Dietary Patterns

Effect of Whole Foods and Dietary Patterns on Markers of Subclinical Inflammation in Weight-Stable Overweight and Obese Adults: A Systematic Review


Significance: This systematic review found no effect of foods or dietary patterns on inflammatory markers in weight-stable adults.

Context: Reduction of subclinical inflammation is a potential target for chronic disease management. Adiposity is a known modifier of meta-inflammation; however, the influence of dietary factors is less clear. Objective: This review examines evidence from human trials evaluating effects of whole foods or dietary patterns on circulating inflammatory markers in weight-stable overweight and obese adults. It is the first review to investigate effects of diet on inflammation, independent of changes in adiposity.

Data Sources: The Ovid MEDLINE, EMBASE, Cinahl, and Cochrane databases were searched. Data Extraction: Data extraction was conducted using the Cochrane Collaboration Handbook for Systematic Reviews of Interventions. Data Analysis: Study quality was evaluated using the Cochrane Collaboration Risk of Bias Assessment tool. Thirty-three studies were included assessing effects of 17 foods and dietary patterns on 39 inflammatory markers.

Conclusions: Overall, foods and dietary patterns were not found to have significant effects on inflammatory markers in weight-stable individuals. Inconsistencies among studies were largely due to methodological limitations. Future research should invest in longer intervention periods and standardization of inflammatory marker panels paired with novel technologies, while ensuring anthropometric measures are monitored and adequately controls are used. Systematic Review Registration: Prospero registration number CRD42017067765.

Nutritional Biomarkers

Perspective: Dietary Biomarkers of Intake and Exposure—Exploration With Omics Approaches


Significance: This Perspective highlights research needs for developing robust biomarkers of food intake and dietary exposure.

While conventional nutrition research has yielded biomarkers such as doubly labeled water for energy metabolism and 24-h urinary nitrogen for protein intake, a critical need exists for additional, equally robust biomarkers that allow for objective assessment of specific food intake and dietary exposure. Recent advances in high-throughput MS combined with improved metabolomics techniques and bioinformatic tools provide new opportunities for dietary biomarker development. In September 2018, the NIH organized a 2-d workshop to engage nutrition and omics researchers and explore the potential of multiomics approaches in nutritional biomarker research. The current Perspective summarizes key gaps and challenges identified, as well as the recommendations from the workshop that could serve as a guide for scientists interested in dietary biomarkers research. Topics addressed included study designs for biomarker development, analytical and bioinformatic considerations, and integration of dietary biomarkers with other omics techniques. Several clear needs were identified, including larger controlled feeding studies, testing a variety of foods and dietary patterns across diverse populations, improved reporting standards to support study replication, more chemical standards covering a broader range of food constituents and human metabolites, standardized approaches for biomarker validation,

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comprehensive and accessible food composition databases, a common ontology for dietary biomarker literature, and methodologic work on statistical procedures for intake biomarker discovery. Multidisciplinary research teams with appropriate expertise are critical to moving forward the field of dietary biomarkers and producing robust, reproducible biomarkers that can be used in public health and clinical research.

**Personalized Nutrition**

**Perspective: Guiding Principles for the Implementation of Personalized Nutrition Approaches That Benefit Health and Function**


**Significance:** This Perspective proposes a standard definition of “personalized nutrition” and a set of guiding principles to establish a basis for responsible, evidence-based personalized nutrition research and practice.

Personalized nutrition (PN) approaches have been shown to help drive behavior change and positively influence health outcomes. This has led to an increase in the development of commercially available PN programs, which utilize various forms of individual-level information to provide services and products for consumers. The lack of a well-accepted definition of PN or an established set of guiding principles for the implementation of PN creates barriers for establishing credibility and efficacy. To address these points, the North American Branch of the International Life Sciences Institute convened a multidisciplinary panel. In this article, a definition for PN is proposed: “Personalized nutrition uses individual-specific information, founded in evidence-based science, to promote dietary behavior change that may result in measurable health benefits.” In addition, 10 guiding principles for PN approaches are proposed: 1) define potential users and beneficiaries; 2) use validated diagnostic methods and measures; 3) maintain data quality and relevance; 4) derive data-driven recommendations from validated models and algorithms; 5) design PN studies around validated individual health or function needs and outcomes; 6) provide rigorous scientific evidence for an effect on health or function; 7) deliver user-friendly tools; 8) for healthy individuals, align with population-based recommendations; 9) communicate transparently about potential effects; and 10) protect individual data privacy and act responsibly. These principles are intended to establish a basis for responsible approaches to the evidence-based research and practice of PN and serve as an invitation for further public dialog. Several challenges were identified for PN to continue gaining acceptance, including defining the health–disease continuum, identification of biomarkers, changing regulatory landscapes, accessibility, and measuring success. Although PN approaches hold promise for public health in the future, further research is needed on the accuracy of dietary intake measurement, utilization and standardization of systems approaches, and application and communication of evidence.

**Protein**

**Dietary Meat Categories and Descriptions in Chronic Disease Research Are Substantively Different Within and Between Experimental and Observational Studies: A Systematic Review and Landscape Analysis**


**Significance:** This systematic review and landscape analysis calls for a practical muscle food classification system to improve interpretation of evidence regarding muscle food consumption and chronic disease.

This systematic review and landscape analysis describes patterns in dietary meat (skeletal muscle and associated tissues from mammalian, avian, and aquatic species; i.e., muscle foods) categories (CAT) and descriptions (DESCR) used throughout nutrition-related chronic disease literature, as there is anecdotally noted variation. A total of 1020 CAT and 776 DESCR were identified from 369 articles that assessed muscle food consumption and primary prevention of cardiovascular disease, obesity, type 2 diabetes, or cancer in adults ≥19 y from PubMed, Cochrane, and CINAHL up to March 2018. Specificity of CAT was analyzed on an empirical 1–7 ordinal scale as: 1) broad/undescriptive, “fish”; 2) muscle food type, “red meat”; 3) species, “poultry”; 4) broad + 1 descriptor, “processed meat”; 5) type/species + 1 descriptor, “fresh red meat”; 6) broad/type + 2 descriptors, “poached lean fish”; and 7) specific product, “luncheon meat.” Median CAT specificity for randomized controlled trials (RCTs) and observational studies (OBSs) was 2 and 3 points out of 7, respectively, with no differences between chronic disease types. Specificity of OBS CAT was higher in recent articles but RCT CAT became less specific starting in the 2000s. RCT CAT were 400% more likely to include species, 500% more likely to include leanness, but 400% less likely to include processing degree compared with OBS CAT. A DESCR was included for 76% and 82% of OBS and RCT CAT, respectively. Researchers described processed meat, red meat, and total meat CAT more commonly than poultry or fish CAT. Among processed meat DESCR, 31% included a common term used in public regulatory definitions. In conclusion, muscle food categories and descriptions are substantively different within and between experimental and observational studies and do not match regulatory definitions. A practical muscle food classification system is warranted to improve interpretation of evidence regarding muscle food consumption and chronic disease.
**Lipids**

**Omega-3 Fatty Acids for the Management of Hypertriglyceridemia: A Science Advisory From the American Heart Association**


**Significance:** This advisory summarizes the lipid and lipoprotein effects of pharmacological doses of eicosapentaenoic acid and docosahexaenoic acid.

Hypertriglyceridemia (triglycerides 200-499 mg/dL) is relatively common in the United States, whereas more severe triglyceride elevations (very high triglycerides, ≥500 mg/dL) are far less frequently observed. Both are becoming increasingly prevalent in the United States and elsewhere, likely driven in large part by growing rates of obesity and diabetes mellitus. In a 2002 American Heart Association scientific statement, the omega-3 fatty acids (n-3 FAs) eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) were recommended (at a dose of 2-4 g/d) for reducing triglycerides in patients with elevated triglycerides. Since 2002, prescription agents containing EPA+DHA or EPA alone have been approved by the US Food and Drug Administration for treating very high triglycerides; these agents are also widely used for hypertriglyceridemia. The purpose of this advisory is to summarize the lipid and lipoprotein effects resulting from pharmacological doses of n-3 FAs (>3 g/d total EPA+DHA) on the basis of new scientific data and availability of n-3 FA agents. In treatment of very high triglycerides with 4 g/d, EPA+DHA agents reduce triglycerides by ≥30% with concurrent increases in low-density lipoprotein cholesterol, whereas EPA-only did not raise low-density lipoprotein cholesterol in very high triglycerides. When used to treat hypertriglyceridemia, n-3 FAs with EPA+DHA or with EPA-only appear roughly comparable for triglyceride lowering and do not increase low-density lipoprotein cholesterol when used as monotherapy or in combination with a statin. In the largest trials of 4 g/d prescription n-3 FA, non-high-density lipoprotein cholesterol and apolipoprotein B were modestly decreased, indicating reductions in total atherogenic lipoproteins. The use of n-3 FA (4 g/d) for improving atherosclerotic cardiovascular disease risk in patients with hypertriglyceridemia is supported by a 25% reduction in major adverse cardiovascular events in REDUCE-IT (Reduction of Cardiovascular Events With EPA Intervention Trial), a randomized placebo-controlled trial of EPA-only in high-risk patients treated with a statin. The results of a trial of 4 g/d prescription EPA+DHA in hypertriglyceridemia are anticipated in 2020. We conclude that prescription n-3 FAs (EPA+DHA or EPA-only) at a dose of 4 g/d (>3 g/d total EPA+DHA) are an effective and safe option for reducing triglycerides as monotherapy or as an adjunct to other lipid-lowering agents.

**Carbohydrates**

**Whole-Grain Consumption Does Not Affect Obesity Measures: An Updated Systematic Review and Meta-Analysis of Randomized Clinical Trials**


**Significance:** The results from this updated meta-analysis do not support current whole-grain intake recommendations for the control of obesity measures.

Since the release of a previous meta-analysis on the effect of whole-grain intake on obesity measures, several clinical trials have been published. Therefore, we aimed to update the previous meta-analysis on the effect of whole-grain intake on obesity measures by including recently published studies, as well as considering the main limitations in that analysis. We searched the online databases of PubMed, Scopus, Clarivate Web of Science, EmBase, and Google Scholar for relevant studies published up to February 2019, using relevant keywords. Randomized clinical trials investigating the effect of whole-grain products or diets high in whole-grain foods, compared with a control diet, on anthropometric measures [including body weight, BMI, waist circumference, and fat mass (FM)] were included. In total, 21 studies with a total sample of 1798 participants, aged ≥18 years, were considered. Based on 22 effect sizes from 19 studies on body weight, with a total sample of 1698 adults, we found no significant effect of whole-grain consumption on body weight. The same findings were obtained for BMIs, such that using 10 effect sizes from 10 clinical trials with a total sample of 769 individuals we did not find any significant effect. With regards to body fat percentage [weighted mean difference (WMD): 0.27; 95% CI: −0.05 to 0.58%; P = 0.09], FM (WMD: 0.45; 95% CI: −0.12 to 1.02 kg; P = 0.12), fat-free mass (WMD: 0.31; 95% CI: −0.67 to 0.06 kg; P = 0.10), and waist circumference (WMD: 0.06; 95% CI: −0.50 to 0.63 cm; P = 0.82), we failed to find any significant effect of whole-grain consumption. In conclusion, our findings did not support current recommendations of whole-grain intake in attempts to control obesity measures. Given the beneficial effects of whole-grain intake on other measures of human health, additional well-designed studies are required to further investigate the effect on obesity. The protocol has been registered with PROSPERO (registration number CRD42018089176).
Low-Calorie Sweeteners

Epidemiological evidence has demonstrated a positive association between artificially sweetened beverage (ASB) and sugar-sweetened beverage (SSB) consumption and type 2 diabetes (T2D) risk. However, research informing this topic in young adults is limited. Objective: This study examined the association between ASB, SSB, and total sweetened beverage (TSB; combined ASB and SSB) consumption and T2D risk in young adults. Methods: A prospective analysis of 4719 Black and White men and women aged 18–30 y at baseline was conducted from the Coronary Artery Risk Development in Young Adults (CARDIA) study. Each participant’s beverage intake was assessed using the CARDIA Diet History at baseline and at study Years 7 and 20. Multivariable Cox proportional hazards regression models were used to examine cumulative average ASB, SSB, and TSB intakes and risk of T2D. Results: During the 30-y follow-up period, 680 participants developed T2D. ASB consumption was associated with a 12% greater risk of T2D per serving/day (HR 1.12, 95% CI 1.04–1.20) in a model adjusted for lifestyle factors, diet quality, and dieting behavior. Further adjustments for baseline BMI (HR 1.07, 95% CI 0.99–1.14) and weight change during follow-up (HR 1.04, 95% CI 0.97–1.12) attenuated the association. SSB and TSB consumption as continuous variables per 1 serving/day of intake were associated with 6% and 5% increased risks of T2D, respectively (HRSSB 1.06, 95% CI 1.01–1.10; HRTSB 1.05, 95% CI 1.01–1.09), in the model accounting for lifestyle factors, dieting behavior, baseline BMI, and weight change. Results were consistent when the exposures were modeled in categories of consumption and quintiles. Conclusions: In young adults, long-term ASB, SSB, and TSB consumption were associated with increased risks of T2D. However, the estimates for ASB were attenuated when accounting for weight change.

Bioactives

Significance: This systematic review and meta-analysis examines, for the first time, if there is consistent evidence that flavan-3-ols (irrespective of source) reduce cardiometabolic risk.

Background: Although available data suggest that some dietary flavan-3-ol sources reduce cardiometabolic risk, to our knowledge no review has systematically synthesized their specific contribution. Objective: We aimed to examine, for the first time, if there is consistent evidence that higher flavan-3-ol intake, irrespective of dietary source, reduces cardiometabolic risk. Methods: MEDLINE, Cochrane Central, and Commonwealth Agricultural Bureau abstracts were searched for prospective cohorts and randomized controlled trials (RCTs) published from 1946 to March 2019 on flavan-3-ol intake and cardiovascular disease (CVD) risk. Random-effects models meta-analysis was used. The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach assessed the strength of evidence. Results: Of 15 prospective cohorts (23 publications), 4 found highest compared with lowest habitual intakes of flavan-3-ols were associated with a 13% reduction in risk of CHD incidence. Highest compared with lowest habitual intakes of monomers were associated with a reduction in risk of type 2 diabetes mellitus (T2DM) (n = 5) and stroke (n = 4) (10% and 18%, respectively). No association was found for hypertension. Of 156 RCTs, flavan-3-ol intervention resulted in significant improvements in acute/chronic flow-mediated dilation (FMD), systolic (SBP) and diastolic blood pressure (DBP), total cholesterol (TC), LDL and HDL cholesterol, triglycerides (TGs), hemoglobin A1c (HbA1c), and homeostasis model assessment of insulin resistance (HOMA-IR). All analyses, except HbA1c, were associated with moderate/high heterogeneity. When analyses were limited to good methodological quality studies, improvements in TC, HDL cholesterol, SBP, DBP, HOMA-IR, and acute/chronic FMD remained significant. In GRADE evaluations, there was moderate evidence in cohort studies that flavan-3-ol and monomer intakes were associated with reduced risk of CVD mortality, CHD, stroke, and T2DM, whereas RCTs reported improved TC, HDL cholesterol, SBP, and HOMA-IR. Conclusions: Available evidence supports a beneficial effect of flavan-3-ol intake on cardiometabolic outcomes, but there was considerable heterogeneity in the meta-analysis. Future research should focus on an integrated intake/biomarker approach in cohorts and high-quality dose–response RCTs. This review was registered at www.crd.york.ac.uk/PROSPERO/ as CRD42018035782.
**Sodium**

**GWAS for Urinary Sodium and Potassium Excretion Highlights Pathways Shared With Cardiovascular Traits**


**Significance:** This genome-wide association study highlights pathways that are shared between urinary sodium and potassium excretion and cardiovascular traits.

Urinary sodium and potassium excretion are associated with blood pressure (BP) and cardiovascular disease (CVD). The exact biological link between these traits is yet to be elucidated. Here, we identify 50 loci for sodium and 13 for potassium excretion in a large-scale genome-wide association study (GWAS) on urinary sodium and potassium excretion using data from 446,237 individuals of European descent from the UK Biobank study. We extensively interrogate the results using multiple analyses such as Mendelian randomization, functional assessment, colocalization, genetic risk score, and pathway analyses. We identify a shared genetic component between urinary sodium and potassium expression and cardiovascular traits. Ingenuity pathway analysis shows that urinary sodium and potassium excretion loci are over-represented in behavioural response to stimuli. Our study highlights pathways that are shared between urinary sodium and potassium excretion and cardiovascular traits.

**Gut Microbiome**

**Establishing What Constitutes a Healthy Human Gut Microbiome: State of the Science, Regulatory Considerations, and Future Directions**


**Significance:** Academic, government, and industry experts were convened to discuss the state of the science, regulatory considerations, and research needs related to defining a “healthy” human gut microbiome.

On December 17, 2018, the North American branch of the International Life Sciences Institute (ILSI North America) convened a workshop “Can We Begin to Define a Healthy Gut Microbiome Through Quantifiable Characteristics?” with >40 invited academic, government, and industry experts in Washington, DC. The workshop objectives were to 1) develop a collective expert assessment of the state of the evidence on the human gut microbiome and associated human health benefits, 2) see if there was sufficient evidence to establish measurable gut microbiome characteristics that could serve as indicators of “health,” 3) identify short- and long-term research needs to fully characterize healthy gut microbiome–host relationships, and 4) publish the findings. Conclusions were as follows: 1) mechanistic links of specific changes in gut microbiome structure with function or markers of human health are not yet established; 2) it is not established if dysbiosis is a cause, consequence, or both of changes in human gut epithelial function and disease; 3) microbiome communities are highly individualized, show a high degree of interindividual variation to perturbation, and tend to be stable over years; 4) the complexity of microbiome-host interactions requires a comprehensive, multidisciplinary research agenda to elucidate relationships between gut microbiome and host health; 5) biomarkers and/or surrogate indicators of host function and pathogenic processes based on the microbiome need to be determined and validated, along with normal ranges, using approaches similar to those used to establish biomarkers and/or surrogate indicators based on host metabolic phenotypes; 6) future studies measuring responses to an exposure or intervention need to combine validated microbiome-related biomarkers and/or surrogate indicators with multomics characterization of the microbiome; and 7) because static genetic sampling misses important short- and long-term microbiome-related dynamic changes to host health, future studies must be powered to account for inter- and intra-individual variation and should use repeated measures within individuals.