Dietary Patterns

The Weight Optimization Revamping Lifestyle Using the Dietary Guidelines (WORLD) Study: Sustained Weight Loss over 12 Months

Significance: Despite no difference in fat intake between the experimental groups, behavioral theory-based nutrition education resulted in weight loss and improved diet quality that was sustained for over one year in premenopausal women with overweight or obesity.

Objective: This study aimed to compare two energy-restricted, nutrient-dense diets at the upper or lower ends of the dietary fat recommendation range (lower fat [20% energy from fat] versus moderate fat [35%]) on weight loss using behavioral theory-based nutrition education. Methods: A total of 101 premenopausal women with overweight or obesity were randomized to an energy-restricted lower-fat or moderate-fat diet for 1 year. Interventions included 28 behavioral theory-based nutrition education sessions plus weekly exercise sessions. Results: Both treatment groups experienced weight loss (-5.0 kg for lower fat and -4.3 kg for moderate fat; P < 0.0001), but there was no difference in weight loss or fat intake between groups. Total and low-density lipoprotein cholesterol decreased (-3.4 mg/dL and -3.8 mg/dL; P < 0.05), and high-density lipoprotein cholesterol increased (1.9 mg/dL; P < 0.05) in both groups at 12 months. Diet quality, assessed by the Healthy Eating Index, increased significantly at 4 months versus baseline (70.8 [0.9] vs. 77.8 [1.0]) and was maintained through 12 months. Higher Healthy Eating Index scores were associated with greater weight loss at 4 months (r = -0.2; P < 0.05). Conclusions: In the context of a well-resourced, free-living weight-loss intervention, total fat intake did not change; however, theory-based nutrition education underpinned by food-based recommendations resulted in caloric deficits, improvements in diet quality, and weight loss that was sustained for 1 year.

Protein

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

Significance: In this systematic review and meta-analysis, protein intakes greater than the RDA were found to benefit changes in lean mass during energy restriction and after resistance training relative to consuming the RDA.

Under stressful conditions such as energy restriction (ER) and physical activity, the RDA for protein of 0.8 g · kg⁻¹ · d⁻¹ may no longer be an appropriate recommendation. Under catabolic or anabolic conditions, higher protein intakes are proposed to attenuate the loss or increase the gain of whole-body lean mass, respectively. No known published meta-analysis compares protein intakes greater than the RDA with intakes at the RDA. Therefore, we conducted a systematic review and meta-analysis to assess the effects of protein intakes greater than the RDA, compared with at the RDA, on changes in whole-body lean mass. Three researchers independently screened 1520 articles published through August 2018 using the PubMed, Scopus, CINAHL, and Cochrane databases, with additional articles identified in published systematic review articles. Randomized, controlled, parallel studies ≥6 wk long with apparently healthy adults (≥19 y) were eligible for inclusion. Data from 18 studies resulting in 22 comparisons of lean mass.
Nutrition Briefs

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The possible activation of sirtuins by dietary fat manipulation has been related to chronic disease. The best-characterized mechanism highlights oleic acid as a natural activator of SIRT1.

**Conclusion:**

Evaluated were as follows:

- Unadjusted self-reported protein intake from the FFQ (mean = 66.7 g) correlated weakly (r = 0.31) with biomarker protein (mean = 74.9 g).
- DLW-TEE-corrected self-reported protein intake (mean = 90.7 g) had the strongest correlation with biomarker protein (r = 0.47).
- Other energy corrections yielded lower, but still significant correlations: EER, r = 0.44 (mean = 92.1 g); WHI-NBS-TEE, r = 0.37 (mean = 90.4 g); Goldberg cutoff, r = 0.36 (mean = 88.4 g); and residual method, r = 0.35 (mean = 66.7 g).

**Conclusions:** Our data indicate that proportional correction of reported protein intake using a measure of energy requirement from DLW-TEE or IOM-EER performed modestly better than other methods in this cohort. These energy adjustments, however, yielded corrected protein exceeding the biomarker protein, indicating that energy adjustment alone does not eliminate all self-reported protein reporting bias.

**Lipids**

**Dietary Fatty Acids as Nutritional Modulators of Sirtuins: A Systematic Review**


**Context:** The sirtuins (SIRT1 to SIRT7) constitute a family of highly conserved nicotinamide adenine dinucleotide–dependent proteins. When activated, sirtuins control essential cellular processes to maintain metabolic homeostasis, while lack of expression of sirtuins has been related to chronic disease. **Objective:** The aim of this systematic review is to analyze the role of fat consumption as a modulator of human sirtuins. **Data Sources:** This review was conducted according to PRISMA guidelines. Studies were identified by searches of the electronic databases PubMed/MEDLINE, Scopus, and Web of Science. **Study Selection:** Randomized clinical trials assessing the effect of fatty acid consumption on sirtuin mRNA expression, sirtuin protein expression, or sirtuin protein activity were eligible for inclusion. **Data Extraction:** Two authors screened and determined the quality of the studies; disagreements were resolved by the third author. All authors compared the compiled data. **Results:** Seven clinical studies with 3 different types of interventions involving healthy and unhealthy participants were selected. Only SIRT1 and SIRT3 were evaluated. Overall, the evidence from clinical studies to date is insufficient to understand how lipid consumption modulates sirtuins in humans. The best-characterized mechanism highlights oleic acid as a natural activator of SIRT1. **Conclusion:** These results draw attention to a new field of interest in nutrition science. The possible activation of sirtuins by dietary fat manipulation may represent an important nutritional strategy for management of chronic and metabolic disease.
Carbohydrates

Dietary Fiber Intake and Total and Cause-Specific Mortality: The Japan Public Health Center-Based Prospective Study

Significance: Fiber consumption, mainly from fruits, vegetables and beans, was associated with lower all-cause mortality in a study of more than 92,000 Japanese adults.

Background: An inverse association has been shown between dietary fiber intake and several noncommunicable diseases. However, evidence of this effect remains unclear in the Asian population. Objective: We examined the association between dietary fiber intake and all-cause and cause-specific mortality, as well as the association between fiber intake from dietary sources and all-cause mortality. Methods: We conducted a large-scale population-based cohort study (Japan Public Health Center-based prospective study). A validated questionnaire with 138 food items was completed by 92,924 participants (42,754 men and 50,170 women) aged 45–74 y. Dietary fiber intake was calculated and divided into quintiles. HR and 95% CI of total and cause-specific mortality were reported. Results: During the mean follow-up of 16.8 y, 19,400 deaths were identified. In multivariable adjusted models, total, soluble, and insoluble fiber intakes were inversely associated with all-cause mortality. The HRs of total mortality in the highest quintile of total fiber intake compared with the lowest quintile were 0.77 (95% CI: 0.72, 0.82; P_{trend}<0.0001) in men and 0.82 (95% CI: 0.76, 0.89; P_{trend}<0.0001) in women. Increased quintiles of dietary fiber intake were significantly associated with decreased mortality due to total cardiovascular disease (CVD), respiratory disease, and injury in both men and women, whereas dietary fiber intake was inversely associated with cancer mortality in men but not women. Fiber from fruits, beans, and vegetables, but not from cereals, was inversely associated with total mortality. Conclusion: In this large-scale prospective study with a long follow-up period, dietary fiber was inversely associated with all-cause mortality. Since intakes of dietary fiber, mainly from fruits, vegetables, and beans were associated with lower all-cause mortality, these food sources may be good options for people aiming to consume more fiber.

Energy Requirement Is Higher During Weight-Loss Maintenance in Adults Consuming a Low- Compared with High-Carbohydrate Diet

Significance: Energy requirement was higher on a low- versus high-carbohydrate diet during weight-loss maintenance in adults, consistent with the carbohydrate-insulin model.

Background: Longer-term feeding studies suggest that a low-carbohydrate diet increases energy expenditure, consistent with the carbohydrate-insulin model of obesity. However, the validity of methodology utilized in these studies, involving doubly labeled water (DLW), has been questioned. Objective: The aim of this study was to determine whether dietary energy requirement for weight-loss maintenance is higher on a low- compared with high-carbohydrate diet. Methods: The study reports secondary outcomes from a feeding study in which the primary outcome was total energy expenditure (TEE). After attaining a mean Run-in weight loss of 10.5%, 164 adults (BMI ≥25 kg/m²; 70.1% women) were randomly assigned to Low-Carbohydrate (percentage of total energy from carbohydrate, fat, protein: 20/60/20), Moderate-Carbohydrate (40/40/20), or High-Carbohydrate (60/20/20) Test diets for 20 wk. Calorie content was adjusted to maintain individual body weight within ± 2 kg of the postweight-loss value. In analyses by intention-to-treat (ITT, completers, n = 148) and per protocol (PP, completers also achieving weight-loss maintenance, n = 110), we compared the estimated energy requirement (EER) from 10 to 20 wk of the Test diets using ANCOVA. Results: Mean EER was higher in the Low- versus High-Carbohydrate group in models of varying covariate structure involving ITT [ranging from 181 (95% CI: 8–353) to 246 (64–427) kcal/d; P ≤0.04] and PP [ranging from 245 (43–446) to 323 (122–525) kcal/d; P ≤0.02]. This difference remained significant in sensitivity analyses accounting for change in adiposity and possible nonadherence. Conclusions: Energy requirement was higher on a low- versus high-carbohydrate diet during weight-loss maintenance in adults, commensurate with TEE. These data are consistent with the carbohydrate-insulin model and lend qualified support for the validity of the DLW method with diets varying in macronutrient composition.
Testing the Carbohydrate-Insulin Model of Obesity in a 5-Month Feeding Study: The Perils of Post-Hoc Participant Exclusions

Significance: Following a challenge to the study’s validity in a post-hoc analysis, a reanalysis controlling for confounding bias confirmed that total energy expenditure was greater on a low- versus high-carbohydrate diet.

A large feeding study reported that total energy expenditure (TEE) was greater on a low- versus high-carbohydrate diet, supporting the carbohydrate-insulin model of obesity. Recently, the validity of this finding was challenged in a post-hoc analysis excluding participants with putative non-adherence to the study diets. Here, we show why that analysis, based on a post-randomization variable linked to the outcome, introduced severe confounding bias. With control for confounding, the diet effect on TEE remained strong in a reanalysis. Together with sensitivity analyses demonstrating robustness to plausible levels of non-adherence, these data provide experimental support for a potentially novel metabolic effect of macronutrients that might inform the design of more effective obesity treatment.

Low-Calorie Sweeteners

Consumption of Diet Soda Sweetened with Sucralose and Acesulfame-Potassium Alters Inflammatory Transcriptome Pathways in Females with Overweight and Obesity

Significance: Sucralose and acesulfame-potassium alter inflammatory transcriptomic pathways in subcutaneous adipose tissue but do not alter circulating biomarkers of inflammation.

Scope: Low-calorie sweetener (LCS) consumption is associated with metabolic disease in observational studies. However, physiologic mechanisms underlying LCS-induced metabolic impairments in humans are unclear. This study is aimed at identifying molecular pathways in adipose impacted by LCSs. Methods and Results: Seven females with overweight or obesity, who did not report LCS use, consumed 12 ounces of diet soda containing sucralose and acesulfame-potassium (Ace-K) three times daily for 8 weeks. A subcutaneous adipose biopsy from the left abdomen and a fasting blood sample were collected at baseline and post-intervention. Global gene expression were assessed using RNA-sequencing followed by functional pathway analysis. No differences in circulating metabolic or inflammatory biomarkers were observed. However, ANOVA detected 828 differentially expressed annotated genes after diet soda consumption (p < 0.05), including transcripts for inflammatory cytokines. Fifty-eight of 140 canonical pathways represented in pathway analyses regulated inflammation, and several key upstream regulators of inflammation (e.g., TNF-alpha) were also represented. Conclusion: Consumption of diet soda with sucralose and Ace-K alters inflammatory transcriptomic pathways (e.g., NF-κB signaling) in subcutaneous adipose tissue but does not significantly alter circulating biomarkers. Findings highlight the need to examine molecular and metabolic effects of LCS exposure in a larger randomized control trial for a longer duration.

Bioactives

Carotenoid Intake and Circulating Carotenoids Are Inversely Associated with the Risk of Bladder Cancer: A Dose-Response Meta-analysis

Significance: Bladder cancer risk decreased by 42% for every 1 mg increase in daily dietary β-cryptoxanthin intake in a meta-analysis of over 516,000 adults.

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

Sodium

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

Significance: There is marked variation in discretionary salt use around the world, with an inverse correlation between discretionary salt intake and per capita GDP.

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

Dietary Sodium Intake and Health Indicators: A Systematic Review of Published Literature between January 2015 and December 2019

Significance: Standardization of methods used to measure sodium intake is needed to summarize evidence from assessments on sodium and health outcomes.

As the science surrounding population sodium reduction evolves, monitoring and evaluating new studies on intake and health can help increase our understanding of the associated benefits and risks. Here we describe a systematic review of recent studies on sodium intake and health, examine the risk of bias (ROB) of selected studies, and provide direction for future research. Seven online databases were searched monthly from January 2015 to December 2019. We selected human studies that met specified population, intervention, comparison, outcome, time, setting/study design (PICOTS) criteria and abstracted attributes related to the study population, design, intervention, exposure, and outcomes, and evaluated ROB for the subset of studies on sodium intake and cardiovascular disease risks or indicators. Of 41,601 abstracts reviewed, 231 studies were identified that met the PICOTS criteria and ROB was assessed for 54 studies. One hundred and fifty-seven (68%) studies were observational and 161 (70%) focused on the general population. Five types of sodium interventions and a variety of urinary and dietary measurement methods were used to establish and quantify sodium intake. Five observational studies used multiple 24-h urine collections to assess sodium intake. Evidence mainly focused on cardiovascular-related indicators (48%) but encompassed an assortment of outcomes. Studies varied in ROB domains and 87% of studies evaluated were missing information on ≥1 domains. Two or more studies on each of 12 outcomes (e.g., cognition) not previously included in systematic reviews and 9 new studies at low ROB suggest the need for ongoing or updated systematic reviews of evidence on sodium intake and health. Summarizing evidence from assessments on sodium and health outcomes was limited by the various methods used to measure sodium intake and outcomes, as well as lack of details related to study design and conduct. In line with research recommendations identified by the National Academies of Science, future research is needed to identify and standardize methods for measuring sodium intake.
Gut Microbiome

Adaptation of the Gut Microbiota to Modern Dietary Sugars and Sweeteners

Significance: This review suggests novel approaches to assess the consequences of metabolic, ecological and genetic profile changes on host–microbe interactions to determine the safety of novel sugars and sweeteners.

The consumption of sugar has become central to the Western diet. Cost and health concerns associated with sucrose spurred the development and consumption of other sugars and sweeteners, with the average American consuming 10 times more sugar than 100 y ago. In this review, we discuss how gut microbes are affected by changes in the consumption of sugars and other sweeteners through transcriptional, abundance, and genetic adaptations. We propose that these adaptations result in microbes taking on different metabolic, ecological, and genetic profiles along the intestinal tract. We suggest novel approaches to assess the consequences of these changes on host–microbe interactions to determine the safety of novel sugars and sweeteners.