Nutrition Briefs

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Dietary Patterns

Protective Effect of High Adherence to Mediterranean Diet on the Risk of Incident Type-2 Diabetes in Subjects with MAFLD: The Di@bet.es Study

Ana Lago-Sampedro, Wasima Oualla-Bachiri, Sara García-Serrano Cristina Maldonado-Araque, Sergio Valdés, Viyey Doulatram-Gamgaram, Gabriel Olveira et. al. *Nutrients* 2024, 16(21), 3788; doi.org/10.3390/nu16213788. Article link

Objectives: Metabolic Dysfunction-Associated Fatty Liver Disease (MAFLD) increases the risk of Type-2 Diabetes (T2DM). The Mediterranean diet (MD) has shown advantages in the management of MAFLD and preventing co-morbidities; however, its relationship with T2DM development in MAFLD has been less investigated. We aimed to evaluate the association of MD adherence with the risk of incident T2DM in the Spanish adult population with MAFLD and according to their weight gain at 7.5 years follow-up. **Methods:** A cohort of 714 participants (without weight increment: 377; with weight increment: 337) from the Di@bet.es cohort study with MAFLD and without T2DM at baseline were investigated. Anthropometric, sociodemographic, clinical data, and a survey on habits were recorded. OGTT and fasting blood biochemistry determinations were made. Baseline adherence to MD was estimated by the adapted 14-point MEDAS questionnaire and categorized as high and low adherence. **Results:** In total, 98 people developed T2DM at follow-up. The high adherence to MD was inversely associated with the development of T2DM in both the overall population (0.52 [0.31–0.87]) and subjects without weight gain at follow-up (0.35 [0.16–0.78]). **Conclusions:** Our results suggest the protective effect of high adherence to MD regarding the risk of T2DM in subjects with MAFLD, with this health benefit being more evident in men with the absence of weight gain. These results support the recommendations for MD use in these patients.

Food Classification

Ultra-Processed Foods and Cardiovascular Disease: Analysis of Three Large US Prospective Cohorts and a Systematic Review and Meta-Analysis of Prospective Cohort Studies

Kenny Mendozaa, Stephanie A. Smith-Warner, Sinara Laurini Rossatoa, Neha Khandpurd, JoAnn E. Mansonb, Lu Qig. *The Lancet*, Vol. 37, 9 2024. DOI: 10.1016/j.lana.2024.100859. Article link

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Background: Prospective associations between total and groups of ultra-processed foods (UPF) and cardiovascular disease (CVD) remained to be characterised. Our aim was to assess the association of total and group-specific UPF intakes with CVD, coronary heart disease (CHD), and stroke in three large prospective cohorts of US adults. Additionally, we conducted a systematic review and meta-analyses on the existing evidence on the associations of total UPF intake with these outcomes. **Methods:** UPF intake was assessed through food frequency questionnaires in the Nurses' Health Study (NHS; n = 75,735), Nurses' Health Study II (NHSII; n = 90,813), and Health Professionals Follow-Up Study (HPFS; n = 40,409). Cox regression estimated cohort-specific associations of total and group-specific UPF intake with risk of CVD (cases = 16,800), CHD (cases = 10,401), and stroke (cases = 6758), subsequently pooled through fixed-effect models. Random-effects meta-analyses pooled existing prospective findings on the UPF-CVD association identified on Medline and Embase up to April 5, 2024, without language restrictions. Risk of bias was assessed with the Newcastle–Ottawa Scale, funnel plots, and Egger's tests, and meta-evidence was evaluated using NutriGrade. **Findings:** The baseline mean (SD) age was 50.8 years (7.2) for the NHS, 36.7 years (4.6) for the NHSII, and 53.4 years (9.6) for the HPFS. The proportion of participants of White race was 97.7% in the NHS, 96.4% in the NHSII, and 94.9% in the HPFS. Among the three cohorts, multivariable-adjusted hazard ratios [HRs (95% CIs)] for CVD, CHD, and stroke for the highest (vs. lowest) total UPF intake quintile were 1.11 (1.06–1.16), 1.16 (1.09–1.24), and 1.04 (0.96–1.12), respectively. UPF groups demonstrated divergent associations. Sugar-/artificially-sweetened drinks and processed meats were associated with higher CVD risk, whereas inverse associations were observed for bread/cold cereals, yoghurt/dairy desserts, and savoury snacks. Meta-analysing 22 prospective studies showed that total UPF intake at the highest category (vs. lowest) was associated with 17% (11%–24%), 23% (12%–34%), and 9% (3%–15%) higher CVD, CHD, and stroke risk. Meta-evidence quality was high for CHD, moderate for CVD, and low for stroke. **Interpretation:** Total UPF intake was adversely associated with CVD and CHD risk in US adults, corroborated by prospective studies from multiple countries, also suggesting a small excess stroke risk. Nutritional advice for cardiovascular health should consider differential consequences of group-specific UPF. Replication is needed in racially/ethnically-diverse populations.

Carbohydrates

Exposure to Sugar Rationing in the First 1000 Days of Life Protected Against Chronic Disease.

Tadeja Gracner, Claire Boone, Paul J. Gertler. *Science,* 31 Oct. 2024. DOI: 10.1126/science.adn5421. Article link

We examined the impact of sugar exposure within 1000 days since conception on diabetes and hypertension, leveraging quasi-experimental variation from the end of the United Kingdom's sugar rationing in September 1953. Rationing restricted sugar intake to levels within current dietary guidelines, yet consumption nearly doubled immediately post-rationing. Using an event study design with UK Biobank data comparing adults conceived just before or after rationing ended, we found that early-life rationing reduced diabetes and hypertension risk by about 35% and 20%, respectively, and delayed disease onset by 4 and 2 years. Protection was evident with in-utero exposure and increased with postnatal sugar restriction, especially after six months when solid foods likely began. In-utero sugar rationing alone accounted for about one third of the risk reduction.

Protein

High-Density Lipoprotein Cholesterol Level and Risk of Muscle Strength Decline and Sarcopenia in Older Adults

Nan Huaa, Chengfan Qina, Feitong Wuc, Ange Wanga, Jing Chena, Qin Zhanga. *Clinical Nutrition*, Volume 43, Issue 10, p2289-2295, October 2024. Article link

Recent studies have demonstrated that very high high-density lipoprotein cholesterol (HDL-C) level was paradoxically linked with higher risk of cardiovascular mortality, all-cause mortality, and several age-related diseases. However, whether very high HDL-C level is associated with a higher risk of sarcopenia in older adults remains unclear. We aimed to investigate the association between HDL-C level and the risk of developing sarcopenia and low grip strength over time in older adults. **Methods:** Participants were from the ongoing China Health and Retirement Longitudinal Study (CHARLS), which includes a nationally representative sample of adults aged ≥45 years and was performed from 2011 to 2020 with follow-ups every two to three years. The current study included 4031 participants aged ≥60 years. Muscle health-related data were collected in waves 2011, 2013, and 2015. Based on HDL-C level at baseline, participants were categorized into five groups: <35 mg/dl, 35–40 mg/dl, 40–60 mg/dl, 60–70 mg/dl and >70 mg/dl. The main outcomes were incident sarcopenia and incident low grip

strength over follow-up. Low grip strength and sarcopenia were defined according to the 2019 Consensus by the Asian Working Group for Sarcopenia. Cox proportional-hazard regression was performed to investigate the association between HDL-C level and the risk of developing sarcopenia and low grip strength in older adults. **Results:** The mean age of study sample was 67.3 (SD 6.1) years, and 49.6% were male. During an average 3.7-year follow-up, 409 (10.1%) participants developed sarcopenia and 771 (21.1%) developed low grip strength. Non-linear association was observed between HDL-C level and the hazard of developing sarcopenia and low grip strength. The multivariable model showed that compared to the reference group (40–60 mg/dl), older adults with very high HDL-C level (>70 mg/dl) had a significantly higher risk of developing sarcopenia (HR 1.69, 95% CI 1.28–2.23) and low grip strength (HR 1.23 95% CI 1.00–1.51). Stratified analyses by sex revealed similar association. **Conclusions:** We present the first longitudinal evidence that very high HDL-C level was associated with a significantly higher risk of muscle strength decline and developing sarcopenia in older adults. It is essential to monitor the muscle health of older adults with very high HDL-C level in clinical practice.

Low- and No-Calorie Sweeteners

Deciphering the Multifaceted Effects of Artificial Sweeteners on Body Health and Metabolic Functions: A Comprehensive Review and Future Perspectives

Qiang Liu, Min Wang, Yuting Hou, Rui Chen, Haixia Liu, Tianlong Han. *CRFSN,* 5 Oct. 2024. doi.org/10.1080/10408398.2024.2411410. Article link

As the rates of chronic diseases such as obesity and diabetes rise worldwide, there is a growing demand for low-calorie or no-calorie sweeteners to reduce sugar intake without sacrificing the sweetness of foods and beverages. Artificial sweeteners have become indispensable as substitutes for sugar due to their high sweetening power and low impact on blood sugar levels and are used in a variety of low-calorie foods and beverages. Although artificial sweeteners offer an alternative for reducing sugar intake while maintaining sweetness, research into their long-term health effects, particularly at high doses, is ongoing, further scientific research and regulatory review are needed to clarify these potential health risks. This article reviews the latest research on the health effects of artificial sweeteners, based on recent studies, introduces the classification, performance, and safety standards for artificial sweeteners, analyses their potential harms to the nervous, immune, and circulatory systems, reproductive system, as well as their effects on gut microbiota, liver function, cancer, diabetes, and obesity. In addition, consumer perceptions of artificial sweeteners and future research directions are discussed, providing insights into current research controversies and knowledge gaps, as well as the health research and market application of artificial sweeteners.

Cognitive Health

Associations of the 'Weekend Warrior' Physical Activity Pattern with Mild Dementia: Findings from the Mexico City Prospective Study

Gary O'Donovan, Fanny Petermann-Rocha, Gerson Ferrari, Catalina Medina, Carolina Ochoa-Rosales, Olga L Sarmiento, Agustín Ibáñez. *BJSM,* 29 October 2024. doi: 10.1136/bjsports-2024-108460. Article link

Objectives: To investigate associations of the 'weekend warrior' physical activity pattern with mild dementia. **Methods:** Participants in the Mexico City Prospective Study were surveyed from 1998 to 2004 and re-surveyed from 2015 to 2019. Participants were asked about leisure time physical activity at baseline. Those who exercised up to once or twice per week were termed 'weekend warriors' and those who exercised more often were termed 'regularly active'. A Mini Mental State Examination (MMSE) was used to assess mild dementia at re-survey. Cox models were adjusted for age, sex, education, income, blood pressure, smoking, body mass index, civil status, sleep, diet and alcohol at baseline. The attributable fraction was defined as the proportion of cases that would not exist if all adults were to exercise once or twice per week or more often. **Results:** The analysis included 10 033 adults of mean (SD) age 51 (10) years followed for 16 (2) years. There were 2400 cases when mild dementia was defined as a score of ≤22 on the MMSE. Compared with the group that reported no sport or exercise, the hazard ratio was 0.75 (95% CI 0.61 to 0.91) in the weekend warrior group, 0.89 (95% CI 0.78 to 1.02) in the regularly active group and 0.84 (95% CI 0.75 to 0.95) in the combined group. The attributable fraction was 13% (95% CI 5% to 21%). Similar results were observed when mild dementia was defined as a score of ≤23 on the MMSE. **Conclusions:** This longitudinal analysis suggests that the weekend warrior physical activity pattern is associated with a reduced risk of mild dementia.

Lipids

Postprandial Metabolomic Profiling: Insights into Macronutrient-Specific Metabolic Responses in Healthy Individuals

Awad Alshahrani, Shereen M. Aleidi, Mohammed Al Dubayee, Reem AlMalki, Rajaa Sebaa, Mahmoud Zhra, Anas M. Abdel Rahman. *Nutrients* 2024, 16(21), 3783; doi.org/10.3390/nu16213783. Article link

Objectives: Understanding the metabolic responses to different macronutrients is crucial for assessing their impacts on health. This study aims to investigate the postprandial metabolomic profiles of healthy individuals following the consumption of glucose, protein, and lipids. **Methods:** Twenty-three healthy, normal-weight adults participated in the study, randomly assigned to consume 300 kcal from glucose, protein, or lipids after an overnight fast. Blood samples were collected at baseline and at 1, 2, and 3 h post-ingestion. An untargeted metabolomic approach using mass spectrometry was employed to analyze plasma metabolites. **Results:** In total, 21, 59, and 156 dysregulated metabolites were identified after glucose, protein, and lipid intake, respectively. Notably, 3'-O-methylguanosine levels decreased significantly after glucose consumption while remaining stable during lipid intake before increasing at 2 h. Common metabolites shared between glucose and lipid groups included 3'-O-methylguanosine, 3-oxotetradecanoic acid, poly-g-D-glutamate, and triglyceride (TG) (15:0/18:4/18:1). **Conclusions:** The findings highlight distinct metabolic responses to macronutrient intake, emphasizing the role of specific metabolites in regulating postprandial metabolism. These insights contribute to understanding how dietary components influence metabolic health and insulin sensitivity.

Overnutrition Causes Insulin Resistance and Metabolic Disorder through Increased Sympathetic Nervous System Activity

Li Ling, Adham Shawkat, et al. *Cell Metab*. Oct. 2024. doi.org/10.1016/j.cmet.2024.09.012 (2024). Article link

Summary: The mechanisms underlying obesity-induced insulin resistance remain incompletely understood, as impaired cellular insulin signaling, traditionally considered the primary driver of insulin resistance, does not always accompany impaired insulin action. Overnutrition rapidly increases plasma norepinephrine (NE), suggesting overactivation of the sympathetic nervous system (SNS). However, the role of the SNS in obesity is controversial, as both increased and decreased SNS activity (SNA) have been reported. Here, we show that reducing catecholamine (CA) release from the SNS protects against overnutrition-induced insulin resistance as well as hyperglucagonemia, adipose tissue dysfunction, and fatty liver disease, as we demonstrate utilizing a mouse model of inducible and peripherally restricted deletion of tyrosine hydroxylase (th; THΔper). A key mechanism through which heightened SNA induces insulin resistance is by triggering adipose tissue lipolysis. Increased SNA emerges as a critical driver in the pathogenesis of overnutrition-induced insulin resistance and metabolic disease independent of cellular insulin signaling.

Sodium

Joint Association of Serum Sodium and Frailty with Mild Cognitive Impairment among Hospitalized Older Adults with Chronic Diseases: A Cross-Sectional Study

Zhaozhao Hui, Zhaozhao Hui, Lina Wang, Jing Deng, Feng Liu, Liping Cheng, Yajing Li, Yuxin Tian, et. al. *Front. Nutr.*, 20 October 2024, Vol. 11 – 2024, doi.org/10.3389/fnut.2024.1467751. Article link

Background: To examine the associations of serum sodium and frailty with the risk of mild cognitive impairment (MCI) among hospitalized older adults with chronic diseases. **Methods:** A cross-sectional study was conducted in 403 hospitalized older adults with chronic diseases. Serum sodium concentration was assessed by the ion-selective electrode method, frailty status was evaluated by the FRAIL scale, and MCI was determined by the Montreal Cognitive Assessment (MoCA). Multiple logistic regression models were used to estimate the associations of serum sodium and frailty with MCI. **Results:** Participants with the lowest tertile of serum sodium had a higher risk of MCI than those in the middle tertile group (OR = 1.75, 95% CI: 1.01–3.04). Below 143 mmol/L, the risk of MCI was 1.38 (95% CI: 1.03–1.84) for per 1 SD decrease in serum sodium. Compared with the robust group, frailty was significantly associated with an increased risk of MCI (OR = 3.94, 95% CI: 1.92–8.10). Moreover, in comparison with participants with the middle tertile of serum sodium and who were robust/prefrail, those with frailty and either the lowest (OR = 5.53, 95% CI: 2.08–14.67) or the highest tertile of serum sodium (OR = 3.48, 95% CI: 1.20–10.05) had higher risks of MCI. **Conclusion:** Both lower and higher serum sodium impose a significantly higher risk for MCI in older adults with frailty. This could inform the design of clinical trials and the development of guidelines and recommendations for correcting serum sodium and frailty in hospitalized older adults with chronic diseases.

Gut Health

Enteric Pathogens Relationship with Small Bowel Histologic Features of Environmental Enteric Dysfunction in a Multicountry Cohort Study

Najeeha T Iqbal, Sarah Lawrence, Tahmeed Ahmed, Phillip I Tarr, Donna M Denno. *AJCN* Vol. 120, 9 2024, DOI 10.1016/j.ajcnut.2024.02.026. Article link

Objectives: The objective of this study was to determine if fecal enteropathogenic detection predicts subsequent EED histology. **Methods:** Fecal samples were obtained from undernourished children aged <2 y without diarrhea enrolled in 3 cohort studies, who failed nutritional intervention and subsequently underwent endoscopy. Duodenal biopsies from 245 (Bangladesh n = 120, Pakistan n = 57, and Zambia n = 68) children were scored using a semiquantitative histologic grading protocol. Thirteen enteropathogens were sought in common across the 3 centers using TaqMan array cards (TAC) (Bangladesh and Pakistan) and the Luminex platform (Zambia). An additional 18 pathogens and 32 virulence loci were sought by TAC and included in sensitivity analyses restricted to TAC data. **Results:** Multivariable linear regressions adjusting for study center, age at stool collection, and stool-to-biopsy interval demonstrated the following: 1) an association of norovirus and Shigella detection with subsequent enterocyte injury [β 0.2 (95% CI: 0.1, 0.3); P = 0.002 and β 0.2 (95% CI: 0.0, 0.3); P = 0.008, respectively], 2) association of Campylobacter with intraepithelial lymphocytes [β 0.2 (95% CI: 0.0, 0.4); P = 0.046], and 3) association of Campylobacter and enterotoxigenic Escherichia coli with a summative EED histopathology index score [β 4.2 (95% CI: 0.8, 7.7); P = 0.017 and β 3.9 (95% CI: 0.5, 7.3); P = 0.027, respectively]. All but 2 of these associations (Shigella-enterocyte injury and Campylobacter-index score) were also demonstrated in TAC-only sensitivity analyses, which identified additional associations between other pathogens, pathogen burden, or virulence loci primarily with the same histologic parameters. **Conclusions:** The detection of some enteropathogens in asymptomatic infections is associated with subsequent EED histopathology. These novel findings offer a basis for future EED etiology and pathogenesis studies.

Emerging Science Areas

Emerging Nutrition Topic: Diet and Behavior

The Full Picture of People's Realities Must be Considered to Deliver Better Diets for All

Corinna Hawkes, Charlotte Gallagher-Squires, Mark Spires, Nicky Hawkins, Kimberley Neve, Jessica Brock, Anna Isaacs, et. al. *Nature Food*. Oct 17, 2024. doi.org/10.1038/s43016-024-01064-0. Article link

Efforts to address poor-quality diets have stepped up considerably in recent years, but the problem of inadequate, unhealthy, unsustainable and unequal diets persists. Here we argue that to get policies and interventions working more effectively and equitably, a fresh approach is needed—one that considers the full picture of people's realities. People's realities interact to shape the way people respond to and engage with policies and interventions, thereby influencing their impact, particularly, albeit not only, on dietary inequalities. We propose a tool that brings together key realities that shape impact, including the material, economic and psychosocial realities that people face in their households, families, food environments, social interactions and cultures. The purpose of the tool is to help policymakers, intervention practitioners and researchers committed to improving diets achieve greater success by helping them think through the full picture of people's realities when identifying, designing, implementing and evaluating policies and interventions.

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November 19, 2024, Virtual Event
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Tufts University introduced the Food Compass nutrient profiling system and its authors have updates based on new nutritional data and scientific feedback.
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