Dietary Patterns

Adherence to the Mediterranean Diet in Relation to All-Cause Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies


Significance: This meta-analysis of recently published prospective studies found an inverse dose-response relationship between adherence to a Mediterranean diet and risk of all-cause mortality.

A previous meta-analysis provided convincing evidence for an inverse association between adherence to a Mediterranean diet (MedDiet) and the risk of all-cause mortality. Since then, 19 prospective studies have been published. We updated the evidence from these prospective studies and conducted a dose-response meta-analysis to test the linear and potential nonlinear dose-response associations between adherence to a MedDiet and the risk of all-cause mortality. The PubMed, Scopus, ISI Web of Knowledge, and Embase bibliographic databases were systematically searched up to August 24, 2018. Summary HRs were estimated with the use of a random-effects meta-analysis to assess the association between a 2-point increment in MedDiet adherence and the risk of all-cause mortality. Sensitivity and subgroup analyses were performed and potential publication bias was tested. Twenty-nine prospective studies with 1,676,901 participants and 221,603 cases of all-cause mortality were included in the final analysis. The pooled HR of all-cause mortality was 0.90 (95% CI: 0.89, 0.91; \( I^2 = 81.1\% \)) for a 2-point increment in adherence to a MedDiet. Subgroup analyses showed that a significant inverse association was stronger in participants who lived in the Mediterranean region compared with non-Mediterranean areas (HRs: 0.82 compared with 0.92, respectively), and in studies that used the Panagiotakos MedDiet score. A nonlinear dose-response meta-analysis indicated that the risk of all-cause mortality linearly decreased with the increase in adherence to a MedDiet. The robustness of findings was confirmed in the sensitivity analyses. In conclusion, low-quality evidence from prospective cohort studies suggests an inverse association between adherence to a MedDiet and the risk of all-cause mortality, especially in Mediterranean regions. An inverse linear dose-response relation was also observed between adherence to a MedDiet and the risk of all-cause mortality.

Improving Fruit and Vegetable Intake Attenuates the Genetic Association With Long-Term Weight Gain


Significance: This study of participants in the Nurse’s Health Study and Health Professionals Follow-Up Study found that fruit and vegetable intake mitigated genetically associated increased BMI and body weight, particularly among those with greater genetic susceptibility.

Background: Whether changes in fruit and vegetable intake can modify the effect of genetic susceptibility to obesity on long-term changes in BMI and body weight are uncertain. Objective: We analyzed the interactions of changes in total and specific fruit and vegetable intake with genetic susceptibility to obesity in relation to changes in BMI and body weight. Methods: We calculated a genetic risk score on the basis of 77 BMI-associated loci to determine the genetic susceptibility to obesity, and examined the interactions of changes in total and specific fruit and vegetable intake with the genetic risk score on changes in BMI and body weight within five 4-y intervals over 20 y of follow-up in 8943 women from the Nurses’ Health Study (NHS) and 5308 men from the Health Professionals Follow-Up Study (HPFS). Results: In the combined cohorts, repeated 4-y BMI change per 10-risk allele increment was 0.09 kg/m² among participants with the greatest decrease in total fruit and vegetable intake and −0.02
among those with the greatest increase in intake (P-interaction <0.001; corresponding weight change: 0.20 kg compared with −0.06 kg). The magnitude of decrease in BMI associated with increasing fruit and vegetable intake was more prominent among participants with high genetic risk than those with low risk. Reproducible interactions were observed for fruits and vegetables separately (both P-interaction <0.001). Based on similar nutritional content, the interaction effect was greatest for berries, citrus fruits, and green leafy vegetables, and the interaction pattern persisted regardless of the different fiber content or glycemic load of fruits and vegetables. Conclusions: Genetically associated increased BMI and body weight could be mitigated by increasing fruit and vegetable intake, and the beneficial effect of improving fruit and vegetable intake on weight management was more pronounced in individuals with greater genetic susceptibility to obesity.

Dietary Guidelines

A Global Review of Food-Based Dietary Guidelines

Significance: This review highlights universally echoed and variable guidance found in food-based dietary guidelines across 90 countries, and highlights future frontiers in food-based dietary guidance.

The objective of this review is to provide a concise, descriptive global review of current food-based dietary guidelines (FBDG), and to assess similarities and differences in key elements of a healthy diet articulated across countries. Information was sourced from the FBDG repository of the FAO, which catalogs FBDG for all countries where they are available, including a description of the food guide (the graphic representation of the dietary guidelines), a set of key messages, and downloadable documents provided by the countries. FBDG are currently available for 90 countries globally: 7 in Africa, 17 in Asia and the Pacific, 33 in Europe, 27 in Latin America and the Caribbean, 4 in the Near East, and 2 in North America. The year of publication of current versions ranges from 1986 to 2017 (mean 2009). This review provides summaries of the key messages and food guides that are used to communicate national dietary guidance, organized by food group, and evaluates the extent to which each set of FBDG includes existing recommendations articulated by the WHO. Some guidance appears nearly universally across countries: to consume a variety of foods; to consume some foods in higher proportion than others; to consume fruits and vegetables, legumes, and animal-source foods; and to limit sugar, fat, and salt. Guidelines on dairy, red meat, fats and oils, and nuts are more variable. Although WHO global guidance encourages consumption of nuts, whole grains, and healthy fats, these messages are not universally echoed across countries. Future frontiers in FBDG development include the incorporation of environmental sustainability and increased attention to sociocultural factors including rapidly changing dietary trends. Steps toward regional and global dietary recommendations could be helpful for refinement of country-level FBDG, and for clear communication and measurement of diet quality both nationally and globally.

Protein

Soy, Soy Isoflavones, and Protein Intake in Relation to Mortality from All Causes, Cancers, and Cardiovascular Diseases: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies

Significance: This meta-analysis found an inverse association between soy isoflavone intake and all-cause mortality risk.

Objective: We conducted a systematic review and dose–response meta-analysis of prospective studies to summarize findings on the associations between intakes of soy, soy isoflavones, and soy protein and risk of mortality from all causes, cancers, and cardiovascular diseases. Methods: Online databases were systematically searched to identify relevant articles published earlier than May 2018. We applied restricted cubic splines using random-effects analysis to assess dose–response associations. Between-study heterogeneity was assessed by I² value and Cochrane Q test. Potential publication bias was assessed by visual inspection of funnel plots and Begg regression test. Results: In total, 23 prospective studies with an overall sample size of 330,826 participants were included in the current systematic review and the meta-analysis. Soy/soy products consumption was inversely associated with deaths from cancers (pooled relative risk 0.88, 95% CI 0.79 to 0.99; P=0.03; I²=47.1%, 95% CI 0.0% to 75.4%) and cardiovascular diseases (pooled effect size: 0.85, 95% CI 0.72 to 0.99; P=0.04; I²=50.0%, 95% CI 0.0% to 77.6%). Such significant associations were also observed for all-cause
mortality in some subgroups of the included studies, particularly those with higher quality. In addition, higher intake of soy was associated with decreased risk of mortality from gastric, colorectal, and lung cancers as well as ischemic cardiovascular diseases. Participants in the highest category of dietary soy isoflavones intake had a 10% lower risk of all-cause mortality compared with those in the lowest category. We also found that a 10-mg/day increase in intake of soy isoflavones was associated with 7% and 9% decreased risk of mortality from all cancers and also breast cancer respectively. Furthermore, a 12% reduction in breast cancer death was indicated for each 5-g/day increase in consumption of soy protein. However, intake of soy protein was not significantly associated with all-cause and cardiovascular diseases mortality. Conclusions: Soy and its isoflavones may favorably influence risk of mortality. In addition, soy protein intake was associated with a decreased risk in the mortality of breast cancer. Our findings may support the current recommendations to increase intake of soy for greater longevity.

**Lipids**

**Negative Effects of a High-Fat Diet on Intestinal Permeability: A Review**


**Significance:** This review highlights the known mechanisms by which a high-fat diet disrupts the gut barrier system.

The intestinal tract is the largest barrier between a person and the environment. In this role, the intestinal tract is responsible not only for absorbing essential dietary nutrients, but also for protecting the host from a variety of ingested toxins and microbes. The intestinal barrier system is composed of a mucus layer, intestinal epithelial cells (IECs), tight junctions (TJs), immune cells, and a gut microbiota, which are all susceptible to external factors such as dietary fats. When components of this barrier system are disrupted, intestinal permeability to luminal contents increases, which is implicated in intestinal pathologies such as inflammatory bowel disease, necrotizing enterocolitis, and celiac disease. Currently, there is mounting evidence that consumption of excess dietary fats can enhance intestinal permeability differentially. For example, dietary fat modulates the expression and distribution of TJs, stimulates a shift to barrier-disrupting hydrophobic bile acids, and even induces IEC oxidative stress and apoptosis. In addition, a high-fat diet (HFD) enhances intestinal permeability directly by stimulating proinflammatory signaling cascades and indirectly via increasing barrier-disrupting cytokines (TNFα, interleukin (IL) 1B, IL6, and interferon γ (IFNγ)) and decreasing barrier-forming cytokines (IL10, IL17, and IL22). Finally, an HFD negatively modulates the intestinal mucus composition and enriches the gut microflora with barrier-disrupting species. Although further research is necessary to understand the precise role HFDs play in intestinal permeability, current data suggest a stronger link between diet and intestinal disease than was first thought to exist. Therefore, this review seeks to highlight the various ways an HFD disrupts the gut barrier system and its many implications in human health.

**Intake of Palm Olein and Lipid Status in Healthy Adults: A Meta-Analysis**


**Significance:** This study found no significant difference in the effects of palm olein oil on lipoprotein biomarkers versus other dietary oils.

It is not clear whether a saturated fatty acid-rich palm olein diet has any significant adverse effect on established surrogate lipid markers of cardiovascular disease (CVD) risk. We reviewed the effect of palm olein with other oils on serum lipid in healthy adults. We searched in MEDLINE and CENTRAL: Central Register of Controlled Trials from 1975 to January 2018 for randomized controlled trials of ≥2 wk intervention that compared the effects of palm olein (the liquid fraction of palm oil) with other oils such as coconut oil, lard, canola oil, high-oleic sunflower oil, olive oil, peanut oil, and soybean oil on changes in serum lipids. Nine studies were eligible and were included, with a total of 533 and 542 subjects on palm olein and other dietary oil diets, respectively. We extracted and compared all the data for serum lipids, such as total cholesterol (TC), LDL cholesterol, HDL cholesterol, triglyceride, and TC/HDL cholesterol ratio. When comparing palm olein with other dietary oils, the overall weighted mean differences for TC, LDL cholesterol, HDL cholesterol, triglycerides, and the TC/HDL cholesterol ratio were -0.10 (95% CI: -0.30, 0.10; P = 0.34), -0.06 (95% CI: -0.29, 0.16; P = 0.59), 0.02 (95% CI: -0.01, 0.04; P = 0.20), 0.01 (95% CI: -0.05, 0.06; P = 0.85), and -0.15 (95% CI: -0.43, 0.14; P = 0.32), respectively. Overall, there are no significant differences in the effects of palm olein intake on lipoprotein biomarkers (P > 0.05) compared with other dietary oils. However, dietary palm olein was found to have effects comparable to those of other unsaturated dietary oils (monounsaturated fatty acid- and polyunsaturated fatty acid-rich oils) but differed from that of saturated fatty acid-rich oils with respect to the serum lipid profile in healthy adults.
**Carbohydrates**

**The Effect of Isolated and Synthetic Dietary Fibers on Markers of Metabolic Diseases in Human Intervention Studies: A Systematic Review**


**Significance:** This systematic review highlights confounding factors in existing research related to the effects of isolated and synthetic fibers on metabolic outcomes, and provides recommendations for future work in this area.

Observational studies provide strong evidence for the health benefits of dietary fiber (DF) intake; however, human intervention studies that supplement isolated and synthetic DFs have shown inconsistent results. Therefore, we conducted a systematic review to summarize the effects of DF supplementation on immunometabolic disease markers in intervention studies in healthy adults, and considered the role of DF dose, DF physicochemical properties, intervention duration, and the placebo used. Five databases were searched for studies published from 1990 to 2018 that assessed the effect of DF on immunometabolic markers. Eligible studies were those that supplemented isolated or synthetic DFs for ≥2 wk and reported baseline data to assess the effect of the placebo. In total, 77 publications were included. DF supplementation reduced total cholesterol (TC), LDL cholesterol, HOMA-IR, and insulin AUC in 36–49% of interventions. In contrast, <20% of the interventions reduced C-reactive protein (CRP), IL-6, glucose, glucose AUC, insulin, HDL cholesterol, and triglycerides. A higher proportion of interventions showed an effect if they used higher DF doses for CRP, TC, and LDL cholesterol (40–63%), viscous and mixed plant cell wall DFs for TC and LDL cholesterol (>50%), and longer intervention durations for CRP and glucose (50%). Half of the placebo-controlled studies used digestible carbohydrates as the placebo, which confounded findings for IL-6, glucose AUC, and insulin AUC. In conclusion, interventions with isolated and synthetic DFs resulted mainly in improved cholesterol concentrations and an attenuation of insulin resistance, whereas markers of dysglycemia and inflammation were largely unaffected. Although more research is needed to make reliable recommendations, a more targeted supplementation of DF with specific physicochemical properties at higher doses and for longer durations shows promise in enhancing several of its health effects.

**Low-Calorie Sweeteners**

**Brain Activity and Connectivity Changes in Response to Nutritive Natural Sugars, Non-Nutritive Natural Sugar Replacements and Artificial Sweeteners**


**Significance:** This study found differing effects of nutritive sugars, low-nutritive sweeteners and non-nutritive sweeteners on whole brain functional responses, which may in turn differentially affect reward and satiety responses and feeding behavior.

**Introduction:** The brain plays an important regulatory role in directing energy homeostasis and eating behavior. The increased ingestion of sugars and sweeteners over the last decades makes investigating the effects of these substances on the regulatory function of the brain of particular interest. We investigated whole brain functional response to the ingestion of nutrient shakes sweetened with either the nutritive natural sugars glucose and fructose, the low- nutritive natural sugar replacement allulose or the non-nutritive artificial sweetener sucralose. **Methods:** Twenty healthy, normal weight, adult males underwent functional MRI on four separate visits. In a double-blind randomized study setup, participants received shakes sweetened with glucose, fructose, allulose or sucralose. Resting state functional MRI was performed before and after ingestion. Changes in Blood Oxygen Level Dependent (BOLD) signal, functional network connectivity and voxel based connectivity by Eigenvector Centrality Mapping (ECM) were measured. **Results:** Glucose and fructose led to significant decreased BOLD signal in the cingulate cortex,insula and the basal ganglia. Glucose led to a significant increase in eigenvector centrality throughout the brain and a significant decrease in eigenvector centrality in the midbrain. Sucralose and allulose had no effect on BOLD signal or network connectivity but sucralose did lead to a significant increase in eigenvector centrality values in the cingulate cortex, central gyri and temporal lobe. **Discussion:** Taken together our findings show that even in a shake containing fat and protein, the type of sweetener can affect brain responses and might thus affect reward and satiety responses and feeding behavior. The sweet taste without the corresponding energy content of the non-nutritive sweeteners appeared to have only small effects on the brain. Indicating that the while ingestion of nutritive sugars could have a strong effect on feeding behavior, both in a satiety aspect as well as rewarding aspects, non-nutritive sweeteners appear to not have these effects. **Trial registration:** This study is registered at clinicaltrials.gov under number NCT02745730.
Bioactives

Effects of Hesperidin Consumption on Cardiovascular Risk Biomarkers: A Systematic Review of Animal Studies and Human Randomized Clinical Trials

Significance: This evaluation of animal and human clinical studies did not find conclusive evidence of a cardioprotective effect of the flavonoid hesperidin.

Context: The cardioprotective effects of the flavonoid hesperidin, which is present in citrus products, are controversial and unclear. This systematic review was conducted in accordance with the PRISMA 2015 guidelines. Objective: To evaluate the current evidence from animal and human clinical studies and thus determine whether the consumption of hesperidin exerts beneficial effects on cardiovascular risk factors. Data sources: PICOS (Population, Intervention, Comparison, Outcome, and Study Design) criteria defined the research question. Searches of the PubMed and Cochrane Plus databases were conducted and studies that met the inclusion criteria and were published in English in the last 15 years were included. Data extraction: The first author, year of publication, study design, characteristics of animals and humans, intervention groups, dose of hesperidin, route of administration, duration of the intervention, cardiovascular risk biomarkers assessed, and results observed were extracted from the included articles. Results: A total of 12 animal studies and 11 randomized clinical trials met the inclusion criteria. In the animal studies, the glucose, total and LDL cholesterol, and triglyceride levels decreased with chronic flavonoid consumption. In the human studies, endothelial function improved with flavonoid consumption, whereas no conclusive results were observed for the other biomarkers. Conclusions: Animal studies have revealed that hesperidin and hesperetin consumption reduces glucose levels and various lipid profile parameters. However, a definitive conclusion cannot be drawn from the existing human clinical trials. Further research is needed to confirm whether the findings observed in animal models can also be observed in humans. Systematic Review Registration: Prospero registration number CRD42018088942.

Sodium

Sodium-Intake Reduction and the Food Industry

Significance: This article provides context for current recommendations for the food industry to reduce the amount of sodium in the U.S. food supply.

A recent report adds overwhelming weight to the imperative to reduce the amount of sodium in the U.S. food supply. Collaborations between the food industry and government agencies could help achieve this goal.

Gut Microbiome

Importance of Gut Microbiota in Obesity

Significance: This article highlights the roles that the gut microbiota play in obesity, as well as proposed tools to control obesity and metabolic disease.

Recently, a number of studies have related the development of highly prevalent disorders such as type 2 diabetes and obesity to gut microbiota. Obesity itself have been associated with modifications in gut microbiota composition, and a tendency towards an overgrowth of microorganisms that obtain more efficient energy from diet. It’s capacity to decompose the polysaccharides that cannot be digested by the host, increase monosaccharide and short chain fatty acid (SCFA) production. However, the increase in fat mass is not only due to a more efficient harvest of energy, but also the microbiota participates in changes in endotoxemia, bowel permeability, insulin resistance, hormonal environment, expression of genes regulating lipogenesis, interaction with bile acids, as well as changes in the proportion of brown adipose tissue, and effects associated with the use of drugs such as metformin. Currently, use of prebiotics and probiotics and other innovative techniques like antibiotic therapy or gut microbiota transplant, has been proposed as suitable tools to control the development of metabolic diseases such as obesity or insulin resistance through the diet.
Taste

Variations in Marginal Taste Perception by Body Mass Index Classification: A Randomized Controlled Trial


Significance: This randomized, controlled trial found differences in taste perception among obese versus normal-weight and overweight individuals.

Background: The propensity to overeat may, in part, be a function of the satisfaction derived from eating. If levels of satisfaction derived from food differ among normal-weight, overweight, and obese adults, the quantification of satisfaction from food may help explain why some people eat more than others. Objective: To quantify the satisfaction obtained from eating one specific food, chocolate, by measuring taste perception as normal-weight, overweight, and obese participants consumed additional pieces of chocolate. To measure the effect of nutritional information on chocolate consumption. Design: Randomized, controlled trial. Participants/setting: We analyzed data on 290 adults; 161 had a body mass index (BMI) that was considered normal (<25), 78 had a BMI considered overweight (≥25 and <30), and 51 had a BMI considered obese (≥30). Intervention: Participants were given samples of chocolate, one at a time, until they chose to stop eating. With each sample, participants were given a questionnaire. Half of the study participants were randomly selected to receive nutritional information (n=150). Main outcome measures: Perceived taste for each sample. Statistical analyses performed: We used time-series-regression to model perceived taste changes while controlling for participant characteristics. Results: Study participants consumed between 2 and 51 pieces of chocolate with a mean of 12.1 pieces. Average taste perception decreased with each piece. We found no significant difference in taste perceptions between normal- and overweight participants. However, obese participants had higher levels of initial taste perception than normal- and overweight participants (P=0.02). Also, obese participants reported taste perceptions that declined at a more gradual rate than normal- and overweight participants (P<0.01). Self-reported hunger, prior to the study, affected taste perception, but providing nutritional information did not. Conclusions: Obese participants started with higher levels of perceived taste and also experienced slower rates of decline than did normal-weight and overweight individuals.