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Dietary Patterns

Food Additive Mixtures and Type 2 Diabetes Incidence: Results from the NutriNet-Santé Prospective Cohort

Marie Payen de la Garanderie, Anaïs Hasenbohler, Nicolas Dechamp, Guillaume Javaux, Fabien Szabo de Edelenyi, Cédric Agaësse, Alexandre De Sa, et. al. *PLOS Medicine*, 8 April 2025, doi.org/10.1371/journal.pmed.1004570, Article link

Background: Mixtures of food additives are daily consumed worldwide by billions of people. So far, safety assessments have been performed substance by substance due to lack of data on the effect of multiexposure to combinations of additives. Our objective was to identify most common food additive mixtures and investigate their associations with type 2 diabetes incidence in a large prospective cohort. **Methods and Findings**: Participants (n = 108,643, mean follow-up = 7.7 years (standard deviation (SD) = 4.6), age = 42.5 years (SD = 14.6), 79.2% women) were adults from the French NutriNet-Santé cohort (2009–2023). Dietary intakes were assessed using repeated 24h-dietary records, including industrial food brands. Exposure to food additives was evaluated through multiple food composition databases and laboratory assays. Mixtures were identified through nonnegative matrix factorization (NMF), and associations with type 2 diabetes incidence were assessed using Cox models adjusted for potential socio-demographic, anthropometric, lifestyle and dietary confounders. A total of 1,131 participants were diagnosed with type 2 diabetes. Two out of the five identified food additive mixtures were associated with higher type 2 diabetes incidence: the first mixture included modified starches, pectin, guar gum, carrageenan, polyphosphates, potassium sorbates, curcumin, and xanthan gum (hazard ratio (HR)per an increment of 1SD of the NMF mixture score = 1.08 [1.02, 1.15], p = 0.006), and the other mixture included citric acid, sodium citrates, phosphoric acid, sulphite ammonia caramel, acesulfame-K, aspartame, sucralose, arabic gum, malic acid, carnauba wax, paprika extract, anthocyanins, guar gum, and pectin (HR = 1.13 [1.08,1.18], p < 0.001). No association was detected for the three remaining mixtures: HR = 0.98 [0.91, 1.06], p = 0.67; HR = 1.02 [0.94, 1.10], p = 0.68; and HR = 0.99 [0.92, 1.07], p = 0.78. Several synergistic and antagonist interactions between food additives were detected in exploratory analyses. Residual confounding as well as exposure or outcome misclassifications cannot be entirely ruled out and causality cannot be established based on this single observational study. **Conclusions:** This study revealed positive associations between

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exposure to two widely consumed food additive mixtures and higher type 2 diabetes incidence. Further experimental research is needed to depict underlying mechanisms, including potential synergistic/antagonist effects. These findings suggest that a combination of food additives may be of interest to consider in safety assessments, and they support public health recommendations to limit nonessential additives.

Carbohydrates

A Meta-Analysis: Dietary Carbohydrates Do Not Increase Body Fat or Fasted Insulin and Glucose in Cats

Hannah Godfrey, Jennifer L Ellis, Adronie Verbrugghe. *Jrnl of An. Science*. Vol. 103, 21 April 2025. doi.org/10.1093/jas/skaf071. Article link

Commercial cat foods contain a greater carbohydrate content, such as nitrogen-free extract (NFE), compared to a typical prey species. This has led to postulations that increased carbohydrate intake is causing a rise in obesity and IR in cats. Studies investigating high-carbohydrate diets on insulin and glucose responses show inconsistent results. A meta-analysis using 16 studies was conducted to elucidate the relationship between NFE content and body fat mass (BFM, $n = 9$), fasted insulin ($n = 12$), and fasted glucose concentrations ($n = 14$). Dietary NFE, fat, and protein content (% metabolizable energy), as well as daily energy intake (DEI), body weight, body condition (lean, obese), and study design metrics were considered as fixed effects in univariate and multivariate models using proc mixed in SAS, treating study as a random effect. Model evaluation was conducted using corrected Akaike Information Criteria, concordance correlation coefficient, and the root mean square prediction error. The best-fitting model for BFM was the interaction between NFE content and DEI, predicting BFM to decrease when NFE content increased as a proportion of the DEI ($P < 0.05$). From univariate models, fasted insulin was positively associated with BFM and dietary fat content ($P < 0.05$), whereas an increase in NFE content was associated with a decrease in fasted insulin in a subgroup of studies ($n = 6$) of only lean cats ($P < 0.05$). No significance was observed for models predicting fasted glucose from diet or body composition variables ($P > 0.05$). The results of this meta-analysis indicate that dietary carbohydrates (NFE), included between 2.8% and 57% ME, are not a risk factor for greater BFM, fasted insulin, and glucose concentrations in cats, suggesting that NFE does not pose a risk for feline obesity, IR, or hyperglycemia. However, future studies should consider postprandial responses of insulin and glucose to macronutrient compositions to further investigate the role of dietary carbohydrates on IR in cats, with particular attention to the role of dietary fat, and the role of body condition.

Protein

Protein-Responsive Gut Hormone Tachykinin Directs Food Choice and Impacts Lifespan

Nadja Ahrentløv, Olga Kubrak, Mette Lassen, Alina Malita, Takashi Koyama, Amalie S. Frederiksen, Casper M. Sigvardsen, et. al. *Nat. Metabolism,* 14 April 2025. doi.org/10.1038/s42255-025-01267-0. Article link

Animals select food based on hungers that reflect dynamic macronutrient needs, but the hormonal mechanisms underlying nutrient-specific appetite regulation remain poorly defined. Here, we identify tachykinin (Tk) as a protein-responsive gut hormone in Drosophila and female mice, regulated by conserved environmental and nutrient-sensing mechanisms. Protein intake activates Tk-expressing enteroendocrine cells (EECs), driving the release of gut Tk through mechanisms involving target of rapamycin (TOR) and transient receptor potential A1 (TrpA1). In flies, we delineate a pathway by which gut Tk controls selective appetite and sleep after protein ingestion, mediated by glucagon-like adipokinetic hormone (AKH) signalling to neurons and adipose tissue. This mechanism suppresses protein appetite, promotes sugar hunger and modulates wakefulness to align behaviour with nutritional needs. Inhibiting protein-responsive gut Tk prolongs lifespan through AKH, revealing a role for nutrient-dependent gut hormone signalling in longevity. Our results provide a framework for understanding EEC-derived nutrient-specific satiety signals and the role of gut hormones in regulating food choice, sleep and lifespan.

Food Classification

Fifteen Years of NOVA Food-Processing Classification: 'Friend or Foe' Among Sustainable Diet Indicators? A Scoping Review

Orsolya Tompa, Anna Kiss, Sándor Soós, Zoltán Lakner, Ana Raner, Gyula Kasza, Dávid Szakos. *Nutrition Reviews*, Vol. 83, Issue 4, April 2025, p771–791, doi.org/10.1093/nutrit/nuae207. Article link

It has been 15 years since the introduction of the NOVA food-processing classification. While it was designed to identify ultra-processed foods linked to noncommunicable diseases, the NOVA system has a holistic concept that fits with sustainable nutrition. However, NOVA's connection to other sustainable diet indicators has not been thoroughly explored. The aim was to summarize the research and methodological context of using the NOVA system with other sustainable diet indicators and to investigate NOVA's synergies and discordance with them. A scoping review was conducted based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses—Extension for Scoping Reviews (PRISMA-ScR). Studies published between 2009 and 2023 were collected from the Web of Science, Scopus, and PubMed databases. 1612 studies were initially screened; in the selected studies (n = 77), the NOVA system was applied in addition to other sustainable diet indicator(s). The studies were analyzed within a qualitative data analysis framework. 77 studies were analyzed in which healthiness (n = 66), environmental pressure (n = 9), affordability (n = 11), other processing classifications (n = 6), and other sustainable diet indicators (n = 10) were applied with NOVA. Among them, the identified relationships between the NOVA system and other healthfulness indicators were synergistic in the majority of studies (n = 70/93). For environmental pressure indicators, a mixed picture was observed; the NOVA classification was predominantly synergistic with greenhouse gas emissions (n = 8/13), while it was mostly discordant with fresh water use (n = 8/12). Economic affordability was also found to be discordant with the NOVA classification in the majority of studies (n = 10/16). To complete the NOVA classification with nutrient profiling would be beneficial to identify healthy diets. In the case of the integration of NOVA into sustainable nutrition research, environmental pressure and economic affordability indicators should be controlled to reach optimal trade-offs for more sustainable diets. The application of NOVA is gaining relevance; thus, its methodological adaptation to sustainable nutrition research is necessary.

Premature Mortality Attributable to Ultraprocessed Food Consumption in 8 Countries

Eduardo A.F. Nilson, Felipe Mendes Delpino, Carolina Batis, Renata Bertazzi Levy, Carlos A. Monteiro, Leandro F.M. Rezende, et. al. *Am. Jrnl. Prev. Medicine,* 28 April 2024. DOI: 10.1016/j.amepre.2025.02.018. Article link

Introduction: Ultraprocessed foods are becoming dominant in the global food supply. Prospective cohort studies have consistently found an association between high consumption of ultraprocessed foods and increased risk of several noncommunicable diseases and all-cause mortality. The study aimed to (1) estimate the risk of all-cause mortality for ultraprocessed foods consumption and (2) estimate the attributable epidemiologic burden of ultraprocessed food consumption in 8 select countries. **Methods:** First, a dose-response meta-analysis of observational cohort studies was performed to assess the association between ultraprocessed food consumption and all-cause mortality and estimated the pooled RR for all-cause mortality per each 10% increment in the percentage ultraprocessed food. Then, the population attributable fractions for premature all-cause mortality attributable to the ultraprocessed foods in consumption were estimated in 8 select countries with relatively low (Colombia and Brazil), intermediate (Chile and Mexico), and high (Australia, Canada, United Kingdom, and the U.S.) ultraprocessed food consumption. Analysis was conducted in November 2023–July 2024. **Results:** The meta-analysis showed a linear dose-response association between the ultraprocessed food consumption and all-cause mortality (RR for each 10% increase in percentage ultraprocessed food=1.03; 95% CI=1.02, 1.04). Considering the magnitude of the association between ultraprocessed foods intake and all-cause mortality and the ultraprocessed food dietary share number (percentage ultraprocessed food) in each of the 8 selected countries, estimations varied from 4% (Colombia) to 14% (United Kingdom and U.S.) of premature deaths attributable to ultraprocessed food intake. **Conclusions:** The findings support that ultraprocessed food intake contributes significantly to the overall burden of disease in many countries, and its reduction should be included in national dietary guideline recommendations and addressed in public policies.

Low- and No-Calorie Sweeteners

Rediscovering Sweetness: The Evolution and Impact of Non-Nutritive and Natural Sweeteners

Yash Patel, Osman Mohamed Elfadil, Suhena Patel, Omar M. Ghanem, Ryan T. Hurt, Manpreet S. Mundi. *Current Nutrit. Reports*, 02 April 2025, Vol. 14, Article #54. doi.org/10.1007/s13668-025-00646-z. Article link

Purpose of the Review: The escalating incidence of obesity and metabolic syndromes has catalyzed a critical evaluation of dietary sugars, leading to an increased interest in non-nutritive and natural sweeteners as viable alternatives. This manuscript reviews the historical developments, safety profiles, and health-related consequences of these sweeteners, tracing the evolution from early discoveries such as saccharin and cyclamate to contemporary compounds like aspartame, sucralose, and plant-derived sweeteners. **Recent Findings:** We explore the physiological mechanisms underpinning sweet taste perception, including the roles of T1R and T2R receptors, and the neurochemical pathways involving dopamine in mediating the rewarding

effects of sugar consumption. The review underscores the adverse health impacts associated with excessive intake of added sugars, which correlate positively with conditions such as obesity, type 2 diabetes, and cardiovascular diseases. Attention is given to the contrasting profiles of non-nutritive sweeteners and natural sweetener alternatives, with an emphasis on emerging concerns regarding the safety and long-term ramifications of synthetic sweeteners. **Summary:** The regulatory context surrounding the approval and utilization of sweeteners varies significantly across different jurisdictions, warranting careful consideration. As consumer inclination shifts towards healthier dietary choices, a nuanced understanding of the implications of sweetener selection on public health is imperative.

Cognitive Health

Brain Activity During a Cognitive Task after Consuming Food of Varying Palatability

Hongjia Li, Siyao Li, Kenji Matsuo, Tsuyoshi Okamoto. *Fron. Psychology*, 28 April 2025. Vol. 16. doi.org/10.3389/fpsyg.2025.1522812. Article link

It has been reported that various physiological and psychological changes occur after consuming delicious food. Additionally, research on task performance efficiency following the consumption of delicious food has garnered significant attention. In particular, studies on physiological states have been actively conducted in recent years, with an increasing number of studies utilizing brain activity measurements. Therefore, in this study, we aimed to investigate the physiological changes that occur after consuming delicious food by administering a cognitive task, the Stroop task, and measuring brain activity during the task. In this study, two experiments were conducted to better understand the effects of consuming delicious food. Before starting the two experiments, we evaluated the taste of fried rice in a preliminary experiment and selected three types of them (delicious, slightly delicious, and normal) for the main experiment. In Experiment 1, 20 healthy students (19–26 years old, 11 females) were divided into two groups: 10 students in group 1 ate delicious fried rice and 10 students in group 2 ate normal fried rice. One experimental block included recording the EEG, performing the Stroop task, eating the given sample, and answering the questionnaire. Results of data analysis indicated that group 1 was significantly shorter (high work efficiency) than group 2 in terms of task work time. Concerning brain activity, group 1 showed lower theta and alpha amplitudes in the frontal regions (high arousal), and alpha band activity was lower in the left frontal region than in the right region (high approach motivation). In Experiment 2, 28 healthy students were asked to eat delicious fried rice and slightly delicious fried rice on different days. The daily experimental flow was set up as in Experiment 1. Results of data analysis showed that deliciousness and EEG were negatively correlated at theta and alpha band. This study provides novel evidence that eating delicious food increases work efficiency, arousal, and motivation for the task and decreases theta and alpha activities in limited brain regions. The observed neural profiles may enhance attentional states in high-demand occupational settings, while providing preliminary insights into neurophysiological mechanisms that might underlie food-related motivational processes.

Lipids

Consuming Pecans as a Snack Improves Lipids/Lipoproteins and Diet Quality Compared with Usual Diet in Adults at Increased Risk of Cardiometabolic Diseases: A Randomized Controlled Trial

Tricia L Hart, Penny M Kris-Etherton, Kristina S Petersen. *AJCN*, Vol. 121, Issue 4, April 2025, p769-778. doi.org/10.1016/j.ajcnut.2025.01.024. Article link

Background: The vascular and cardiometabolic effects of pecans are relatively understudied. **Objectives:** The aim was to examine how substitution of usual snack foods with 57 g/d of pecans affects vascular health, risk factors for cardiometabolic diseases, and diet quality, compared with continuing usual intake in individuals at risk of cardiometabolic diseases. **Methods:** A 12-wk single-blinded, parallel, randomized controlled trial was conducted. Adults with ≥1 criterion for metabolic syndrome who were free from cardiovascular disease and type 2 diabetes were included. Participants were provided with 57 g/d of pecans and instructed to replace the snacks usually consumed with the provided pecans. The control group was instructed to continue consuming their usual diet. Flow-mediated dilation (FMD),primary outcome, along with blood pressure, carotid-femoral pulse wave velocity (cf-PWV), lipids/lipoproteins, and glycemic control were measured at baseline and following the intervention. Participants completed 3 24-h recalls at 3 time points (baseline, week 6, and week 12) during the study (9 recalls in total). The Healthy Eating Index-2020 (HEI-2020) was calculated to assess diet quality. **Results:** In total, 138 participants (mean ± SD; 46 ± 13 y, 29.8 ± 3.7 kg/m2) were randomly assigned (69 per group). No between-group differences in FMD,

cf-PWV, or blood pressure were observed. Compared with the usual diet group, pecan intake reduced total cholesterol (−8.1 mg/dL; 95% confidence interval [CI]: −14.5, −1.7), LDL cholesterol (−7.2 mg/dL; 95% CI −12.3, −2.1), non-HDL-cholesterol (−9.5 mg/dL; 95% CI −15.3, −3.7), and triglycerides concentrations (−16.4 mg/dL; 95% CI −30.0, −2.9). Weight tended to increase in the pecan group compared with the usual diet group (0.7 kg; 95% CI −0.1, 1.4). The HEI-2020 increased by 9.4 points (95% CI 5.0, 13.7) in the pecan group compared with the usual diet group. **Conclusions:** Replacing usual snacks with 57 g/d of pecans for 12-wk improves lipids/lipoproteins and diet quality but does not affect vascular health in adults at risk of cardiometabolic disease.

Gut Health

Best Practices and Considerations for Conducting Research on Diet-Gut Microbiome Interactions and their Impact on Health in Adult Populations: An Umbrella Review

This research was supported by IAFNS Nutrition for Gut Health Committee

Diacova T, Cifelli CJ, Davis CD, Holscher HD, Kable ME, Lampe JW, Latulippe ME, Swanson KS, Karl JP. *Adv. in Nutrition*. Vol. 16, Issue 5, 25 April 2025. doi.org/10.1016/j.advnut.2025.100419. Article link

Diet modulates gut microbiome composition and function. However, determining causal links between diet–gut microbiome interactions and human health is complicated by inconsistencies in the evidence, arising partially from variability in research methods and reporting. Widespread adoption of standardized best practices would advance the field but require those practices to be identified, consolidated, and discussed. This umbrella review aimed to identify recommended best practices, define existing gaps, and collate considerations for conducting research on diet–gut microbiome interactions and their impact on human health outcomes. Reviews meeting inclusion criteria and published after 2013 were identified using a systematic search. Recommendations, considerations, and gaps relating to the best practices associated with study design, participant selection, dietary intervention/assessment, biological sample collection, and data analysis and reporting were extracted and consolidated. Eight narrative reviews were included. Several general points of agreement were identified, and a recurring theme was that best practices are dependent upon the research aims, outcomes, and feasibility. Multiple gaps were also identified. Some, such as suboptimal diet assessment methods and lack of validated dietary intake biomarkers, are particularly relevant to nutrition science. Others, including defining a “healthy” gut microbiome and the absence of standardized sample and data collection/analysis protocols, were relevant specifically to gut microbiome research. Gaps specific to diet–gut microbiome research include the underrepresentation of microbiome-modulating dietary components in food databases, lack of knowledge regarding interventions eliciting changes in the gut microbiome to confer health benefits, lack of in situ measurement methods, and the need to further develop and refine statistical approaches for integrating diet and gut microbiome data. Future research and cross-disciplinary exchange will address these gaps and evolve the best practices. In the interim, the best practices and considerations discussed herein, and the publications from which that information was extracted provide a roadmap for conducting diet–gut microbiome research.

Sodium

Monitoring Sodium Content in Packaged Foods Sold in the Americas and Compliance with the Updated Regional Sodium Reduction Targets

Yahan Yang, Nadia Flexner, Maria Victoria Tiscornia, Leila Guarnieri, Adriana Blanco-Metzler, Hilda Núñez-Rivas, Marlene Roselló-Araya, et. al. *PLOS One*, 3 April 2025. doi.org/10.1371/journal.pone.0304922. Article link

Background: Sodium reduction is a cost-effective measure to prevent noncommunicable diseases. The World Health Organization (WHO) established a target of a 30% relative reduction in mean population intake of sodium by 2025. The Pan American Health Organization (PAHO) published sodium reduction targets (SRTs) for packaged foods in 2015, expanding and updating the targets in 2021 to help Member States with its efforts in reducing population sodium intake. **Objective:** This study examined the current sodium levels in packaged foods among five countries in the Americas and monitored cross-sectional and longitudinal compliance with the sodium targets from 2015 to 2022. **Methods:** Food labels were systematically collected from the main supermarkets in five countries in the Americas region in 2022. Sodium levels per 100g and per kcal for collected food labels in 16 PAHO categories and 75 subcategories were analyzed and compared against the updated SRTs. Further analysis of three countries that have longitudinal data for 2015–2016, 2017–2018 and 2022 was conducted to compare sodium per 100 g against the 2015 SRTs. **Results:** A total of 25,569 food items were analyzed. Overall, ‘processed meat and poultry’ had the highest sodium levels, although there were large variations within categories. 47% and 45% of products met the sodium per 100g and per kcal 2022 SRTs, respectively. Peru had the highest compliance, whereas Panama had the lowest for both targets. Among Argentina, Costa Rica and Peru, the proportion of foods meeting the 2015 PAHO lower targets were 48, 53 and 61% for 2015–2016, 2017–2018 and 2022, respectively ($p < 0.001$). **Conclusions:** This study showed that around half of the examined foods met their respective SRTs and

there have been small improvements in compliance over time. Further efforts are required to reach the WHO's global sodium reduction goal by 2025, such as implementation of mandatory SRTs and front-of-pack labelling regulations.

Emerging Science Areas

Emerging Areas: Mitigating Bias in Nutrition Research Design

Wash-In and Washout Effects: Mitigating Bias in Short-Term Dietary and Other Trials

David S Ludwig, Walter C Willett, Mary E Putt. *BMJ*, 22 April 2025;389. doi.org/10.1136/bmj-2024-082963. Article link

Short term trials with surrogate measures instead of hard outcomes are often used to study chronic diseases. The effects of an intervention may, however, take time to develop and persist after discontinuation, producing wash-in and washout effects that threaten trial validity. This problem, especially involving carryover effects in crossover trials, is well recognized in the pharmacology and statistics literature but commonly disregarded in some areas of non-pharmaceutical research. Dietary trials, including feeding studies, are highly susceptible to bias because physiological adaptation to a major change in nutrients may take several weeks or longer. This article describes the nature and extent of this bias in nutrition research, as an important and illustrative case; considers implications for various other interventions; and proposes measures to strengthen causal inference.

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