To satisfy consumer demand, sugar is replaced with other types of natural or artificial sweeteners, resulting in food products with high sweetness intensity. The prevalence of snacks and beverages with a high sweetness sets the preference and craving for sweet food. On the other hand, a sharp reduction in products' sweetness without considering sensory perceptions results in low consumer acceptance and product failure. The objective was to evaluate children's perception of two snacks with reduced sugar content using the analysis of their facial expressions. Methods: 94 children (47 girls and 47 boys, 9-15y), tested two products with reduced sugar content: muffins (M, 1g sugar/85g) and brownies (B, 3g sugar/44g). The pleasantness was measured using 9-point (pt) Peryam & Kroll (P&K) and 100mm visual analogue (VAS) scales, and the facial expressions to food tasting were assessed using Noldus FaceReader-8. Results: The pleasantness was 6.7±2.0pt-P&K, 66.0±29.1mm VAS for B and 5.0±2.2pt-P&K, 44.1±30.3mm VAS for M ($P<0.0001$). Tasting M resulted in a higher facial expression of disgust and sadness than tasting B ($P<0.05$), while the expression of surprise was higher for tasting B than M ($P<0.05$). The valence was more negative, and the arousal was lower for tasting M compared to B ($P<0.05$). Conclusion: The analysis of children's facial expressions during food tasting reliably predicts the hedonic acceptance and can be used to evaluate the perception of new and reformulated food products with reduced sugar content.

Weight- and non-weight-based approaches to diabetes remission: a scoping review

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Background: The global prevalence of type 2 diabetes mellitus continues to rise, where obesity is the driving risk factor. Diabetes remission (defined as an HbA1c <6.5% without glucose-lowering medications for ≥3 months) has recently emerged as an established therapeutic goal. Remission can be achieved through surgical, pharmacological, or behavioural interventions, most of which target weight loss as the principal mechanism. However, emerging research suggests that remission may also be attainable through weight-independent pathways. The scope and characteristics of both weight- and non–weight-based approaches to diabetes remission remains unclear.

Aim: To conduct a scoping review and map evidence from published and registered randomized controlled trials of interventions for diabetes remission.

Methods: We followed the Cochrane Handbook for systematic reviews and PRISMA-extension for scoping reviews. Medline, Embase, the Cochrane Library, and ClinicalTrials.gov were searched through January 8, 2025 for relevant randomized controlled trials of interventions for diabetes remission ≥8 weeks.

Results: Of 471 reports identified, 101 unique trials met the eligibility criteria. Of 101 unique trials, 54 were published (24 bariatric, 4 pharmacological, 17 lifestyle, 9 combination interventions) and 34 are underway (7 bariatric, 7 pharmacological, 14 lifestyle, 6 combination interventions) and 13 are status unknown/terminated (4 bariatric, 5 pharmacological, 3 lifestyle [1 terminated], 1 combination interventions) on ClinicalTrials.gov. Approximately half (49%) identified diabetes remission as the primary outcome, comprised of 21 (43%) published trials, 19 (39%) underway and 10 (20%) with unknown status/terminated on ClinicalTrials.gov. Of the 54 published trials, 44 were weight-based and 10 were non-weight-based. Of the 44 weight-based trials, 22 (50%) compared the intervention to a standard of care, with the majority (N=19/22, 86%) showing a direction of effect that favoured the intervention compared to control and 32% of bariatric, 42% of lifestyle, and 26% of combination interventions showing statistically significant diabetes remission. The remaining 22 trials compared interventions to active comparators, such as bariatric to lifestyle, bariatric to pharmacological, or comparisons within bariatric approaches, with 6 showing directionality favouring bariatric surgery over other approaches. Of the 10 non-weight-based trials, 5 compared the intervention to standard of care, with 2 (40%) favouring the intervention over the control and 50% of lifestyle and 50% of pharmacological interventions showing statistically significant diabetes remission. The remaining 5 trials compared interventions to active comparators (within pharmacological or

within lifestyle approaches). Of the 34 trials underway, 68% employ weight-based approaches, including lifestyle (35%), bariatric (30%), combination (22%) and pharmacological (13%) interventions.

Conclusions: These preliminary findings underscore the evolving landscape of diabetes remission research, emphasizing the role of both weight- and non-weight-based approaches.

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Consumption of fructose-containing food and beverage sources in childhood through to adulthood and risk of hypertension

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Background: High intakes of fructose-containing sugars among children and adolescents is implicated in obesity and related comorbidities, including hypertension. However, sugar-sweetened beverages (SSBs), fruit juices, and whole fruit, have very different nutritional profiles and matrices, which confer different effects on blood pressure.

Aims: To use prospective data from the Growing Up Today Study (GUTS) to investigate the association between intake of SSBs, fruit juice, and whole fruit in childhood through to adulthood and risk of hypertension.

Methods: The GUTS is a longitudinal cohort enrolling 25,749 children and adolescents (age at enrollment mean = 12 years, SD =1.86) followed prospectively from 1996-2021. Participants provided updated information on lifestyle, health status, and habitual diet via validated food frequency questionnaires every 1-4 years. We conducted multivariate adjusted cox proportional hazards regression models to estimate the associations of SSB, fruit juice, and whole fruit intake (categories of servings/day) with incident hypertension (hazard ratios [HR] and 95% confidence intervals [CI]), adjusting for age, sex, other diet, lifestyle, and other risk factors. We also modeled substitutions (per 1 serving/day) of SSBs for fruit juice, whole fruit, milk, and water as well as substitutions of fruit juice for whole fruit, milk, and water.

Results: During 25 years of follow-up, 1625 participants reported a diagnosis of hypertension. In adjusted models, participants with the highest intake of SSBs (≥ 2servings/day) and fruit juice (≥

1.5 servings/day) had a higher risk of hypertension compared to lowest intake (HR, 1.52; 95% CI, 1.27, 1.83; P-trend < 0.01 and HR, 1.35; 95% CI, 1.06, 1.71; P-trend = 0.02, respectively). In contrast, whole fruit was not associated with hypertension (highest vs. lowest category HR, 0.79; 95% CI, 0.59, 1.05; P-trend = 0.08). Replacing 1 serving per day of SSBs with milk, water, or whole fruit was associated with 13%, 9%, and 22% lower risk of hypertension, respectively. Additionally, replacing fruit juice with whole fruit was associated with a 19% lower risk of hypertension.

Conclusions: SSBs and fruit juice were positively associated with a dose-response higher risk of hypertension, independent of overall diet quality, physical activity, and other factors. No significant associations were found for whole fruit. Our findings support public health guidelines to limit the overconsumption of SSBs and fruit juice starting in childhood to protect against the development of cardiometabolic risk factors, including hypertension

Ultra-processed foods and cognitive health in older adults: A 2-year prospective cohort analysis

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Background: Ultra-processed foods (UPFs), which are often rich in sugars, unhealthy fats, salt, and additives, have become increasingly prevalent in modern diets, raising concerns about their impact on health. Higher UPF consumption has been associated with increased cardiovascular risk, and cardiometabolic health. However, the relationship between UPF consumption and cognitive health, particularly in older populations, remains understudied.

Aims: To investigate the association between UPF consumption and cognitive performance in older Spanish adults at high cardiovascular risk

Methods: A 2-year prospective analysis was conducted with a cohort of 4,600 adults (aged 55-75) with overweight/obesity (BMI ≥27 to <40 kg/m²) and metabolic syndrome from the PREDIMED-Plus study. UPF consumption (g/day) was assessed annually using a validated 143-item semi-quantitative food frequency questionnaire, with foods categorized by their degree of processing using the NOVA classification system. Cognitive function was assessed as z-score change from baseline to 2 years using an extensive neuropsychological battery. Multivariable linear regression models were used to assess associations between sex- and energy-adjusted, cumulative average UPF consumption and 2-year changes in cognitive performance.

Results: In multivariable-adjusted models, higher UPF consumption (comparing the highest to the lowest tertile) was negatively associated with 2-year change in global cognitive function (β coefficient = -0.042; 95% CI: -0.082 to -0.002; p-trend = 0.037) and attention (β = -0.059; 95% CI: -0.113 to -0.005; p-trend = 0.016). Continuously, per each 100 g incremental increase in energy-adjusted UPF consumption were associated with lower global cognitive function (β=-0.017, 95% CI: -0.032 to -0.003, p-value = 0.018).

Conclusions: Higher UPF consumption was associated with a decline in cognitive performance compared to those with lower UPF consumption over 2 years in older Mediterranean adults with

overweight/obesity and metabolic syndrome. These findings highlight the potential adverse impact of UPFs on cognitive health, warranting further investigation, particularly in at-risk populations.

Carbohydrate Quality Index and Mortality Risk: Insights from the PREDIMED Trial

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Background: Carbohydrates are the global primary source of dietary energy, yet there is still controversy regarding the health attributes of carbohydrate quality.

Aims: We investigated the association of carbohydrate quality with all-cause and cause-specific mortality (cardiovascular disease [CVD], cancer, and other causes) in older adults at high cardiovascular risk.

Methods: Within the PREDIMED trial, an observational analysis was conducted involving 7,210 participants (aged 55-80 years, 57.5% women). Carbohydrate quality variables were determined as cumulative averages from dietary information obtained annually from validated, semi-quantitative 137-item food frequency questionnaires. A carbohydrate quality index (CQI) was estimated adding quintiles of four dimensions: total dietary fiber intake, whole-grain-to-total grain ratio, solid carbohydrate-to-total carbohydrate ratio, and low glycemic index. CQI was the primary outcome assessed, with secondary outcomes of interest being the individual carbohydrate quality dimensions. Mortality was assessed based on annual visit examinations, yearly review of medical records and linkage to the National Death Index. Multivariate Cox proportional hazard models were utilized.

Results: During 6 years of median follow-up, 425 deaths were documented (103 cardiovascular deaths, 169 cancer deaths, and 153 other deaths). Multivariable-adjusted hazard ratios (95% confidence intervals) for the second versus first tertile of CQI were 0.75 (0.59 to 0.95) for all-cause mortality, 0.60 (0.37 to 0.97) for cardiovascular mortality, and 0.59 (0.40 to 0.87) for cancer mortality. Similar associations were observed when early cases of mortality were excluded. Additionally, glycemic index, whole grains, and the ratio of solid to total carbohydrates, but not dietary fiber or glycemic load, were significantly associated with some mortality outcomes.

Conclusions: Findings suggest that dietary carbohydrate quality may be linked to reduced mortality risk. However, further research is needed to explore additional aspects of carbohydrate quality and to examine these associations in diverse, large-scale populations.

A cross-sectional study to assess awareness and practice of complications and its screening among Diabetes and Hypertension patients in rural central India.

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Background: Noncommunicable diseases kill 41 million people per year and account for 71% of all deaths worldwide. It is essential to focus on reducing the risk factors associated with these diseases, as well as monitoring the progression and trends of Diabetes and Hypertensions and their risk in order to prevent premature mortality from these diseases, which is primarily caused by patients' lack of awareness of the complications, as well as poor screening opportunities for the complications.

Aim: Assess the knowledge of Diabetes and Hypertension complications based on screening practices.

Methods: A community-based cross-sectional study of 220 patients was conducted in rural central India villages to better understand their awareness and screening practices for Diabetes and Hypertension complications.

Results: The majority of the participants (28.2%) were only aware of one of the complications, with cardiovascular complications being the most well-known (88.7%), followed by cerebrovascular and ophthalmic complications (62.9%). More than a quarter of those polled were aware that uncontrolled diabetes and hypertension can result in medical emergencies. When asked about screening practices, very few (9.5%) had had blood tests, ECG (4.5%), Urine (6.8%), Ophthalmic (5.5%), or HBA1c (4.1%). Logistic regression revealed that those with higher education and participants with both HTN and diabetes had a higher odds of screening practices.

Conclusion: Our findings revealed that there is average awareness and low screening practices for Diabetes and Hypertension complications, implying that the component on health education and promotion of screening practices to prevent further complications for those already diagnosed with Diabetes and Hypertension should be expanded.

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Alcohol consumption, smoking and their synergy as risk factors for Incident Type 2 Diabetes

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Background and aims: Smoking has been independently related to an increased risk of type 2 diabetes (T2D). Controversial results have been reported for the association between alcohol and T2D onset, while the joint exposure to tobacco and alcohol use has not been explored. Here, we investigated the association of individual and combined tobacco-alcohol exposure with T2D risk.

Methods: Participants in the NutriNet-Santé web-based cohort (2009-2023) who were free of T2D and had data on alcohol consumption and smoking habits at enrollment were included in these prospective analyses (N = 110,076; mean age 42.9±14.6 years, 79.2% women). Multivariable Cox regression models were fitted to explore the relationships of alcohol consumption (<2 portions/day vs. ≥2 portions/day, <10 portions/week vs. ≥10 portions/week, and as grams of ethanol/day), tobacco use (never vs. former/current smoker), and the combined effect of smoking-alcohol consumption with risk of T2D.

Results: During a median follow-up of 7.5 years (820,470 person-years), 1,175 incident T2D cases were identified. In the fully-adjusted models, no significant differences in T2D risk were detected among categories of alcohol consumption or by alcohol intake (g/day). Compared to never-smokers, former/current smokers showed an increased risk for T2D (HR: 1.36;1.20-1.53). An increased risk of T2D was observed for heavy smokers compared to light/moderate smokers (HR: 2.10;1.46–3.02). Being a former/current smoker with an alcohol consumption ≥10 portions/week was not associated with a higher risk of T2D (HR: 1.11;0.95–1.29) compared to having one or neither of these exposures.

Conclusions: These findings support smoking as an independent risk factor for T2D, and showed that alcohol consumption does not confer any protection against T2D risk. The combined effect of alcohol and tobacco use on T2D risk, and the mechanisms behind this relationship should be further explored.

Metabolomic profiles related to glycemic index, glycemic load, and carbohydrate quality and its association with type 2 diabetes, cardiovascular disease, and mortality.

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Background: The glycemic index (GI), glycemic load (GL), and carbohydrate quality index (CQI) are intended to measure carbohydrate quality and have been associated with type 2 diabetes (T2D) and cardiovascular disease (CVD) onset, with limited evidence regarding mortality. However, evidence regarding their ability to predict these health outcomes and the specific metabolomic pathways involved is still scarce.

Aims: To identify metabolomic profiles related to GI, GL, and CQI in an older population at high cardiovascular risk and to elucidate their longitudinal association with T2D, CVD and all-cause mortality.

Methods: The study was conducted in a subset of 1,865 participants from the PREvención con DIeta MEDiterranea trial, who had various cardiovascular risk factors at baseline but no CVD. Plasma metabolites were analyzed using LC-MS/MS methods. Metabolomic signatures for GI, GL, and CQI were derived using elastic net regression applying nested 10-fold cross-validation for model refinement. Pearson's coefficients were estimated from weighted metabolite profiles.

Cox proportional hazard models (HR;95%CI) assessed the association of these metabolomic profiles with incident T2D, CVD, and all-cause mortality.

Results: The metabolic profiles included 45 metabolites for GI, 71 for GL, and, and 63 for CQI metabolites. The GI metabolomic profile was associated with a higher risk of CVD, T2D, and mortality (HR;95%CI: 1.75;1.27–2.42; 1,52;1.19-1.95, and 1.13;1.01-1.27, respectively). The GL metabolomic profile was associated with an increased risk of CVD (HR;95%CI, 1.96;1.41–2.73), and mortality (HR;95%CI, 1.13;1.01–1.27). Conversely, the CQI metabolomic profile was associated with a 50% and 18% lower CVD and mortality risk (all p<0.001), but not with T2D.

Conclusion: In an older population at high cardiometabolic risk, GI, GL and CQI metabolomic signatures were identified and associated with T2D, CVD, and mortality. A metabolic profile associated with a higher CQI might reduce future CVD events and death.

Metabolomic Profiling of Ultra-processed Food Consumption: Early Indicators of Cardiometabolic Risk in Children Aged 3 to 6 Years

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Background: The increasing consumption of ultra-processed foods (UPFs) during early childhood has raised concerns about their potential impact on cardiometabolic risk factors (CMRF). Understanding how the UPF consumption affects the metabolome in early childhood could provide insights into the early origins of cardiometabolic risk.

Aims: To identify metabolomic profiles associated with UPF consumption and their relationship with CMRF in children aged 3–6 years.

Methods: Children from Childhood Obesity Risk Assessment Longitudinal Study (CORALS), with baseline metabolomic data were included in this cross-sectional analysis (n= 1,148). Energy-adjusted UPF consumption (grams/day) was estimated using a validated, food frequency

questionnaire and classified according to NOVA system. A composite of cardiometabolic risk score (CMRs) was calculated using the age- and sex-specific z-scores for fat mass index (FMI), blood pressure (systolic and diastolic), HDL-c (inverted), LDL-c, triglycerides, and HOMA-IR (glucose, insulin). Plasma metabolites were quantified by NMR spectroscopy. UPF-related metabolites were identified using linear regressions. Lipid (LS) and amino acid (AAS) scores were derived via partial least squares regression and tested for association with CMR using FDR-adjusted robust generalized linear models.

Results: Nineteen metabolites (13 lipids, 6 amino acids) associated with UPF consumption (FDR <0.05). The LS was linked (β, [95%CI]) to lower HDL (-0.22, [-0.24, -0.20]), and higher triglycerides (0.22[0.17, 0.23]) and CMRs (0.38[0.28, 0.48]; all FDR < 0.01). The AAS was associated with lower triglycerides (-0.20, [-0.26, -0.15]), HOMA-IR (-0.06, [-0.10, -0.03]), insulin (-0.07, [0.10, -0.03]), CMRs (-0.47, [-0.64, -0.30]), and higher HDL (0.24, [0.20, 0.27]; all FDR <0.01).

Conclusion: Metabolomic profiles associated with UPF consumption in pre-schoolers showed differential associations with cardiometabolic risk. These findings highlight the potential of metabolomics to uncover early dietary-related biomarkers relevant to cardiometabolic health.

Impact of early vs. late time-restricted eating on glucose and lipid profiles and internal circadian time in overweight or obese women

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Background: Time-restricted eating (TRE) is a promising strategy to improve metabolic outcomes but there is a lack of carefully controlled trials.

Aims: We investigated whether timing of the eating window during the isocaloric TRE affects diurnal rhythms of circadian clock and improves glycemic control and lipid profile.

Methods: A randomized cross-over trial was completed by 31 overweight or obese non-diabetic women (age 58.4y; BMI 30.5kg/m2). They followed a two-week early TRE (eTRE, eating 8a.m.-4p.m.) and two-week late TRE (lTRE, eating 1p.m.-9p.m.) being asked to consume their usual food quality and quantity. Glycemic control was assessed by continuous glucose monitoring (CGM). Lipid profiling was conducted by high throughput shotgun plasma lipidomics. Internal circadian time was assessed by the BodyTime assay in blood monocytes.

Results: Participants showed a high timely adherence, unchanged dietary composition, minor daily calorie deficit (eTRE:-167kcal) and weight reduction (eTRE:-1.1kg, lTRE:-0.4kg). Circadian phase in blood monocytes was advanced by 40 min after the lTRE compared to the eTRE. The 24-hour glucose profiles were also shifted accordingly to the eating timing. The mean 24h glucose levels, mean amplitude of glycemic excursion (MAGE), and glucotypes were unchanged by both TRE interventions. Mean of daily difference (MODD) index slightly decreased during both eTRE (p=0.037) and lTRE (p=0.003). The eTRE intervention affected 103 lipid species, reducing ceramide (P = 0.043) and phosphatidylcholine (P = 0.043) classes, and altered the activity indices of desaturases D5D, D6D, and D9D, as well as elongase ELOVL6. The lTRE altered D5D index but caused no substantial changes in lipid species and classes.

Conclusion: A nearly isocaloric TRE induced changes of circadian systems but does not clinically relevantly alter glycemic control in overweight or obese women. However, eTRE has more pronounced effects on the plasma lipid profile compared to lTRE, suggesting that TRE effects depend on the eating timing.

Free and healthy grocery delivery for adults recovering from an acute coronary event: three-armed randomised controlled trial

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Background: Dietary strategies for the management of diabetes and heart disease are similar in their focus on carbohydrate and fat quality. We conducted a three-arm parallel trial of free grocery provision in adults recovering from an acute coronary event.

Aims: To compare the effectiveness of usual care and 12-weeks free delivered groceries with usual care alone for adults recovering from an acute coronary event.

Methods: This study was in free living adults aged 18-80 years recruited between 6 weeks and 6 months from their most recent acute coronary event. Multiple events or further comorbidities do not exclude participation. Unstratified block randomisation was to: usual care in acute coronary event recovery (Usual Care), usual care and 12-weeks free delivery of high fibre foods (High Fibre), or usual care and 12-weeks free delivery of foods high in unsaturated fats (Healthy Fats). Primary outcome: LDL cholesterol. Secondary outcomes were additional cardiometabolic risk factors, medication change, dietary intakes, measures of bowel health and wellbeing.

Results: 309 participants (mean 63.2 years, 32% female, 34.5% BF, 15% with T2) were randomised to Usual Care (101), High Fibre (103), or Healthy Fats (105). Fibre intake increased in the High fibre intervention while unsaturated fat intake increased in the Healthy Fat intervention when compared with both other interventions. In intention to treat analysis there were no differences in LDL or any other cardiometabolic outcome between interventions. When compared with Usual Care alone, self-reported bowel habits improved for High Fibre (-1.43 (-2.29, -0.57) and Healthy Fats (-1.06 (-1.92, -0.20) participants.

Conclusions: Three months of free and healthy grocery delivery did not influence LDL cholesterol or other cardiometabolic markers of health in adults recovering from an acute coronary event, indicating prescribed medication use at this time is sufficient to control immediate risk of secondary event.

Rationale and Design of the SWITCH (Substitution of high With low ultra-processed soy protein foods In a guideline-based diet inTervention for Cardiometabolic Health) trial

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Background: Clinical guidelines for hypertension, diabetes, and cardiovascular disease recommend plant-based dietary patterns. Soy protein, a high-quality, complete plant protein, is a key component of these diets, particularly the Portfolio Diet, recognized for its cardiometabolic benefits. However, soy stands at a nutritional "crossroad". While it aligns with plant-based dietary advice, most soy-based foods are classified as ultra-processed foods (UPFs) under the NOVA classification system. Research links higher total UPF intake to adverse cardiometabolic outcomes, highlighting the need for a relevant UPF definition and high-quality studies to understand the role of nutrient-dense soy-protein UPFs within recommended dietary patterns.

Aim: To determine whether a high-UPF soy-containing DASH-enhanced Portfolio Diet is non-inferior to a low-UPF soy-containing DASH-enhanced Portfolio Diet in replacing standard of care for systolic blood pressure (SBP) reduction and other UPF-related cardiometabolic factors.

Methods: The SWITCH (Substitution of high With low ultra-processed soy protein foods In a guideline-based diet inTervention for Cardiometabolic Health) trial is a parallel, 3-arm, 12-week randomized controlled trial to assess the effect of the DASH-enhanced Portfolio Diet Program (PortfolioDiet.app, online behavior change curriculum, plus 10 servings of vegetables and fruit), with or without high UPF soy-containing proteins compared to standard of care (usual care) on SBP (primary outcome) and other intermediate cardiometabolic outcomes in 300 adults (≥18 years of age) with obesity and hypertension, including 50% with type 2 diabetes. Participants will be randomized into three groups: 1) Active Treatment: High-UPF soy DASH-enhanced Portfolio Diet (≥4 servings/day of NOVA Group 4 soy products: ≥2 servings of soy milk and ≥2 servings of other soy foods like soy yogurt or burgers), 2) Reference Treatment: Low-UPF soy DASH-enhanced Portfolio Diet (≥4 servings/day of NOVA non-Group 4 soy products: ≥2 servings of Group 1 soy milk, ≥1 serving of Group 1 foods like edamame or roasted

soy nuts, and ≥1 serving of Group 3 foods like tofu or tempeh), or 3) Standard of Care: Usual care from family physicians/specialists. The study is powered at >80% to detect a minimum absolute difference of 5mmHg in superiority testing between groups on the primary outcome SBP over 12-weeks, and non-inferiority of the active vs. reference treatment with a 4-mmHg margin based on the lower limit of efficacy of the starting dose of established antihypertensive medications. Our primary analyses will follow intention-to-treat principles, using inverse probability weighting.

Conclusion: Findings will provide high-quality evidence on the cardiometabolic effects of nutrient-dense soy foods, including those classified as UPFs, to support guideline-based dietary strategies for cardiometabolic risk reduction.

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Effects of genetic risk on type 2 diabetes in a 3-year lifestyle intervention (T2D-GENE study)

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Background: It is known that lifestyle intervention prevents type 2 diabetes (T2D). However, it is not known whether genetic background modifies the effect of lifestyle intervention.

Aims: The effect of a 3-year group and internet-based lifestyle intervention (diet and physical activity) was studied in middle-aged and aging men.

Methods: Altogether 628 men with either a low (n=315) or a high (n=313) genetic risk score (GRS) for T2D were recruited from the Metabolic Syndrome in Men (METSIM) cohort. The inclusion criteria were age 50-75 years, BMI≥25 kg/m2, fasting plasma glucose 5.6-6.9 mmol/l, and hemoglobin A1c<48 mmol/mol. Population-based control groups with either a low (n=196) or a high (n=149) GRS for T2D were recruited with a general health advice as a part of the METSIM cohort protocol.

Results: In the group with a high GRS the intervention significantly lowered the risk for T2D [hazards ratio (HR) 0.30, 95% confidence interval (CI) 0.16-0.56, P<0.001). In the group with a low GRS the intervention had no significant effect for the risk of T2D (HR 0.69, 95% CI 0.36-1.32, P=0.262). There was no difference in the effect of the intervention between the high and the low GRS groups (P=0.135). The intervention ameliorated the worsening of glycemia and decreased body weight in both intervention groups (P<0.05). The intervention decreased total and LDL cholesterol concentrations in the low GRS group (P<0.001), whereas in the high GRS group there was no change (P=0.316 and P=0.769, respectively).

Conclusions: A 3-year group and internet-based lifestyle intervention significantly decreased the risk for T2D in participants with a high GRS for T2D. So, lifestyle changes should be encouraged to all individuals at risk for T2D regardless of the genetic risk.

Does improving food biodiversity lower mortality in older Mediterranean adults with high cardiometabolic risk?

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Background: The increasing frequency of extreme temperatures and rainfall unequivocally supports the "One Planet, One Health" approach. Given that the food system is a key determinant of population and planetary health, evaluating "food biodiversity" is increasingly important. Nevertheless, to convincingly inform dietary guidelines, it is necessary to determine the value of improving food biodiversity in high-quality diets, such as the Mediterranean diet (MedDiet), and ascertain its association with long-term endpoints such as mortality in high-risk populations.

Aims: We evaluated the associations of food biodiversity with all-cause and cause-specific mortality in a Spanish cohort of older adults at high cardiovascular risk.

Methods: Food biodiversity was measured as dietary species richness (DSR), the count of unique plants and animal species in an individual's diet, and extracted from the yearly food frequency questionnaire data. Using DSR calculated cumulatively over the follow-up, we evaluated the correlation between food biodiversity and level of MedDiet adherence. Cox regression models were used to assess the association of food biodiversity with all-cause and cause-specific mortality.

Results: In 7,210 PREDIMED participants, with a median age of 67 years (58% women), the DSR ranged between 16 and 57 (median: 48). A total of 425 deaths were recorded (103 cardiovascular diseases (CVD) deaths, 169 cancer deaths, and 153 deaths due to other-causes) over a median follow-up of 6 years. DSR was only moderately correlated with adherence to the MedDiet. When fully adjusted, every additional species over the follow-up period was associated with an HR of (95% CI) 0·91(0·90,0·93) for all-cause mortality, 0·93(0·90,0·96) for CVD mortality, 0·92 (0·89,0·94) for cancer deaths, and 0·91(0·89,0·94) for deaths from other causes. Standardized comparisons showed no significant differences between plant and animal-origin species in their association with mortality.

Conclusion: Improving food biodiversity in addition to diet quality may increase longevity in high-risk populations.

Replacing animal with plant protein in individuals with type 2 diabetes reduces CRP: a systematic review and meta-analysis of randomized controlled trials

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Introduction: Inflammation contributes to elevated cardiovascular disease risk in individuals with type 2 diabetes. While guidelines encourage plant-based diets, the impact of replacing animal with plant proteins on inflammatory markers in individuals with type 2 diabetes levels remains unclear.

Objective: To explore the effect of replacing animal with plant protein sources on C-reactive protein (CRP) in individuals with type 2 diabetes in a systematic review and meta-analysis of randomized controlled trials (RCTs).

Methods: We searched MEDLINE, Embase, and Cochrane Library through February 2025 for RCTs ≥3 weeks. Two independent reviewers extracted data and assessed Risk of Bias (Cochrane Risk of Bias 2.0 tool). The primary outcome was CRP. Data were pooled using random-effects models with results expressed as mean differences (MD) with 95% confidence intervals (CI). Heterogeneity was evaluated (Cochran Q) and quantified (I^2 statistic). The certainty of evidence was evaluated using GRADE.

Results: The analysis included 5 RCTs, providing data on 6 trial comparisons in participants with type 2 diabetes (n=221). Intervention arms included soy-based products (n=3), or dietary pulses (n=3), as substitutes for animal meat (n=2), dairy products (n=1), or mixed animal-based proteins (n=3). Replacement of animal with plant protein sources significantly reduced CRP (MD -0.34mg/L [95% CI -0.69, -0.00] P=0.049; substantial heterogeneity, I2=50.51% PQ=0.07). Sensitivity analyses by baseline CRP level showed that there was a significant CRP reduction when restricting analyses to trials with elevated average baseline CRP of ≥3 mg/L (Centres for Disease Control-American Heart Association threshold for increased cardiovascular risk), showed (MD -0.78mg/L [95% CI -1.49, -0.07]; no substantial heterogeneity, I^2=55.49% PQ=0.11). The overall certainty of evidence was moderate.

Conclusion: The available evidence provides a good indication that replacing animal with plant protein from soy and pulse sources results in trivial reductions in CRP in type 2 diabetes. The

magnitude of effect of replacing animal with plant protein on CRP appears dependant on the baseline CRP level with limited evidence suggesting that the replacement of animal with plant protein results in small important reductions in CRP in individuals with type 2 diabetes and elevated CRP of ≥3 mg/L.

Registration: ClinicalTrials.gov identifier, NCT02037321"

Mediterranean diet, physical activity, and bone health in older adults: the PREDIMED-Plus randomized clinical trial

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Background: Understanding the modifiable effects of diet and physical activity on bone health could help develop strategies to mitigate undesirable effects of concomitant weight loss and age-related bone decline.

Aims: To evaluate the effects of a weight loss lifestyle intervention on bone mineral density (BMD), total bone mineral content (BMC), and low BMD prevalence over three years.

Methods: We analyzed data from 924 older adults with overweight/obesity and metabolic syndrome (mean age 65y, 49% women). Participants were randomized (1:1) to a control group (n=464) advised to adhere to an ad libitum Mediterranean diet with no physical activity promotion, or an intervention group (n=460) following an intensive weight-loss lifestyle intervention based on an energy-reduced Mediterranean diet and physical activity promotion. BMD in total femur, lumbar spines (L1–L4), and femoral trochanter, as well as total BMC, were measured using Dual-energy X-ray Absorptiometry scans at baseline, one, and 3-years of follow-up. T-scores from BMD variables were also determined, and osteopenia/osteoporosis status was defined as low BMD. Linear and logistic two-level mixed models stratified by sex were used for main analyses. Intention-to-treat analysis, completers case analysis, and sensitivity analysis were additionally performed.

Results: Significant differences in mean changes between groups were observed with an overall three-year intervention increase in the intervention group compared to the control group in lumbar spines L1-L4 BMD (P=0.047). This protective association was observed specifically for women (P=0.005), but not for men (P for interaction ≤0.05). No overall 3-year intervention effect on total BMC and low BMD prevalence was shown.

Conclusion: An energy-reduced Mediterranean diet and physical activity lifestyle intervention mitigated the weight loss– and age-related BMD decline, especially among older women with overweight or obesity and metabolic syndrome compared to with conventional ad libitum Mediterranean diet recommendations with no physical activity promotion.

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Supporting healthcare providers to translate diabetes clinical practice guidelines on nutrition therapy: content and face validation of the Portfolio Diet toolkit for healthcare providers

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Background: Type 2 diabetes (T2D) is a major public health concern worldwide, contributing significantly to premature morbidity and mortality. The Portfolio Diet is an evidence-based dietary pattern shown to reduce LDL-C, HbA1c, improve other cardiometabolic outcomes, and lower the incidence of T2D. Although diabetes clinical practice guidelines support the Portfolio Diet, healthcare providers (HCPs) often report a lack of knowledge and confidence to advise patients effectively. To address this gap, we developed an HCP-facing Portfolio Diet toolkit to enhance HCP knowledge and support clinical application of the diet. To ensure effective uptake in clinical practice, content and face validation of the toolkit is needed.

Aim: To assess the content and face validity of the HCP-facing Portfolio Diet toolkit among HCPs.

Methods: Using Lynn's method for face and content validity, physicians, dietitians, pharmacists, and nurse practitioners were recruited to review the toolkit's infographic and video and complete a mixed-methods questionnaire. Content validity was assessed for the six sections of the infographic using a 4-point Likert scale (1 = irrelevant to 4 = extremely relevant), and face validity was assessed using 17 items rated on a 5-point Likert scale (1 = strongly disagree to 5 = strongly agree). The content validity index (CVI) and face validity index (FVI) were calculated, with a threshold of ≥0.7 indicating substantial agreement and validity. Participants also provided qualitative feedback, which informed revisions to the toolkit. A second round of evaluation was conducted with a new cohort of HCPs.

Results: Twenty-one HCPs (7 physicians, 7 dietitians, 5 pharmacists, and 2 nurse practitioners) participated in the first round of review. Content validity for five out of the six sections of the infographic was achieved with CVIs ranging from 0.86 to 0.95, while one section did not meet the threshold (CVI=0.67). FVIs for all items ranged from 0.76 to 1.00, all meeting substantial agreement for face validity. Quantitative and qualitative feedback was used to create a revised toolkit, including providing explicit food examples, improving format, and reducing jargon. Most HCPs (86%) rated the revised version as improved. In the second round, 28 new HCPs reviewed the revised toolkit. All six sections achieved content validity with CVIs ranging from 0.86 to 1.00, and FVIs ranged from 0.76 to 1.00, confirming face validity. In both rounds, all HCPs reported increased knowledge and confidence in recommending the Portfolio Diet after viewing the toolkit.

Conclusions: The final HCP-facing Portfolio Diet toolkit demonstrated excellent content and face validity, and enhanced HCP-reported knowledge and confidence in its clinical application. Now hosted on the Canadian Cardiovascular Society website supporting credibility and free access, the toolkit will address a critical gap in clinical practice guideline translation, supporting HCPs in recommending the Portfolio Diet to prevent and manage T2D and reducing its burden across Canada and beyond.

Gut microbiota, plasma hippuric acid, fiber intake, and cardiometabolic health in U.S. populations.

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Background: Hippuric acid is a gut microbiota-derived metabolite linked with fiber intake. However, its role in linking dietary fiber intake to gut microbial activity and cardiometabolic health remains unclear.

Aims: To identify gut microbial species associated with plasma hippuric acid levels, investigate the relationships between dietary fiber intake, gut microbiota composition, and hippuric acid concentrations, and explore the prospective associations of circulating hippuric acid with the risks of type 2 diabetes (T2D), cardiovascular disease (CVD), and weight gain (WG) in free-living individuals through a systematic, integrated approach.

Methods: We included 287 men from the Men's Lifestyle Validation Study (MLVS), a substudy of the Health Professionals Follow-up Study (HPFS), with plasma metabolomics and fecal metagenomic data. Fiber intake was assessed using 7-day diet records. Prospective associations between hippuric acid concentrations and T2D, CVD, and WG risk were examined in 5,472 participants from the Nurses' Health Study (NHS), NHSII, and HPFS.

Results: We identified 26 microbial species significantly associated with plasma hippuric acid concentrations, with most species from the Lachnospiraceae and Oscillospiraceae families. A microbial species-derived score was developed in MLVS and showed a strong correlation with hippuric acid (Pearson r = 0.73). The association between fiber intake and hippuric acid levels was partially mediated by hippuric acid-associated gut bacteria, primarily fiber-fermenting Firmicutes. Higher plasma hippuric acid concentrations were associated with a lower risk of T2D (Quintile5 vs. Quintile1: HR = 0.77 [95% CI: 0.64 to 0.94]) and reduced likelihood of excess WG, but the association with CVD was null.

Conclusions: Our findings highlight the gut microbiota's role in mediating the relationship between dietary fiber intake and plasma hippuric acid levels, which predict better metabolic health. Overall these data elucidate novel pathways partially underlying the health benefits of fiber intake on improving cardiometabolic health.

Body Weight, Human Gut Microbiome, Blood Metabolome, and Cardiometabolic Health – A Multi-Omics Integration Study

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Background: Few prospective human studies have comprehensively characterized interrelationships between body weight, the gut microbiome, human metabolome, and cardiometabolic health.

Aims: To characterize weight-associated microbiome profiles, identify metabolomic signatures responsive to this microbial profile, and examine the links to future weight change and incident coronary heart disease (CHD) risk.

Methods: Body mass index (BMI), waist-to-hip ratio (WHR), and total fat percentage (fat%) measured using DEXA, fecal metagenomics, and plasma metabolomics data collected from 307 healthy men participating in the Men's Lifestyle Validation Study (MLVS) were integrated and analyzed. A microbial signature of body weight was developed in the MLVS and replicated in 233 women participating in the Mind Body Study (MBS). Prospective associations of identified microbial signatures with weight change(n=1,052) and CHD incidence (n=76 case-control pairs) risks were further examined in Nurses' Health Study II (NHSII) participants who provided stool samples in 2019-2023.

Results: We identified 23 microbial species that significantly correlated with the concurrent BMI (FDR<0.05), predominantly in the phylum of Firmicutes (n=19). A non-parametric microbial score summarizing these species was significantly correlated with BMI (rs=0.46), WHR (rs=0.23), and fat% (rs=0.65), and replicated in MBS (rs=0.34 with BMI). Elastic net regression

analysis further derived a score of 32 plasma metabolites that predicted the BMI microbial score in the MLVS (rs =0.66) and MBS (rs =0.38). In the NHSII, higher microbial score was significantly associated with faster BMI gain (β= 0.22, P = 0.003), and a non-significant, increased CHD risk [HR=1.69, 95%CI: (0.89-3.23), P=0.11].

Conclusions: Concurrent body weight is associated with a specific microbial profile, which predicts future BMI gain and elevated heart disease risk. These data collectively support the notion that the human gut microbiome is significantly influence by the body weight and may significantly contribute to the etiology of weight gain and subsequent cardiometabolic risk.

Co-design of a Digital Tool to Translate Low Glycemic Index Diet Guidelines for Diabetes Prevention

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Background: Type 2 diabetes (T2D) presents public health challenges in Canada. Low glycemic index (GI) diets are recommended in guidelines globally to prevent and manage diabetes. However, there are insufficient resources to support healthcare providers and communities in the adoption of low GI diets. With 94% of Canadians having internet access, innovative digital interventions using mobile health applications provide an opportunity to engage communities and healthcare providers in delivering nutrition interventions.

Aim: We plan to develop and apply a theory-based and community-driven methodology to co-design the GI Education Program, with the basis as GIDiet.app, as a digital education and engagement tool to translate Diabetes Canada's clinical practice guidelines on low GI diets.

Methods: Our study follows the Consolidated Framework for Implementation Research to assess barriers and facilitators in collaboration with interest holders, the Co-design Evaluation Framework, and the REAIM framework to develop and evaluate our program.We will hold 4 meetings with key interest holders, including individuals from ethnically diverse communities at elevated risk of diabetes, to identify barriers and facilitators to the use of digital tools and uptake of low GI dietary patterns. Discussions will focus on identifying preferred features in digital tools to support engagement and education on low GI diets. Mixed-form questionnaires and transcripts from meetings will be analyzed descriptively and thematically. Findings will inform the co-design of the program.

Preliminary Results: We have established collaborations with interest holders including: Diabetes Action Canada, Diabetes Canada, Certified Diabetes Educator committee, people with lived experiences advisory committee, community partners supporting individuals at high risk of or living with diabetes, and decision makers and initiated the beta-version of GIDiet.app.

Conclusions: Through theory-based and community-driven design, this project provides an innovative approach to translate and support the implementation of low GI diets to reduce the burden of T2D, especially in high-risk communities.

Designing an Effective Nutrition Curriculum to Translate the Portfolio Diet for the Prevention and Management of Type 2 Diabetes in the Peel Region of Ontario

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Background: The Peel Region, home to Ontario's largest immigrant and racialized population, faces significant health disparities, including a 40% higher type 2 diabetes (T2D) prevalence than the provincial average. The Portfolio Diet, a plant-based dietary pattern, has been associated with reduced risk for T2D and risk factors for cardiometabolic diseases. A gap exists in translating the Portfolio Diet into community-level practice. Development of a translational tool, the Portfolio Diet Program, is underway. One of the Program's four components—a 16-module curriculum—remains to be developed and tested. The Program is designed with evidence-based theories (EBTs), including behaviour change and learning theories, since previous health interventions that integrate EBTs have demonstrated effective behaviour change.

Aims: 1) To develop a 16-module online nutrition education curriculum with integration of EBTs to translate the Portfolio Diet for T2D risk reduction in high-risk communities. 2) To evaluate the acceptability of the Portfolio Diet curriculum in adults at high risk of T2D through a mixed-methods study.

Methods: 1) The 16-module curriculum will be co-designed with an advisory committee of diverse interest holders from Peel through quarterly meetings. The modules will be designed using Articulate, an e-learning design platform. Six EBTs will be integrated into module design with all features of the modules mapped to each of the domains within the EBTs. Regular meetings with EBT experts and registered dietitians will be held to review content quality. 2) 60 participants recruited from Peel will be randomized into 4 groups, each evaluating 4 modules of the curriculum using questionnaires to assess acceptability, usability (mHealth app usability questionnaire (MAUQ)), knowledge acquisition and cultural relevance, followed by a guided focus group session. Quantitative data will be analyzed descriptively and compared against thresholds (e.g. MAUQ >5/7 demonstrating good usability). Qualitative data will be analyzed thematically using NVivo.

Conclusions: This project will demonstrate how a nutrition curriculum mapped to EBTs meets the needs of a community at high T2D risk. The curriculum will be used in multiple upcoming trials to assess the implementation of the Portfolio Diet Program in diverse settings. By providing culturally relevant, accessible nutrition education, the project aims to reduce health disparities and scale chronic disease prevention in various urban populations.

Global Pan-Databases Synthesis of Ecological Factors Influencing Diabetes from 1990 to 2021

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Background: Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia due to impaired insulin secretion or action. Its global prevalence has risen sharply, imposing significant healthcare burdens. While various risk factors have been identified, most studies focus on isolated variables or specific regions, limiting broader applicability. A comprehensive global analysis is needed to elucidate the complex interplay of factors influencing diabetes prevalence and mortality.

Aims: This study conducts the most extensive and systematic analysis to date on the socio-economic, environmental, lifestyle, dietary, and physiological determinants of diabetes prevalence and mortality worldwide.

Methods: We analyzed data from 18 international databases covering 201 countries over three decades (1990–2021 for prevalence, 1980–2021 for mortality). Using multivariate regression and ranking analyses, we examined associations between diabetes outcomes and ecological factors, including 74 socio-economic and environmental indicators, 126 lifestyle and dietary factors, 27 physiological metrics, and 100 diseases. Data visualization techniques, such as heatmaps and multidimensional scaling, were employed to illustrate correlations.

Results: By integrating 327 ecological factors, our study reaffirmed high fasting blood glucose (HFBG) and obesity as primary drivers of diabetes prevalence and mortality. Interestingly, rising average minimum temperatures emerged as a significant risk factor, while lower temperatures appeared protective. Previously underexplored contributors included prolonged work hours, social inequalities, high poultry consumption, and deficiencies in zinc, calcium, and vitamins. Protective factors included moderate alcohol intake and elevated high-density lipoprotein (HDL) levels. Diabetes mortality was strongly associated with social inequality indices (Gini Index, Gender Inequality Index).

Conclusions: This study highlights the multifaceted nature of diabetes risk, emphasizing the interplay of socio-economic, environmental, and lifestyle factors. A holistic approach that integrates these determinants is essential for developing more effective strategies to mitigate the global diabetes burden and improve public health outcomes."

Effects of different dietary patterns on glucose management in type 1 diabetes: a systematic review and meta-analysis of randomized controlled trials

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Background: Effective glucose management is essential to prevent complications in type 1 diabetes. While nutrition therapy is vital, the optimal diet remains uncertain.

Aims: Our systematic review and meta-analysis aimed to synthesize evidence from randomized controlled trials (RCTs) on the impact of various diets on glucose management in type 1 diabetes.

Methods: We systematically searched Medline, Embase, and Cochrane Library through November 2024 for RCTs on dietary patterns and glucose control outcomes in type 1 diabetes, including HbA1c, time in range (TIR), coefficient of variation (CV), hypoglycemia, insulin dose, and anthropometric characteristics. Two reviewers independently extracted data and assessed study quality using the RoB-2 tool. We estimated summary mean differences (MD) with 95% confidence intervals (CI) using random-effects models. The certainty of the evidence was evaluated using GRADE. The study protocol was registered in PROSPERO (CRD42023479252).

Results: Out of 5,287 studies, 35 RCTs involving children, adolescents and adults with type 1 diabetes were eligible. Higher-fiber diets ($\geq$35 g/day, n=5 RCTs) reduced HbA1c (MD=-0.46%, 95% CI -0.93 to 0.00, I2=65%) and hypoglycemia (MD=-0.81 episodes/month, 95% CI -1.34 to -0.28, I2=0%), with moderate and low certainty of evidence, respectively. Carbohydrate-restricted diets ($\leq$45% energy, n=20 RCTs) improved TIR (MD=3.84%, 95% CI 2.24 to 5.44, I2=0%), CV (MD=-3.24%, 95% CI -5.51 to -0.97, I2=53%), and insulin dose (MD=-5.63 U/day, 95% CI -9.51 to -1.74, I2=70%), but not HbA1c, with low to moderate certainty of evidence. Higher-protein, low-glycemic index, gluten-free, Mediterranean, vegan, and intermittent fasting diets showed no effects on glucose management (n=1-6 RCTs), although certainty of evidence was low.

Conclusions: Maintaining a high-fiber diet while restricting other carbohydrate intakes may improve glycemic control in individuals with type 1 diabetes. Further investigation is needed into long-term effects and other diets.