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Dietary Patterns

Longitudinal Associations of Healthy Dietary Pattern Scores with Coronary Artery Calcification and Pericardial Adiposity in United States Adults with and without Type 1 Diabetes

Leigh Ann Richardson, Arpita Basu, Lung-Chang Chien, Amy C Alman, Janet K Snell-Bergeon. *J Nutr.* 2023 Jul;153(7):2085-2093. doi: 10.1016/j.tjnut.2023.05.016. [Article link](#)

Significance: This study demonstrates a link between pericardial adipose tissue volume and coronary cardiac calcification, and for individuals with Type 1 Diabetes, the DASH diet may be beneficial for lowering odds of coronary disease progression.

Background: Pericardial adipose tissue volume (PAT) and coronary artery calcification (CAC) are prognostic indicators for future cardiovascular events; however, no studies have assessed the long-term associations of adherence to dietary patterns (DPs) with PAT and CAC in adults with and without type 1 diabetes (T1D). **Objectives:** We investigated the longitudinal associations of the Mediterranean Diet (MedDiet) and Dietary Approaches to Stop Hypertension (DASH) diet with PAT and CAC progression in adults with and without T1D. **Methods:** The Coronary Artery Calcification in Type 1 Diabetes (CACTI) study is a population-based, prospective study of 652 T1D and 764 nondiabetic mellitus (nonDM) (19-56 y) participants that began in 2000-2002 with follow-up visits in 2003-2004 and 2006-2007. At each visit, food frequency questionnaires were collected and used to develop adherence scores for the MedDiet and DASH diets. PAT and CAC were measured at each visit using electron beam computed tomography. CAC progression was defined as a ≥ 2.5 mm square root-transformed volume. Mixed effect models were used to conduct statistical analyses. **Results:** Combined models found a significant -0.09 cm³ (95% CI: -0.14, -0.03; P = 0.0027) inverse association in PAT for every 1-point increase in the MedDiet score and a significant -0.26 cm³ (95% CI: -0.38, -0.14; P < 0.0001) inverse association in PAT for every 1-point increase in the DASH score. In combined models, the DPs were not significantly associated with lower odds of CAC progression; however, both DPs had significant interactions by diabetes status for CAC. Only the DASH diet was associated with lower odds of CAC progression in the nonDM group (OR: 0.96; 95% CI: 0.93, 0.99; P = 0.0224). **Conclusions:** These data suggest that the DPs are associated with lower PAT, which may reduce future cardiovascular events. The DASH diet may be beneficial for lower odds of CAC progression in those without T1D.

Carbohydrates

Carbohydrate Intakes Below Recommendations with a High Intake of Fat are Associated with Higher Prevalence of Metabolic Syndrome

Dakota Dustin, Corina Kowalski, Meredith Salesses, Acree McDowell, Penny M Kris-Etherton, Martha Belury, LuAnn K Johnson. *J Acad Nutr Diet.* 2023 Jul;123(7):1022-1032.e13. doi: 10.1016/j.jand.2023.02.011. [Article link](#).

Significance: Individuals with carbohydrate intake below recommendations when compared to those who met recommendations have increased odds of prevalent metabolic syndrome based on a cross-sectional study of adults from the 1999-2018 NHANES survey.

Background: More than one-third of adults in the United States have metabolic syndrome, and dietary carbohydrate intake may modify the likelihood of developing this condition. Currently, there is a lack of consistent evidence demonstrating the relationship between carbohydrate intake that falls below recommendations and metabolic syndrome. Not accounting for the differences in fatty acid classes of these dietary patterns may be a reason for inconsistent findings. **Objective:** This study evaluated the association between a carbohydrate intake below recommendations and metabolic syndrome stratified by fat quantity and fatty acid classes in a nationally representative sample of US adults. **Design:** This cross-sectional study acquired

data on food and nutrient intake and markers of metabolic syndrome from respondents in the National Health and Nutrition Examination Survey 1999-2018. **Participants/setting:** This study included 19,078 respondents who were aged 20 years or older, had reliable and complete data on food and nutrient intake and markers of metabolic syndrome, and were not pregnant or breastfeeding. **Main outcome measures:** The main outcome was prevalence of metabolic syndrome. **Statistical analyses performed:** Usual dietary intake was estimated using the National Cancer Institute's usual intake methodology. Multivariable logistic regression models assessed the relative odds of prevalent metabolic syndrome between those who had a carbohydrate intake below recommendations and those who met carbohydrate recommendations. **Results:** Those who had a carbohydrate intake below recommendations had 1.067 (95% CI 1.063 to 1.071) times greater odds of having metabolic syndrome compared with those who met carbohydrate recommendations ($P < 0.001$). High intake of fat of any class was associated with higher odds of metabolic syndrome (total fat: 1.271, 95% CI 1.256 to 1.286; saturated fatty acid: 1.072, 95% CI 1.060 to 1.085; monounsaturated fatty acid: 1.317, 95% CI 1.300 to 1.333; polyunsaturated fatty acid: 1.056, 95% CI 1.047 to 1.066; $P < 0.001$ for all comparisons) in those who had a carbohydrate intake below recommendations. **Conclusions:** The odds of prevalent metabolic syndrome were higher among individuals who had a carbohydrate intake below recommendations compared with individuals who met carbohydrate recommendations.

Protein

The Association between Total Protein, Animal Protein and Animal Protein Sources with Risk of Inflammatory Bowel Diseases: A Systematic Review and Meta-Analysis of Cohort Studies

Sepide Talebi, Sheida Zeraattalab-Motlagh, Mehran Rahimlou, Fatemeh Naeini, Mahsa Ranjbar, Ali Talebi, Hamed Mohammadi. *Adv Nutr.* 2023 Jul;14(4):752-761. doi: 10.1016/j.advnut.2023.05.008. [Article link](#)

Significance: A dose-dependent meta-analysis reported increased risk of IBD with increased total meat intake, while intake of proteins from dairy sources was protective against IBD risk.

We aimed to conduct this dose-dependent meta-analysis to examine the relation between total protein, animal protein, and its sources with inflammatory bowel disease (IBD). We searched databases, comprising PubMed/Medline, Web of Science (ISI), Embase, and Google Scholar, for the published studies up to 28 March 2023. Prospective cohort study designs that investigated associations between dietary intake of various animal protein sources and with risk of IBD in the general population were identified. Eleven prospective cohort studies with 4,302,554 participants and 8067 cases were considered eligible. Findings indicated that higher intake of dairy was significantly associated with a lower risk of IBD (relative risk [RR]: 0.81; 95% confidence interval [CI]: 0.72, 0.90), Crohn disease (RR: 0.69; 95% CI: 0.56, 0.86), and ulcerative colitis (RR: 0.84; 95% CI: 0.75, 0.94). There was no association between different sources of animal protein and the risk of IBD. The dose-response analysis suggested that each 100 g/d increment in dietary total meat consumption was associated with a 38% greater risk of IBD. Moreover, a positive linear association was found between total meat intake and risk of IBD ($P_{\text{nonlinearity}} = 0.522$, $P_{\text{dose-response}} = 0.005$). Overall, among the dietary sources of protein, the risk of IBD increased only with increasing total meat intake, and the consumption of protein from dairy products was found to be a protective factor against the IBD risk.

Low- and No-Calorie Sweeteners

Sucrose Intake Elevates Erythritol in Plasma and Urine in Male Mice

Semira R Ortiz, Martha S Field. *J Nutr.* 2023 Jul;153(7):1889-1902. doi: 10.1016/j.tjnur.2023.05.022. [Article link](#)

Significance: Sucrose intake, not high-fat diets, increases erythritol synthesis and excretion in male mice. Loss of ADH1 or SORD enzyme activity did not significantly affect erythritol concentrations in mice.

Background: Elevated serum erythritol concentration is a predictive biomarker of diabetes and cardiovascular incidence and complications. Erythritol is synthesized endogenously from glucose, but little is known regarding the origin of elevated circulating erythritol in vivo. **Objectives:** In vitro evidence indicates that intracellular erythritol is elevated by high-glucose cell culture conditions and that final step of erythritol synthesis is catalyzed by the enzymes sorbitol dehydrogenase (SORD) and alcohol dehydrogenase (ADH) 1. The purpose of this study was to determine whether dietary intake and/or diet-induced obesity affect erythritol synthesis in mice and whether this relationship is modified by the loss of the enzymes SORD or ADH1. **Methods:** First, 8-wk-old male *Sord*^{+/+}, *Sord*^{-/-}, *Adh1*^{+/+}, and *Adh1*^{-/-} mice were fed either low-fat diet (LFD) with

10% fat-derived calories or diet-induced obesity high-fat diet (HFD) with 60% fat-derived calories for 8 wk. Plasma and tissue erythritol concentrations were measured using gas chromatography-mass spectrometry. Second, male wild-type 8-wk-old C57BL/6J mice were fed LFD or HFD with plain drinking water or 30% sucrose water for 8 wk. Blood glucose and plasma and urinary erythritol concentrations were measured in nonfasted and fasted samples. Tissue erythritol was measured after killing. Finally, male *Sord*^{+/+} and *Sord*^{-/-} mice were fed LFD with 30% sucrose water for 2 wk; then, nonfasted plasma, urine, and tissue erythritol concentrations were quantified. **Results:** Plasma and tissue erythritol concentrations were not affected by loss of *Sord* or *Adh1* in mice fed LFD or HFD. In wild-type mice, consumption of 30% sucrose water significantly elevated plasma and urinary erythritol concentrations on both LFD-fed and HFD-fed mice compared with that of plain water. *Sord* genotype did not affect plasma or urinary erythritol concentration in response to sucrose feeding, but *Sord*^{-/-} mice had reduced kidney erythritol content compared with wild-type littermates in response to sucrose. **Conclusions:** Sucrose intake, not HFD, elevates erythritol synthesis and excretion in mice. Loss of *ADH1* or *SORD* does not significantly affect erythritol concentration in mice.

Assessing the Relationship between Low-Calorie Sweetener Use and Quality of Life Measures in Adults with T1D

Halis K Akturk, Janet Snell-Bergeon, Kagan E Karakus, Viral N Shah. *BMC Endocrine Disorders*, Vol. 23, Article Number: 147 (2023). doi.org/10.1186/s12902-023-01399-y. [Article link](#)

Significance: Though most adults with Type 1 Diabetes perceived improvement in r QOL and glycemic control with LCS use, this was not backed with questionnaires. It may be that associations between the exposure and outcome are bi-directional.



This work was supported by IAFNS [Low- and No-Calorie Sweeteners Committee](#).

Background: To evaluate use of low-calorie sweeteners (LCS) among adults with type 1 diabetes (T1D) and its impact on quality of life (QOL). **Methods:** In this single center, cross-sectional survey study with 532 adults with T1D, Food related QOL (FRQOL), LCS specific questionnaire (LCSSQ), Diabetes Self-Management Questionnaire (DSMQ), Food Frequency Questionnaire (FFQ), Audit of Diabetes-Dependent QOL (AddQOL), Type 1 Diabetes and Life (T1DAL) questionnaires were administered through RedCAP, a secure, HIPAA-compliant web-based application. Demographics and scores of adults who used LCS in last month (recent users) and others (non-users) were compared. Results were adjusted for age, sex, diabetes duration and other parameters. **Results:** Of 532 participants (mean age 36 ± 13, 69% female), 99% heard LCS before, 68% used them in the last month, 73% reported better glucose control with LCS use and 63% reported no health concerns about LCS use. Recent LCS users were older and had a longer diabetes duration and more complications (hypertension, or any complication) than non-users. However, A1c, AddQOL, T1DAL, FRQOL scores did not differ significantly between recent LCS users and non-users. DSMQ scores, DSMQ management, diet, health care scores did not differ between two groups; however, recent LCS users had lower physical activity score than non-users ($p = 0.001$). **Conclusions:** Most of the adults with T1D have used LCS and perceived that LCS use improved their QOL and glycemic control; however, these were not verified with questionnaires. There was no difference in QOL questionnaires except DSMQ physical activity between recent LCS users and not users with T1D. However, more patients in need to increase their QOL may be using LCS; therefore, associations between the exposure and outcome can be bi-directional.

Cognitive Health

Trial of the MIND Diet for Prevention of Cognitive Decline in Older Persons

Lisa L Barnes, Klodian Dhana, Xiaoran Liu, Vincent J Carey, Jennifer Ventrelle, Kathleen Johnson, Chiquia S Hollings, et. al. *N Engl J Med*. 2023 Jul 18. doi: 10.1056/NEJMoa2302368. [Article link](#)

Significance: A three-year study of subjects with family history of dementia but had unimpaired cognition found no significant difference between the groups on the MIND and control diets, both with caloric restriction.

Background: Findings from observational studies suggest that dietary patterns may offer protective benefits against cognitive decline, but data from clinical trials are limited. The Mediterranean–DASH Intervention for Neurodegenerative Delay, known as the MIND diet, is a hybrid of the Mediterranean diet and the DASH (Dietary Approaches to Stop Hypertension) diet, with modifications to include foods that have been putatively associated with a decreased risk of dementia. **Methods:** We performed a two-site, randomized, controlled trial involving older adults without cognitive impairment but with a family history of dementia, a body-mass index (the weight in kilograms divided by the square of the height in meters) greater than 25, and a suboptimal diet, as determined by means of a 14-item questionnaire, to test the cognitive effects of the MIND diet with mild caloric restriction as compared with a control diet with mild caloric restriction. We assigned the participants in a 1:1 ratio to follow the

follow the intervention or the control diet for 3 years. All the participants received counseling regarding adherence to their assigned diet plus support to promote weight loss. The primary end point was the change from baseline in a global cognition score and four cognitive domain scores, all of which were derived from a 12-test battery. The raw scores from each test were converted to z scores, which were averaged across all tests to create the global cognition score and across component tests to create the four domain scores; higher scores indicate better cognitive performance. The secondary outcome was the change from baseline in magnetic resonance imaging (MRI)-derived measures of brain characteristics in a nonrandom sample of participants. **Results:** A total of 1929 persons underwent screening, and 604 were enrolled; 301 were assigned to the MIND-diet group and 303 to the control-diet group. The trial was completed by 93.4% of the participants. From baseline to year 3, improvements in global cognition scores were observed in both groups, with increases of 0.205 standardized units in the MIND-diet group and 0.170 standardized units in the control-diet group (mean difference, 0.035 standardized units; 95% confidence interval, -0.022 to 0.092; $P=0.23$). Changes in white-matter hyperintensities, hippocampal volumes, and total gray- and white-matter volumes on MRI were similar in the two groups. **Conclusions:** Among cognitively unimpaired participants with a family history of dementia, changes in cognition and brain MRI outcomes from baseline to year 3 did not differ significantly between those who followed the MIND diet and those who followed the control diet with mild caloric restriction.

Lipids

The Potential Cardiometabolic Effects of Long-Chain ω -3 Polyunsaturated Fatty Acids: Recent Updates and Controversies

Jae Hyun Bae, Hyunjung Lim, Soo Lim. *Adv Nutr.* 2023 Jul;14(4):612-628. doi: 10.1016/j.advnut.2023.03.014. [Article link](#)

Significance: This review focuses on recent research and challenges of the potential benefits and safety of LC ω -3 PUFAs in cardiometabolic functions.

Various health-related effects of long-chain (LC) ω -3 PUFAs, EPA, and DHA have been suggested. LC ω -3 PUFAs reduce TG concentrations and have anti-inflammatory, immunomodulatory, antiplatelet, and vascular protective effects. Controversially, they might help in restoring glucose homeostasis via the gut microbiota. However, previous studies have not shown the clear benefits of LC ω -3 PUFAs for CVDs. REDUCE-IT and STRENGTH-representative randomized controlled trials (RCTs) that examined whether LC ω -3 PUFAs would prevent major adverse cardiovascular (CV) events (MACE)-showed conflicting results with differences in the types, doses, or comparators of LC ω -3 PUFAs and study populations. Therefore, we performed a meta-analysis using major RCTs to address this inconsistency and assess the clinical and biological effects of LC ω -3 PUFAs. We included RCTs that involved ≥ 500 participants with ≥ 1 y follow-up. Of 17 studies involving 143,410 people, LC ω -3 PUFA supplementation showed beneficial effects on CV death (RR: 0.94; 95% CI: 0.88, 0.99; $P = 0.029$) and fatal or nonfatal MI (RR: 0.83; 95% CI: 0.72, 0.95; $P = 0.010$). RCTs on EPA alone showed better results for 3-point MACE, CV death, and fatal or nonfatal MI. However, the benefits were not found for fatal or nonfatal stroke, all-cause mortality, and hospitalization for heart failure. Of note, studies of both the EPA/DHA combination and EPA alone showed a significant increase in risk of new-onset atrial fibrillation. Thus, well-designed studies are needed to investigate the underlying mechanisms involved in the distinct effects of EPA compared with DHA on cardiometabolic diseases. This review discusses the potential benefits and safety of LC ω -3 PUFAs from a cardiometabolic perspective focusing on recent updates and controversies.

Sodium

Impact of Serum Sodium Concentrations, and Effect Modifiers on Mortality in the Irish Health System

Conor Walsh, Leonard D Browne, Robert Gilligan, Rose Galvin, Liam Glynn, Cathal Walsh, Austin G Stack. *BMC Nephrol.* 2023 Jul 6;24(1):203. doi: 10.1186/s12882-023-03251-w. [Article link](#)

Significance: A retrospective 5.5-year study of participants in the National Kidney Disease Surveillance System found serum sodium levels outside of normal range (135-145mmole/l) adversely impact mortality and were linked to specific causes of death. The level of risks varied with age and renal function.

Background: Abnormalities of serum sodium are associated with increased mortality risk in hospitalised patients, but it is unclear whether, and to what extent other factors influence this relationship. We investigated the impact of dysnatraemia on total and cause-specific mortality in the Irish health system while exploring the concurrent impact of age, kidney function and designated clinical work-based settings. **Methods:** A retrospective cohort study of 32,666 participants was conducted using data from the National Kidney Disease Surveillance System. Hyponatraemia was defined as < 135 mmol/L and hypernatraemia as > 145 mmol/L with normal range 135-145 mmol/L. Multivariable Cox proportional hazards regression was

used to estimate hazard ratios (HR's) and 95% Confidence Intervals (CIs) while penalised spline models further examined patterns of risk. **Results:** There were 5,114 deaths (15.7%) over a median follow up of 5.5 years. Dysnatraemia was present in 8.5% of patients overall. In multivariable analysis, both baseline and time-dependent serum sodium concentrations exhibited a U-shaped association with mortality. Hyponatremia was significantly associated with increased risk for cardiovascular [HR 1.38 (1.18-1.61)], malignant [HR: 2.49 (2.23-2.78)] and non-cardiovascular/non-malignant causes of death [1.36 (1.17-1.58)], while hypernatremia was significantly associated with cardiovascular [HR: 2.16 (1.58-2.96)] and non-cardiovascular/ non-malignant deaths respectively [HR: 3.60 (2.87-4.52)]. The sodium-mortality relationship was significantly influenced by age, level of kidney function and the clinical setting at baseline ($P < 0.001$). For hyponatraemia, relative mortality risks were significantly higher for younger patients (interaction term $P < 0.001$), for patients with better kidney function, and for patients attending general practice [HR 2.70 (2.15-3.36)] than other clinical settings. For hypernatraemia, age and kidney function remained significant effect modifiers, with patients attending outpatient departments experiencing the greatest risk [HR 9.84 (4.88-18.62)] than patients who attended other clinical locations. Optimal serum sodium thresholds for mortality varied by level of kidney function with a flattening of mortality curve observed for patients with poorer kidney function. **Conclusion:** Serum sodium concentrations outside the standard normal range adversely impact mortality and are associated with specific causes of death. The thresholds at which these risks appear to vary by age, level of kidney function, and are modified in specific clinical settings within the health system

Gut Microbiome

Exploring the Influence of Gut Microbiome on Energy Metabolism in Humans

Julia Montenegro, Anissa M Armet, Benjamin P Willing, Edward C Deehan, Priscila G Fassini, João F Mota, Jens Walter, et. al. *Adv Nutr.* 2023 Jul;14(4):840-857. doi: 10.1016/j.advnut.2023.03.015. [Article link](#)

Significance: This research review of human studies found no consistent gut microbiome patterns associated with energy metabolism, and that most interventions were ineffective in modulating the gut microbiome to influence energy metabolism. Future longitudinal and randomized control trials are necessary to establish cause-and-effect mechanisms and approaches to modulate gut microbiome for energy regulation.

The gut microbiome has a profound influence on host physiology, including energy metabolism, which is the process by which energy from nutrients is transformed into other forms of energy to be used by the body. However, mechanistic evidence for how the microbiome influences energy metabolism is derived from animal models. In this narrative review, we included human studies investigating the relationship between gut microbiome and energy metabolism —i.e., energy expenditure in humans and energy harvest by the gut microbiome. Studies have found no consistent gut microbiome patterns associated with energy metabolism, and most interventions were not effective in modulating the gut microbiome to influence energy metabolism. To date, cause-and-effect relationships, and mechanistic evidence on the impact of the gut microbiome on energy expenditure have not been established in humans. Future longitudinal observational studies and randomized controlled trials utilizing robust methodologies and advanced statistical analysis are needed. Such knowledge would potentially inform the design of therapeutic avenues and specific dietary recommendations to improve energy metabolism through gut microbiome modulation.

Emerging Science Areas

Emerging Areas: Nutrition

Vitamin D Supplementation and Major Cardiovascular Events: D-Health Randomized Controlled Trial

Thompson B, Waterhouse M, English D R, McLeod D S, Armstrong B K, Baxter C et al. *BMJ* 2023; 381, doi:10.1136/bmj-2023-075230. [Article link](#)

Significance: A five-year study in older adults found Vitamin D3 supplementation (60,000 units/month) might reduce the incidence of major cardiovascular events particularly in individuals on cardiovascular drugs at baseline. The rate of myocardial infarction and coronary revascularization was lower in the vitamin D group, but no difference in the rate of stroke. The absolute risk difference was small with a confidence interval consistent with a null finding.

Objective: To investigate whether supplementing older adults with monthly doses of vitamin D alters the incidence of major cardiovascular events. **Design:** Randomized, double blind, placebo-controlled trial of monthly vitamin D (the D-Health Trial). Computer generated permuted block randomisation was used to allocate treatments. **Setting:** Australia from 2014 to 2020.

Participants: 21 315 participants aged 60-84 years at enrolment. Exclusion criteria were self-reported hypercalcaemia, hyperparathyroidism, kidney stones, osteomalacia, sarcoidosis, taking >500 IU/day supplemental vitamin D, or unable to give consent because of language or cognitive impairment. **Intervention:** 60 000 IU/month vitamin D₃ (n=10 662) or placebo (n=10 653) taken orally for up to five years. 16 882 participants completed the intervention period: placebo 8270 (77.6%); vitamin D 8552 (80.2%). **Main outcome measures:** The main outcome for this analysis was the occurrence of a major cardiovascular event, including myocardial infarction, stroke, and coronary revascularisation, determined through linkage with administrative datasets. Each event was analysed separately as secondary outcomes. Flexible parametric survival models were used to estimate hazard ratios and 95% confidence intervals. **Results:** 21 302 people were included in the analysis. The median intervention period was five years. 1336 participants experienced a major cardiovascular event (placebo 699 (6.6%); vitamin D 637 (6.0%)). The rate of major cardiovascular events was lower in the vitamin D group than in the placebo group (hazard ratio 0.91, 95% confidence interval 0.81 to 1.01), especially among those who were taking cardiovascular drugs at baseline (0.84, 0.74 to 0.97; P for interaction=0.12), although the P value for interaction was not significant (<0.05). Overall, the difference in standardised cause specific cumulative incidence at five years was -5.8 events per 1000 participants (95% confidence interval -12.2 to 0.5 per 1000 participants), resulting in a number needed to treat to avoid one major cardiovascular event of 172. The rate of myocardial infarction (hazard ratio 0.81, 95% confidence interval 0.67 to 0.98) and coronary revascularisation (0.89, 0.78 to 1.01) was lower in the vitamin D group, but there was no difference in the rate of stroke (0.99, 0.80 to 1.23). **Conclusions:** Vitamin D supplementation might reduce the incidence of major cardiovascular events, although the absolute risk difference was small and the confidence interval was consistent with a null finding. These findings could prompt further evaluation of the role of vitamin D supplementation, particularly in people taking drugs for prevention or treatment of cardiovascular disease.

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