Nutrition Briefs
North America    May 2019

Dietary Patterns

Ultra-Processed Diets Cause Excess Calorie Intake and Weight Gain: An Inpatient Randomized Controlled Trial of Ad Libitum Food Intake


Significance: This randomized controlled trial found that consumption of a diet consisting of ultra-processed foods leads to increased energy intake and weight gain.

We investigated whether ultra-processed foods affect energy intake in 20 weight-stable adults, aged (mean ± SE) 31.2 ± 1.6 years and BMI = 27 ± 1.5 kg/m². Subjects were admitted to the NIH Clinical Center and randomized to receive either ultra-processed or unprocessed diets for 2 weeks immediately followed by the alternate diet for 2 weeks. Meals were designed to be matched for presented calories, energy density, macronutrients, sugar, sodium, and fiber. Subjects were instructed to consume as much or as little as desired. Energy intake was greater during the ultra-processed diet (508 ± 106 kcal/day; p = 0.0001), with increased consumption of carbohydrate (280 ± 54 kcal/day; p < 0.0001) and fat (230 ± 53 kcal/day; p = 0.0004), but not protein (2 ± 12 kcal/day; p = 0.85). Weight changes were highly correlated with energy intake (r = 0.8, p < 0.0001), with participants gaining 0.9 ± 0.3 kg (p = 0.009) during the ultra-processed diet and losing 0.9 ± 0.3 kg (p = 0.007) during the unprocessed diet. Limiting consumption of ultra-processed foods may be an effective strategy for obesity prevention and treatment.

Dietary Intake Recommendations

Milestones in DRI Development: What Does the Future Hold?


Significance: A historical view of dietary guidance in the United States and considerations for adapting the DRI model to meet future needs are discussed.

The state of nutritional health in the United States in the early part of the twentieth century was very different from today. Nutrient deficiencies and dental caries were prevalent health concerns for many Americans. In 1940, the US National Defense Advisory Commission asked the National Academy of Sciences for help in studying problems of nutrition in the United States. The outcome was issuance of the first RDAs. The goal of the RDAs was to recommend “…allowances sufficiently liberal to be suitable for maintenance of good nutritional status.” In the subsequent decades, a very different nutritional health challenge began to emerge for an increasing proportion of the population, that of overweight and obesity and risk of diet-related chronic disease. In part, as a response to this challenge, the RDA process was revised and the Dietary Reference Intakes (DRIs) were developed. The DRIs are a set of reference values that, when adhered to, predict a low probability of nutrient inadequacy or excessive intake. Recently, new DRI guidelines were proposed to define reference points for nutrient and food component intakes that influence risk of chronic disease. Developing DRIs for chronic disease endpoints presents unique challenges, notably, chronic diseases are multifactorial in nature and not directly nutrient-specific; the body of evidence supporting nutrients and other food

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substances as modifiers of risk of chronic disease is generally limited; and there is a lack of consistency in findings across study types. In addition, the latency of dietary exposures and chronic disease outcomes makes it difficult to demonstrate causality. Adapting the DRI model to meet the needs of the general population in the current context suggests a need to redefine the boundaries that describe the health of the population and to re-examine how indicators of chronic disease can be integrated effectively into the DRI process.

**Protein**

**Dietary Protein and Changes in Biomarkers of Inflammation and Oxidative Stress in the Framingham Heart Study Offspring Cohort**


**Significance:** The associations between dietary protein and changes in biomarkers of inflammation and oxidative stress over the long term in a community-dwelling population are presented.

**Background:** Chronic inflammation is thought to be a major characteristic of aging, which may increase need for substrates, specifically protein, to support anti-inflammatory processes. **Objectives:** The aim of this study was to assess associations between dietary protein and changes in biomarkers of inflammation and oxidative stress over the long term in a community-dwelling population. **Methods:** In 2061 participants of the Framingham Heart Study Offspring cohort who attended exams 7 (1998–2001; mean ± SD age 60.0 ± 8.8 y, 56% female) and 8 (2005–2008), total, animal, and plant protein intakes were assessed by food-frequency questionnaire at each exam, energy adjusted, and averaged. We defined an inflammation and oxidative stress score as the sum of rank-normalized values of 9 circulating biomarkers (C-reactive protein, osteoprotegerin, P-selectin, tumor necrosis factor receptor II, soluble intercellular adhesion molecule-1, interleukin 6, monocyte chemoattractant protein 1, and lipoprotein phospholipase A2 mass and activity), and urinary isoprostanes, along with 2 subscores. Adjusted least-square means of changes in the scores and log individual biomarkers in quartile categories of intake were estimated with the use of linear regression models, across mean ± SD 6.6 ± 0.7 y of follow-up. **Results:** Protein intake was inversely associated with changes in the inflammation and oxidative stress score (mean ± SE in Q1 compared with Q4: 0.77 ± 0.17 compared with 0.31 ± 0.19; P-trend = 0.02), indicating overall inflammation/oxidative stress increased less in those with the highest intake than in those with the lowest. Favorable associations were observed for plant protein (Q1 compared with Q4: 0.89 ± 0.25 compared with 0.14 ± 0.25; P-trend = 0.001), but only trended toward significance for animal protein (Q1 compared with Q4: 0.70 ± 0.26 compared with 0.31 ± 0.26; P-trend = 0.05). Total protein and plant protein intakes were also inversely associated with changes in monocyte chemoattractant protein 1 (total: Q1 compared with Q4: 0.19 ± 0.01 compared with 0.15 ± 0.01 log-pg/mL; P-trend = 0.03; plant: Q1 compared with Q4: 0.21 ± 0.01 compared with 0.16 ± 0.01 log-pg/mL; P-trend = 0.003). **Conclusions:** Dietary protein, particularly from plant sources, may be associated with beneficial changes in the inflammatory burden in aging populations.

**Perspective: The Public Health Case for Modernizing the Definition of Protein Quality**


**Significance:** A modernized definition of protein quality that incorporates health and environmental outcomes associated with specific food sources of protein is proposed.

Prevailing definitions of protein quality are predicated on considerations of biochemistry and metabolism rather than the net effects on human health or the environment of specific food sources of protein. In the vernacular, higher “quality” equates to desirability. This implication is compounded by sequential, societal trends in which first dietary fat and then dietary carbohydrate were vilified during recent decades, leaving dietary protein under an implied halo. The popular concept that protein is “good” and that the more the better, coupled with a protein quality definition that favors meat, fosters the impression that eating more meat, as well as eggs and dairy, is desirable and preferable. This message, however, is directly opposed to current Dietary Guidelines for Americans, which encourage consumption of more plant foods and less meat, and at odds with the literature on the environmental impacts of foods, from carbon emissions to water utilization, which decisively favor plant protein sources. Thus, the message conveyed by the current definitions of protein quality is at odds with imperatives of public and planetary health alike. We review the relevant literature in this context and make the case that the definition of protein quality is both misleading and antiquated. We propose a modernized definition that incorporates the quality of health and environmental outcomes associated with specific food sources of protein. We demonstrate how such an approach can be adapted into a metric and applied to the food supply.
Lipids

Using Metabolic Profiling and Gene Expression Analyses to Explore Molecular Effects of Replacing Saturated Fat With Polyunsaturated Fat—A Randomized Controlled Dietary Intervention Study

Significance: The biological and molecular effects of substituting dietary saturated fatty acids with polyunsaturated fatty acids were evaluated in this double-blind randomized controlled trial.

Background: Replacing dietary saturated fatty acids (SFAs) with polyunsaturated fatty acids (PUFAs) reduces the plasma low-density lipoprotein (LDL) cholesterol and subsequently the risk of cardiovascular disease. However, beyond changes in LDL cholesterol, we lack a complete understanding of the physiologic alterations that occur when improving dietary fat quality. Objectives: The aim of this study was to gain knowledge of metabolic alterations paralleling improvements in the fat quality of the diet. Methods: We recently conducted an 8-wk, double-blind, randomized controlled trial replacing SFAs with PUFAs in healthy subjects with moderate hypercholesterolemia (n = 99). In the present substudy, we performed comprehensive metabolic profiling with multiple platforms (both nuclear magnetic resonance- and mass spectrometry-based technology) (n = 99), and analyzed peripheral blood mononuclear cell gene expression (n = 95) by quantitative real-time polymerase chain reaction. Results: A large number of lipoprotein subclasses, myristoylcarnitine and palmitoylcarnitine, and kynurenine were reduced when SFAs were replaced with PUFAs. In contrast, bile acids, proprotein convertase subtilisin/kexin type 9, acetate, and acetoacetate were increased by the intervention. Some amino acids were also altered by the intervention. The mRNA levels of LXRA and LDLR were increased, in addition to several liver X receptor α target genes and genes involved in inflammation, whereas the mRNA levels of UCP2 and PPARD were decreased in peripheral blood mononuclear cells after replacing SFAs with PUFAs. Partial least squares-discriminant analysis showed that the 30 most important variables that contributed to class separation spanned all classes of biomarkers, and was in accordance with the univariate analysis. Conclusions: Applying metabolomics in randomized controlled dietary intervention trials has the potential to extend our knowledge of the biological and molecular effects of dietary fat quality. This study was registered at clinicaltrials.gov as NCT 01679496.

The Effect of Canola Oil on Body Weight and Composition: A Systematic Review and Meta-Analysis of Randomized Controlled Clinical Trials

Significance: This systematic review and meta-analysis found that canola oil consumption reduced body weight but did not affect other measures of adiposity in adults.

A number of clinical trials have examined the effect of canola oil (CO) on body composition in recent years; however, the results have been inconsistent. The present investigation aims to examine the effect of CO on body weight (BW) and body composition using a systematic review and meta-analysis of controlled clinical trials. Online databases including PubMed, Scopus, and Google Scholar were searched up to February, 2018 for randomized controlled clinical trials that examined the effect of CO on anthropometric measures and body composition indexes in adults. The Cochrane Collaboration’s tool was used to assess the risk of bias in individual studies. A random-effects model was used to evaluate the effect of CO consumption on several outcomes: BW, body mass index, waist circumference, hip circumference, waist-to-hip ratio, android-to-gynoid ratio, and body lean and fat mass. In total, 25 studies were included in the systematic review. The meta-analysis revealed that CO consumption reduces BW [weighted mean difference (WMD) = −0.30 kg; 95% CI: −0.52, −0.08 kg, P = 0.007; n = 23 effect sizes], particularly in participants with type 2 diabetes (WMD = −0.63 kg; 95% CI: −1.09, −0.17 kg, P = 0.007), in studies with a parallel design (WMD = −0.49 kg; 95% CI: −0.85, −0.14 kg, P = 0.006), in nonfeeding trials (WMD = −0.32 kg; 95% CI: −0.55, −0.09 kg, P = 0.006), and when compared with saturated fat (WMD = −0.40 kg; 95% CI: −0.74, −0.06 kg, P = 0.019). CO consumption did not significantly affect any other anthropometric measures or body fat markers (P > 0.05). Although CO consumption results in a modest decrease in BW, no significant effect was observed on other adiposity indexes. Further well-constructed clinical trials that target BW and body composition as their primary outcomes are needed.

Intake of Palm Olein and Lipid Status in Healthy Adults: A Meta-Analysis
Voon PT, Lee ST, Ng TKW, Ng YT, Yong XS, Lee VKM, Ong ASH. Adv Nutr. 2019 May 16. doi: 10.1093/advances/nmy122. Article Link

Significance: This meta-analysis found no differences in the effects of palm olein intake on lipoprotein biomarkers relative to unsaturated 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**

**Review of the Scientific Evidence Used for Establishing US Policies on Added Sugars**


**Significance:** This review provides an overview of the scientific evidence considered by health authorities and highlights issues in the evaluations and interpretations of this evidence.

The 2015 Dietary Guidelines for Americans Advisory Committee has set recommendations to limit added sugars. This action was based on the association between dietary pattern quality scores and chronic disease risk, the results of meta-analyses conducted for the World Health Organization, and data from modeling of dietary patterns for establishing the US Department of Agriculture’s Healthy US-Style Eating Patterns. Recommendations provided by the 2015-2020 Dietary Guidelines for Americans were used by the US Food and Drug Administration to establish, for the first time, the mandatory declaration of added sugars and a Daily Value of added sugars for the Nutrition Facts label. This review provides an overview of the scientific evidence considered by the World Health Organization, the 2015-2020 Dietary Guidelines for Americans, and the US Food and Drug Administration for setting recent polices and regulations on added sugars and highlights important issues and inconsistencies in the evaluations and interpretations of the evidence.

**Low-Calorie Sweeteners**

**Non-Nutritive Sweeteners and Their Association With the Metabolic Syndrome and Non-Alcoholic Fatty Liver Disease: A Review of the Literature**


**Significance:** The relationships between non-nutritive sweeteners and features of the metabolic syndrome are evaluated.

Purpose: Non-alcoholic fatty liver disease (NAFLD) is increasing in incidence worldwide, paralleling epidemics in obesity and metabolic syndrome. Widely considered the hepatic manifestation of the metabolic syndrome, NAFLD is associated with significant morbidity, mortality, and increased healthcare costs. There is an abundance of data linking sugar-sweetened beverages, and fructose, in particular, to the metabolic syndrome and NAFLD. As a result, non-nutritive sweeteners (NNSs) are frequently substituted for sugar in drinks and a variety of foods. However, despite the widespread consumption of NNSs, there is growing concern about their impact on metabolic health. Methods: This review examines the experimental and clinical evidence on non-nutritive sweetener (NNS) consumption and features of the metabolic syndrome, including NAFLD. Results: Experimental animal studies show that NNS consumption can induce glucose intolerance, increased food consumption, and weight gain, with proposed mechanisms including altered gut microbiome, inhibition of protective intestinal enzymes, and increased appetite. The evidence from clinical studies is more controversial. Observational studies overwhelmingly show an association between NNS consumption and features of the metabolic syndrome, and this includes NAFLD when analyses are not adjusted for obesity. The evidence from randomized-controlled trials in humans is sparse and conflicting, and primarily evaluates weight-related outcomes. Conclusion: Further research is urgently needed to evaluate NNS consumption and its relationship with NAFLD and the gut microbiome in humans.
Bioactives

**Dietary Polyphenol Intake, Blood Pressure, and Hypertension: A Systematic Review and Meta-Analysis of Observational Studies**


**Significance:** This systematic review and meta-analysis found no significant association between total flavonoid intake and hypertension risk, but anthocyanin intake was associated with an 8% reduction in risk of hypertension.

**Background:** Dietary polyphenols, including flavonoids, have been the focus of major recent attentions due to their wide content in a variety of foods commonly consumed and the findings from numerous studies showing evidence of an association with positive outcomes on human health. **Methods:** A systematic search using electronic databases PubMed and EMBASE was performed to retrieve English language studies published from the earliest indexing year of each database to April 2019, reporting on the association between dietary flavonoids intake and hypertension. **Results:** The search strategy resulted in the final selection of 20 studies including 15 cross-sectional investigations and 7 prospective cohorts (1 study reported on 3 prospective cohorts). 5 prospective cohorts, comprising 200,256 individuals and 45,732 cases of hypertension were included in the quantitative analysis. Analysis by extreme quantiles of intake of flavonoid showed a non-significant association with decreased risk of hypertension (RR (risk ratio): 0.96, 95% CI (confidence interval): 0.89, 1.03). Taking into consideration individual flavonoid subclasses, dietary anthocyanins intake was associated with 8% reduction in risk of hypertension, when comparing highest vs. lowest exposure (RR: 0.92, 95% CI: 0.88, 0.97). **Conclusions:** Further studies are needed to strengthen the retrieved association between anthocyanins consumption and decreased risk of hypertension and clarify whether total flavonoids or rather individual subclasses may exert beneficial effects on blood pressure.

Sodium

**Sodium-Intake Reduction and the Food Industry**


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.

**Dose-Response Relation Between Dietary Sodium and Blood Pressure: A Meta-Regression Analysis of 133 Randomized Controlled Trials**


**Significance:** The dose-response relations between sodium reduction and blood pressure in individuals with blood pressure above and below the 75th percentile of the general population are presented.

**Background:** The projected reduced mortality effect of reduced sodium intake in model-based studies conflicts with the observed increased mortality associated with low sodium intake in population studies. This may reflect an overestimation of the dose-response relation between sodium reduction (SR) and blood pressure (BP) used in mortality modeling studies. **Objectives:** The present meta-regression analysis sought to estimate the dose-response relations between SR and BP in study groups with mean BP above or below the 75th percentile of the general population. **Methods:** Based on a literature search from 1 January 1946 to 11 April 2018, we identified 133 randomized controlled trials allocating healthy or hypertensive individuals to SR or usual sodium intake. Multivariable regression analyses of the mean SR versus the mean blood pressure effect adjusted for effect modifiers were performed. **Results:** In study groups with mean BP above the 75th percentile [131/78 mm Hg systolic BP (SBP)/diastolic BP (DBP)], there was strong evidence of a linear dose-response relation between SR and BP. For SBP, the dose-response relation was −7.7 mm Hg/100 mmol SR (95% CI: −10.4, −5.0), and for DBP it was −3.0 mm Hg/100 mmol SR (95% CI: −4.6, −1.4). In study groups with mean BP ≤ 131/78 mm Hg, the relation between SR and BP was weak. For SBP it was −1.46 mm Hg/100 mmol SR (95% CI: −2.7, −0.20) and for DBP it was: −0.07 mm Hg/100 mmol SR (95% CI: −1.5, 1.4). **Conclusions:** Only study groups with a BP in the highest 25th percentile of the population showed a clinically significant drop in BP with SR. The policy of lowering dietary sodium intake in the general population may need to be reframed to target patients with hypertension. This study was registered at PROSPERO 2015 as CRD42015017773.
Microbiome

Associations Between Usual Diet and Gut Microbiota Composition: Results From the Milieu Intérieur Cross-Sectional Study


Significance: The associations between diet and gut microbiota composition in healthy French adults are assessed.

Background: Diet is widely recognized as one of the main modifiable drivers of gut microbiota variability, and its influence on microbiota composition is an active area of investigation. Objective: The present work aimed to explore the associations between usual diet and gut microbiota composition in a large sample of healthy French adults. Methods: Gut microbiota composition was established through sequencing of the 16S rRNA gene in stool samples from 862 healthy French adults of the Milieu Intérieur study. Usual dietary consumptions were determined through the administration of a food-frequency questionnaire. The associations between dietary variables and α- and β-diversity indexes and relative taxa abundances were tested using Spearman correlations, permutational ANOVAs, and multivariate analyses with linear models, respectively. Results: Foods generally considered as healthy (raw fruits, fish) were positively associated with α-diversity, whereas food items for which a limited consumption is generally recommended (fried products, sodas or sugary drinks, fatty sweet products, processed meats, ready-cooked meals, and desserts) were negatively associated with α-diversity. Fruits, fried products, ready-cooked meals, and cheese contributed to shifts within microbiota composition (β-diversity). Our results also highlighted a number of associations between various food group intakes and abundances of specific phyla, genera, and species. For instance, the consumption of cheese was negatively associated with Akkermansia muciniphila abundance. Conclusions: This large-scale population-based study supports that the usual consumption of certain food items is associated with several gut microbial features, and extends the mechanistic arguments linking Western diet to an altered microbiota composition. These results provide new insights into the understanding of complex diet–gut microbiota relations, and their implications for host health deserve further investigation because altered microbiota diversity was consistently linked to increased risk of several health outcomes. This trial was registered at clinicaltrials.gov as NCT01699893.

Personalized Nutrition

Development of a Genetic Score to Predict an Increase in HDL Cholesterol Concentration After a Dietary Intervention in Adults with Metabolic Syndrome


Significance: The proposed genetic predisposition score can be used to predict the HDL cholesterol response to diet in individuals with metabolic syndrome.

Background: Dietary intervention (DI) is a primary strategy to attenuate some of the metabolic abnormalities associated with metabolic syndrome (MetS), including low HDL cholesterol. There is no biomarker that can identify individuals who respond to DI by increasing HDL cholesterol. Objective: The aim of this study was to assess the predictive power of a genetic predisposition score (GPS) in Mexican adults with MetS to identify HDL cholesterol responders to DI. Methods: This study followed a prospective cohort design. Sixty-seven Mexican adults aged 20–60 y (21% men) with BMI ≥25 and ≤39.9 kg/m², who had at least 3 of 5 positive criteria for MetS, were included. Participants consumed a low saturated fat diet for 2.5 mo (<7% energy as saturated fat, <200 mg of cholesterol/d) and reduced their usual diet by ~440 kcal/d, a reduction in total energy intake of about 25%. Anthropometry and serum biochemical markers, including HDL cholesterol, were measured before and after DI. A multilocus GPS was constructed using previously reported genetic variants associated with response to diet in subjects with MetS. GPS values, designed to predict the response of HDL cholesterol to the DI, were computed for each individual as the sum of the number of effect alleles across 14 SNPs. Results: Individuals were dichotomized as high and low GPS according to median GPS (~2.12) and we observed a difference in HDL cholesterol changes on DI of +3 mg/dl (6.3%) in subjects with low GPS, whereas those with high GPS had HDL cholesterol decreases of ~3 mg/dl (~7.9%) (P = 0.04). Conclusions: Individuals with low GPS showed greater increases in their HDL cholesterol than those with high GPS. Therefore, the GPS can be useful for predicting the HDL cholesterol response to diet.