**Dietary Patterns**

**Diet Quality of Vegetarian Diets Compared with Nonvegetarian Diets: A Systematic Review**


**Significance:** Overall diet quality is higher among lacto-ovo vegetarians and vegans compared to non-vegetarians, but the effect of confounders such as health consciousness is not known.

Objective: Vegetarian diets are consistently associated with improved health outcomes, and higher diet quality may contribute to improved health outcomes. This systematic review aims to qualitatively compare the a priori diet quality of vegetarian and nonvegetarian diets.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) protocol, 2 online databases (Web of Science and PubMed) were searched for English language studies comparing diet quality among vegetarian and nonvegetarian adults using an a priori diet quality index. Two reviewers assessed study eligibility. Comparisons were made between total and component (when available) diet quality scores among the 12 studies meeting inclusion criteria. Conclusions: Lacto-ovo vegetarians or vegans had higher overall diet quality (4.5–16.4 points higher on the Healthy Eating Index 2010 [HEI-2010]) compared with nonvegetarians in 9 of 12 studies. Higher HEI-2010 scores for vegetarians were driven by closer adherence to recommendations for total fruit, whole grains, seafood and plant protein, and sodium. However, nonvegetarians had closer adherence to recommendations for refined grains and total protein foods. Higher diet quality in vegetarian diets may partially explain improvements in health outcomes compared with nonvegetarians; however, more research controlling for known confounders like health consciousness is needed.

**The Associations of Fruit and Vegetable Intakes with Burden of Diseases: A Systematic Review of Meta-Analyses**


**Significance:** This systematic review supports existing recommendations for fruit and vegetable intakes.

Background: Low fruit and vegetable intakes are recognized risk factors for noncommunicable diseases. This systematic review summarizes published meta-analyses of global burden of diseases attributable to low fruit and vegetable intakes, and the best relative risk estimates. Methods: A published novel assessment process combining Cochrane Review measures, Assessing the Methodological Quality of Systematic Reviews checklist, and Newcastle-Ottawa Quality Assessment Scale was employed. Results: Sixty-four reports investigating 98 risk–disease pairs were included in the systematic review. Fifty-six pairs from 39 reports were assessed as statistically significant, involving 29 burden of diseases. Dose responses were identified for 31 negative and two positive associations. High against low intake relative risks were identified for 22 negative and one positive association. The highest identified linear dose response for each 100 g/day increase in fruit intakes was 0.56 (95% CI 0.42 to 0.74) for esophageal cancer, followed by 0.72 (95% CI 0.59 to 0.87) for mouth, pharynx, and larynx cancer; nonlinear dose response for the first 100 g/day of fruit intakes were 0.86 (95% CI 0.84 to 0.88) for stroke, followed by 0.89 (95% CI 0.88 to 0.90) for all-cause mortality. The highest identified linear dose response for each 100 g/day increase in vegetable intakes was 0.88 (95% CI 0.80 to 0.95) for renal cell cancer, followed by 0.89 (95% CI 0.84 to 0.95) for non-Hodgkin lymphoma; nonlinear dose responses for the first 100 g/day of vegetable intake were 0.86 (95% CI 0.84 to 0.89) for coronary heart disease, followed by 0.87 (95% CI 0.84 to 0.90) for all-cause mortality. For nonlinear associations, clear increases in protective associations were observed with the first 200 g/day of intakes, whereas little further increase or even decrease in protective associations were reported beyond 300 g/day.
g/day intakes. Canned fruit intakes were positively associated with all-cause and cardiovascular disease mortality, and pickled vegetable intakes were positively associated with stomach cancer. Conclusions: This systematic review supports existing recommendations for fruit and vegetable intakes. Current comparative risk assessments might significantly underestimate the protective associations of fruit and vegetable intakes.

**Protein**

The Impact of Dairy Protein Intake on Muscle Mass, Muscle Strength, and Physical Performance in Middle-Aged to Older Adults with or without Existing Sarcopenia: A Systematic Review and Meta-Analysis


**Significance:** Dairy protein is shown to be effective as part of a nutrition strategy to improve muscle mass and strength in middle-aged and older adults.

Sarcopenia is an age-related condition associated with a progressive loss of muscle mass and strength. Insufficient protein intake is a risk factor for sarcopenia. Protein supplementation is suggested to improve muscle anabolism and function in younger and older adults. Dairy products are a good source of high-quality proteins. This review evaluates the effectiveness of dairy proteins on functions associated with sarcopenia in middle-aged and older adults. Randomized controlled trials were identified using PubMed, CINAHL/EBSCO, and Web of Science databases (last search: 10 May 2017) and were quality assessed. The results of appendicular muscle mass and muscle strength of handgrip and leg press were pooled using a random-effects model. The analysis of the Short Physical Performance Battery is presented in narrative form. Adverse events and tolerability of dairy protein supplementation were considered as secondary outcomes. Fourteen studies involving 1424 participants aged between 61 and 81 y met the inclusion criteria. Dairy protein significantly increased appendicular muscle mass (0.13 kg; 95% CI: 0.01, 0.26 kg; P = 0.04); however, it had no effect on improvement in handgrip (0.84 kg; 95% CI: −0.24, 1.93 kg; P = 0.13) or leg press (0.37 kg; 95% CI: −4.79, 5.53 kg; P = 0.89). The effect of dairy protein on the Short Physical Performance Battery was inconclusive. Nine studies reported the dairy protein to be well tolerated with no serious adverse events. Although future high-quality research is required to establish the optimal type of dairy protein, the present systematic review provides evidence of the beneficial effect of dairy protein as a potential nutrition strategy to improve appendicular muscle mass in middle-aged and older adults.

**Carbohydrates**

Dietary Carbohydrates: A Review of International Recommendations and the Methods Used to Derive Them


**Significance:** Recommendations for reducing variation among recent dietary carbohydrate guidelines published by international health authorities are presented.

Background/objectives: Renewed dietary recommendations for carbohydrates have recently been published by various international health authorities. The present work (1) reviews the methods and processes (systematic approach/review, inclusion of public consultation) used to identify, select and grade the evidence underpinning the recommendations, particularly for total carbohydrate (CHO), fibre and sugar consumption, and (2) examines the extent to which variation in the methods and processes applied relates to any differences in the final recommendations. Subjects/methods: A search of WHO, US, Canada, Australia and European sources identified 19 documents from 13 authorities with the desired detailed information. Processes and methods applied to derive recommendations were compiled and compared. Results: (1) A relatively high total CHO and fibre intake and limited intake of (added or free) sugars are generally recommended. (2) Even where recommendations are similar, the specific justifications for quantitative/qualitative recommendations differ across authorities. (3) Differences in recommendations mainly arise from differences in the underlying definitions of CHO exposure and classifications, the degree to which specific CHO-providing foods and food components were considered, and the choice and number of health outcomes selected. (4) Differences in the selection of source material, time frames or data aggregation and grading methods appeared to have minor influence. Conclusions: Despite general consistency, apparent differences among the recommendations of different authorities would likely be minimized by: (1) More explicit quantitative justifications for numerical recommendations and communication of uncertainty, and (2) greater international harmonization, particularly in the underlying definitions of exposures and range of relevant nutrition-related outcomes.
Association Between Added Sugar Intake and Mortality is Nonlinear and Dependent on Sugar Source in 2 Swedish Population-Based Prospective Cohorts


**Significance:** The associations between sugar intake and mortality risk are dependent on the sugar source.

Background: Although sugar consumption has been associated with several risk factors for cardiometabolic diseases, evidence for harmful long-term effects is lacking. In addition, most studies have focused on sugar-sweetened beverages (SSBs), not sugar per se. Objective: The aim of this study was to examine the associations between added and free sugar intake, intake of different sugar sources, and mortality risk. Methods: Two prospective population-based cohorts were examined: the Malmö Diet and Cancer Study (MDCS; n = 24,272), which collected dietary data by combining a food diary, interview, and food-frequency questionnaire (FFQ), and the Northern Swedish Health and Disease Study (NSHDS; n = 24,475), which assessed diet with an FFQ. Sugar intakes defined as both added and free sugar and different sugar sources were examined. The associations with mortality were examined using a multivariable Cox proportional hazards regression. Results: Higher sugar consumption was associated with a less favorable lifestyle in general. The lowest mortality risk was found with added sugar intakes between 7.5% and 10% of energy (E%) intake in both cohorts. Intakes >20E% were associated with a 30% increased mortality risk, but increased risks were also found at intakes <5E% [23% in the MDCS and 9% (nonsignificant) in the NSHDS]. Similar U-shaped associations were found for both cardiovascular and cancer mortality in the MDCS. By separately analyzing the different sugar sources, the intake of SSBs was positively associated with mortality, whereas the intake of treats was inversely associated. Conclusions: Our findings indicate that a high sugar intake is associated with an increased mortality risk. However, the risk is also increased among low sugar consumers, although they have a more favorable lifestyle in general. In addition, the associations are dependent on the type of sugar source.

**Bioactives**

**Carotenoids, Vitamin A, and their Association with the Metabolic Syndrome: A Systematic Review and Meta-Analysis**


**Significance:** The findings from this meta-analysis suggest that total and individual carotenoids, but not retinol, are inversely related to the risk of metabolic syndrome.

Context: Modifiable factors that reduce the burden of the metabolic syndrome (MetS), particularly plant-derived biomarkers, have been a recent focus of rising interest. Objective: This systematic review and meta-analysis, which follows PRISMA guidelines, evaluates evidence from a period of 20 years that links vitamin A and carotenoids with the occurrence of MetS and following the PRISMA guidelines. Data Sources: PubMed and Cochrane databases (January 1997 through March 2017) were systematically assessed for studies, including case–control, cross-sectional, and cohort studies, that evaluated the associations of MetS with carotenoids and retinyl esters and retinol (vitamin A). Data Extraction: Key measures of associations were harmonized into odds ratios (ORs) and 95% confidence intervals (95%CI) of MetS per 1 standard deviation (SD) of exposure using forest plots and random effects models that pooled data points from 11 cross-sectional studies. Begg’s funnel and harvest plots were constructed. Results: An inverse association between total carotenoids and MetS was found [ORpooled, 0.66; 95%CI, 0.56–0.78; 1 SD ~ 0.82 µmol/L; n = 5 studies]. This association was the strongest for β-carotene, followed by α-carotene and β-cryptoxanthin. No association was detected between retinol and MetS (ORpooled, 1.00; 95%CI, 0.88–1.13; 1 SD ~ 2.14 µmol/L; n = 6 studies). Publication bias was absent, and harvest plots indicated consistency upon replication for β-carotene and total carotenoid exposures. Conclusions: This review and meta-analysis suggests that, unlike retinol, total and individual carotenoids were inversely related to MetS.

**Sodium**

**Association of Usual 24-h Sodium Excretion with Measures of Adiposity Among Adults in the United States: NHANES, 2014**


**Significance:** This cross-sectional study found that high usual sodium excretion is associated with overweight/obesity and central adiposity.
Background: Both excessive sodium intake and obesity are risk factors for hypertension and cardiovascular disease. The association between sodium intake and obesity is unclear, with few studies assessing sodium intake using 24-h urine collection. Objectives: Our objective was to assess the association between usual 24-h sodium excretion and measures of adiposity among US adults. Methods: Cross-sectional data were analyzed from a sample of 730 nonpregnant participants aged 20–69 y who provided up to 2 complete 24-h urine specimens in the NHANES 2014 and had data on overweight or obesity (body mass index (kg/m^2) ≥25) and central adiposity (waist circumference (WC): >88 cm for women, >102 cm for men). Measurement error models were used to estimate usual sodium excretion, and multiple linear and logistic regression models were used to assess its associations with measures of adiposity, adjusting for sociodemographic, health, and dietary variables [i.e., energy intake or sugar-sweetened beverage (SSB) intake]. All analyses accounted for the complex survey sample design. Results: Unadjusted mean ± SE usual sodium excretion was 3727 ± 43.5 mg/d and 3145 ± 55.0 mg/d among participants with and without overweight/obesity and 3653 ± 58.1 mg/d and 3443 ± 35.3 mg/d among participants with or without central adiposity, respectively. A 1000-mg/d higher sodium excretion was significantly associated with 3.8-units higher BMI (95% CI: 2.8, 4.8) and a 9.2-cm greater WC (95% CI: 6.9, 11.5 cm) adjusted for covariates. Compared with participants in the lowest quartile of sodium excretion, the adjusted prevalence ratios in the highest quartile were 1.93 (95% CI: 1.69, 2.20) for overweight/obesity and 2.07 (95% CI: 1.74, 2.46) for central adiposity. The associations also were significant when adjusting for SSBs, instead of energy, in models. Conclusions: Higher usual sodium excretion is associated with overweight/obesity and central adiposity among US adults.

### Lipids

**Unsaturated Fatty Acid Intakes During Midlife Are Positively Associated with Later Cognitive Function in Older Adults with Modulating Effects of Antioxidant Supplementation**


**Significance:** The protective effect of omega-3 fatty acids on cognitive health may be dependent on the individual’s antioxidant status.

Background: Given the drastic demographic changes characterized as “population aging,” the disease burden related to dementia is a major public health problem. The scientific literature documenting the link between mono- and polyunsaturated fatty acids (MUFA, PUFA) and cognitive function during aging is plentiful, but findings are inconsistent. Objectives: We aimed to evaluate the association between intakes of unsaturated fatty acids at midlife and cognitive performance 13 y later in French adults, and to test for a modulating effect of antioxidant supplementation. Methods: Fatty acid intakes were estimated with the use of repeated 24-h records (1994–1996) among 3362 subjects (mean ± SD age: 65.5 ± 4.6 y) of the SU.VI.MAX (Supplementation with Antioxidant Vitamins and Minerals) study, including an intervention phase (1994–2002) during which participants were randomly assigned to an “antioxidant supplementation” or placebo group. Cognitive performance was assessed at follow-up only (in 2007–2009) via a battery of 6 standardized neuropsychological tests. A global cognitive score was calculated as the sum of T-scores of the 6 tests. Multivariable-adjusted regression analyses were performed to provide regression coefficients and 95% CIs. Results: In multivariable models, total MUFA, total PUFA, and n-6 PUFA (ω-6 PUFA) were positively associated with overall cognitive functioning. n-3 PUFA (ω-3 PUFA) intakes showed positive associations among supplemented participants only (mean difference Tertile3 versus Tertile1: 1.40; 95% CI: 0.30, 2.51; P-trend = 0.01, P-interaction = 0.01). A detrimental role of arachidonic acid for cognitive functioning was only detected in the placebo group (mean difference Tertile3 versus Tertile1: −1.38; 95% CI: −2.57, −0.18; P-trend = 0.02, P-interaction = 0.07). Conclusion: Whereas higher total MUFA and n-6 PUFA intakes may be generally beneficial for maintaining cognitive health during aging, a higher consumption of n-3 fatty acids may only be beneficial among individuals with an adequate antioxidant status. These findings underline the importance of not only focusing on specific nutrients for dementia prevention, but also considering the complex interaction between consumed nutrients. This trial was registered at clinicaltrials.gov as NCT00272428.

**Habitual Consumption of Long-Chain n-3 PUFAs and Fish Attenuates Genetically Associated Long-Term Weight Gain**


**Significance:** This study provides evidence that high intake of fish and long-chain omega-3 polyunsaturated fatty acids may attenuate the genetic association with long-term weight gain in Caucasians.

Background: A growing amount of data suggests that n-3 (ω-3) polyunsaturated fatty acid (PUFA) intake may modify the genetic association with weight change. Objectives: We aimed to prospectively test interactions of habitual consumption of n-3 PUFAs or fish, the major food source,
with overall genetic susceptibility on long-term weight change. Design: Gene–diet interactions were examined in 11,330 women from the Nurses’ Health Study (NHS), 6773 men from the Health Professionals Follow-Up Study (HPFS), and 6254 women from the Women’s Health Initiative (WHI). Results: In the NHS and HPFS cohorts, food-sourced long-chain n–3 PUFA intake showed directionally consistent interactions with genetic risk score on long-term changes in BMI (P-interaction = 0.01 in the HPFS, 0.15 in the NHS, and 0.01 in both cohorts combined). Such interactions were successfully replicated in the WHI, an independent cohort (P-interaction = 0.02 in the WHI and 0.01 in the combined 3 cohorts). The genetic associations with changes in BMI (in kg/m²) consistently decreased (0.15, 0.10, 0.07, and −0.14 per 10 BMI-increasing alleles) across the quartiles of long-chain n–3 PUFA intake in the combined cohorts. In addition, high fish intake also attenuated the genetic associations with long-term changes in BMI in the HPFS (P-interaction = 0.01), NHS (P-interaction = 0.03), WHI (P-interaction = 0.10), and the combined cohorts (P-interaction = 0.01); and the differences in BMI changes per 10 BMI-increasing alleles were 0.16, 0.06, −0.08, and −0.18, respectively, across the categories (≤1, 1–4, 4–6, and ≥7 servings/wk) of total fish intake. Similar interactions on body weight were observed for fish intake (P-interaction = 0.003) and long-chain n–3 PUFA intake (P-interaction = 0.12). Conclusion: Our study provides replicable evidence to show that high intakes of fish and long-chain n–3 PUFA are associated with an attenuation of the genetic association with long-term weight gain based on results from 3 prospective cohorts of Caucasians.

Fine Mapping of Genome-Wide Association Study Signals to Identify Genetic Markers of the Plasma Triglyceride Response to an Omega-3 Fatty Acid Supplementation


Significance: Genetic determinants of plasma triglyceride response to omega-3 fatty acid supplementation were identified.

Background: Using a genome-wide association study (GWAS) approach, our group previously computed a genetic risk score (GRS) from single nucleotide polymorphisms (SNPs) of 10 loci that affect the plasma triglyceride (TG) response to an omega-3 (n–3) fatty acid (FA) supplementation. Objectives: The objective was to compute a novel and more refined GRS using fine mapping to include a large number of genetic variants. Methods: A total of 208 participants of the Fatty Acid Sensor (FAS) Study received 5 g fish oil/d, containing 1.9–2.2 g eicosapentaenoic acid and 1.1 g docosahexaenoic acid, for 6 wk. Plasma TG concentrations were measured before and after supplementation. Dense genotyping and genotype imputation were used to refine mapping around GWAS hits. A GRS was computed by summing the number of at-risk alleles of tagging SNPs. Analyses were replicated in samples of the FINGEN study. Results: A total of 31 tagging SNPs associated with the TG response were used for GRS calculation in the FAS study. In a general linear model adjusted for age, sex, and body mass index, the GRS explained 49.73% of TG response variance (P < 0.0001). Nonresponders to the n–3 FA supplementation had a higher GRS than did responders. In the FINGEN replication study, the GRS explained 3.67% of TG response variance (P = 0.0006). Conclusions: Fine mapping proved to be effective to refine the previous GRS. Carrying increasing numbers of at-risk alleles of 31 SNPs confers a higher risk of being nonresponsive to n–3 FAs. The genetic profile therefore appears to be an important determinant of the plasma TG response to an n–3 FA supplementation and could be used to target those most likely to gain clinical benefit. This trial was registered at http://www.clinicaltrials.gov as NCT01343342.

Microbiome

The Gut–Brain Axis and the Microbiome: Mechanisms and Clinical Implications


Significance: Programming of the brain gut microbiome axis occurs during the first three years of life, but targets within this axis can be targeted to treat brain gut disorders.

Background & Aims: Based largely on results from preclinical studies, the concept of a brain gut microbiome axis has been established, mediating bidirectional communication between the gut, its microbiome, and the nervous system. Limited data obtained in human beings suggest that alterations in these interactions may play a role in several brain gut disorders. Methods: We reviewed the preclinical and clinical literature related to the topic of brain gut microbiome interactions. Results: Well-characterized bidirectional communication channels, involving neural, endocrine, and inflammatory mechanisms, exist between the gut and the brain. Communication through these channels may be modulated by variations in the permeability of the intestinal wall and the blood-brain barrier. Brain gut microbiome interactions are programmed during the first 3 years of life, including the prenatal period, but can be modulated by diet, medications, and stress throughout life. Based on correlational studies, alterations in these interactions have been implicated in the regulation of food intake, obesity, and in irritable bowel syndrome, even though causality remains to be established. Conclusions: Targets within the brain gut microbiome axis have the potential to become targets for novel drug development for brain gut disorders.