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Dietary Patterns

The Healthy Eating Index-2015 and All-Cause/Cause-Specific Mortality: A Systematic Review and Dose-Response Meta-Analysis

Xuanyu Hao, Dongyang Li. *Adv Nutr*. 2024 Mar;15(3):100166. doi: 10.1016/j.advnut.2023.100166. [Article link](#)

This meta-analysis was undertaken to determine the predictive value of Healthy Eating Index (HEI)-2015 in all-cause, cancer-cause, and cardiovascular disease (CVD)-cause mortality. This review was registered with PROSPERO as CRD42023421585. PubMed and Web of Science were searched for articles published by September 15, 2023. The hazard ratio (HR) was calculated with exact confidence intervals (CIs) of 95%. Statistical heterogeneity among studies was measured by Cochran's Q test (χ^2) and the I² statistic. Eighteen published studies were finally identified in this meta-analysis. The results showed that the HEI-2015 was associated with all-cause mortality either as a categorical variable (HR: 0.80; 95% CI: 0.79, 0.82) or continuous variable (HR: 0.90; 95% CI: 0.88, 0.92). The HEI-2015 was also associated with cancer-cause mortality as categorical variable (HR: 0.81; 95% CI: 0.78, 0.83) or continuous variable (HR: 0.90; 95% CI: 0.81, 0.99). The categorical HEI-2015 was also independently correlated with decreasing CVD-cause mortality (HR: 0.81; 95% CI: 0.75, 0.87). A nonlinear dose-response relation between the HEI-2015 and all-cause mortality was found. In the linear dose-response analysis, the risk of mortality from cancer decreased by 0.42% per 1 score increment of the HEI-2015 and the risk of CVD-cause mortality decreased by 0.51% with the increment of the HEI-2015 per 1 score. Our analysis indicated a significant relationship between the HEI-2015 and all-cause, cancer-cause, and CVD-cause mortality.

Carbohydrates

Effects of Low-Carbohydrate Diets, with and without Caloric Restriction, on Inflammatory Markers in Adults: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Fatemeh Kazeminasab, Maryam Miraghajani, Mousa Khalafi, Mohammad Hossein Sakhaei, Sara K Rosenkranz, Heitor O Santos. *Eur J Clin Nutr*. 2024 Mar 18. doi: 10.1038/s41430-024-01431-x. [Article link](#)

Low-carbohydrate diets (LCDs) have gained interest due to their favorable effects on health outcomes, such as inflammation. However, further research is needed to ascertain the overall effects of LCDs on inflammatory parameters, but at the same time considering weight loss and calorie intake. Thus, a systematic review and meta-analysis of randomized clinical trials was performed to investigate the effects of LCDs compared with low-fat diets (LFDs), with and without caloric restriction, on inflammatory markers in adults. PubMed, Scopus, and Web of Science were searched through March 2022 to select intervention studies addressing LCDs vs. LFDs, in which the following circulating inflammatory markers were used: C-reactive protein (CRP), tumor necrosis factor alpha (TNF- α), and interleukin (IL-6). Analyses were conducted comparing LCDs vs. LFDs through weighted mean differences (WMD) or standardized mean differences (SMD) and 95% confidence intervals (95% CIs) using random effects models. The systematic review and meta-analysis included a total of 51 studies with a total sample of 4,164 adults, with or without other chronic diseases. Intervention durations ranged from 2-144 weeks. LCDs, compared with LFDs, significantly decreased body weight [WMD = -1.35%, $p = 0.001$], CRP [SMD = -0.1, $p = 0.03$], and IL-6 [SMD = -0.15, $p = 0.09$]. However, LCDs did not significantly decrease TNF- α [SMD = -0.02, $p = 0.7$] compared to LFDs. In conclusion, LCDs have a beneficial effect on markers of inflammation by decreasing CRP and IL-6; this effect has an association with weight loss. However, LCDs were not more effective than LFDs in decreasing TNF- α .

Protein

Lack of Change in Blood Pressure and Arterial Stiffness after High Dairy Intake in Hyperinsulinemic Subjects: A Cross-Over Randomized Controlled Trial

Hana Arghavani, Sarah O'Connor et. al. *Ap Ph Nutr Met.* 2024 Mar 1;49(3):350-359. doi: 10.1139/apnm-2023-0053. [Article link](#)

To evaluate the effects of high dairy (HD) (≥ 4 servings/day), compared to adequate dairy (AD) (2-3 servings/day as per Canada's Food Guide for Healthy Eating (2007)), on blood pressure (BP) and measures of arterial stiffness in hyperinsulinemic subjects. In this cross-over clinical trial, hyperinsulinemic adults were randomized to AD and HD for 6 weeks. Anthropometric, glycemic, and lipid parameters were analyzed and dietary intake was evaluated; BP, carotid-femoral pulse wave velocity, augmentation index, and measures of arterial stiffness were assessed. 27 participants completed the study. Dairy intake was 2.2 ± 1.2 servings/day during AD. In addition, lower total and low-density lipoprotein (LDL) cholesterol were observed without significant change in BP or arterial stiffness between before and after AD. During HD, the subjects consumed 5.8 ± 1.9 servings/day of dairy products, providing a higher intake of protein, saturated fat, calcium, phosphorus, sodium, and potassium compared to the baseline diet. After the HD, subjects had higher body fat, fasting insulin, homeostatic model assessment for insulin resistance (HOMA-IR) index, and triglycerides without altering BP or arterial stiffness compared to before HD. Overall, adequate or high intake of total dairy did not modify BP or arterial stiffness in hyperinsulinemic adults after 6 weeks.

Low- and No-Calorie Sweeteners

The Molecular Theory of Sweet Taste: Revisit, Update, and Beyond

Hong Zheng, Xiangqun Xu, Yishan Fang, Rui Sun, Bo Liu. *J Med Chem.* 2024 Mar 14;67(5):3232-3243. doi: 10.1021/acs.jmedchem.3c02055. [Article link](#)

The molecular origin of the sweet taste is still elusive. Herein, the canonical AH-B-X theory of sweet taste is extended by resurveying various sweeteners, which provides deeper insights into an analogous intramolecular connectivity pattern of both glucophores in sweeteners and their interaction counterparts in sweet taste receptor TAS1R2/TAS1R3: electrostatic complementarity and topochemical compatibility. Furthermore, their complementary interaction is elaborately illustrated, accounting for the common molecular feature of eliciting sweetness. Moreover, it highlights that multiple glucophores in a topological system synergistically mediate the elicitation and performance of sweetness. This perspective presents a meaningful framework for the structure-activity relationship-based molecular design and modification of sweeteners and sheds light on the mechanism of molecular evolution of TAS1R2s/TAS1R3s. The link between palatability of sweeteners and harmony relationships between their structural components via stereochemistry and network has significant implications to illuminate the underlying mechanisms by which nature designs chemical reactions to elicit the most important taste.

Cognitive Health

Diet Patterns Associated with Cognitive Decline: Methods to Harmonize Data from European and US Cohort Studies

Amaia Ayala-Garcia, Natalia Soldevila-Domenech, So-Yun Yi, Rafael de la Torre, Lyn M. Steffen, for the IAFNS Retrospective Harmonization Expert Working Group. *Front. Nutr.*, 21 March, Vol. 11 – 2024. doi.org/10.3389/fnut.2024.1379531. [Article link](#)

This work was supported by IAFNS [Cognitive Health Committee](#).



The impact of dietary intake on cognitive outcomes and dementia prevention is a topic of increasing interest. Meta-analyses of observational studies, mostly conducted within US and European populations, have reported benefits of healthy diet patterns on cognitive performance, but results from individual studies have been inconsistent. These inconsistencies are likely due to the diverse methodology used in studies, including different diet and cognitive function assessment instruments, follow-up periods, and analytical methods, which make drawing conclusions relevant to dietary guidance challenging. The objective of this project is to describe a protocol to conduct a retrospective harmonization study on dietary intake and cognitive health using data from European and US studies. The recommendations resulting from the project can be used to support evidence-based synthesis for future iterations of the Dietary Guidelines for Americans or other population-based dietary guidance. Additionally, this study will serve as a harmonization guide for future research on the relationship between diet patterns and cognition. The approach outlined ultimately aims to optimize resources and expedite research efforts for dementia prevention.

A Review of the Effects of Mushrooms on Mood and Neurocognitive Health across the Lifespan

Sara Cha, Lynne Bell, Barbara Shukitt-Hale, Claire M Williams. *Neurosci Biobehav Rev.* 2024 Mar;158:105548. doi: 10.1016/j.neubiorev.2024.105548. [Article link](#)

Mushrooms contain bioactive compounds with documented antioxidant and anti-inflammatory actions. Here, we present a systematic evaluation of epidemiological and clinical studies that investigate the role of mushrooms, either as a separate or integral dietary component, on neurocognition and mood. Following a search of four databases, a total of 34 human studies examining the effect of different mushrooms across varying age cohorts and health statuses were selected for inclusion. Epidemiological studies included in this review ($n = 24$) revealed a significant benefit of dietary patterns that included mushrooms of any species on cognition and mood in both healthy and compromised populations. However, the results obtained from intervention studies ($n = 10$) were mixed. Studies mainly investigated Lion's Mane (*Hericium erinaceus*), showing some enhancement of mood and cognitive function in middle-aged and older adults. Further acute and chronic human intervention studies are needed, using adequate sample sizes, employing appropriately sensitive neurocognitive tests, and investigating a range of dietary mushrooms, to confirm the effects of mushroom supplementation on neurocognition and mood in humans.

Lipids

Can the Gut Microbiome Inform the Effects of Omega-3 Fatty Acid Supplementation Trials on Cognition?

Bilal E Kerman, Wade Self, Hussein N Yassine. *Curr Opin Clin Nutr Metab Care.* 2024 Mar 1;27(2):116-124. doi: 10.1097/MCO.0000000000001007. [Article link](#)

Purpose of review: Most omega-3 polyunsaturated fatty acid (n-3 PUFA) supplementation clinical trials report inconsistent or null findings on measures of cognition or Alzheimer's disease (AD) with a relatively large variability in the response to n-3 PUFA supplementation. The purpose of this review is to identify whether the gut microbiome together with the metabolome can provide critical insights to understand this heterogeneity in the response to n-3 PUFA supplementation. Recent findings: A Western diet with high saturated fat and omega-6 fatty acid content, obesity, and lack of exercise puts strain on the gut microbiome resulting in imbalance, dysbiosis, reduced bacterial diversity, and increased abundance of the pro-inflammatory taxa. A plant-based diet has beneficial effects on the gut microbiota even when deficient in n-3 PUFAs. Human and animal studies show that increased intake of the n-3 PUFAs correlates with increased beneficial intestinal bacteria when compared to a Western diet. Summary: The composition of the gut microbiota can help define the effects of n-3 PUFA supplementation on the brain and lead to more personalized nutritional interventions.

Sodium

Modifying Dietary Sodium and Potassium Intake: An End to the 'Salt Wars'?

Robert Little, David H Ellison. *Hypertension.* 2024 Mar;81(3):415-425. doi: 10.1161/HYPERTENSIONAHA.123.19487. [Article link](#)

Excessive salt intake raises blood pressure, but the implications of this observation for human health have remained contentious. It has also been recognized for many years that potassium intake may mitigate the effects of salt intake on blood pressure and possibly on outcomes such as stroke. Recent large randomized intervention trials have provided strong support for the benefits of replacing salt (NaCl) with salt substitute (75% NaCl, 25% KCl) on hard outcomes, including stroke. During the same period of time, major advances have been made in understanding how the body senses and tastes salt, and how these sensations drive intake. Additionally, new insights into the complex interactions between systems that control sodium and potassium excretion by the kidneys, and the brain have highlighted the existence of a potassium switch in the kidney distal nephron. This switch seems to contribute importantly to the blood pressure-lowering effects of potassium intake. In recognition of these evolving data, the United States Food and Drug Administration is moving to permit potassium-containing salt substitutes in food manufacturing. Given that previous attempts to reduce salt consumption have not been successful, this new approach has a chance of improving health and ending the 'Salt Wars'.

Gut Health

Exploring the Influence of Gut-Brain Axis Modulation on Cognitive Health: A Comprehensive Review of Prebiotics, Probiotics, and Symbiotics

Mónika Fekete, Andrea Lehoczki, Dávid Major, Vince Fazekas-Pongor, Tamás Csípő, Stefano Tarantini, Zoltán Csizmadia, et. al. *Nutrients*. 2024 Mar 10;16(6):789. doi: 10.3390/nu16060789. [Article link](#)

Recent research exploring the relationship between the gut and the brain suggests that the condition of the gut microbiota can influence cognitive health. A well-balanced gut microbiota may help reduce inflammation, which is linked to neurodegenerative conditions. Prebiotics, probiotics, and symbiotics are nutritional supplements and functional food components associated with gastrointestinal well-being. The bidirectional communication of the gut-brain axis is essential for maintaining homeostasis, with pre-, pro-, and symbiotics potentially affecting various cognitive functions such as attention, perception, and memory. Numerous studies have consistently shown that incorporating pre-, pro-, and symbiotics into a healthy diet can lead to improvements in cognitive functions and mood. Maintaining a healthy gut microbiota can support optimal cognitive function, which is crucial for disease prevention in our fast-paced, Westernized society. Our results indicate cognitive benefits in healthy older individuals with probiotic supplementation but not in healthy older individuals who have good and adequate levels of physical activity. Additionally, it appears that there are cognitive benefits in patients with mild cognitive impairment and Alzheimer's disease, while mixed results seem to arise in younger and healthier individuals. However, it is important to acknowledge that individual responses may vary, and the use of these dietary supplements should be tailored to each individual's unique health circumstances and needs.

Gut Microbiome and Metabolome Profiling in Framingham Heart Study Reveals Cholesterol-Metabolizing Bacteria

Chenhao Li, Martin Stražar, Ahmed M.T. Mohamed, Stanley Y. Shaw, Damian R. Plichta, Ramnik J. Xavier. *Cell*. April 02, 2024. doi.org/10.1016/j.cell.2024.03.014. [Article link](#)

Summary:

- Multi-omic profiling in FHS reveals microbes and metabolites associated with CVD
- *Oscillibacter* species are associated with decreased blood and stool cholesterol
- Homology searches and molecular networking predict cholesterol enzymes and products
- *Oscillibacter* species encode for conserved cholesterol-metabolizing enzymes

Accumulating evidence suggests that cardiovascular disease (CVD) is associated with an altered gut microbiome. Our understanding of the underlying mechanisms has been hindered by lack of matched multi-omic data with diagnostic biomarkers. To comprehensively profile gut microbiome contributions to CVD, we generated stool metagenomics and metabolomics from 1,429 Framingham Heart Study participants. We identified blood lipids and cardiovascular health measurements associated with microbiome and metabolome composition. Integrated analysis revealed microbial pathways implicated in CVD, including flavonoid, γ -butyrobetaine, and cholesterol metabolism. Species from the *Oscillibacter* genus were associated with decreased fecal and plasma cholesterol levels. Using functional prediction and *in vitro* characterization of multiple representative human gut *Oscillibacter* isolates, we uncovered conserved cholesterol-metabolizing capabilities, including glycosylation and dehydrogenation. These findings suggest that cholesterol metabolism is a broad property of phylogenetically diverse *Oscillibacter* spp., with potential benefits for lipid homeostasis and cardiovascular health.

Emerging Science

Emerging Nutrition Areas: Ultra-Processed Food and Adverse Outcomes

Ultra-Processed Food Exposure and Adverse Health Outcomes: Umbrella Review of Epidemiological Meta-Analyses

Melissa M Lane, Elizabeth Gamage, Shutong Du, Deborah N Ashtree, Amelia J McGuinness, Sarah Gauci, Phillip Baker, et. al. *BMJ*. 2024 Feb 28;384:e077310. doi: 10.1136/bmj-2023-077310. [Article link](#)

Objective: To evaluate the existing meta-analytic evidence of associations between exposure to ultra-processed foods, as defined by the Nova food classification system, and adverse health outcomes. Design: Systematic umbrella review of existing meta-analyses. Data sources: MEDLINE, PsycINFO, Embase, and the Cochrane Database of Systematic Reviews, as

manual searches of reference lists from 2009 to June 2023. Eligibility criteria for selecting studies: Systematic reviews and meta-analyses of cohort, case-control, and/or cross-sectional study designs. To evaluate the credibility of evidence, pre-specified evidence classification criteria were applied, graded as convincing ("class I"), highly suggestive ("class II"), suggestive ("class III"), weak ("class IV"), or no evidence ("class V"). The quality of evidence was assessed using the GRADE (Grading of Recommendations, Assessment, Development, and Evaluations) framework, categorised as "high," "moderate," "low," or "very low" quality. Results: The search identified 45 unique pooled analyses, including 13 dose-response associations and 32 non-dose-response associations (n=9 888 373). Overall, direct associations were found between exposure to ultra-processed foods and 32 (71%) health parameters spanning mortality, cancer, and mental, respiratory, cardiovascular, gastrointestinal, and metabolic health outcomes. Based on the pre-specified evidence classification criteria, convincing evidence (class I) supported direct associations between greater ultra-processed food exposure and higher risks of incident cardiovascular disease related mortality (risk ratio 1.50, 95% confidence interval 1.37 to 1.63; GRADE=very low) and type 2 diabetes (dose-response risk ratio 1.12, 1.11 to 1.13; moderate), as well as higher risks of prevalent anxiety outcomes (odds ratio 1.48, 1.37 to 1.59; low) and combined common mental disorder outcomes (odds ratio 1.53, 1.43 to 1.63; low). Highly suggestive (class II) evidence indicated that greater exposure to ultra-processed foods was directly associated with higher risks of incident all cause mortality (risk ratio 1.21, 1.15 to 1.27; low), heart disease related mortality (hazard ratio 1.66, 1.51 to 1.84; low), type 2 diabetes (odds ratio 1.40, 1.23 to 1.59; very low), and depressive outcomes (hazard ratio 1.22, 1.16 to 1.28; low), together with higher risks of prevalent adverse sleep related outcomes (odds ratio 1.41, 1.24 to 1.61; low), wheezing (risk ratio 1.40, 1.27 to 1.55; low), and obesity (odds ratio 1.55, 1.36 to 1.77; low). Of the remaining 34 pooled analyses, 21 were graded as suggestive or weak strength (class III-IV) and 13 were graded as no evidence (class V). Overall, using the GRADE framework, 22 pooled analyses were rated as low quality, with 19 rated as very low quality and four rated as moderate quality. Conclusions: Greater exposure to ultra-processed food was associated with a higher risk of adverse health outcomes, especially cardiometabolic, common mental disorder, and mortality outcomes. These findings provide a rationale to develop and evaluate the effectiveness of using population based and public health measures to target and reduce dietary exposure to ultra-processed foods for improved human health. They also inform and provide support for urgent mechanistic research.

Engage with IAFNS

Host-Microbiota Interactions: A Personalized Point of View

April 18, 2024, 10:00-11:00 a.m. ET, Virtual Webinar.

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