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Dietary Patterns

Traditional Atlantic Diet and Its Effect on Health and the Environment: A Secondary Analysis of the GALIAT Cluster Randomized Clinical Trial

Cristina Cambeses-Franco, Francisco Gude, Alfonso J. Benítez-Estévez, Sara González-García, Rosaura Leis, Juan Sánchez-Castro, María Teresa Moreira, et. al. *JAMA Netw Open.* 2024;7(2):e2354473.
doi:10.1001/jamanetworkopen.2023.54473. [Article link](#)

Importance: The universal call to action for healthier and more sustainable dietary choices is the framework of the United Nations's Sustainable Development Goals. The Atlantic diet, originating from the northwest of the Iberian Peninsula, represents an example of a traditional diet that aligns with these principles. **Objective:** To explore a 6-month intervention based on the Atlantic diet's effects on metabolic and environmental health, assessing metabolic syndrome (MetS) incidence and the carbon footprint. **Design, Setting and Participants:** The Galician Atlantic Diet study was a 6-month randomized clinical trial designed to assess the effects of this regional traditional diet on families' eating habits. The study was conducted from March 3, 2014, to May 29, 2015, at a local primary health care center in the rural town of A Estrada in northwestern Spain and involved a multisectoral collaboration. Families were randomly selected from National Health System records and randomized 1:1 to an intervention or control group. This secondary analysis of the trial findings was performed between March 24, 2021, and November 7, 2023. **Interventions:** Over 6 months, families in the intervention group received educational sessions, cooking classes, written supporting material, and foods characteristic of the Atlantic diet, whereas those randomized to the control group continued with their habitual lifestyle. **Main Outcomes and Measures:** The main outcomes were MetS incidence, defined per National Cholesterol Education Program Adult Treatment Panel III guidelines, and carbon footprint



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emissions as an environmental metric using life cycle assessment with daily dietary intake as the functional unit. **Results:** Initially, 250 families were randomized (574 participants; mean [SD] age, 46.8 [15.7] years; 231 males [40.2%] and 343 females [59.8%]). The intervention group included 126 families (287 participants) and the control group, 124 families (287 participants). Ultimately, 231 families completed the trial. The intervention significantly reduced the risk of incident cases of MetS (rate ratio, 0.32; 95% CI, 0.13-0.79) and had fewer MetS components (proportional odds ratio, 0.58; 95% CI, 0.42-0.82) compared with the control condition. The intervention group did not have a significantly reduced environmental impact in terms of carbon footprint emissions compared with the control group (-0.17 [95% CI, -0.46 to 0.12] kg CO₂ equivalents/person/d). **Conclusions and Relevance:** These findings provide important evidence that a family-focused dietary intervention based on a traditional diet can reduce the risk of incident MetS. Further research is needed to understand the underlying mechanisms and determine the generalizability to other populations, taking into account regional cultural and dietary variations.

Carbohydrates

Impact of Dietary Carbohydrate, Fat, or Protein Restriction on the Human Gut Microbiome: A Systematic Review

Marjolein P Schoonakker, Petra G van Peet, Elske L van den Burg, Mattijs E Numans, Quinten R Ducarmon, Hanno Pijl, Maria Wiese. *Nutr Res Rev.* 2024 Apr 11:1-47. doi: 10.1017/S0954422424000131. [Article link](#)

Restriction of dietary carbohydrates, fat, and/or protein is often used to reduce body weight and/or treat (metabolic) diseases. Since diet is a key modulator of the human gut microbiome, which plays an important role in health and disease, this review aims to provide an overview of current knowledge of the effects of macronutrient-restricted diets on gut microbial composition and metabolites. A structured search strategy was performed in several databases. After screening for in- and exclusion criteria, 36 articles could be included. Data are included in the results only when supported by at least three independent studies to enhance the reliability of our conclusions. Low-carbohydrate (<30 energy%) diets tended to induce a decrease in the relative abundance of several health-promoting bacteria, such as *Bifidobacterium*, as well as a reduction in short-chain fatty acid (SCFA) levels in faeces. In contrast, low-fat diets (<30 energy%) increased alpha diversity, faecal SCFA levels, and abundance of some beneficial bacteria, including *F. prausnitzii*. There was insufficient data to draw conclusions concerning the effects of low-protein (<10 energy%) diets on gut microbiota. Although the data of included studies unveils possible benefits of low-fat and potential drawbacks of low-carbohydrate diets for human gut microbiota, the diversity in study designs made it difficult to draw firm conclusions. Using a more uniform methodology in design, sample processing and sharing raw sequence data could foster our understanding of the effects of macronutrient restriction on gut microbiota composition and metabolic dynamics relevant to health.

Protein

Daily Dietary Protein Distribution Does Not Influence Changes in Body Composition During Weight Loss in Women of Reproductive Years with Overweight or Obesity: A Randomized Controlled Trial

Angela De Leon, James N Roemmich, Shanon L Casperson. *J Nutr.* 2024 Apr;154(4):1347-1355. doi: 10.1016/j.tjnut.2024.02.009. [Article link](#)

Background: Preservation of fat-free mass (FFM) during intentional weight loss is challenging yet important to maintain a resting metabolic rate. A balanced protein distribution of 25-30 g per meal improves 24-h muscle protein synthesis, which may promote FFM maintenance and greater reductions in fat mass (FM) during weight loss in women. **Objectives:** We aimed to determine whether the daily dietary protein distribution pattern during energy restriction influences changes in body composition in women of reproductive age. We hypothesized that evenly distributing protein across meals compared with the

usual intake pattern of consuming most of the protein at the dinner meal would be superior in preserving FFM while reducing FM during weight loss. **Methods:** Healthy women (n = 43) aged 20-44 y with a BMI of 28-45 kg/m² completed a randomized parallel feeding study testing 2 patterns of daily protein intake (even distribution across all meals compared with a skewed distribution with most protein consumed at the evening meal). Participants completed an 8-wk controlled 20% energy restriction (all foods provided), followed by an 8-wk self-choice phase in which participants were asked to maintain a similar diet and dietary pattern when purchasing and consuming their own foods. Body composition was measured at baseline, week 8, and week 16. Data were analyzed using mixed models. Statistical significance was set at P < 0.05. Data are presented as differences in least squares means ± SE. **Results:** No significant main effects of group or group-by-time interactions were observed. All measures exhibited the main effect of time (P < 0.001). Overall, body weight, FFM, FM, and body fat percentage decreased 5.6 ± 0.4, 1.0 ± 0.2, 4.6 ± 0.4 kg, and 2.3 ± 0.2%, respectively, during this 16-wk study. **Conclusion:** Daily dietary protein distribution at a fixed protein level does not appear to influence changes in body composition during weight loss in women of reproductive age.

Low- and No-Calorie Sweeteners

Comparison of a Daily Steviol Glycoside Beverage compared with a Sucrose Beverage for Four Weeks on Gut Microbiome in Healthy Adults

David Kwok, Corey Scott, Noah Strom, Fei Au-Yeung, Caanan Lam, Anirikh Chakrabarti, Thomas Hutton, Thomas Ms Wolever. *J Nutr.* 2024 Apr;154(4):1298-1308. doi: 10.1016/j.tjnut.2024.01.032. [Article link](#)

Background: Recent studies suggest that some nonnutritive sweeteners (NNS) have deleterious effects on the human gut microbiome (HGM). The effect of steviol glycosides on the HGM has not been well studied. **Objective:** We aimed to evaluate the effects of stevia- compared with sucrose-sweetened beverages on the HGM and fecal short-chain fatty acid (SCFA) profiles. **Methods:** Using a randomized, double-blinded, parallel-design study, n = 59 healthy adults [female/male, n = 36/23, aged 31±9 y, body mass index (BMI): 22.6±1.7 kg/m²] consumed 16 oz of a beverage containing either 25% of the acceptable daily intake (ADI) of stevia or 30 g of sucrose daily for 4 weeks followed by a 4-week washout. At weeks 0 (baseline), 4, and 8, the HGM was characterized via shotgun sequencing, fecal SCFA concentrations were measured using ultra-high performance liquid chromatography-tandem mass spectrometry and anthropometric measurements, fasting serum glucose, insulin and lipids, blood pressure, pulse, and 3-d diet records were obtained. **Results:** There were no significant differences in the HGM or fecal SCFA between the stevia and sucrose groups at baseline (P > 0.05). At week 4 (after intervention), there were no significant differences in the HGM at the phylum, family, genus, or species level between the stevia and sucrose groups and no significant differences in fecal SCFA. At week 4, BMI had increased by 0.3 kg/m² (P = 0.013) in sucrose compared with stevia, but all other anthropometric and cardiometabolic measures and food intake did not differ significantly (P > 0.05). At week 8 (after washout), there were no significant differences in the HGM, fecal SCFA, or any anthropometric or cardiometabolic measure between the stevia and sucrose groups (P > 0.05). **Conclusions:** Daily consumption of a beverage sweetened with 25% of the ADI of stevia for 4 weeks had no significant effects on the HGM, fecal SCFA, or fasting cardiometabolic measures, compared with daily consumption of a beverage sweetened with 30 g of sucrose.

Cognitive Health

Systematic Evaluation and Meta-Analysis of the Effects of Major Dietary Patterns on Cognitive Function in Healthy Adults

HanQing Guo, Qi Tian, XueMei Qin, Qing Luo, XiuMei Gong, Qinghan Gao. *Nutr Neurosci.* 2024 Apr 30:1-17. doi: 10.1080/1028415X.2024.2342164. [Article link](#)

Purpose: Evidence shows diet promotes brain health. Combining foods and nutrients may have beneficial synergistic effects, but the effects on cognitive function interventions are inconsistent. So, a meta-analysis of RCTs was conducted to examine the specific effects on cognitive function. **Methods:** We searched four databases from creation to April 2023. Eligible randomized controlled trials were identified. A random-effects meta-analysis was used to combine standardized mean differences (SMD) (95% confidence intervals [CI]), and homogeneity tests for a variance were calculated. **Results:** A total of 19 studies involving 12,119 participants were included in this systematic review. The dietary intervention group had a positive effect on overall cognitive functioning compared to the control group (SMD = 0.14, 95% CI [0.08, 0.20], P < 0.00001). The dietary intervention improved executive function, processing speed and language skills (SMD = -0.10, 95% CI [-0.17,-0.04], P = 0.002, I² = 0%),

(SMD = -0.16, 95% CI [-0.23,-0.09], P < 0.00001, I² = 0%), (SMD = 0.10, 95% CI [0.01, 0.20], P = 0.03, I² = 0%). The dietary intervention had no effect on delayed memory and spatial ability (SMD = 0.04, 95% CI [-0.02, 0.09], P = 0.20, I² = 0%), (SMD = 0.08, 95% CI [-0.01, 0.16], P = 0.08, I² = 0%). **Conclusion:** The Mediterranean diet, a diet with restricted caloric intake, a diet incorporating aerobic exercise, a low-carbohydrate diet, and a healthy lifestyle diet (increased intake of fruits and vegetables, and weight and blood pressure management) appear to have positive effects on cognitively healthy adults, as reflected in their overall cognitive, processing speed, executive, and language functions.

Internet Marketing of Dietary Supplements for Improving Memory and Cognitive Abilities

Jelena Banović Fuentes, Maja Amidžić, Jovica Banović, Ljilja Torović March 2024. *PharmaNutrition* 27(6):100379. DOI:10.1016/j.phanu.2024.100379. [Article link](#)

Background: The use of the internet for researching and purchasing dietary supplements (DS) is rapidly increasing, especially after the COVID-19 pandemic influenced people to seek information related to health problems online. However, internet marketing is not subject to strict controls and can potentially mislead consumers. **Methods:** The study assessed information obtained through internet search on websites for online sale of 75 DS intended for cognitive improvement and prevention of cognitive degeneration. **Results:** The analysis revealed a wide array of active substances (126), most often three or more being present in one DS (61.3%). Data on auxiliary substances were present in 74.3% of DS, with 92.7% of DS specifying usage instructions. However, information on references (10.7%), mechanism of action (50.7%), pharmacological (9.3%) and toxicological (5.3%) effects, as well as presence or absence of allergens (21.3%), were considerably less represented. Warnings were not provided in 41.3% of DS, while 77.3% had some information on potential adverse/side effects. Claims, as the primary drivers of supplement promotion, were present in all assessed DS, but in case of USA products were not always followed by FDA disclaimer (8.2%), while in case of EU products, as many as 90.9% had at least one unapproved claim. **Conclusion:** Stricter regulations for advertising and selling DS are necessary, along with harmonization among countries, as the internet is a global space that transcends national borders and laws. There is a necessity to enhance inspection oversight and public education on recognizing verified information on the internet.

Lipids

Short-Chain Fatty Acids: Linking Diet, the Microbiome and Immunity

Elizabeth R Mann, Ying Ka Lam, Holm H Uhlig. *Nat Rev Immunol.* 2024 Apr 2. doi: 10.1038/s41577-024-01014-8. [Article link](#)

The short-chain fatty acids (SCFAs) butyrate, propionate and acetate are microbial metabolites and their availability in the gut and other organs is determined by environmental factors, such as diet and use of antibiotics, that shape the diversity and metabolism of the microbiota. SCFAs regulate epithelial barrier function as well as mucosal and systemic immunity via evolutionary conserved processes that involve G protein-coupled receptor signalling or histone deacetylase activity. Indicatively, the anti-inflammatory role of butyrate is mediated through direct effects on the differentiation of intestinal epithelial cells, phagocytes, B cells and plasma cells, and regulatory and effector T cells. Intestinally derived SCFAs also directly and indirectly affect immunity at extra-intestinal sites, such as the liver, the lungs, the reproductive tract and the brain, and have been implicated in a range of disorders, including infections, intestinal inflammation, autoimmunity, food allergies, asthma and responses to cancer therapies. An ecological understanding of microbial communities and their interrelated metabolic states, as well as the engineering of butyrogenic bacteria may support SCFA-focused interventions for the prevention and treatment of immune-mediated diseases.

Sodium

Long-Term Effect of Salt Substitution for Cardiovascular Outcomes: A Systematic Review and Meta-Analysis

Hannah Greenwood, , Katelyn Barnes. *Annals of Internal Medicine.* 9 April 2024. doi.org/10.7326/M23-2626. [Article link](#)

Background: Salt substitution is a simple yet increasingly promising strategy to improve cardiovascular outcomes. **Purpose:** To evaluate the long-term effects of salt substitution on cardiovascular outcomes. **Data Sources:** PubMed, EMBASE, Cochrane CENTRAL, and CINAHL searched from inception to 23 August 2023. Trial registries, citation analysis, and hand-search were also done. **Study Selection:** Randomized controlled trials (RCTs) comparing provision of or advice to use a salt substitute with no intervention or use of regular salt among adults for 6 months or longer in total study duration.

Data Extraction: Two authors independently screened articles, extracted data, and assessed risk of bias. Primary outcomes include mortality, major cardiovascular events (MACE), and adverse events at 6 months or greater. Secondary and post hoc outcomes include blood pressure, cause-specific mortality, and urinary excretion at 6 months or greater. Random-effects meta-analyses were done and certainty of effect estimates were assessed using GRADE (Grading of Recommendations Assessment, Development and Evaluation). **Data Synthesis:** Of the 16 included RCTs, 8 reported on primary outcomes. Most ($n = 7$ of 8) were done in China or Taiwan, 3 were done in residential facilities, and 7 included populations of older age (average 62 years) and/or with higher-than-average cardiovascular risk. In this population, salt substitute may reduce risk for all-cause mortality (6 RCTs; 27 710 participants; rate ratio [RR], 0.88 [95% CI, 0.82 to 0.93]; low certainty) and cardiovascular mortality (4 RCTs; 25 050 participants; RR, 0.83 [CI, 0.73 to 0.95]; low certainty). Salt substitute may result in a slight reduction in MACE (3 RCTs; 23 215 participants; RR, 0.85 [CI, 0.71 to 1.00]; very low certainty), with very low-certainty evidence of serious adverse events (6 RCTs; 27 995 participants; risk ratio, 1.04 [CI, 0.87 to 1.25]). **Limitations:** The evidence base is dominated by a single, large RCT. Most RCTs were from China or Taiwan and involved participants with higher-than-average cardiovascular risk; therefore, generalizability to other populations is very limited. **Conclusion:** Salt substitution may reduce all-cause or cardiovascular mortality, but the evidence for reducing cardiovascular events and for not increasing serious adverse events is uncertain, particularly for a Western population. The certainty of evidence is higher among populations at higher cardiovascular risk and/or following a Chinese diet.

Gut Health

Variability and Bias in Microbiome Metagenomic Sequencing: An Interlaboratory Study Comparing Experimental Protocols

Samuel P. Forry, Stephanie L. Servetas, Jason G. Kralj, Keng Soh, Michalis Hadjithomas, Raul Cano, Martha Carlin, et. al. *Nature: Scientific Reports*. 29 April. 9785 (2024). doi.org/10.1038/s41598-024-57981-4. [Article link](#)

Several studies have documented the significant impact of methodological choices in microbiome analyses. The myriad of methodological options available complicate the replication of results and generally limit the comparability of findings between independent studies that use differing techniques and measurement pipelines. Here we describe the Mosaic Standards Challenge (MSC), an international interlaboratory study designed to assess the impact of methodological variables on the results. The MSC did not prescribe methods but rather asked participating labs to analyze 7 shared reference samples (5 × human stool samples and 2 × mock communities) using their standard laboratory methods. To capture the array of methodological variables, each participating lab completed a metadata reporting sheet that included 100 different questions regarding the details of their protocol. The goal of this study was to survey the methodological landscape for microbiome metagenomic sequencing (MGS) analyses and the impact of methodological decisions on metagenomic sequencing results. A total of 44 labs participated in the MSC by submitting results (16S or WGS) along with accompanying metadata; thirty 16S rRNA gene amplicon datasets and 14 WGS datasets were collected. The inclusion of two types of reference materials (human stool and mock communities) enabled analysis of both MGS measurement variability between different protocols using the biologically-relevant stool samples, and MGS bias with respect to ground truth values using the DNA mixtures. Owing to the compositional nature of MGS measurements, analyses were conducted on the ratio of Firmicutes: Bacteroidetes allowing us to directly apply common statistical methods. The resulting analysis demonstrated that protocol choices have significant effects, including both bias of the MGS measurement associated with particular methodological choices, as well as effects on measurement robustness as observed through the spread of results between labs making similar methodological choices. In the analysis of the DNA mock communities, MGS measurement bias was observed even when there was general consensus among the participating laboratories. This study was the result of a collaborative effort that included academic, commercial, and government labs. In addition to highlighting the impact of different methodological decisions on MGS result comparability, this work also provides insights for consideration in future microbiome measurement study design.

Next-Generation Probiotics: The Upcoming Biotherapeutics

Omnia Momtaz Al-Fakhrany. *Mol Biol Rep*. 2024 Apr 15;51(1):505. doi: 10.1007/s11033-024-09398-5. [Article link](#)

Recent and continuing advances in gut microbiome research have pointed out the role of the gut microbiota as an unexplored source of potentially beneficial probiotic microbes. Along the lines of these advances, both public awareness and acceptance of probiotics are increasing. That's why; academic and industrial research is dedicated to identifying and investigating new microbial strains for the development of next-generation probiotics (NGPs). At this time, there is a growing interest in NGPs

as biotherapeutics that alter the gut microbiome and affect various diseases development. In this work, we have focused on some emergent and promising NGPs, specifically *Eubacterium hallii*, *Faecalibacterium prausnitzii*, *Roseburia spp.*, *Akkermansia muciniphila*, and *Bacteroides fragilis*, as their presence in the gut can have an impact on the development of various diseases. Emerging studies point out the beneficial roles of these NGPs and open up novel promising therapeutic options. Interestingly, these NGPs were found to enhance gastrointestinal immunity, enhance immunotherapy efficacy in cancer patients, retain the intestinal barrier integrity, generate valuable metabolites, especially short-chain fatty acids, and decrease complications of chemotherapy and radiotherapy. Although many of these NGPs are considered promising for the prevention and treatment of several chronic diseases, research on humans is still lacking. Therefore, approval of these microbes from regulatory agencies is rare. Besides, some issues limit their wide use in the market, such as suitable methods for the culture and storage of these oxygen-sensitive microbes. The present review goes over the main points related to NGPs and gives a viewpoint on the key issues that still hinder their wide application. Furthermore, we have focused on the advancement in NGPs and human healthiness investigations by clarifying the limitations of traditional probiotic microorganisms, discussing the characteristics of emerging NGPs and defining their role in the management of certain ailments. Future research should emphasize the isolation, mechanisms of action of these probiotics, safety, and clinical efficacy in humans.

Emerging Science

Emerging Areas: UPF and IBS risk

Ultra-Processed Food Consumption and Long-Term Risk of Irritable Bowel Syndrome: A Large-Scale Prospective Cohort Study

Shanshan Wu, Zhirong Yang, Si Liu, Qian Zhang, Shutian Zhang, Shengtao Zhu. *CJH*. March 21, 2024. DOI:<https://doi.org/10.1016/j.cgh.2024.01.040>. [Article link](#)

Background & Aims: The considerable disease burden of irritable bowel syndrome (IBS) has coincided with the increase of ultraprocessed food (UPF) consumption over the past few decades. However, epidemiologic evidence for an association is lacking. We aimed to examine the long-term risk of IBS associated with UPF consumption in a large-scale prospective cohort. **Methods:** Participants who completed 24-hour dietary recalls during 2009 to 2012 from the UK Biobank, and free of IBS, celiac disease, inflammatory bowel disease, and any cancer at baseline, were included (N = 178,711; 53.1% female). UPF consumption was defined according to the NOVA food classification system, expressed as a percentage of UPF content in the total diet intake (as grams per day). The primary outcome was incident IBS. A Cox proportional hazard model was performed to estimate associated risk. **Results:** The mean UPF consumption was 21.0% (SD, 11.0%) of the total diet. During a median of 11.3 years of follow-up, 2690 incident IBS cases were identified. An 8% higher risk of IBS (hazard ratio, 1.08; 95% CI, 1.04–1.12) was associated with every 10% increment of UPF consumption. Compared with the lowest quartile of UPF consumption, the highest quartile was associated with a significantly increased risk of incident IBS (hazard ratio, 1.19; 95% CI, 1.07–1.33; P_{trend} < .001). Subgroup analyses by age, sex, body mass index, smoking, and alcohol drinking status also showed similar results, except for the never/previous drinking subgroup. Further sensitivity analyses confirmed the positive association with a higher UPF consumption. **Conclusions:** Our findings provide evidence that a higher UPF consumption is associated with an increased risk of incident IBS, with a significant dose-response relationship.

Emerging Area: Potential Health Protective Properties of Marine Algae

The Ocean's Pharmacy: Health Discoveries in Marine Algae

Mélanie Silva, Dorit Avni, João Varela, Luísa Barreira. *Molecules*. 2024 Apr 22;29(8):1900. doi:10.3390/molecules29081900. [Article link](#)

Non-communicable diseases (NCDs) represent a global health challenge, constituting a major cause of mortality and disease burden in the 21st century. Addressing the prevention and management of NCDs is crucial for improving global public health, emphasizing the need for comprehensive strategies, early interventions, and innovative therapeutic approaches to mitigate their far-reaching consequences. Marine organisms, mainly algae, produce diverse marine natural products with significant therapeutic potential. Harnessing the largely untapped potential of algae could revolutionize drug development and contribute to combating NCDs, marking a crucial step toward natural and targeted therapeutic approaches. This review examines

bioactive extracts, compounds, and commercial products derived from macro- and microalgae, exploring their protective properties against oxidative stress, inflammation, cardiovascular, gastrointestinal, metabolic diseases, and cancer across *in vitro*, cell-based, *in vivo*, and clinical studies. Most research focuses on macroalgae, demonstrating antioxidant, anti-inflammatory, cardioprotective, gut health modulation, metabolic health promotion, and anti-cancer effects. Microalgae products also exhibit anti-inflammatory, cardioprotective, and anti-cancer properties. Although studies mainly investigated extracts and fractions, isolated compounds from algae have also been explored. Notably, polysaccharides, phlorotannins, carotenoids, and terpenes emerge as prominent compounds, collectively representing 42.4% of the investigated compounds.

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