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: A review of 33 studies concluded that foods and dietary patterns were not found to have significant effects on inflammatory markers in weight-stable individuals.

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. 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. Sources: The Ovid MEDLINE, EMBASE, CINAHL, and Cochrane databases were searched. Data extraction was conducted using the Cochrane Collaboration Handbook for Systematic Reviews of Interventions. 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. 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.

Protein

Protein Intake Greater Than the RDA Differentially Influences Whole-Body Lean Mass Responses to Purposeful Catabolic and Anabolic Stressors: A Systematic Review and Meta-Analysis


Significance: Among all comparisons, protein intakes greater than the RDA benefitted changes in lean mass relative to consuming the RDA.

Under stressful conditions such as energy restriction (ER) and physical activity, the RDA for protein of 0.8 g · kg⁻¹ · d⁻¹ may no longer be an appropriate recommendation. Under catabolic or anabolic conditions, higher protein intakes are proposed to attenuate the loss or increase the gain of whole-body lean mass, respectively. No known published meta-analysis compares protein intakes greater than the RDA with intakes at the RDA. Therefore, we conducted a systematic review and meta-analysis to assess the effects of protein intakes greater than the RDA, compared with at the RDA, on changes in whole-body lean mass. Three researchers independently screened 1520 articles published through August 2018 using the PubMed, Scopus, CINAHL, and Cochrane databases, with additional articles identified in published systematic review articles. Randomized, controlled, parallel studies ≥6 wk long with apparently healthy adults (≥19 y) were eligible for inclusion. Data from 18 studies resulting in 22 comparisons of lean mass changes were included in the final overall analysis. Among all comparisons, protein intakes greater than the RDA benefitted changes in lean mass relative to consuming the RDA [weighted mean difference (95% CI): 0.32 (0.01, 0.64) kg, n = 22 comparisons]. In the subgroup analyses, protein intakes greater than the RDA attenuated lean mass loss after ER [0.36 (0.06, 0.67) kg, n = 14], increased lean mass after resistance training (RT) [0.77 (0.23, 1.31) kg, n = 3], but did not differentially affect changes in lean mass [0.08 (−0.59, 0.75) kg, n = 7] under nonstressed conditions (no ER + no RT). Protein intakes greater...
than the RDA beneficially influenced changes in lean mass when adults were purposefully stressed by the catabolic stressor of dietary ER with and without the anabolic stressor of RT. The RDA for protein is adequate to support lean mass in adults during nonstressed states. This review was registered at www.crd.york.ac.uk/prospero as CRD 42018106532.

**Mycoprotein as a Possible Alternative Source of Dietary Protein to Support Muscle and Metabolic Health**


**Significance:** Emerging data suggest that the amino acid composition and bioavailability of mycoprotein may also position it as a promising dietary protein source to support skeletal muscle protein metabolism and promote training adaptations in athletes and the maintenance of muscle mass to support healthy aging.

The world’s population is expanding, leading to an increased global requirement for dietary protein to support health and adaptation in various populations. Though a strong evidence base supports the nutritional value of animal-derived dietary proteins, mounting challenges associated with sustainability of these proteins have led to calls for the investigation of alternative, non-animal-derived dietary protein sources. Mycoprotein is a sustainably produced, protein-rich, high-fiber, whole food source derived from the fermentation of fungus. Initial investigations in humans demonstrated that mycoprotein consumption can lower circulating cholesterol concentrations. Recent data also report improved acute postprandial glycemic control and a potent satiety effect following mycoprotein ingestion. It is possible that these beneficial effects are attributable to the amount and type of dietary fiber present in mycoprotein. Emerging data suggest that the amino acid composition and bioavailability of mycoprotein may also position it as a promising dietary protein source to support skeletal muscle protein metabolism. Mycoprotein may be a viable dietary protein source to promote training adaptations in athletes and the maintenance of muscle mass to support healthy aging. Herein, current evidence underlying the metabolic effects of mycoprotein is reviewed, and the key questions to be addressed are highlighted.

**Lipids**

**Long-Chain Omega-3 Polyunsaturated Fatty Acids and Cognitive Decline in Non-Demented Adults: A Systematic Review and Meta-Analysis**


**Significance:** Results from randomized controlled trials indicate that LCn-3PUFAs have no effect on global cognitive function.

**Context:** Long-chain omega-3 polyunsaturated fatty acids (LCn-3PUFAs) are widely considered as nootropic agents that may be beneficial in reversing cognitive impairment. **Objective:** The present systematic review of randomized controlled trials was conducted to determine the changes in cognitive function after intervention with LCn-3PUFA supplementation in non-demented adults, including those with mild cognitive impairment. **Data Sources:** Five databases (MEDLINE, CINAHL, Scopus, EMBASE, and the Cochrane Library) were searched systematically along with reference lists of selected articles. **Study Selection:** Studies were eligible for inclusion if they measured the effect of LCn-3PUFA supplementation on cognition in non-demented adults. **Data Extraction:** A total of 787 records were screened, of which 25 studies were eligible for inclusion. Treatment effects were summarized as global cognitive function for primary outcome and measured using the Mini-Mental State Examination and individual cognitive domains for secondary outcome. The pooled effect sizes were estimated using Hedge’s g and random-effects modeling. **Data Analysis:** Results from randomized controlled trials indicate that LCn-3PUFAs have no effect on global cognitive function (Hedge’s g = 0.02; 95% confidence interval, −0.12 to 0.154), and among the specific cognitive domains, only memory function showed a mild benefit (Hedge’s g = 0.31; P = 0.003; z = 2.945). **Conclusion:** The existing literature suggests that LCn-3PUFA supplementation could provide a mild benefit in improving memory function in non-demented older adults. **Systematic Review Registration:** PROSPERO registration no. CRD42017078664.

**Carbohydrates**

**Very Low and Higher Carbohydrate Diets Promote Differential Appetite Responses in Adults With Type 2 Diabetes: A Randomized Trial**


**Significance:** The high carbohydrate diet resulted in greater “daily overall” fullness and reduced prospective consumption.
Effects of very low carbohydrate (VLC) diets on appetite response in individuals with type 2 diabetes remain unclear. A secondary analysis was conducted to determine appetite responses to an energy-restricted (30% of energy (%E) deficit) very low carbohydrate (VLC) diet compared with a higher carbohydrate (HC) diet in adults who were overweight or obese with type 2 diabetes. Forty-four men and 40 women (mean ± SD; age: 58.7 ± 6.6 y; weight: 100.4 ± 15.5 kg; BMI: 34.5 ± 4.1 kg/m²; glycated hemoglobin: 7.3 ± 1.0%; duration of diabetes: 6.7 ± 5.6 y) were randomly assigned to diets categorized as VLC [14%E carbohydrate (<50 g/d), 28%E protein, 58%E fat (<10%E saturated fat)], or energy-matched HC [53%E carbohydrate, 17%E protein, 30%E fat (<10%E saturated fat)] combined with progressive multicomponent exercise (60 min; 3 d/wk). Body weight, average weekly “daily fasting” and “daily overall” appetite perceptions (hunger, fullness, prospective consumption, and desire to eat-visual analog scales) were assessed at baseline and after 4 and 16 wk. Changes between diets over time were assessed using repeated measures ANOVA. Significant decreases in body weight did not differ between groups (VLC: -11.0 ± 5.4 kg/16 wk compared with HC: -10.1 ± 4.3 kg/16 wk, P = 0.40). There was no difference between diet groups in “daily fasting” appetite ratings (P ≥ 0.30) or “daily overall” hunger and desire to eat (P ≥ 0.21). Compared with HC, VLC had greater decreases in “daily overall” ratings of fullness at Week 4 (VLC: -6 ± 2 compared with HC: 1 ± 2 arbitrary units, P = 0.001) and Week 16 (VLC: -3 ± 1 compared with HC: 3 ± 2 arbitrary units, P = 0.019) and reduced prospective consumption ratings at Week 4 (VLC: 5 ± 1 compared with HC: 0 ± 1 arbitrary units, P = 0.008). In the context of energy restriction, both HC and VLC energy-matched diets promoted comparable effects on fasting perceptions of appetite, but the HC diet resulted in greater “daily overall” fullness and reduced prospective consumption. Further research is required to evaluate the effects of ad libitum diets differing in amounts of carbohydrate on appetite response in populations with type 2 diabetes. This trial was registered at www.anzctr.org.au as ACTRN12612000369820.

**Effects of High-Fiber Diets Enriched With Carbohydrate, Protein, or Unsaturated Fat on Circulating Short Chain Fatty Acids: Results From the OmniHeart Randomized Trial**


**Significance:** Macronutrient composition of high-fiber diets affects circulating SCFAs, which are associated with measures of appetite and cardiometabolic health.

Short chain fatty acids (SCFAs; e.g., acetate, propionate, and butyrate) are produced by microbial fermentation of fiber in the colon. Evidence is lacking on how high-fiber diets that differ in macronutrient composition affect circulating SCFAs. We aimed to compare the effects of 3 high-fiber isocaloric diets differing in %kcal of carbohydrate, protein, or unsaturated fat on circulating SCFAs. Based on previous literature, we hypothesized that serum acetate, the main SCFA in circulation, increases on all high-fiber diets, but differently by macronutrient composition of the diet. OmniHeart is a randomized crossover trial of 164 men and women (≥30 y old); 163 participants with SCFA data were included in this analysis. We provided participants 3 isocaloric high-fiber (~30 g/2100 kcal) diets, each for 6 wk, in random order: a carbohydrate-rich (Carb) diet, a protein-rich (Prot) diet (protein predominantly from plant sources), and an unsaturated fat-rich (Unsat) diet. We used LC-MS to quantify SCFA concentrations in fasting serum, collected at baseline and the end of each diet period. We fitted linear regression models with generalized estimating equations to examine change in ln-transformed SCFAs from baseline to the end of each diet; differences between diets; and associations of changes in SCFAs with cardiometabolic parameters. From baseline, serum acetate concentrations were increased by the Prot (β: 0.24; 95% CI: 0.12, 0.35), Unsat (β: 0.21; 95% CI: 0.10, 0.33), and Carb (β: 0.12; 95% CI: 0.01, 0.24) diets; between diets, only Prot compared with Carb was significant (P = 0.02). Propionate was decreased by the Carb (β: -0.10; 95% CI: -0.16, -0.03) and Unsat (β: -0.10; 95% CI: -0.16, -0.04) diets, not the Prot diet; between diet comparisons of Carb vs. Prot (P = 0.006) and Unsat vs. Prot (P = 0.002) were significant. The Prot diet increased butyrate (β: 0.05; 95% CI: 0.00, 0.09) compared with baseline, but not compared with the other diets. Increases in acetate were associated with decreases in insulin and glucose; increases in propionate with increases in leptin, LDL cholesterol, and blood pressure; and increases in butyrate with increases in insulin and glucose, and decreases in HDL cholesterol and ghrelin (Ps < 0.05). Macronutrient composition of high-fiber diets affects circulating SCFAs, which are associated with measures of appetite and cardiometabolic health. This trial was registered at clinicaltrials.gov as NCT00051350.

**Low-Calorie Sweeteners**

**Perspective: Standards for Research and Reporting on Low-Energy (“Artificial”) Sweeteners**


**Significance:** This perspective identifies a number of issues which may contribute toward apparent inconsistencies in the content and understanding of past studies on LCS, and it provides a set of recommendations for authors, reviewers, and journal editors to standardize aspects of LES research. Widely differing views exist among experts, policy makers, and the general public with regard to the potential risks and benefits of reduced- or low-energy sweeteners (LES) in the diet. These views are informed and influenced by different types of research.
in LES, with differing hypotheses, designs, interpretation, and communication. Given the high level of interest in LES, and the public health relevance of the research evidence base, it is important that all aspects of the research process are framed and reported in an appropriate and balanced manner. In this Perspective, we identify and give examples of a number of issues relating to research and reviews on LES, which may contribute toward apparent inconsistencies in the content and understanding of the totality of evidence. We conclude with a set of recommendations for authors, reviewers and journal editors, as general guidance to improve and better standardize the quality of LES research design, interpretation, and reporting. These focus on clarity of underlying hypotheses, characterization of exposures, and the placement and weighting of new research within the wider context of related prior work.

**Bioactives**

**Carotenoid Intake and Circulating Carotenoids Are Inversely Associated With the Risk of Bladder Cancer: A Dose-Response Meta-Analysis**


**Significance:** Dose-response analysis showed that bladder cancer risk decreased by 42% for every 1-mg increase in daily dietary β-cryptoxanthin intake.

Some evidence indicates that carotenoids may reduce the risk of bladder cancer (BC), but the association is unclear. We conducted a systematic review and meta-analysis of case-control and cohort studies investigating the relation between carotenoid intake or circulating carotenoid concentrations and BC risk in men and women. All relevant epidemiologic studies were identified by a search of PubMed and Scopus databases, and the Cochrane Library from inception to April 2019 with no restrictions. A random-effects model was used to calculate pooled RRs and their 95% CIs across studies for high compared with low categories of intake or circulating concentrations. We also performed a dose-response meta-analysis using the Greenland and Longnecker method and random-effects models. A total of 22 studies involving 516,740 adults were included in the meta-analysis. The pooled RRs of BC for the highest compared with the lowest category of carotenoid intake and circulating carotenoid concentrations were 0.88 (95% CI: 0.76, 1.03) and 0.36 (95% CI: 0.12, 1.07), respectively. The pooled RR of BC for the highest compared with lowest circulating lutein and zeaxanthin concentrations was 0.53 (95% CI: 0.33, 0.84). Dose-response analysis showed that BC risk decreased by 42% for every 1 mg increase in daily dietary β-cryptoxanthin intake (RR: 0.58; 95% CI: 0.36, 0.94); by 76% for every 1 μmol/L increase in circulating concentration of α-carotene (RR: 0.24; 95% CI: 0.08, 0.67); by 27% for every 1 μmol/L increase in circulating concentration of β-carotene (RR: 0.73; 95% CI: 0.57, 0.94); and by 56% for every 1 μmol/L increase in circulating concentrations of lutein and zeaxanthin (RR: 0.44; 95% CI: 0.28, 0.67). Dietary β-cryptoxanthin intake and circulating concentrations of α-carotene, β-carotene, and lutein and zeaxanthin were inversely associated with BC risk. The protocol was registered at PROSPERO as CRD42019133240.

**Sodium**

**A Systematic Review of the Sources of Dietary Salt Around the World**


**Significance:** Bread products, cereal and grains, meat products, and dairy products were the major contributors to dietary salt intake in international populations. Salt use is correlated with economic development.

Excess salt intake contributes to hypertension and increased cardiovascular disease risk. Efforts to implement effective salt-reduction strategies require accurate data on the sources of salt consumption. We therefore performed a systematic review to identify the sources of dietary salt around the world. We systematically searched peer-reviewed and gray literature databases for studies that quantified discretionary (salt added during cooking or at the table) and nondiscretionary sources of salt and those that provided information about the food groups contributing to dietary salt intake. Exploratory linear regression analysis was also conducted to assess whether the proportion of discretionary salt intake is related to the gross domestic product (GDP) per capita of a country. We identified 80 studies conducted in 34 countries between 1975 and 2018. The majority (n = 44, 55%) collected data on dietary salt sources within the past 10 y and were deemed to have a low or moderate risk of bias (n = 75, 94%). Thirty-two (40%) studies were judged to be nationally representative. Populations in Brazil, China, Costa Rica, Guatemala, India, Japan, Mozambique, and Romania received more than half of their daily salt intake from discretionary sources. A significant inverse correlation between discretionary salt intake and a country’s per capita GDP was observed (P < 0.0001), such that for every $10,000 increase in per capita GDP, the amount of salt obtained from discretionary sources was lower by 8.7% (95% CI: 5.1%, 12%). Bread products, cereal and grains, meat products, and dairy products were the major contributors to dietary salt intake in international populations. Salt use is correlated with economic development.
products, and dairy products were the major contributors to dietary salt intake in most populations. There is marked variation in discretionary salt use around the world that is highly correlated with the level of economic development. Our findings have important implications for the type of salt-reduction strategy likely to be effective in a country.

**Gut Microbiome**

**Tryptophan Metabolism: A Link Between the Gut Microbiota and Brain**

**Significance:** This review summarizes recent advances in research on the influence of the gut microbiota on tryptophan metabolism, which affects brain function.

The gut-brain axis (GBA) is a bilateral communication network between the gastrointestinal (GI) tract and the central nervous system. The essential amino acid tryptophan contributes to the normal growth and health of both animals and humans and, importantly, exerts modulatory functions at multiple levels of the GBA. Tryptophan is the sole precursor of serotonin, which is a key monoamine neurotransmitter participating in the modulation of central neurotransmission and enteric physiological function. In addition, tryptophan can be metabolized into kynurenine, tryptamine, and indole, thereby modulating neuroendocrine and intestinal immune responses. The gut microbial influence on tryptophan metabolism emerges as an important driving force in modulating tryptophan metabolism. Here, we focus on the potential role of tryptophan metabolism in the modulation of brain function by the gut microbiota. We start by outlining existing knowledge on tryptophan metabolism, including serotonin synthesis and degradation pathways of the host, and summarize recent advances in demonstrating the influence of the gut microbiota on tryptophan metabolism. The latest evidence revealing those mechanisms by which the gut microbiota modulates tryptophan metabolism, with subsequent effects on brain function, is reviewed. Finally, the potential modulation of intestinal tryptophan metabolism as a therapeutic option for brain and GI functional disorders is also discussed.

**Understanding the Interaction of Diet Quality With the Gut Microbiome and Their Effect on Disease**

**Significance:** These findings add to evidence of the linkage between dietary patterns, presence of prediabetes, and gut microbiota composition.

As evidence emerges that higher diet quality predicts lower mortality and incidence of type 2 diabetes, possible biologic mechanisms for this relation have been hypothesized. Besides the positive influence of diet quality on body weight, body fat distribution, and inflammatory status, food components and dietary patterns have been linked to the composition of gut microbiota. In addition, evidence has accumulated for a relation between gut microbial characteristics and type 2 diabetes. The cross-sectional investigation among Swedish adults in the current issue of the Journal of Nutrition adds new evidence to the triangular relation of dietary patterns, the presence of prediabetes as an indicator of risk to develop diabetes, and gut microbiota composition.