

July 2022

Nutrition Science Briefs



Dietary Patterns

Biomarkers of Dietary Patterns: A Systematic Review of Randomized Controlled Trials

Shuang Liang, Reeja F Nasir, Kim S Bell-Anderson, Clémence A Toniutti, Fiona M O'Leary, Michael R Skilton. *Nutr Rev.* 2022 Jul 7;80(8):1856-1895. doi: 10.1093/nutrit/nuac009. [Article link](#)

Significance: A systematic review of RCT found no consistent biomarkers or biomarker profiles that can identify specific dietary patterns, calling for the need for future research to validate novel biomarkers or biomarker panels that can be applied to identify pattern characteristics and compliance.



Context: Most methods for assessing dietary intake have considerable measurement error. Dietary biomarkers are objective tools for dietary assessment. Dietary biomarkers of dietary patterns have not been well described, despite modern dietary guidelines endorsing dietary patterns. **Objective:** This systematic review sought to describe the dietary biomarkers commonly used to assess dietary patterns, and the novel biomarkers of dietary patterns identified by exploratory studies. **Data sources:** MEDLINE, Embase, Cochrane Central, PreMEDLINE, and CINAHL databases were searched. **Data Extraction:** Data extraction and bias assessment were undertaken in duplicate. **Data Analysis:** A qualitative approach was applied, without statistical analysis. **Conclusion:** In controlled settings, dietary biomarkers of single nutrients or of individual foods or food groups are commonly used to assess compliance with dietary patterns. However, currently, there are no dietary biomarkers or biomarker profiles that are able to identify the specific dietary pattern that

has been consumed by an individual. Future work should seek to validate novel dietary biomarkers and biomarker profiles that are indicative of specific dietary patterns and their characteristics. A dietary biomarker panel consisting of multiple biomarkers is almost certainly necessary to capture the complexity of dietary patterns.

Poor Reporting Quality in Basic Nutrition Research: A Case Study Based on a Scoping Review of Recent Folate Research in Mouse Models (2009-2021)

Esther Munezero, Nathalie A Behan, Stephanie Diaz G, Eva-Marie Neumann, Amanda J MacFarlane. *Advances in Nutrition*, 12 July 2022. doi.org/10.1093/advances/nmac056. [Article link](#)

Significance: The lack of in-depth reporting of crucial details on generic and nutrition-specific study design in nutrition studies may limit their generalizability, reproducibility and interpretation. The use of consistent checklists when performing animal studies will greatly enhance quality of animal-based studies.

Transparent reporting of nutrition research promotes rigor, reproducibility and relevance to human nutrition. We performed a scoping review of recent articles reporting dietary folate interventions in mice as a case study to determine the reporting frequency of generic study design items (i.e. sex, strain and age) and nutrition-specific items (i.e. base diet composition, intervention doses, duration, and exposure verification) in basic nutrition research. We identified 798 original research articles in the EMBASE, Medline, Food Science and Technology Abstracts (FSTA), Global Health and International Pharmaceutical Abstracts (IPA) databases published between January 2009 and July 2021 in which a dietary folic acid (FA) intervention was used in mice. We identified 312 original peer-reviewed articles including 191 studies in non-pregnant and 126 in pregnant mice. Most studies reported sex (99%), strain (99%) and age (83%). The majority of studies used C57BL/6 (53%) or BALB/c (11%) mice aged 3-9 weeks. Non-pregnancy studies were more likely to use only male mice (57%). Dietary FA interventions varied considerably and overlapped: deficiency (0-3

mg/kg), control (0-16 mg/kg) and supplemented (0-50 mg/kg). Only 63% of studies used an open-formula base diet with a declared FA content and 60% of studies verified FA exposure using folate status biomarkers. The duration of intervention ranged from 1-104 weeks for non-pregnancy studies. The duration of intervention for pregnancy studies was 1-19 weeks occurring variably before pregnancy and/or during pregnancy and/or lactation. Overall, 17% of studies did not report ≥1 generic study design item(s) and 40% did not report ≥1 nutrition-specific study design item(s). The variability and frequent lack of reporting of important generic and nutrition-specific study design details in nutrition studies limits their generalizability, reproducibility and interpretation. The use of reporting checklists for animal research would enhance reporting quality of key study design and conduct factors in animal-based nutrition research.

An Analysis of the Recent U.S. Dietary Guidelines Process in Light of its Federal Mandate and a National Academies Report

Cheryl Achterberg, Arne Astrup, Dennis M Bier, Janet C King, Ronald M Krauss, Nina Teicholz, Jeff S Volek. *PNAS Nexus*, 20 July 2020. doi.org/10.1093/pnasnexus/pgac107. [Article link](#)

Significance: An analysis of recent Dietary Guidelines concluded that they may not have fully met the recommendations proposed by the NASEM on the need for enhanced transparency, greater scientific rigor, and updates to the scientific methodology for the DGA process. This oversight may have diminished scientific independence and rigor of the review process for producing consistent and trustworthy guidelines for the public.

The U.S. Dietary Guidelines for Americans is an enormously influential policy that has guided US nutrition programs since 1980. During these last forty years, some researchers have expressed concern that the guidelines are based on an insufficiently rigorous assessment of the scientific evidence, a view that was largely substantiated by a Congressionally mandated 2017 report by the National Academies of Sciences, Engineering, and Medicine, which identified a need for enhanced transparency, greater scientific rigor, and updates to the scientific methodology for the DGA process. This paper traces the history of these ideas and contextualizes the DGA within the law and regulations that govern its process. The paper also discusses how recent iterations of the Dietary Guidelines have not fully adhered to these guiding documents, which has resulted in diminished independence of the expert committee in charge of evaluating the science for the DGA and a continued lack of a fully rigorous scientific process for producing consistent and trustworthy guidelines for the public.

Carbohydrates

3D Printed Foods-Carbs from the Lab for Better Health

Jyoti Singh, Jaspreet Kaur, Prasad Rasane, Sawinder Kaur. *Curr Opin Clin Nutr Metab Care*. 2022 Jul 1;25(4):271-276. doi: 10.1097/MCO.0000000000000837. [Article link](#)

Significance: Current 3D printed food products have focused on texture modulation using carbohydrates. However future efforts involving adding prebiotics and probiotics to the carbohydrate ingredient may enhance nutritional and sensory benefits of carbohydrate-based 3D printed food products.

Purpose of Review: The purpose of the review is to describe carbohydrate-based 3D food printing technology in light of how it is affected by the use of various ingredients of ink and the properties associated with carbohydrate inks used for printing. Special focus is diverted to evaluate its effect on texture and corresponding health implications associated with carbohydrate based printed foods. **Recent findings:** The focus of 3D food printed products has revolved around texture modulation and carbohydrates are the best possible additives to achieve this modification. Carbohydrate based inks are used to design healthy texturized printed foods to provide various health benefits to consumer in addition to satisfy their aesthetic requirements. Other ingredients such as prebiotics and probiotics are major adjuncts that add value to these carbohydrates-based 3D food printed foods and may have synergistic effects. **Summary:** Although much of the current attention is on texture modulation, health aspects of the foods naturally drive the future course of research associated with the carbohydrate-based 3D food printed foods.

Protein

Approximately Half of Total Protein Intake by Adults must be Animal-Based to Meet Non-Protein Nutrient-Based Recommendations with Variation Due to Age and Sex

Florent Vieux, Didier Rémond, Jean-Louis Peyraud, Nicole Darmon. *J Nutr*. 2022 Jul 11. doi: 10.1093/jn/nxac150. [Article link](#)

Significance: A cross-sectional survey representative of French adults found that the amount of animal protein contribution to total proteins that will meet all nutrient-based recommendations at no added cost may range between

45% and 60% depending on the group of adults considered.

Background: Shifting towards a more plant-based diet, as promoted in Western countries, will reduce the animal protein contribution to total proteins. Such a reduction may not only impair protein adequacy, but also the adequacy in other nutrients. **Objectives:** We determined, for different adult subpopulations, the minimum total protein level and the minimum animal protein contribution to total proteins that are compatible with the fulfillment of all non-protein nutrient-based recommendations. **Methods:** Mean nutritional content and mean diet cost for 5 French subpopulations were estimated using a French cross-sectional representative survey: Women < 50 years (A), Women 50-64 years (B), Women ≥ 65 years (C), Men < 65 years (D), Men ≥ 65 years (E). For each subpopulation, linear programming optimization was used to assess the minimum protein level (Model Set#1) and the minimum animal protein contribution to total proteins (Model Set#2) that are compatible with the fulfillment of all nutrient-based recommendations (except proteins for which levels were analyzed as output). Total diet cost was not allowed to increase. Eating habits were considered in Model Set#2 only. **Results:** The minimum amount of protein that was theoretically compatible with the fulfillment of nutrient-based recommendations (Model Set#1) was below the minimum recommended protein intake for all subpopulations except A. In Model Set#2, for women and men over 65 years (C and E), decreasing animal protein contribution to total proteins below 55% and 60% respectively led to protein levels below recommend levels. For the other subpopulations (A, B, and D), the lowest animal protein contribution to total proteins compatible with a nutritionally adequate diet (including protein adequacy) was 55%, 50% and 45%, respectively. **Conclusion:** This study provides factual information about the animal protein contribution to total proteins compatible with meeting all nutrient-based recommendations at no additional cost and shows that it varies between 45% and 60% depending on the group of adults considered.

Low- and No-Calorie Sweeteners

The Convolutional Neural Network as a Tool to Classify Electroencephalography Data Resulting from the Consumption of Juice Sweetened with Caloric or Non-Caloric Sweeteners

Gustavo Voltani von Atzingen, Hubert Arteaga, Amanda Rodrigues da Silva, Nathalia Fontanari Ortega, Ernane Jose Xavier Costa, Ana Carolina de Sousa Silva. *Front Nutr.* 2022 Jul 19;9. doi: 10.3389/fnut.2022.901333.

[Article link](#)

Significance: Little is known how the brain processes the sensory characteristics of different artificial sweeteners. A recent study in 11 healthy subjects found that convolutional neural networks (CNN) may provide a viable tool for electroencephalography (EEG) analyses and classification of perceptually similar tastes of the different sweeteners.

Sweetener type can influence sensory properties and consumer's acceptance and preference for low-calorie products. An ideal sweetener does not exist, and each sweetener must be used in situations to which it is best suited. Aspartame and sucralose can be good substitutes for sucrose in passion fruit juice. Despite the interest in artificial sweeteners, little is known about how artificial sweeteners are processed in the human brain. Here, we applied the convolutional neural network (CNN) to evaluate brain signals of 11 healthy subjects when they tasted passion fruit juice equivalently sweetened with sucrose (9.4 g/100 g), sucralose (0.01593 g/100 g), or aspartame (0.05477 g/100 g). Electroencephalograms were recorded for two sites in the gustatory cortex (i.e., C3 and C4). Data with artifacts were disregarded, and the artifact-free data were used to feed a Deep Neural Network with tree branches that applied a Convolutions and pooling for different feature filtering and selection. The CNN received raw signal as input for multiclass classification and with supervised training was able to extract underlying features and patterns from the signal with better performance than handcrafted filters like FFT. Our results indicated that CNN is a useful tool for electroencephalography (EEG) analyses and classification of perceptually similar tastes.

Cognitive Health

Empirical Dietary Inflammatory Pattern Scores Are Not Associated with Worse Cognitive Performance in the Nurses' Health Study

Debora Melo van Lent, Cécilia Samieri, Francine Grodstein, Sudha Seshadri. *J Nutr.* 2022 Jul 26. doi: 10.1093/jn/nxac157. [Article link](#)

Significance: No relationship was found in a study in older Caucasian women (70+ years) between long term adherence to pro-inflammatory diets (based on EDIP scores) and cognitive functions (measured by averaged global cognitive function and verbal memory). Studies involving longer duration, in men and different ethnic groups are warranted to further investigate the relationship between inflammatory diets and cognitive health.

Background: Low-grade chronic inflammation associated with unhealthy diets may lead to cognitive aging.

Objectives: We evaluated whether higher long-term adherence to an Empirical Dietary Inflammatory Pattern (EDIP) was associated with lower cognitive function after age 70 years(y) in the Nurses' Health Study. **Methods:** 16,058 older (mean \pm SD, age 74 \pm 2y) highly educated (\geq bachelor degree) completed up to five validated 116-item Food Frequency Questionnaires. An EDIP score, previously derived with the use of reduced rank regression to predict circulating inflammatory markers (i.e., C-reactive protein, tumor necrosis factor- α receptor 2 and interleukin-6), was computed based on nine anti-inflammatory and nine pro-inflammatory components. A long-term EDIP score was calculated by averaging across five exams. The EDIP score was categorized into quintiles, taking the first (anti-inflammatory) quintile as the reference category. Cognitive testing was performed through telephone interviews over four follow-up exams (1995-2008). A composite global cognition score, a composite verbal memory score and the Telephone Interview for Cognitive Status (TICS) were calculated and averaged across the four exams (six years of follow-up). Multivariable linear regressions were used to examine longitudinal relationships under study. Results: Higher long-term EDIP scores (i.e., more pro-inflammatory) were significantly associated with worse performance on global cognitive function (P-for trend < 0.01) and TICS (P-for trend < 0.001) after adjustment for demographic and lifestyle factors. Both associations became non-significant after additional adjustments for disease (related) risk factors for dementia. No association was observed between the EDIP score and verbal memory. **Conclusions:** We observed no relationship between long-term EDIP scores and averaged global cognitive function and verbal memory among older women. Our findings suggest no relationship between long-term adherence to pro-inflammatory diet and cognitive function in a large population of mostly Caucasian and generally highly educated older women. Future studies are encouraged to investigate the relationship between inflammatory diets and cognitive function in other race/ethnicities and men, and over a longer follow-up period.

Lipids

A Randomized Trial of ω -3 Fatty Acid Supplementation and Circulating Lipoprotein Subclasses in Healthy Older Adults

Darya Moosavi, Ivan Vuckovic, Hawley E Kunz, Ian R Lanza. *J Nutr.* 2022 Jul 6;152(7):1675-1689. doi: 10.1093/jn/nxac084. [Article link](#)

Significance: This study suggests potential benefits of n-3-PUFA supplementation to lipoprotein profiles in healthy older adults without dyslipidemia. The study found despite an increased in small, dense LDL particles, n-3 PUFAs reduced total triglycerides, maintained HDL, reduced systolic blood pressure, and shifted the HDL particle distribution toward a favorable cardioprotective profile in healthy older adults without dyslipidemia.

Background: Omega-3 (n-3) PUFAs are recognized for triglyceride-lowering effects in people with dyslipidemia, but it remains unclear if n-3-PUFA intake influences lipoprotein profiles in older adults without hypertriglyceridemia. **Objectives:** The objective was to determine the effect of n-3-PUFA supplementation on plasma lipoprotein subfractions in healthy older men and women in the absence of cardiovascular disease (CVD) or hypertriglyceridemia. This was a secondary analysis and considered exploratory. **Methods:** Thirty young (20-35 y old) and 54 older (65-85 y old) men and women were enrolled in the study. Fasting plasma samples were collected. After baseline sample collection, 44 older adults were randomly assigned to receive either n-3-PUFA ethyl esters (3.9 g/d) or placebo (corn oil) for 6 mo. Pre- and post-intervention plasma samples were used for quantitative lipoprotein subclass analysis using high-resolution proton NMR spectroscopy. **Results:** The number of large, least-dense LDL particles decreased 17%-18% with n-3 PUFAs compared with placebo (<1% change; P < 0.01). The number of small, dense LDL particles increased 26%-44% with n-3 PUFAs compared with placebo (~11% decrease; P < 0.01). The cholesterol content of large HDL particles increased by 32% with n-3 PUFAs and by 2% in placebo (P < 0.01). The cholesterol content of small HDL particles decreased by 23% with n-3 PUFAs and by 2% in placebo (P < 0.01). **Conclusions:** Despite increasing abundance of small, dense LDL particles that are associated with CVD risk, n-3 PUFAs reduced total triglycerides, maintained HDL, reduced systolic blood pressure, and shifted the HDL particle distribution toward a favorable cardioprotective profile in healthy older adults without dyslipidemia. This study suggests potential benefits of n-3-PUFA supplementation to lipoprotein profiles in healthy older adults without dyslipidemia, which should be considered when weighing the potential health benefits against the cost and ecological impact of widespread use of n-3-PUFA supplements.

Sodium

Blood Pressure Interactions with the DASH Dietary Pattern, Sodium, and Potassium: The International Study of Macro-/Micronutrients and Blood Pressure (INTERMAP)

Queenie Chan, Gina M Wren, Chung-Ho E Lau, Timothy M D Ebbels, Rachel Gibson, Ruey Leng Loo, Ghadeer S Aljurai-ban et. al. *Am J Clin Nutr.* 2022 Jul 6;116(1):216-229. doi: 10.1093/ajcn/nqac067. [Article link](#)

Significance: This study found in free-living individuals in the United States that greater adherence to the DASH diet, which recommended increased intakes of fruits, vegetables and potassium rich foods, was associated with lower BP and

higher potassium intake across levels of sodium intake. More research is needed to identify DASH-specific metabolic pathways that impact blood pressure.

Background: Adherence to the Dietary Approaches to Stop Hypertension (DASH) diet enhances potassium intake and reduces sodium intake and blood pressure (BP), but the underlying metabolic pathways are unclear. **Objectives:** Among free-living populations, we delineated metabolic signatures associated with the DASH diet adherence, 24-hour urinary sodium and potassium excretions, and the potential metabolic pathways involved. **Methods:** We used 24-hour urinary metabolic profiling by proton nuclear magnetic resonance spectroscopy to characterize the metabolic signatures associated with the DASH dietary pattern score (DASH score) and 24-hour excretion of sodium and potassium among participants in the United States (n = 2164) and United Kingdom (n = 496) enrolled in the International Study of Macro- and Micronutrients and Blood Pressure (INTERMAP). Multiple linear regression and cross-tabulation analyses were used to investigate the DASH-BP relation and its modulation by sodium and potassium. Potential pathways associated with DASH adherence, sodium and potassium excretion, and BP were identified using mediation analyses and metabolic reaction networks. **Results:** Adherence to the DASH diet was associated with urinary potassium excretion (correlation coefficient, $r = 0.42$; $P < 0.0001$). In multivariable regression analyses, a 5-point higher DASH score (range, 7 to 35) was associated with a lower systolic BP by 1.35 mmHg (95% CI, -1.95 to -0.80 mmHg; $P = 1.2 \times 10^{-5}$); control of the model for potassium but not sodium attenuated the DASH-BP relation. Two common metabolites (hippurate and citrate) mediated the potassium-BP and DASH-BP relationships, while 5 metabolites (succinate, alanine, S-methyl cysteine sulfoxide, 4-hydroxyhippurate, and phenylacetylglutamine) were found to be specific to the DASH-BP relation. **Conclusions:** Greater adherence to the DASH diet is associated with lower BP and higher potassium intake across levels of sodium intake. The DASH diet recommends greater intake of fruits, vegetables, and other potassium-rich foods that may replace sodium-rich processed foods and thereby influence BP through overlapping metabolic pathways. Possible DASH-specific pathways are speculated but confirmation requires further study.

Gut Microbiome

The Fecal Metabolome Links Diet Composition, Food Processing and the Gut Microbiota to Gastrointestinal Health in a Randomized Trial of Adults Consuming a Processed Diet

J Philip Karl, Nicholes J Armstrong, Robert A Player, Jennifer C Rood, Jason W Soares, Holly L McClung. *J Nutr.* 2022 Jul 26;nxac161. doi: 10.1093/jn/nxac161. [Article link](#)

Significance: A secondary analysis from an RCT study of healthy subjects assigned to usual or military-ration diets suggests observed changes in fecal metabolomes between the groups may be due to differences in dietary composition, diet digestibility and the gut microbiota. Findings underscore the importance of food processing and nutrient composition on diet-gut microbiota interactions.

Background: Food processing alters diet digestibility and composition, thereby influencing interactions between host biology, diet, and the gut microbiota. The fecal metabolome offers insight into those relationships by providing a readout of diet-microbiota interactions impacting host health. **Objectives:** To determine the effects of consuming a processed diet on the fecal metabolome, and to explore relationships between changes in the fecal metabolome with fecal microbiota composition and gastrointestinal health markers. **Methods:** Secondary analysis of a randomized-controlled trial wherein healthy adults (94% male; 18-61 yr; BMI 26 ± 3 kg.m⁻²) consumed their usual diet (CON, n = 27) or a Meal, Ready-to-Eat™ military ration diet comprised of processed, shelf-stable, ready-to-eat items for 21d (MRE, n = 27). Fecal metabolite profiles, fecal microbiota composition, biomarkers of intestinal barrier function, and gastrointestinal symptoms were measured before and after the intervention. Between-group differences and associations were assessed using nonparametric t-tests, partial least squares discriminant analysis, correlation and redundancy analysis. **Results:** Fecal levels of multiple dipeptides (Mann-Whitney effect size (ES) = 0.27-0.50) and long-chain saturated fatty acids (ES = 0.35-0.58) increased, whereas, plant-derived compounds (ES = 0.31-0.60) decreased in MRE versus CON ($P < 0.05$; $q < 0.20$). Changes in dipeptides correlated positively with changes in fecal levels of Maillard-reaction products ($\rho = 0.29$ - 0.70 ; $P < 0.05$) and inversely with changes in serum prealbumin ($\rho = -0.30$ - -0.48 ; $P \leq 0.03$). Multiple bile acids, coffee and caffeine metabolites, and plant-derived compounds were associated with both fecal microbiota composition and gastrointestinal health markers, with changes in fecal microbiota composition explaining 26% of the variability within changes in gastrointestinal health-associated fecal metabolites ($P = 0.001$). **Conclusions:** Changes in the fecal metabolomes of adults consuming a Meal, Ready-to-Eat™ diet implicate interactions between diet composition, diet digestibility and the gut microbiota as contributing to variability within gastrointestinal responses to the diet. Findings underscore the need to consider both food processing and nutrient composition when investigating the impact of diet-gut microbiota interactions on health outcomes.

Emerging Science Areas

Emerging Topic: Climate Change and Food Production

Category: Food & Nutrition

Mechanism of Fertilization-Induced Auxin Synthesis in the Endosperm for Seed and Fruit Development

Lei Guo, Xi Luo, Muzi Li, Dirk Joldersma, Madison Plunkert & Zhongchi Liu *Nature Communications*, Vol.13, Article: 3985, 09 July 2022. [Article link](#)

Significance: The impact of rising global temperature and reduced numbers of plant pollinators on sustainable food production is a major concern. Understanding the mechanism of how flowering plants in staple crops such as strawberry, rice, corns, peanuts produce fruits and seeds are essential to ensure a sustainable food supply. A study funded by the National Science Foundation discovered the AGL62 gene in strawberry responsible for the activation of auxin synthesis in the endosperm which is necessary for viable seedcoat production and fruiting for successful crop pollination.

Background: The dominance of flowering plants on earth is owed largely to the evolution of maternal tissues such as fruit and seedcoat that protect and disseminate the seeds. The mechanism of how fertilization triggers the development of these specialized maternal tissues is not well understood. A key event is the induction of auxin synthesis in the endosperm, and the mobile auxin subsequently stimulates seedcoat and fruit development. However, the regulatory mechanism of auxin synthesis in the endosperm remains unknown. Here, we show that a type I MADS box gene AGL62 is required for the activation of auxin synthesis in the endosperm in both *Fragaria vesca*, a diploid strawberry, and in *Arabidopsis*. Several strawberry FveATHB genes were identified as downstream targets of FveAGL62 and act to repress auxin biosynthesis. In this work, we identify a key mechanism for auxin induction to mediate fertilization success, a finding broadly relevant to flowering plants.

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 - Despite the large body of evidence on the health benefits of specific probiotics and Functional Foods, there is an absence of recommended dietary allowances relating to the consumption of live microbes. Evidence for the benefits of live dietary microbes for health is building. However, the volume and nature of evidence that supports specific health benefits must be characterized, with gaps identified and addressed in order to develop more specific and quantitative guidance. Join in crafting an evidence-map. To learn more, please email science@iafns.org.