Nutrition Research

Perspective: Consideration of Values When Setting Priorities in Nutrition Research: Guidance for Transparency


Significance: Guidance for transparent consideration of values while setting nutrition research priorities is provided.

Nutrition research can guide interventions to tackle the burden of diet-related diseases. Setting priorities in nutrition research, however, requires the engagement of various stakeholders with diverse insights. Consideration of what matters most in research from a scientific, social, and ethical perspective is therefore not an automatic process. Systematic ways to explicitly define and consider relevant values are largely lacking. Here, we review existing nutrition research priority-setting exercises, analyze how values are reported, and provide guidance for transparent consideration of values while setting priorities in nutrition research. Of the 27 (n = 22 peer-reviewed manuscripts and 5 grey literature documents) studies reviewed, 40.7% used a combination of different methods, 59.3% described the represented stakeholders, and 49.1% reported on follow-up activities. All priority-setting exercises were led by research groups based in high-income countries. Via an iterative qualitative content analysis, reported values were identified (n = 22 manuscripts). Three clusters of values (i.e., those related to impact, feasibility, and accountability) were identified. These values were organized in a tool to help those involved in setting research priorities systematically consider and report values. The tool was finalized through an online consultation with 7 international stakeholders. The value-oriented tool for priority setting in nutrition research identifies and presents values that are already implicitly and explicitly represented in priority-setting exercises. It provides guidance to enable explicit deliberation on research priorities from an ethical perspective. In addition, it can serve as a reporting tool to document how value-laden choices are made during priority setting and help foster the accountability of stakeholders involved.

Dietary Patterns

Long-Term Consumption of a Mediterranean Diet Improves Postprandial Lipemia in Patients with Type 2 Diabetes: The Cordioprev Randomized Trial


Background: Patients with type 2 diabetes (T2D) have an elevated postprandial lipemia (PPL) that has been associated with increased cardiovascular risk. Objective: We aimed to analyze whether the long-term consumption of 2 healthy dietary patterns is associated with an improvement in PPL and remnant cholesterol (RC) concentrations in patients with T2D. Design: We selected patients from the Cordioprev study who underwent oral fat load tests (FLTs) at baseline and the 3-y follow-up (241 patients with and 316 patients without T2D). Subjects were randomly assigned to receive either a Mediterranean diet rich in olive oil (MedDiet; 35% of calories from fat [22% monounsaturated fatty acids (MUFAs)] and 50% from carbohydrates) or a low-fat (LF) diet (<30% fat [12-14% MUFAs] and 55% of calories from carbohydrates). Lipids were measured in serial bloods drawn at 0, 1, 2, 3, and 4 h after the FLT. Results: After 3 y of dietary intervention, patients with T2D showed an improvement in their PPL measured as postprandial
triglycerides (TGs) (P < 0.0001), TG area under the curve (AUC) (P = 0.001), and TG-rich lipoproteins (TRLs-TG; P = 0.001) compared with baseline. Subgroup analysis, based on the type of dietary intervention, showed that those T2D patients randomly assigned to the MedDiet presented a reduction in the TG AUC of 17.3% compared with baseline (P = 0.003). However, there were no differences for T2D patients randomly assigned to the LF diet (P > 0.05) or in patients without T2D (P > 0.05) regardless of the dietary intervention. In addition, the MedDiet induced a significant improvement in the RC AUC in patients with T2D (P = 0.04). However, there was no significant improvement in those following the LF diet. Conclusions: Our findings show that the long-term consumption of a MedDiet rich in olive oil improves PPL and RC concentrations mainly in patients with T2D. This trial was registered at clinicaltrials.gov as NCT00924937.

Dietary Intake Assessment

The Failure to Measure Dietary Intake Engendered a Fictional Discourse on Diet-Disease Relations
Article Link

Significance: Decades of flawed epidemiologic research may be potentiating public confusion regarding diet-disease relationships.

Controversies regarding the putative health effects of dietary sugar, salt, fat, and cholesterol are not driven by legitimate differences in scientific inference from valid evidence, but by a fictional discourse on diet-disease relations driven by decades of deeply flawed and demonstrably misleading epidemiologic research. Over the past 60 years, epidemiologists published tens of thousands of reports asserting that dietary intake was a major contributing factor to chronic non-communicable diseases despite the fact that epidemiologic methods do not measure dietary intake. In lieu of measuring actual dietary intake, epidemiologists collected millions of unverified verbal and textual reports of memories of perceptions of dietary intake. Given that actual dietary intake and reported memories of perceptions of intake are not in the same ontological category, epidemiologists committed the logical fallacy of “Misplaced Concreteness.” This error was exacerbated when the anecdotal (self-reported) data were impermissibly transformed (i.e., pseudo-quantified) into proxy-estimates of nutrient and caloric consumption via the assignment of “reference” values from databases of questionable validity and comprehensiveness. These errors were further compounded when statistical analyses of diet-disease relations were performed using the pseudo-quantified anecdotal data. These fatal measurement, analytic, and inferential flaws were obscured when epidemiologists failed to cite decades of research demonstrating that the proxy-estimates they created were often physiologically implausible (i.e., meaningless) and had no verifiable quantitative relation to the actual nutrient or caloric consumption of participants. In this critical analysis, we present substantial evidence to support our contention that current controversies and public confusion regarding diet-disease relations were generated by tens of thousands of deeply flawed, demonstrably misleading, and pseudoscientific epidemiologic reports. We challenge the field of nutrition to regain lost credibility by acknowledging the empirical and theoretical refutations of their memory-based methods and ensure that rigorous (objective) scientific methods are used to study the role of diet in chronic disease.

Nutrient Profile Models with Applications in Government-Led Nutrition Policies Aimed at Health Promotion and Noncommunicable Disease Prevention: A Systematic Review

Significance: A global resource that summarizes the key characteristics of nutrient profile models having applications in government-led nutrition policies.

Nutrient profile (NP) models, tools used to rate or evaluate the nutritional quality of foods, are increasingly used by government bodies worldwide to underpin nutrition-related policies. An up-to-date and accessible list of existing NP models is currently unavailable to support their adoption or adaptation in different jurisdictions. This study used a systematic approach to develop a global resource that summarizes key characteristics of NP models with applications in government-led nutrition policies. NP models were identified from an unpublished WHO catalog of NP models last updated in 2012 and from searches conducted in different databases of the peer-reviewed (n = 3; e.g., PubMed) and gray literature (n = 15). Included models had to meet the following inclusion criteria (selected) as of 22 December 2016: 1) developed or endorsed by governmental or intergovernmental organizations, 2) allow for the evaluation of individual food items, and 3) have publicly available nutritional criteria. A total of 387 potential NP models were identified, including n = 361 from the full-text assessment of >600 publications and n = 26 exclusively from the catalog. Seventy-eight models were included. Most (73%) were introduced within the past 10 y, and 44% represent adaptations of ≥1 previously built model. Models were primarily built for school food standards or guidelines (n = 27), food labeling (e.g., front-of-pack; n = 12), and restriction of the marketing of food products to children (n = 10). All models consider nutrients to limit, with sodium, saturated fatty acids, and total sugars being included most frequently; and 86% also consider ≥1 nutrient to encourage (e.g., fiber). No information on validity testing could be identified for 58% of the models. Given the proliferation of NP models worldwide, this new resource will be highly valuable for assisting health professionals and
policymakers in the selection of an appropriate model when the establishment of nutrition-related policies requires the use of nutrient profiling.

**Obesity**

No Consistent Evidence of a Disproportionately Low Resting Energy Expenditure in Long-Term Successful Weight-Loss Maintainers


**Significance:** Significance: Sustained weight loss may not always result in a substantial and disproportionately low resting energy expenditure.

**Background:** Evidence in humans is equivocal in regards to whether resting energy expenditure (REE) decreases to a greater extent than predicted for the loss of body mass with weight loss, and whether this disproportionate decrease in REE persists with weight-loss maintenance. Objectives: We aimed to: 1) determine if a lower-than-predicted REE is present in a sample of successful weight-loss maintainers (WLMs) and 2) determine if amount of weight loss or duration of weight-loss maintenance are correlated with a lower-than-predicted REE in WLMs.

**Design:** Participants (18-65 y old) were recruited in 3 groups: WLMs (maintaining ≥13.6 kg weight loss for ≥1 y, n = 34), normal-weight controls [NCs, body mass index (BMI; in kg/m2) similar to current BMI of WLMs, n = 35], and controls with overweight/obesity (OCs, BMI similar to pre-weight-loss maximum BMI of WLMs, n = 33). REE was measured (REEm) with indirect calorimetry. Predicted REE (REEp) was determined via 1) a best-fit linear regression developed with the use of REEm, age, sex, fat-free mass, and fat mass from our control groups and 2) three standard predictive equations.

**Results:** REEm in WLMs was accurately predicted by equations developed from NCs and OCs (±1%) and by 3 standard predictive equations (±3%). In WLMs, individual differences between REEm and REEp ranged from -257 to +163 kcal/d. A lower REEm compared with REEp was correlated with amount of weight lost (r = 0.36, P < 0.05) but was not correlated with duration of weight-loss maintenance (r = 0.04, P = 0.81). Conclusions: We found no consistent evidence of a significantly lower REE than predicted in a sample of long-term WLMs based on predictive equations developed from NCs and OCs as well as 3 standard predictive equations. Results suggest that sustained weight loss may not always result in a substantial, disproportionately low REE. This trial was registered at clinicaltrials.gov as NCT03422380.

Is Abdominal Obesity at Baseline Influencing Weight Changes in Observational Studies and During Weight Loss Interventions?


**Significance:** Significance: This study found no association between baseline abdominal obesity and short- and long-term weight change.

**Background:** Body fat distribution is a marker of metabolic health independent of body size. Visceral fat accumulation has been suggested to result from a decreased expandability of the subcutaneous fat depots. Furthermore, the visceral fat may be easier to mobilize than the peripheral fat. We examined whether differences in abdominal obesity at baseline influenced prospective body-weight changes. OBJECTIVE: In this study we examined whether body-fat distribution at baseline was associated with long-term and short-term weight changes. DESIGN: We included 3 observational studies (ntotal = 7271) with mean follow-up times of 5-9 y and two 8-10-wk weight loss intervention studies (ntotal = 1091). We examined the association between baseline waist circumference and weight changes in a substitution regression model, where body weight, height, and fat-free mass were fixed so that a difference in waist circumference would reflect a difference in body fat distribution alone. The results were summarized in meta-analyses. RESULTS: In the observational studies, we found no associations between baseline waist circumference and subsequent weight change in men (β: 0.03 kg; 95% CI: -0.01, 0.08 kg; P = 0.19), but a negligible inverse association in women (β: -0.05 kg; 95% CI: -0.08, -0.01 kg; P = 0.01). There was no association between baseline waist circumference and weight loss in the intervention studies (men: β: -0.05 kg; 95% CI: -0.13, 0.03 kg; P = 0.25; women: β: -0.00 kg; 95% CI: -0.03, 0.03 kg; P = 0.84). However, in all studies, the SDs of the weight change residuals were greater, the greater the waist circumference at baseline. This trend was statistically significant in women in most studies as well as in men in 1 of the studies. CONCLUSIONS: With narrow CIs in 3 observational studies and 2 weight loss interventions, we did not find any clinically or epidemiologically relevant association between baseline abdominal obesity and weight change. However, the present study suggests that a greater baseline abdominal obesity is a marker for greater weight fluctuations. The CCHS trial was registered at www.clinicaltrials.gov as
NCT02993172. The Health2006 trial was registered at www.clinicaltrials.gov as NCT00316667. The ORG study was conducted before trial registration was required. The NUGENOB trial was registered at www.isrctn.com as ISRCTN25867281. The DiOGenes trial was registered at www.clinicaltrials.gov as NCT00390637.

**Protein**

**Effects of Protein Supplementation on Lean Body Mass, Muscle Strength, and Physical Performance in Nonfrail Community-Dwelling Older Adults: A Systematic Review and Meta-Analysis**


**Significance:** Protein supplementation does not improve lean body mass, muscle strength or physical performance in nonfrail older adults.

**Background:** Increasing protein intake has been suggested as an effective strategy to ameliorate age-related loss of muscle mass and strength. Current reviews assessing the effect of protein supplementation are strongly influenced by the inclusion of studies with frail older adults. **Objectives:** We assessed the effect of protein supplementation on lean body mass, muscle strength, and physical performance in exclusively nonfrail community-dwelling older adults. Moreover, we assessed the superior effects of protein supplementation during concomitant resistance exercise training on muscle characteristics. **Design:** A systematic literature search was conducted on PubMed, Embase, and Web of Science up to 15 May 2018. We included randomized controlled trials that assessed the effect of protein supplementation on lean body mass, muscle thigh cross-sectional area, muscle strength, gait speed, and chair-rise ability and performed random-effects meta-analyses. **Results:** Data from 36 studies with 1682 participants showed no significant effects of protein supplementation on changes in lean body mass (standardized mean difference (SMD): 0.11; 95% CI: -0.06, 0.28), handgrip strength (SMD: 0.58; 95% CI: -0.08, 1.24), lower extremity muscle strength (SMD: 0.03; 95% CI: -0.20, 0.27), gait speed (SMD: 0.41; 95% CI: -0.04, 0.85), or chair-rise ability (SMD: 0.10; 95% CI: -0.08, 0.28) compared with a control condition in nonfrail community-dwelling older adults. Moreover, no superior effects of protein supplementation were found during concomitant resistance exercise training on muscle characteristics. **Conclusions:** Protein supplementation in nonfrail community-dwelling older adults does not lead to increases in lean body mass, muscle cross-sectional area, muscle strength, or physical performance compared with control conditions; nor does it exert superior effects when added to resistance exercise training. Habitual protein intakes of most study participants were already sufficient, and protein interventions differed in terms of type of protein, amount, and timing. Future research should clarify what specific protein supplementation protocol is beneficial for nonfrail community-dwelling older adults with low habitual protein intake.

**Bioactives**

**Assessing the Respective Contributions of Dietary Flavanol Monomers and Procyanidins in Mediating Cardiovascular Effects in Humans: Randomized, Controlled, Double-Masked Intervention Trial**


**Significance:** Flavanol monomers and circulating SREMs are primarily responsible for cocoa flavanol-related improvements in vascular function.

**Background:** Flavanols are an important class of food bioactives that can improve vascular function even in healthy subjects. Cocoa flavanols (CFs) are composed principally of the monomer (-)-epicatechin (~20%), with a degree of polymerisation (DP) of 1 (DP1), and oligomeric procyanidins (~80%, DP2-10). **Objective:** Our objective was to investigate the relative contribution of procyanidins and (-)-epicatechin to CF intake-related improvements in vascular function in healthy volunteers. **Design:** In a randomized, controlled, double-masked, parallel-group dietary intervention trial, 45 healthy men (aged 18-35 y) consumed the following once daily for 1 mo: 1) a DP1-10 cocoa extract containing 130 mg (-)-epicatechin and 560 mg procyanidins, 2) a DP2-10 cocoa extract containing 20 mg (-)-epicatechin and 540 mg procyanidins, or 3) a control capsule, which was flavanol-free but had identical micro- and macronutrient composition. **Results:** Consumption of DP1-10, but not of either DP2-10 or the control capsule, significantly increased flow-mediated vasodilation (primary endpoint) and the concentration of structurally related (-)-epicatechin metabolites (SREMs) in the circulatory system while decreasing pulse wave velocity and blood pressure. Total cholesterol significantly decreased after daily intake of both DP1-10 and DP2-10 as compared with the control. **Conclusions:** CF-related improvements in vascular function are predominantly related to the intake of flavanol monomers and circulating
SREMs in healthy humans but not to the more abundant procyanidins and gut microbiome-derived CF catabolites. Reduction in total cholesterol was linked to consumption of procyanidins but not necessarily to that of (-)-epicatechin. This trial was registered at clinicaltrials.gov as NCT02728466.

Lycopene and Metabolic Syndrome: A Systematic Review of the Literature

Significance: This is the first systematic review to demonstrate a favorable effect of lycopene consumption on components of the metabolic syndrome.

Cardiometabolic risk factors increase the likelihood of cardiovascular disease development by 2-fold. Lycopene, a potent lipophilic antioxidant, may be able to mediate oxidative stress, a mechanism underpinning metabolic syndrome (MetS) and its risk factors. This is, to our knowledge, the first systematic review of the literature with the purpose of investigating the relation between circulating lycopene or dietary intake of lycopene and MetS as well as its risk factors. The review was conducted using PubMed and EBSCOhost databases with the search terms “lycopene” and “metabolic syndrome.” Inclusion criteria included human studies published in English in a scholarly, peer-reviewed journal and evaluation of lycopene in relation to ≥3 of the 5 MetS risk factors as defined by the National Cholesterol Education Program’s Adult Treatment Panel III (ATP III) report. The process identified 11 studies, including 8 cross-sectional and 3 intervention studies. Cross-sectional studies were grouped into 3 categories, with several studies falling into >1 category, based on results reporting associations of lycopene with the prevalence and outcomes of MetS (5 studies), presence of ATP III risk factors (4 studies), and variables mediating lycopene’s influence on MetS risk (3 studies). All studies in each category reported significant protective associations. Of the 3 intervention studies, all reported significant protective effects from a lycopene-rich beverage, despite varying doses and durations of intake. Although a protective relation between lycopene and MetS was generally supported, different MetS components appeared to be influenced by lycopene rather than demonstrating consistent improvement in a single component. Thus, additional research is needed to elucidate the mechanistic effects of lycopene on MetS, as well as to determine evidence-based recommendations concerning dose-duration effects of lycopene and MetS risk reduction. In conclusion, the evidence of lycopene’s benefit exists such that lycopene status or lycopene consumption may be associated with favorable alterations to the components of MetS.

Sodium

Mineral Intake Ratios Are a Weak but Significant Factor in Blood Pressure Variability in US Adults

Significance: Lower sodium:potassium intake ratios may help protect against hypertension in US adults.

Background: Hypertension contributes substantially to chronic disease and mortality. Mineral intakes can modify blood pressure. Objective: Individual minerals and their intake ratios in US adults and their association with blood pressure were examined. Methods: Regression models were used to examine the associations of sodium, potassium, and calcium intakes and their ratios from food and supplements with blood pressure in 8777 US adults without impaired renal function from the 2011-2014 NHANES. We evaluated men (n = 4395) and women (n = 4382) separately. Models for predicting blood pressure were developed using age, blood pressure medication, race, body mass index (BMI), and smoking as explanatory variables. Results: Few adults met the recommended intake ratios for sodium:potassium (1.2% and 1.5%), sodium:calcium (12.8% and 17.67%), and sodium:magnesium (13.7% and 7.3%) for men and women, respectively. Approximately half of adults (55.2% of men and 54.8% of women) met calcium:magnesium intake ratio recommendations. In our regression models, the factors that explained the largest amount of variability in blood pressure were age, blood pressure medication, race/ethnicity, BMI, and smoking status. Together, these factors explained 31% and 15% of the variability in systolic blood pressure in women and men, respectively. The sodium:potassium (men and women), sodium:magnesium (women), and sodium:calcium (men) intake ratios were positively associated with systolic blood pressure, whereas calcium intake was inversely associated with systolic blood pressure in men only. When mineral intake ratios were added individually to our regression models, they improved the percentage of variability in blood pressure explained by the model by 0.13-0.21%. Conclusions: Strategies to lower blood pressure are needed. Lower sodium:potassium intake ratios provide a small benefit for protection against hypertension in US adults.

Effect of Monitoring Salt Concentration of Home-Prepared Dishes and Using Low-Sodium Seasonings on Sodium Intake Reduction

Significance: Monitoring salt concentrations of home-prepared dishes may have a stronger salt-reducing effect than using
low-sodium seasonings.

Background/Objectives: Objective methods such as the monitoring of salt concentrations in home-prepared dishes may be effective in reducing salt intake. We investigated the effect of monitoring the salt concentration of home-prepared dishes (Monitoring) on salt reduction and change in taste threshold, and the effect of the simultaneous use of low-sodium seasonings (Seasoning) to compare the effect of Monitoring with the conventional method. Subjects/Methods: We conducted a double-blind randomized controlled study using a 2 × 2 factorial design with two interventions. A total of 50 participants (40-75 years-old) were recruited among residents of Niigata Prefecture, a high sodium-consuming population in Japan, then randomly allocated to four groups. After excluding participants with incomplete urine collection, change in salt intake was evaluated using 24-hour urinary excretion as a surrogate of intake for 43 participants. Change in taste threshold was evaluated in 48 participants after excluding those with incomplete threshold measurement. Results: The Monitoring intervention group showed a significant decrease in sodium intake (-777 mg/24 h), whereas the decrease in the Seasoning intervention group was not significant (-413 mg/24 h). Sodium intake did not statistically differ between the intervention and control groups (-1011 mg/24 h and -283 mg/24 h for Monitoring and Seasoning, respectively). The changes in taste threshold measurement were very small and did not markedly differ between groups. Conclusions: Monitoring the salt concentration of dishes had a potentially stronger salt-reducing effect than the use of low-sodium seasonings, a conventional method. Confirmation requires additional study with a larger sample size.

Comparison of Label and Laboratory Sodium Values in Popular Sodium-Contributing Foods in the United States


Significance: Underdeclaration of sodium label values in US foods is limited.

Background: Nutrition labels are important tools for consumers and for supporting public health strategies. Recent, published comparison of label and laboratory sodium values for US foods, and differences by brand type (national or private-label) or source (store or restaurant [fast-food and sit-down]) is unavailable. Objective: The objective was to compare label and laboratory values for sodium and related nutrients (ie, total sugars, total fat, and saturated fat) in popular, sodium-contributing foods, and examine whether there are differences by brand type, and source. Design: During 2010 to 2014, the Nutrient Data Laboratory of the US Department of Agriculture collected 3,432 samples nationwide of 125 foods, combined one or more samples of the same food (henceforth referred to as composites), and chemically analyzed them. For this comparative post hoc analysis, the Nutrient Data Laboratory linked laboratory values for 1,390 composites (consisting of one or more samples of the same food) of 114 foods to corresponding label or website (restaurant) nutrient values. Main Outcome Measures: Label and laboratory values and their ratio for each composite, for each of the four nutrients (sodium, total fat, total sugars, and saturated fat). Statistical Analyses Performed: Nutrient Data Laboratory analysis determined the ratio of laboratory to label value for each composite, and categorized them into six groups: ≥141%, 121% to 140%, 101% to 120%, 81% to 100%, 61% to 80%, and ≤60%. For sodium, the Nutrient Data Laboratory analysis determined the distribution of the ratios by food, food category, brand type, and source. Results: For sodium, 5% of the composites had ratios of laboratory to label values >120% and 14% had ratios ≤80%. Twenty-two percent of private-label brand composites had ratios ≤80%, compared with 12% of national brands. Only 3% of store composites had ratios >120% compared with 11% of restaurant composites. Ratios ≤80% were more prevalent among sit-down restaurants (37%) compared with fast-food restaurants (9%). Conclusions: This study shows that a majority of label and laboratory values sampled agree and underdeclaration of label values is limited. However, there is some disagreement. Periodic monitoring of the nutrient content of foods through laboratory analyses establishes validity of the food labels and helps identify foods and food categories where the label and laboratory values do not compare well, and hence may need laboratory analyses to support accuracy of food composition data.

Lipids

Differential Effects of Medium- and Long-Chain Saturated Fatty Acids on Blood Lipid Profile: A Systematic Review and Meta-Analysis

**Significance:** This systematic review and meta-analysis found differential effects of medium- and long-chain saturated fatty acids on HDL cholesterol concentrations.

**Background:** Medium-chain saturated fatty acids (MCFAs) may affect circulating lipids and lipoproteins differently than long-chain saturated fatty acids (LCSFAs), but the results from human intervention trials have been equivocal. Objective: The aim of this study was to determine whether MCFAs and LCSFAs have differential impacts on blood lipids and lipoproteins. Design: Five databases were searched (EMBASE, MEDLINE, CINAHL, Cochrane, and Scopus) until April 2018, and published clinical trials investigating the differential effects of dietary MCFAs and LCSFAs on blood lipids were included. Searches were limited to the English language and to studies with adults aged >18 y. Where possible, studies were pooled for meta-analysis using RevMan 5.2. The principle summary measure was the mean difference between groups calculated using the random-effects model. Results: Eleven eligible crossover and 1 parallel trial were identified with a total of 299 participants [weighted mean ± SD age: 38 ± 3 y; weighted mean ± SD body mass index (kg/m2): 24 ± 2]. All studies were pooled for the meta-analysis. Diets enriched with MCFAs led to significantly higher high-density lipoprotein (HDL) cholesterol concentrations than diets enriched with LCSFAs (0.11 mmol/L; 95% CI: 0.07, 0.15 mmol/L) with no effect on triglyceride, low-density lipoprotein (LDL) cholesterol, and total cholesterol concentrations. Consumption of diets rich in MCFAs significantly increased apolipoprotein A-I (apoA-I) concentrations compared with diets rich in LCSFAs (0.08 g/L; 95% CI: 0.02, 0.14 g/L). There was no evidence of statistical heterogeneity for HDL cholesterol, apoA-I, and triglyceride concentrations; however, significant heterogeneity was observed for the total cholesterol (I² = 49%) and LDL cholesterol analysis (I² = 58%). Conclusion: The findings of this research demonstrate a differential effect of MCFAs and LCSFAs on HDL cholesterol concentrations. Further investigations are warranted to elucidate the mechanism by which the lipid profile is altered. This trial was registered at www.crd.york.ac.uk/PROSPERO as CRD42017078277.

**Progress and Perspectives in Plant Sterol and Plant Stanol Research**

**Significance:** This review summarizes the health effects of plant sterols and stanols, and identifies research gaps related to endpoints of cardiovascular disease.

Current evidence indicates that foods with added plant sterols or stanols can lower serum levels of low-density lipoprotein cholesterol. This review summarizes the recent findings and deliberations of 31 experts in the field who participated in a scientific meeting in Winnipeg, Canada, on the health effects of plant sterols and stanols. Participants discussed issues including, but not limited to, the health benefits of plant sterols and stanols beyond cholesterol lowering, the role of plant sterols and stanols as adjuncts to diet and drugs, and the challenges involved in measuring plant sterols and stanols in biological samples. Variations in interindividual responses to plant sterols and stanols, as well as the personalization of lipid-lowering therapies, were addressed. Finally, the clinical aspects and treatment of sitosterolemia were reviewed. Although plant sterols and stanols continue to offer an efficacious and convenient dietary approach to cholesterol management, long-term clinical trials investigating the endpoints of cardiovascular disease are still lacking.

**Microbiome**

**Importance of Gut Microbiota in Obesity**

**Significance:** The modulators and health effects of the gut microbiome are discussed within the context of obesity.

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 has 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 can not be digested by the host, increase monosaccharides 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.
Microbial Enterotypes in Personalized Nutrition and Obesity Management


Significance: Stratification of individuals by microbial enterotype may be useful in predicting responses to obesity-management interventions.

Human gut microbiota has been suggested to play an important role in nutrition and obesity. However, formulating meaningful and clinically relevant dietary advice based on knowledge about gut microbiota remains a key challenge. A number of recent studies have found evidence that stratification of individuals according to 2 microbial enterotypes (dominance of either Prevotella or Bacteroides) may be useful in predicting responses to diets and drugs. Here, we review enterotypes in a nutritional context and discuss how enterotype stratification may be used in personalized nutrition in obesity management. Enterotypes are characterized by distinct digestive functions with preference for specific dietary substrate, resulting in short-chain fatty acids that may influence energy balance in the host. Consequently, the enterotype potentially affects the individual’s ability to lose weight when following a specific diet. In short, a high-fiber diet seems to optimize weight loss among Prevotella-enterotype subjects but not among Bacteroides-enterotype subjects. In contrast, increasing bifidobacteria in the gut among Bacteroides-enterotype subjects improves metabolic parameters, suggesting that this approach can be used as an alternative weight loss strategy. Thus, enterotypes, as a pretreatment gut microbiota biomarker, have the potential to become an important tool in personalized nutrition and obesity management, although further interventions assessing their applicability are warranted.

Personalized Nutrition

Diet Quality and Genetic Association with Body Mass Index: Results from 3 Observational Studies


Significance: Diet quality may modulate genetic predisposition to obesity.

Background: It is unknown whether dietary quality modifies genetic association with body mass index (BMI). OBJECTIVE: This study examined whether dietary quality modifies genetic association with BMI. Design: We calculated 3 diet quality scores including the Alternative Healthy Eating Index 2010 (AHEI-2010), the Alternative Mediterranean Diet score (AMED), and the Dietary Approach to Stop Hypertension (DASH) diet score. We examined the interactions of a genetic risk score (GRS) based on 97 BMI-associated variants with the 3 diet quality scores on BMI in 30,904 participants from 3 large cohorts. Results: We found significant interactions between total GRS and all 3 diet scores on BMI assessed after 2-3 y, with an attenuated genetic effect observed in individuals with healthier diets (AHEI: P-interaction = 0.003; AMED: P = 0.001; DASH: P = 0.004). For example, the difference in BMI (kg/m²) per 10-unit increment of the GRS was smaller among participants in the highest tertile of AHEI score compared with those in the lowest tertile (0.84; 95% CI: 0.72, 0.96 compared with 1.14; 95% CI: 0.99, 1.29). Results were consistent across the 3 cohorts with no significant heterogeneity. The interactions with diet scores on BMI appeared more significant for central nervous system GRSs (P < 0.01 for 3 diet scores) than for non-central nervous system GRSs (P > 0.05 for 3 diet scores). Conclusions: A higher diet quality attenuated genetic predisposition to obesity. These findings underscore the importance of maintaining a healthful diet for the prevention of obesity, particularly for those individuals with a strong genetic predisposition to obesity. This trial was registered with the Clinical Trial Registry as NCT03577639.