Dietary Patterns

Efficacy of Different Dietary Patterns on Lowering of Blood Pressure Level: An Umbrella Review

**Significance:** Adherence to the DASH, Nordic and portfolio diets effectively reduced blood pressure. Evidence of blood pressure-lowering effects for other diets examined was inconsistent.

**Background:** Many systematic reviews and meta-analyses have assessed the efficacy of dietary patterns on blood pressure (BP) lowering but their findings are largely conflicting. **Objective:** This umbrella review aims to provide an update on the available evidence for the efficacy of different dietary patterns on BP lowering. **Methods:** PubMed and Scopus databases were searched to identify relevant studies through to June 2020. Systematic reviews with meta-analyses of randomized controlled trials (RCTs) were eligible if they measured the effect of dietary patterns on systolic (SBP) and/or diastolic blood pressure (DBP) levels. The methodological quality of included systematic reviews was assessed by A Measurement Tool to Assess Systematic Review version 2. The efficacy of each dietary pattern was summarized qualitatively. The confidence of the effect estimates for each dietary pattern was graded using the NutriGrade scoring system.

**Results:** Fifty systematic reviews and meta-analyses of RCTs were eligible for review. Twelve dietary patterns namely the Dietary Approaches to Stop Hypertension (DASH), Mediterranean, Nordic, vegetarian, low-salt, low-carbohydrate, low-fat, high-protein, low glycemic index, portfolio, pulse, and Paleolithic diets were included in this umbrella review. Among these dietary patterns, the DASH diet was associated with the greatest overall reduction in BP with unstandardized mean differences ranging from -3.20 to -7.62 mmHg for SBP and from -2.50 to -4.22 mmHg for DBP. Adherence to Nordic, portfolio, and low-salt diets also significantly decreased SBP and DBP levels. In contrast, evidence for the efficacy of BP lowering using the Mediterranean, vegetarian, Paleolithic, low-carbohydrate, low glycemic index, high-protein, and low-fat diets was inconsistent. **Conclusion:** Adherence to the DASH, Nordic, and portfolio diets effectively reduced BP. Low-salt diets significantly decreased BP levels in normotensive Afro-Caribbean people and in hypertensive patients of all ethnic origins.

The Mediterranean Dietary Pattern and Inflammation in Older Adults: A Systematic Review and Meta-analysis

**Significance:** The findings from this systematic review and meta-analysis suggest that the Mediterranean diet is associated with lower inflammation in older adults.

This systematic review and meta-analysis aimed to explore the association between the Mediterranean dietary pattern and inflammation in older adults. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. A search of the literature was conducted up to June 2020 in 7 electronic databases, namely PubMed, Embase, Web of Science, Scopus, Cochrane Library, Cumulative Index to Nursing and Allied Health Literature (CINAHL), and ProQuest. The Joanna Briggs Institute Critical Appraisal Checklists and the Newcastle-Ottawa Scale were used to assess the methodological quality. The overall standardized mean difference (SMD) and 95% CIs were estimated in random-effects meta-analyses. Thirteen studies were identified as having acceptable quality and were included in this systematic review: 3 randomized controlled trials (RCTs), 1 quasi-experimental study, 1 cohort study, and 8 cross-sectional studies. The circulating C-reactive protein (CRP) concentration was the most common inflammation indicator used. Results of the meta-analysis on 5 cross-sectional studies revealed a significant inverse association between the Mediterranean dietary pattern and inflammation as assessed by CRP (SMD = -0.26; 95% CI: -0.41, -0.11; P < 0.001). Other studies that investigated a variety of inflammation indicators other than CRP showed mixed results with regard to the relation between the Mediterranean dietary pattern and inflammation in older adults. Our
findings suggest that the Mediterranean dietary pattern may be associated with lower inflammation in older adults. However, more long-term RCTs are required to demonstrate the effects of the Mediterranean dietary pattern on multiple inflammation parameters in older adults.

**Methods**

**Nutrition Study Design Issues—Important Issues for Interpretation**


**Significance:** Randomized clinical trials have limits when comparing two diet types, but apparently inconsistent findings may be more aligned once these limits are understood.

Of the many study designs used in nutrition science, the randomized clinical trial (RCT) is largely held in highest regard for its clinical relevance and ability to address cause and effect relationships. Researchers utilize RCTs to provide scientific evidence addressing controversial topics about what to eat or avoid. However, RCTs have their own challenges, particularly when it comes to comparing 2 diet types or patterns – e.g. Diet A vs. Diet B. A better understanding and appreciation of these challenges and limitations can help show how seemingly conflicting, confusing and controversial findings are often more aligned and consistent than it may seem.

**Protein**

**Replacing the Consumption of Red Meat With Other Major Dietary Protein Sources and Risk of Type 2 Diabetes Mellitus: A Prospective Cohort Study**


**Significance:** A prospective analysis found that replacing red meat consumption with other protein sources was associated with a lower risk of type 2 diabetes over a four-year period.

**Background:** Greater consumption of red meat has been associated with a higher risk of type 2 diabetes mellitus (T2DM). A decreased intake of red meat and simultaneous increased intake of other high-protein foods may be associated with a lower risk of T2DM. These analyses of specific food replacements for red meat may provide more accurate dietary advice. **Objective:** We examined the association between a decrease in intake of red meat accompanied by an increase in other major dietary protein sources and risk of T2DM. **Methods:** We prospectively followed 27,634 males in the Health Professionals Follow-up Study, 46,023 females in the Nurses’ Health Study, and 75,196 females in the Nurses’ Health Study II. Diet was assessed by a validated FFQ and updated every 4 y. Cox proportional hazards models adjusted for T2DM risk factors were used to model the food replacements. We calculated HRs and 95% CIs for the T2DM risk associated with replacements of 1 daily serving of red meat with another common protein food. **Results:** During 2,113,245 person-years of follow-up, we identified 8763 incident T2DM cases from 1990 to 2013. In the pooled analyses, a decrease in total red meat intake during a 4-y period replaced with another common protein food was associated with a lower risk of T2DM in the subsequent 4-y period. The HR (95% CI) per 1 serving/d was 0.82 (0.75, 0.90) for poultry, 0.87 (0.77, 0.98) for seafood, 0.82 (0.78, 0.86) for low-fat dairy, 0.82 (0.77, 0.86) for high-fat dairy, 0.90 (0.81, 0.99) for eggs, 0.89 (0.82, 0.98) for legumes, and 0.83 (0.78, 0.89) for nuts. The associations were present for both unprocessed and processed red meat, although stronger for the replacement of processed red meat. **Conclusions:** Replacing red meat consumption with other protein sources was associated with a lower risk of T2DM.

**The Impact of Protein Supplementation on Appetite and Energy Intake in Healthy Older Adults: A Systematic Review With Meta-Analysis**


**Significance:** Protein supplementation may be an effective solution to increase protein intakes in healthy older adults without compromising energy intake through appetite suppression.

Protein supplementation is an attractive strategy to prevent loss of muscle mass in older adults. However, it could be counterproductive due to adverse effects on appetite. This systematic review and meta-analysis aimed to determine the effects of protein supplementation on appetite and/or energy intake (EI) in healthy older adults. MEDLINE, The Cochrane Library, CINAHL, and Web of Science were searched up to June 2020. Acute and longitudinal studies in healthy adults ≥60 y of age that reported effects of protein supplementation (through supplements or whole foods) compared with control and/or preintervention (for
longitudinal studies) on appetite ratings, appetite-related peptides, and/or EI were included. Random-effects model meta-analysis was performed on EI, with other outcomes qualitatively reviewed. Twenty-two studies (9 acute, 13 longitudinal) were included, involving 857 participants (331 males, 526 females). In acute studies (n = 8), appetite ratings were suppressed in 7 out of 24 protein arms. For acute studies reporting EI (n = 7, n = 22 protein arms), test meal EI was reduced following protein preload compared with control [mean difference (MD): -164 kJ; 95% CI: -299, -29 kJ; P = 0.02]. However, when energy content of the supplement was accounted for, total EI was greater with protein compared with control (MD: 649 kJ; 95% CI: 438, 861 kJ; P < 0.00001). Longitudinal studies (n = 12 protein arms) showed a higher protein intake (MD: 0.29 g · kg⁻¹ · d⁻¹; 95% CI: 0.14, 0.45 g · kg⁻¹ · d⁻¹; P < 0.001) and no difference in daily EI between protein and control groups at the end of trials (MD: -54 kJ/d; 95% CI: -300, 193 kJ/d; P = 0.67). While appetite ratings may be suppressed with acute protein supplementation, there is either a positive effect or no effect on total EI in acute and longitudinal studies, respectively. Therefore, protein supplementation may represent an effective solution to increase protein intakes in healthy older adults without compromising EI through appetite suppression.

**Lipids**

**Small Amounts of Dietary Medium-Chain Fatty Acids Protect Against Insulin Resistance During Caloric Excess in Humans**


**Significance:** Substituting small LCFAs with MCFAs rescues insulin action under conditions of lipid-induced energy excess.

Medium-chain fatty acids (MCFAs) have in rodents been shown to have protective effects on glucose homeostasis during high-fat overfeeding. In this study, we investigated whether dietary MCFAs protect against insulin resistance induced by a hypercaloric high-fat diet in humans. Healthy, lean men ingested a eucaloric control diet and a three-day hypercaloric high-fat diet (+75% energy, 81-83%E% fat) in randomized order. For one group (n=8), the high-fat diet was enriched with saturated long-chain FAs (LCSFA-HFD), while the other group (n=9) ingested a matched diet, but with ∼30 g (5E%) saturated MCFAs (MCSFA-HFD) in substitution for a corresponding fraction of the saturated LCSFAs. A hyperinsulinemic-euglycemic clamp with femoral arteriovenous balance and glucose tracer was applied after the control and hypercaloric diets. In LCSFA-HFD, whole body insulin sensitivity and peripheral insulin-stimulated glucose disposal were reduced. These impairments were prevented in MCSFA-HFD, accompanied by increased basal FA oxidation, maintained glucose metabolic flexibility, increased non-oxidative glucose disposal related to lower starting glycogen content and increased glycogen synthase activity, together with increased muscle lactate production. In conclusion, substitution of a small amount of dietary LCFAs with MCFAs rescues insulin action in conditions of lipid-induced energy excess.

**Carbohydrates**

**Whole Grain Food Definition Effects on Determining Associations of Whole Grain Intake and Body Weight Changes: A Systematic Review**


**Significance:** How whole grain foods are operationally defined affects research conclusions. Going forward, application of a standardized methodology to calculate whole grain intake is important.

Within epidemiological and intervention studies, whole grain consumption has generally shown positive associations with reductions in markers of overweight and obesity. However, studies use varied methods of determining whole grain intake, including different definitions of a whole grain food, which may explain varied results. This systematic review aimed to identify how different methods of reporting and calculating whole grain intake, including whole grain food definitions, affect reported associations between whole grain intake and body weight measures in adults. Systematic searching of PubMed, Scopus, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Cochrane Central Register for Controlled Trials (CENTRAL), and MEDLINE (all years to 11 June, 2020) identified eligible studies. Cohort and cross-sectional studies assessing whole grain intake and body weight measures in adults were included. Studies that did not specify methods used to calculate whole grain intake were excluded. Twenty-one cross-sectional studies (from 24 articles) and 9 prospective cohort studies (from 7 articles) were included in the review. Many cross-sectional studies showed whole grain intake was, to some degree, significantly associated with body weight measures, whereas associations varied greatly among cohort studies. Studies
calculating whole grain intake using total grams of intake, USDA databases, or ≥25% whole grain in combination with listing specific foods, showed consistent beneficial effects of increasing whole grain intake on body weight. Studies with general lists of foods included as “whole grain foods” or lower cut-offs for whole grain content were inconsistent. The majority of studies reported whole grain intake as servings/day or grams whole grain/day. This review suggests that an association between whole grain and body weight measures remains likely, although precise associations are difficult to determine due to heterogeneity in methodologies and an inability to formally compare studies. Moving forward, application of a standardized methodology to calculate whole grain intake is essential.

Low-Calorie Sweeteners

Impacts of Acute Sucralose and Glucose on Brain Activity during Food Decisions in Humans

Significance: This study revealed attenuation of central nervous system signaling associated with food valuation after consumption of glucose and sucralose.

It is not known how acute sucralose and glucose alter signaling within the brain when individuals make decisions about available food. Here we examine this using Food Bid Task in which participants bid on visually depicted food items, while simultaneously undergoing functional Magnetic Resonance Imaging. Twenty-eight participants completed three sessions after overnight fast, distinguished only by the consumption at the start of the session of 300 mL cherry flavored water with either 75 g glucose, 0.24 g sucralose, or no other ingredient. There was a marginally significant \( p = 0.05 \) effect of condition on bids, with 13.0% lower bids after glucose and 16.6% lower bids after sucralose (both relative to water). Across conditions, greater activity within regions a priori linked to food cue reactivity predicted higher bids, as did greater activity within the medial orbitofrontal cortex and bilateral frontal pole. There was a significant attenuation within the a priori region of interest (ROI) after sucralose compared to water \( p < 0.05 \). Activity after glucose did not differ significantly from either of the other conditions in the ROI, but an attenuation in signal was observed in the parietal cortex, relative to the water condition. Taken together, these data suggest attenuation of central nervous system (CNS) signaling associated with food valuation after glucose and sucralose.

Bioactives

Systematic Review and Meta-Analysis of the Relative Dose-Response Tests to Assess Vitamin A Status

Significance: The Relative Dose-Response and Modified RDR are sensitive tests for determining a population’s vitamin A status and assessing interventions using vitamin A.

Vitamin A (VA) is an essential nutrient often lacking in the diets of people in developing countries. Accurate biomarkers of VA status are vital to inform public health policy and monitor interventions. The relative dose-response (RDR) and modified-RDR (MRDR) tests are semi-quantitative screening tests for VA deficiency that have been used in Demographic and Health Surveys and VA intervention studies. A systematic review and meta-analysis of sensitivity and specificity were conducted to summarize the physiological evidence to support the RDR tests as methods to assess VA status and investigate the impact of different pathological and physiological states on the tests. A total of 190 studies were screened for inclusion, with 21 studies comparing the RDR tests with the gold-standard biomarker, liver VA concentration (68% and 80% sensitivity and 85% and 69% specificity for the RDR and MRDR, respectively). Nearly all studies with VA interventions in VA-deficient populations demonstrated a response of the tests to VA intake that would be expected to improve VA status. The impacts of chronic liver disease, protein malnutrition, age, pregnancy and lactation, infection and inflammation, and various other conditions were examined in 51 studies. The RDR and MRDR tests were reported to have been used in 39 observational studies, and the MRDR has been used in at least 6 national micronutrient surveys. The RDR and MRDR are sensitive tests for determining population VA status and assessing VA interventions. Although they are robust to most physiological and pathological states, caution may be warranted when using the tests in neonates, individuals with chronic liver disease, and those with protein or iron malnutrition. Research on further improvements to the tests to increase accessibility, such as sampling breast milk instead of blood or using intramuscular doses in subjects with malabsorption, will allow wider adoption.
**Sodium**

**Associations of Sodium and Potassium Consumption with the Gut Microbiota and Host Metabolites in a Population-Based Study in Chinese adults**  

**Significance:** Sodium and potassium consumption is linked with taxa and metabolites that have been implicated in cardiometabolic health.

**Background:** There is increasing evidence that sodium consumption alters the gut microbiota and host metabolome in murine models and small studies in humans. However, there is a lack of population-based studies that capture large variations in sodium consumption as well as potassium consumption. **Objective:** We examined the associations of energy-adjusted dietary sodium (milligrams/kilocalorie), potassium, and sodium-to-potassium (Na/K) ratio with the microbiota and plasma metabolome in a well-characterized Chinese cohort with habitual excessive sodium and deficient potassium consumption. **Methods:** We estimated dietary intakes from 3 consecutive validated 24-h recalls and household inventories. In 2,833 adults (18-80 y old, 51.2% females), we analyzed microbial (genus-level 16S ribosomal RNA) between-person diversity, using distance-based redundancy analysis (dbRDA), and within-person diversity and taxa abundance using linear regression, accounting for geographic variation in both. In a subsample (n = 392), we analyzed the overall metabolome (dbRDA) and individual metabolites (linear regression). P values for specific taxa and metabolites were false discovery rate adjusted (q-value). **Results:** Sodium, potassium, and Na/K ratio were associated with microbial between-person diversity (dbRDA P < 0.01) and several specific taxa with large geographic variation, including pathogenic *Staphylococcus* and *Moraxellaceae*, and SCFA-producing *Phascolarctobacterium* and *Lachnospiraceae* (q-value < 0.05). For example, sodium and Na/K ratio were positively associated with *Staphylococcus* and *Moraxellaceae* in Liaoning, whereas potassium was positively associated with 2 genera from *Lachnospiraceae* in Shanghai. Additionally, sodium, potassium, and Na/K ratio were associated with the overall metabolome (dbRDA P ≤ 0.01) and several individual metabolites, including butyrate/isobutyrate and gut-derived phenolics such as 1,2,3-benzenetriol sulfate, which was negatively associated with sodium in Guizhou (q-value < 0.05). **Conclusions:** Our findings suggest that sodium and potassium consumption is associated with taxa and metabolites that have been implicated in cardiometabolic health, providing insights into the potential roles of gut microbiota and host metabolites in the pathogenesis of sodium- and potassium-associated diseases. More studies are needed to confirm our results.

**Gut Microbiome**

**Current Explorations of Nutrition and the Gut Microbiome: A Comprehensive Evaluation of the Review Literature**  

**Significance:** Nutrition has profound effects on microbial composition, in turn affecting wide-ranging metabolic, hormonal and neurological processes.

**Context:** The ability to measure the gut microbiome led to a surge in understanding and knowledge of its role in health and disease. The diet is a source of fuel for and influencer of composition of the microbiome. **Objective:** To assess the understanding of the interactions between nutrition and the gut microbiome in healthy adults. **Data Sources:** PubMed and Google Scholar searches were conducted in March and August 2018 and were limited to the following: English, 2010-2018, healthy adults, and reviews. **Data Extraction:** A total of 86 articles were independently screened for duplicates and relevance, based on preidentified inclusion criteria. **Data Analysis:** Research has focused on dietary fiber - microbiota fuel. The benefits of fiber center on short-chain fatty acids, which are required by colonocytes, improve absorption, and reduce intestinal transit time. Contrastingly, protein promotes microbial protein metabolism and potentially harmful by-products that can stagnate in the gut. The microbiota utilize and produce micronutrients; the bidirectional relationship between micronutrition and the gut microbiome is emerging. **Conclusions:** Nutrition has profound effects on microbial composition, in turn affecting wide-ranging metabolic, hormonal, and neurological processes. There is no consensus on what defines a “healthy” gut microbiome. Future research must consider individual responses to diet.
Probiotics Contribute to Glycemic Control in Patients with Type 2 Diabetes Mellitus: A Systematic Review and Meta-Analysis

Significance: Probiotics may have a glucose-lowering effect in individuals with type 2 diabetes. The effect appeared to be stronger in participants with poorly controlled diabetes and those not receiving insulin therapy.

This systematic review aimed to evaluate the effectiveness and safety of probiotics for glycemic control in adults with impaired glucose control, including prediabetes and type 2 diabetes mellitus (T2DM). We searched PubMed, Embase, and Cochrane databases, and trial registries up to February 2019. We included randomized controlled trials (RCTs) of participants with prediabetes or T2DM. Eligible trials compared probiotics versus either placebo, no intervention, or comparison probiotics, or compared synbiotics versus prebiotics. Primary outcomes were mean change in fasting blood glucose (FBG) and glycated hemoglobin (HbA1c) from baseline to short term (<12 wk) and long term (≥12 wk). We performed meta-analyses using the random-effects model. We included 28 RCTs (1947 participants). Overall, probiotics reduced FBG more than the placebo/no intervention group with a mean difference (MD) of -12.99 mg/dL (95% CI: -23.55, -2.42; P value: 0.016) over the short term; and -2.99 mg/dL (95% CI: -5.84, -0.13; P value: 0.040) over the long term. There was also some evidence for reduced HbA1c in the probiotics group at both short term (MD: -0.17; 95% CI: -0.37, 0.02; P value: 0.084) and long term (MD: -0.14; 95% CI: -0.34, 0.06; P value: 0.172), however, these did not reach statistical significance possibly because only a few trials reported HbA1c as an outcome. Subgroup analyses showed a greater reduction in HbA1c in participants not receiving insulin therapy than those receiving insulin therapy. Furthermore, the effect of probiotics on the reduction of FBG was more pronounced in participants with FBG >130 mg/dL and those not receiving insulin therapy than their counterparts. Probiotics were also effective in lowering serum cholesterol over the short and long term. In conclusion, we found that probiotics may have a glucose-lowering effect in T2DM participants. The effect appeared to be stronger in participants with poorly controlled diabetes and those not on insulin therapy.