April 2023

Nutrition Briefs

Dietary Patterns

Ultra-Processed Foods and Obesity Risk: A Critical Review of Reported Mechanisms

Vinicius M Valicente, Ching-Hsuan Peng, Kathryn N Pacheco, Luotao Lin, Elizabeth I Kielb, Elina Dawoodani, et. al. *Adv Nutr*. 2023 Apr 18;S2161-8313(23)00291-0. doi: 10.1016/j.advnut.2023.04.006. **Article link**

Significance: A review of current evidence failed to identify specific mechanistic evidence that directly linked ultra-processed food intake with increased body mass index and questioned the adoption of the NOVA system for dietary guidance at this stage.

Epidemiological evidence supports a positive association between ultra-processed food (UPF) consumption and BMI. This has led to recommendations to avoid UPF despite very limited evidence establishing causality. Many mechanisms have been proposed and this review critically evaluates selected possibilities for specificity, clarity, and consistency related to food choice (i.e., low cost, shelf-life, food packaging, hyper-palatability, and stimulation hunger/suppression of fullness); food composition (i.e., macronutrients, food texture, added sugar, fat salt, energy density, low calorie sweeteners, and additives); and digestive processes (i.e., oral processing/eating rate, gastric emptying time, gastrointestinal transit time, and microbiome). For some purported mechanisms (e.g., fiber content, texture, gastric emptying, intestinal transit time), data directly contrasting effects of UPF and non-UPF food intake on indices of appetite, food intake and adiposity are available and do not support a unique contribution of UPF. In other instances, data are not available (e.g., microbiome, food additives) or are insufficient (e.g., packaging, food cost, shelf life, macronutrient intake, appetite stimulation) to judge the benefits versus risks of UPF avoidance. There are yet other evoked mechanisms where the preponderance of evidence indicates ingredients in UPF moderate body weight (e.g., LCS use for weight management; beverage consumption as it dilutes energy density; higher fat content because it reduces glycemic responses). Because avoidance of UPF holds potential adverse effects (e.g., reduced diet quality, increased risk of food poisoning, food wastage), it is imprudent to make recommendations about their role in diets before causality and plausible mechanisms have been verified.

Carbohydrates

Low-Carbohydrate Diet and Human Health

Sousana K. Papadopoulos, Pantelis T. Nikolaidis. *Nutrients 2023,* 15(8), 2004; April 21, 2023. doi.org/10.3390/

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nu15082004. **Article link**

Significance: This special issue presents new knowledge on the impact of low-carbohydrate diets on quality of life, disease prevention and nutritional intakes. It focuses on older adults, individuals with cardiovascular disease, and children from low socio-economic environments. The long-term benefits of a personalized approach to such diets warrant further investigation.

Low-carbohydrate diets were initially recommended as a therapeutic dietary scheme for epilepsy, while increasing evidence suggests their potential application in the management of several other pathologies, such as diabetes, neoplasms, gastrointestinal and lung diseases, diseases of the cardiovascular system, as well as obesity. For the present editorial, four manuscripts were gathered, including two systematic reviews and two research articles. Novel knowledge is presented regarding the adoption of low-carbohydrate diets in older adults, people with chronic diseases, children, and those living in a low socio-economic environment, with special focus on patients' quality of life, disease prevention, and nutritional coverage. Further studies are needed to identify the patients' and general population subgroups that could benefit from a low-carbohydrate diet in a personalized approach.

Protein

Protein Source Influences Acute Appetite and Satiety but Not Subsequent Food Intake in Healthy Adults

Morgan L Braden, Jess A Gwin, Heather J Leidy. *J Nutr*. 2023 Apr 6;S0022-3166(23)35542-1. doi: 10.1016/j.tjnut.2023.04.001. **Article link**

Significance: A protein preloading study in healthy adults found casein and pea protein preloads — but not whey — led to greater acute changes in appetite and satiety compared with soy, although no difference in overall energy intake was found.

Background: Although current recommendations encourage plant-based dietary patterns, data is limited as to whether the equivalent substitution of animal-based protein-rich foods with plant-based versions impacts ingestive behavior. **Objectives:** To compare higher-protein preloads, varying in protein source, on appetite, satiety, and subsequent energy intake. **Methods:** Thirty-two adults (age: 25 ± 1 y; body mass index (BMI) measured in kg/m2: 24.2 ± 0.5 kg/m2) randomly consumed 250 kcal, protein-preload beverages (24 g protein), varying in protein source [whey, soy, and pea protein isolates (WHEY, SOY, and PEA) or micellar casein (CAS)] each morning for 3 acclimation days/preload. On day 4, participants completed a 4-h clinical testing day in which the respective preload was consumed, followed by blood sampling and questionnaires every 30 min for appetite and satiety. In addition, an ad libitum lunch was provided 4-h postpreload. On day 5, participants consumed the respective preload at home, followed by an ad libitum breakfast 30 min afterward. For normally-distributed data, repeated-measures analysis of variance (ANOVA) or Friedman nonparametric test were utilized to compare the main effects of protein source on study outcomes. Post hoc pairwise comparisons using least-significant differences (LSD) were then performed. **Results:** CAS (-3330 ± 690 mm ~ 240 min) and PEA (-2840 ± 930mm ~ 240 min) reduced 4-h appetite compared with SOY (-1440 ± 936 mm ~ 240 min; both, $P < 0.05$). WHEY was not different (-2290 ± 930 mm ~ 240 min). CAS (3520 ± 84 pg/mm ~ 240 min) and PEA (3860 ± 864 pg/mL ~ 240 min) increased 4-h peptide YY concentrations compared with SOY (2200 ± 869 pg/mL ~ 240 min; both, $P < 0.05$). WHEY was not different (3870 ± 932 pg/mL ~ 240 min). No differences in ad libitum energy intake were observed. **Conclusions**: CAS and PEA, but not WHEY, elicited greater acute changes in appetite and satiety compared with SOY in healthy adults, supporting that not all protein sources are equivalent.

Low- and No-Calorie Sweeteners

Important Food Sources of Fructose-Containing Sugars and Adiposity: A Systematic Review and Meta-Analysis of Controlled Feeding Trials

Laura Chiavaroli, Annette Cheung, Sabrina Ayoub-Charette, Amna Ahmed, Danielle Lee, Fei Au-Yeung, XinYe Qi, et. al. *Am J Clin Nutr*. 2023 Apr;117(4):741-765. doi: 10.1016/j.ajcnut.2023.01.023. **Article link**

Significance: This systematic review and meta-analysis found excess intakes of energy from sugars (sugar-sweetened beverages at high doses) increased adiposity. Their removal decreased adiposity. Other food sources had no effect, with some showing decreases, including fruits.

Background: Sugar-sweetened beverages (SSBs) providing excess energy increase adiposity. The effect of other food sources of sugars at different energy control levels is unclear. Objectives: To determine the effect of food

sources of fructose-containing sugars by energy control on adiposity. Methods: In this systematic review and meta-analysis, MEDLINE, Embase, and Cochrane Library were searched through April 2022 for controlled trials ≥2 wk. We prespecified 4 trial designs by energy control: substitution (energy-matched replacement of sugars), addition (energy from sugars added), subtraction (energy from sugars subtracted), and ad libitum (energy from sugars freely replaced). Independent authors extracted data. The primary outcome was body weight. Secondary outcomes included other adiposity measures. Grading of Recommendations Assessment, Development, and Evaluation (GRADE) was used to assess the certainty of evidence. Results: We included 169 trials (255 trial comparisons, n = 10,357) assessing 14 food sources at 4 energy control levels over a median 12 wk. Total fructose-containing sugars increased body weight (MD: 0.28 kg; 95% CI: 0.06, 0.50 kg; PMD = 0.011) in addition trials and decreased body weight (MD: -0.96 kg; 95% CI: -1.78, -0.14 kg; PMD = 0.022) in subtraction trials with no effect in substitution or ad libitum trials. There was interaction/influence by food sources on body weight: substitution trials [fruits decreased; added nutritive sweeteners and mixed sources (with SSBs) increased]; addition trials [dried fruits, honey, fruits (≤10%E), and 100% fruit juice (≤10%E) decreased; SSBs, fruit drink, and mixed sources (with SSBs) increased]; subtraction trials [removal of mixed sources (with SSBs) decreased]; and ad libitum trials [mixed sources (with/without SSBs) increased]. GRADE scores were generally moderate. Results were similar across secondary outcomes. Conclusions: Energy control and food sources mediate the effect of fructose-containing sugars on adiposity. The evidence provides a good indication that excess energy from sugars (particularly SSBs at high doses ≥20%E or 100 g/d) increase adiposity, whereas their removal decrease adiposity. Most other food sources had no effect, with some showing decreases (particularly fruits at lower doses ≤10%E or 50 g/d).

Cognitive Health

The Relationship of Omega-3 Fatty Acids with Dementia and Cognitive Decline: Evidence from Perspective Cohort Studies of Supplementation, Dietary Intake and Blood Markers

Bao-Zhen Wei, Lin Li, Cheng-Wen Dong, Chen-Chen Tan; Alzheimer's Disease Neuroimaging Initiative; Wei Xu. *Am J Clin Nutr*. 2023 Apr 5;S0002-9165(23)46320-4. doi: 10.1016/j.ajcnut.2023.04.001. **Article link**

Significance: Data from an analysis of prospective cohort studies of participants with dementia found dietary intake, or long-term supplementation, of Omega-3 fatty acids may lower the risk of Alzheimer's disease or cognitive decline.

Previous data have linked omega-3 fatty acids with risk of dementia. We aimed to assess the longitudinal relationships of omega-3 polyunsaturated fatty acid intake as well as blood biomarkers with risk of Alzheimer's disease (AD), dementia, or cognitive decline. Longitudinal data were derived from 1135 participants without dementia (mean age = 73 y) in the Alzheimer's Disease Neuroimaging Initiative (ADNI) cohort to evaluate the associations of omega-3 fatty acid supplementation and blood biomarkers with incident AD during the 6-y follow-up. A meta-analysis of published cohort studies was further conducted to test the longitudinal relationships of dietary intake of omega-3 and its peripheral markers with all-cause dementia or cognitive decline. Causal dose-response analyses were conducted using the robust error meta-regression model. In the ADNI cohort, long-term users of omega-3 fatty acid supplements exhibited a 64% reduced risk of AD (hazard ratio: 0.36, 95% confidence interval: 0.18, 0.72; P = 0.004). After incorporating 48 longitudinal studies involving 103,651 participants, a moderate-to-high level of evidence suggested that dietary intake of omega-3 fatty acids could lower risk of all-cause dementia or cognitive decline by ~ 20%, especially for docosahexaenoic acid (DHA) intake (relative risk [RR]: 0.82, I2 = 63.6%, P = 0.001) and for studies that were adjusted for apolipoprotein APOE ε4 status (RR: 0.83, I2 = 65%, P = 0.006). Each increment of 0.1 g/d of DHA or eicosapentaenoic acid (EPA) intake was associated with an 8% ~ 9.9% (Plinear < 0.0005) lower risk of cognitive decline. Moderate-to-high levels of evidence indicated that elevated levels of plasma EPA (RR: 0.88, I2 = 38.1%) and erythrocyte membrane DHA (RR: 0.94, I2 = 0.4%) were associated with a lower risk of cognitive decline. Dietary intake or long-term supplementation of omega-3 fatty acids may help reduce risk of AD or cognitive decline

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 Apr 7;S2161-8313(23)00283-1. doi: 10.1016/j.advnut.2023.03.014. **Article link**

Significance: Potential benefits and safety of LC ω-3 polyunsaturated fatty acids on cardiometabolic health is

covered in this review which presents current updates and controversies.

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

A Qualitative Look at Perception and Experience of Sodium Reduction Strategies in the Food Industry through Focus Groups and Individual Interviews

Aubrey N. Dunteman, Youngsoo Lee, Soo-Yeun Lee. *Journal of Food Science*.10 April 2023. doi.org/10.1111/1750-3841.16564. **Article link**

Significance: Extensive interviews led researchers to conclude that future efforts to reduce sodium intake should be carried out through multiple avenues.

This paper was supported by **IAFNS Sodium in Food & Health Implications Committee.**

The high incidence of sodium overconsumption in the general population has led sodium reduction in commercial food products to become a topic of importance in the food industry. In order to bridge the gap between sodium reduction understanding in the food industry and academia, focus groups and individual interviews of food industry professionals were conducted. Sodium reduction and influence from external entities such as federal regulations and consumer insight were prominent in the nutritional concerns of food industry professionals. A large variety of sodium reduction strategies were introduced with discussion on the many factors that contribute to their potential for success. Flavor modification methods were most prevalent in the discussion, with particular focus on potassium chloride and incorporating umami taste. Factors that frequently positively contributed to a strategy's success include maintaining functionality and/or important sensory attributes, inexpensive to implement, and being perceived as clean label. Conversely, factors that negatively affect success include adversely impacting flavor, being considered not clean label, and high costs of implementation. Foods important for future sodium reduction varied widely, although those were largely products with high sodium density. Future efforts toward reducing sodium overconsumption and sodium content in the food supply fell into three categories: consumer-focused, industry-focused, and research-focused. Of particular importance for future efforts included greater regulatory pressure and more consumer nutritional education. Findings suggest that future efforts to reduce the incidence of sodium overconsumption should be carried out through multiple avenues rather than focusing on the agency of consumers, the food industry, or research alone.

Modelling Health and Economic Impact of Nutrition Interventions: A Systematic Review

Mariska Dötsch-Klerk, Maaike J Bruins, Patrick Detzel, Janne Martikainen, Reyhan Nergiz-Unal, Annet J C Roodenburg, Ayla Gulden Pekcan. *Eur J Clin Nutr*. 2023 Apr;77(4):413-426. doi: 10.1038/s41430-022-01199-y. **Article link**

Significance: This review evaluated existing models on the health and economic impact of nutrition interventions. It looked at studies of salt and sugar reduction; and increases of Vitamin D, iron, and folate/folic

acid. Methods and study design differences impede cross-study comparisons and interpretation. There is a need to set guidance and standards for future modelling studies to enable better conclusions and projections of the impact of nutritional interventions on health and the economy.

Diet related non-communicable diseases (NCDs), as well as micronutrient deficiencies, are of widespread and growing importance to public health. Authorities are developing programs to improve nutrient intakes via foods. To estimate the potential health and economic impact of these programs there is a wide variety of models. The aim of this review is to evaluate existing models to estimate the health and/or economic impact of nutrition interventions with a focus on reducing salt and sugar intake and increasing vitamin D, iron, and folate/folic acid intake. The protocol of this systematic review has been registered with the International Prospective Register of Systematic Reviews (PROSPERO: CRD42016050873). The final search was conducted on PubMed and Scopus electronic databases and search strings were developed for salt/sodium, sugar, vitamin D, iron, and folic acid intake. Predefined criteria related to scientific quality, applicability, and funding/interest were used to evaluate the publications. In total 122 publications were included for a critical appraisal: 45 for salt/sodium, 61 for sugar, 4 for vitamin D, 9 for folic acid, and 3 for iron. The complexity of modelling the health and economic impact of nutrition interventions is dependent on the purpose and data availability. Although most of the models have the potential to provide projections of future impact, the methodological challenges are considerable. There is a substantial need for more guidance and standardization for future modelling, to compare results of different studies and draw conclusions about the health and economic impact of nutrition interventions.

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, Carla M Prado. *Adv Nutr*. 2023 Apr 7;S2161-8313(23)00284-3. doi: 10.1016/j.advnut.2023.03.015. **Article link**

Significance: A recent review of human studies failed to find a consistent gut microbiome pattern associated with energy metabolism. A cause-and-effect relationship has yet to be established for mechanistic evidence on the impact of the gut microbiome on energy expenditure. More observational and randomized controlled trials are needed for dietary applications.

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 and Bodyweight

Lancet Diabetes & Endocrinology Commission on the Definition and Diagnosis of Clinical Obesity

Francesco Rubino, Rachel L Batterham, Marta Koch, Geltrude Mingrone, Carel W le Roux, I Sadaf Farooqi et al. *The Lancet Diabetes and Endocrinology*. Vol. 11, Issue 4, p226-228, April 2023. doi.org/10.1016/S2213-8587(23)00058-X. **Article Link.**

Significance: This comment by experts from the Lancet Diabetes and Endocrinology Commission outlines current controversies over the idea that obesity is a disease, or alternately, is solely a risk factor for other diseases. Addressing this controversy is critical, given the global prevalence of obesity, and the profound consequences that such classification would have on public health, health policies, clinical practice, and society.

Obesity was first recognized as a disease by the World Health Organization in 1948, then between 2013 and 2022 by several medical societies and countries. However, the notion that obesity is a disease and not merely a risk factor for other illnesses remains highly controversial, both within and beyond medical circles. This debate constitutes far more than arcane semantics, and seriously affects the provision of therapeutic strategies to improve health among people living with obesity.

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Metascience 2023 Conference

May 9, 2023 - May 10, 2023, Washington DC

The scientific community is making a conscious shift towards transparency in science and is seeking prescriptive ideas on how the research process can be improved. The Metascience 2023 Conference will bring together researchers and stakeholders to share ideas to make meaningful change to the practice of research and foster a culture of continuous experimentation and improvement.

Read More.

Food Classification Workshop

May 16 - 17, 2023, Washington, DC

Considerations for formulation and degree of processing in food classification systems that support research.

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Diet-Microbiome Interactions in Older People: Effect on Inflammaging

May 18, 2023, Virtual Event

“Inflammaging” describes the low-grade inflammation that arises from age-related changes to the immune system. Intersecting with age-related inflammation are age-related changes to the gut microbiome. These two systemic changes can modify disease risk.

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IAFNS 2023 Annual Summer Science Symposium

June 13 – June 14, 2023, at the National Press Club, Washington, DC.

A gathering of scientific and regulatory experts to address food and nutrition science, FDA perspectives, artificial intelligence, food packaging innovation, bioactives, food classification systems, science communications and more.

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