Dietary Intake Assessment

A Proposed Nutrient Density Score That Includes Food Groups and Nutrients to Better Align With Dietary Guidance


Significance: A hybrid nutrient density score that integrates food groups and nutrients will provide better alignment between nutrient profiling models and the Dietary Guidelines for Americans.

Current research on diets and health focuses on composite food patterns and their likely impact on health outcomes. The Dietary Guidelines for Americans (DGA) have likewise adopted a more food group-based approach. By contrast, most nutrient profiling (NP) models continue to assess nutrient density of individual foods, based on a small number of individual nutrients. Nutrients to encourage have included protein, fiber, and a wide range of vitamins and minerals. Nutrients to limit are typically saturated fats, total or added sugars, and sodium. Because current NP models may not fully capture the healthfulness of foods, there is a case for advancing a hybrid NP approach that takes both nutrients and desirable food groups and food ingredients into account. Creating a nutrient- and food-based NP model may provide a more integrated way of assessing a food’s nutrient density. Hybrid nutrient density scores will provide for a better alignment between NP models and the DGA, a chief instrument of food and nutrition policy in the United States. Such synergy may lead ultimately to improved dietary guidance, sound nutrition policy, and better public health.

Protein

A Meta-Analysis of 46 Studies Identified by the FDA Demonstrates That Soy Protein Decreases Circulating LDL and Total Cholesterol Concentrations in Adults


Significance: A meta-analysis of 46 controlled trials found an LDL cholesterol-lowering effect of soy protein relative to non-soy protein controls.

Background: Certain plant foods (nuts and soy protein) and food components (viscous fibers and plant sterols) have been permitted by the FDA to carry a heart health claim based on their cholesterol-lowering ability. The FDA is currently considering revoking the heart health claim for soy protein due to a perceived lack of consistent LDL cholesterol reduction in randomized controlled trials. Objective: We performed a meta-analysis of the 46 controlled trials on which the FDA will base its decision to revoke the heart health claim for soy protein. Methods: We included the 46 trials on adult men and women, with baseline circulating LDL cholesterol concentrations ranging from 110 to 201 mg/dL, as identified by the FDA, that studied the effects of soy protein on LDL cholesterol and total cholesterol (TC) compared with non-soy protein. Two independent reviewers extracted relevant data. Data were pooled by the generic inverse variance method with a random effects model and expressed as mean differences with 95% CI. Heterogeneity was assessed and quantified. Results: Of the 46 trials identified by the FDA, 43 provided data for meta-analyses. Of these, 41 provided data for LDL cholesterol, and all 43 provided data for TC. Soy protein at a median dose of 25 g/d during a median follow-up of 6 wk decreased LDL cholesterol by 4.76 mg/dL (95% CI: −6.71, −2.80 mg/dL, P < 0.0001; I² = 55%, P < 0.0001) and decreased TC by 6.41 mg/dL (95% CI: −9.30, −3.52 mg/dL, P < 0.0001; I² = 74%, P < 0.0001) compared with non-soy protein controls. There was no dose–response effect or evidence of publication bias for either outcome. Inspection of the individual trial estimates indicated most trials (~75%) showed a reduction in LDL cholesterol (range: −0.77 to −58.60 mg/dL), although only a minority of these were individually statistically significant. Conclusions: Soy protein significantly reduced LDL cholesterol by approximately 3–4% in adults. Our data support the advice given to the general public internationally to increase plant protein intake. This trial was registered at clinicaltrials.gov as NCT03468127.
Nonessential Amino Acid Usage for Protein Replenishment in Humans: A Method of Estimation

Significance: This study provides the first estimates of nonessential amino acid usage for body protein replacement in humans.

Background: Essential amino acids (EAAs) are key factors in determining dietary protein quality. Their RDAs have been estimated. However, although nonessential amino acids (NEAAs) are utilized for protein synthesis too, no estimates of their usage for body protein replenishment have been proposed so far. Objective: The aim of this study was to provide minimum, approximate estimates of NEAA usage for body protein replenishment/conservation in humans. Methods: A correlation between the pattern of both EAAs and NEAAs in body proteins, and their usage, was assumed. In order to reconstruct an “average” amino acid pattern/composition of total body proteins (as grams of amino acid per gram of protein), published data of relevant human organs/tissues (skeletal muscle, liver, kidney, gut, and collagen, making up ∼74% of total proteins) were retrieved. The (unknown) amino acid composition of residual proteins (∼26% of total proteins) was assumed to be the same as for the sum of the aforementioned organs excluding collagen. Using international EAA RDA values, an average ratio of EAA RDA to the calculated whole-body EAA composition was derived. This ratio was then used to back-calculate NEAA usage for protein replenishment. The data were calculated also using estimated organ/tissue amino acid turnover. Results: The individual ratios of World Health Organization/Food and Agriculture Organization/United Nations University RDA to EAA content ranged between 1.35 (phenylalanine + tyrosine) and 3.68 (leucine), with a mean ± SD value of 2.72 ± 0.81. In a reference 70-kg subject, calculated NEAA usage for body protein replenishment ranged from 0.73 g/d for asparagine to 3.61 g/d for proline. Use of amino acid turnover data yielded similar results. Total NEAA usage for body protein replenishment was ∼19 g/d (45% of total NEAA intake), whereas ∼24 g/d was used for other routes. Conclusion: This method may provide indirect minimum estimates of the usage of NEAAs for body protein replacement in humans.

Lipids

BMI Modifies the Effect of Dietary Fat on Atherogenic Lipids: A Randomized Clinical Trial

Significance: This study found smaller improvements in atherogenic lipid concentrations in response to polyunsaturated fatty acids in subjects who were obese relative to those who were normal weight.

Background: SFA intake increases LDL cholesterol whereas PUFA intake lowers it. Whether the lipid response to dietary fat differs between normal-weight and obese persons is of relevance to dietary recommendations for obese populations. Objectives: We compared the effect of substituting unsaturated fat for saturated fat on LDL cholesterol and apob concentrations in normal-weight (BMI ≤ 25 kg/m²) and obese (BMI: 30–45) subjects with elevated LDL cholesterol. Methods: We randomly assigned 83 men and women (aged 21–70 y) stratified by BMI (normal: n = 44; obese: n = 39) and elevated LDL cholesterol (mean ± SD, normal weight 4.6 ± 0.9 mmol/L; obese 4.4 ± 0.8 mmol/L) to either a PUFA diet enriched with oil-based margarine (n = 42) or an SFA diet enriched with butter (n = 41) for 6 wk. Results: Seven-day dietary records showed differences of ∼9 energy percent (E%) in SFA and ∼4 E% in PUFA between the SFA and PUFA groups. In the total study population, the PUFA diet compared with the SFA diet lowered LDL cholesterol (−0.31 mmol/L; 95% CI: −0.47, −0.15 mmol/L, compared with 0.32 mmol/L; 95% CI: 0.18, 0.47 mmol/L; P < 0.001) and apob (−0.08 g/L; 95% CI: −0.11, −0.05 g/L, compared with 0.07 g/L; 95% CI: 0.03, 0.10 g/L; P < 0.001). Tests of the BMI × diet interaction were significant for total cholesterol, LDL cholesterol, and apob (P values ≤ 0.009). In normal-weight compared with obese participants post-hoc comparisons found that the respective changes in LDL cholesterol were 9.7% (95% CI: 5.3%, 14.2%) compared with 5.3% (95% CI: −0.7%, 11.2%), P = 0.206, in the SFA group, and −10.4% (95% CI: −15.2%, −5.7%) compared with −2.3% (95% CI: −7.4%, 2.8%), P = 0.020, in the PUFA group. ApoB changes were 7.5% (95% CI: 3.5%, 11.4%) compared with 3.0% (95% CI: −1.7%, 7.7%), P = 0.140, in the SFA group, and −8.9% (95% CI: −12.6%, −5.2%) compared with −3.8% (95% CI: −6.3%, −1.2%), P = 0.021, in the PUFA group. Responses to dietary fat were not associated with changes in polyprotein convertase subtilisin/kexin type 9 concentrations. Conclusions: BMI modifies the effect of PUFAs compared with SFAs, with smaller improvements in atherogenic lipid concentrations in obese than in normal-weight individuals, possibly supporting adjustment of dietary recommendations according to BMI. This trial was registered with www.clinicaltrials.gov as NCT02589769.
Carbohydrates

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

Significance: Inconsistencies in the evaluation and interpretation of evidence used for setting recent policies on added sugars are discussed.

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 policies and regulations on added sugars and highlights important issues and inconsistencies in the evaluations and interpretations of the evidence.

Fiber Intake Predicts Weight Loss and Dietary Adherence in Adults Consuming Calorie-Restricted Diets: The POUNDS Lost (Preventing Overweight Using Novel Dietary Strategies) Study

Significance: In overweight and obese adults, fiber intake was found to promote dietary adherence and weight loss independently of macronutrient and caloric intake.

Background: The effects of dietary composition on weight loss are incompletely understood. In addition to energy intake, fiber intake, energy density, macronutrient composition, and demographic characteristics have all been suggested to contribute to weight loss. Objective: The primary aim of this analysis was to assess the role of dietary fiber as a predictor of weight loss in participants who consumed calorie-restricted diets (~750 kcal/d from estimated energy needs) for 6 mo, using data from the POUNDS Lost (Preventing Overweight Using Novel Dietary Strategies) Study—a randomized trial that examined the effects of calorie-restricted diets varying in macronutrient composition on weight loss in adults. Methods: Data were randomly partitioned to a training data set (70%) in which the effects of fiber and other weight-loss predictors were identified using adjusted Least Absolute Shrinkage and Selection Operator and model averaging. The retained predictors were then fit on the testing data set to assess predictive performance. Results: Three hundred and forty-five participants (53.9% female) provided dietary records at baseline and 6 mo. Mean ± SD age and BMI for the full sample was 52.5 ± 8.7 y and 32.6 ± 3.9 kg/m², respectively. Mean ± SD (99% CI) weight change at 6 mo for the full sample was −7.27 ± 5.6 kg (−8.05, −6.48 kg). The final, best fit model (R² = 0.41) included fiber, energy density, fat, age, adherence, baseline weight, race, and changes from baseline in carbohydrate, fiber, PUFA, and MUFA intake, but the most influential predictor was fiber intake (β = −0.37; P < 0.0001). In addition, fiber was strongly associated with adherence to the macronutrient prescriptions (P < 0.0001). Interactions between race and adherence, age, baseline weight, carbohydrate, energy density, and MUFAs were also retained in the final model. Conclusion: Dietary fiber intake, independently of macronutrient and caloric intake, promotes weight loss and dietary adherence in adults with overweight or obesity consuming a calorie-restricted diet. This trial was registered at clinicaltrials.gov as NCT00072995.

Low-Calorie Sweeteners

Associations of Diet Soda and Non-Caloric Artificial Sweetener Use With Markers of Glucose and Insulin Homeostasis and Incident Diabetes: The Strong Heart Family Study

Significance: In an American Indian population, no significant associations were found between reported non-caloric artificial sweetener consumption and fasting insulin and glucose or incident diabetes.

Background/Objectives: Non-caloric artificial sweeteners (NAS) are marketed as healthier alternatives to sugar, but the relationship between consumption of NAS and development of diabetes is unclear. This study assessed the associations of diet soda and NAS consumption with (1) early markers of insulin and glucose homeostasis (cross-sectionally) and (2) incident diabetes (over an average of 8 years of follow-up) among American Indians, a population with high rates of obesity. Subjects/Methods: The study population included Strong Heart Family Study participants without cardiovascular disease or diabetes who participated in the 2007–2009 study exam (n = 1359). Diet soda and NAS consumption were assessed using a Block food frequency questionnaire...
and supplemental NAS questionnaire at the study exam. Fasting plasma glucose and insulin were measured during the study exam after a 12-h overnight fast. Participants were followed for incident diabetes through December 2017 using a single phone interview and medical record review; diabetes was identified by self-report and confirmed by documentation in medical records. Associations of diet soda and NAS consumption with fasting insulin, glucose, and incident diabetes were assessed using generalized estimating equations (failing insulin and glucose analyses) and parametric survival models with Weibull distributions (incident diabetes analyses). Results: Just under half of participants reported regularly consuming diet soda (40%) or using NAS to sweeten their beverages (41%). During an average 8 years of follow-up, we identified 98 cases of incident diabetes. After correction for multiple comparisons, there were no statistically significant associations of reported diet soda and NAS consumption with fasting insulin, fasting glucose, or incident diabetes. Conclusions: Although reported consumption of diet soda and NAS were high, neither were associated with diabetes risk.

Bioactives

Effects of a Diet Naturally Rich in Polyphenols on Lipid Composition of Postprandial Lipoproteins in High Cardiometabolic Risk Individuals: An Ancillary Analysis of a Randomized Controlled Trial


Significance: A high-polyphenol diet modifies postprandial lipoprotein composition in individuals at high cardiometabolic risk.

Background/Objectives: Plasma lipoprotein composition, especially in the postprandial state, could be relevant for cardiovascular risk and could be influenced by eating habits. This study evaluated the effects of a polyphenol-rich diet on postprandial lipoprotein composition in individuals at high cardiometabolic risk. Subjects/Methods: Seventy-eight individuals with high waist circumference and at least another component of the metabolic syndrome were randomized to either a high-polyphenol (HighP) or low-polyphenol (LowP) diet. Before and after the 8-week intervention, chylomicrons, VLDL1, VLDL2, IDL, LDL, HDL particles, and their lipid concentrations were determined over a 6-h high-fat test meal with high or low-polyphenol content, according to the diet assigned. Results: VLDL1 postprandial areas under the curve (AUCs) were lower for cholesterol (Chol) (1.48 ± 0.98 vs. 1.91 ± 1.33 mmol/L × 6 h, M ± SD, p = 0.014) and triglycerides (Tg) (4.70 ± 2.70 vs. 6.02 ± 3.07 mmol/L × 6 h, p = 0.005) after the HighP than after the LowP diet, with no changes in Chol/Tg ratio. IDL Chol AUCs were higher after the HighP than after the LowP diet (1.29 ± 0.77 vs. 1.01 ± 0.51 mmol/L × 6 h, p = 0.037). LDL Tg AUCs were higher after the HighP than after the LowP diet (1.15 ± 0.33 vs. 1.02 ± 0.35 mmol/L × 6 h, p < 0.001), with a lower Chol/Tg ratio (14.6 ± 4.0 vs. 16.0 ± 3.8, p = 0.007). HDL Tg AUCs were lower after the HighP than after the LowP diet (1.20 ± 0.41 vs. 1.34 ± 0.37 mmol/L × 6 h, p = 0.013). Conclusions: A high-polyphenol diet reduces the postprandial lipid content of large VLDL and increases IDL cholesterol; it modifies the composition of LDL particles—which become richer in triglycerides, and of HDL—which become instead triglyceride poor. The overall changes in atherogenicity by these effects warrant further investigation on clinical cardiovascular outcomes.

Sodium


Significance: 24-hour dietary recalls underestimate mean sodium and potassium intake relative to 24-hour urinary excretion, which may lead to attenuation of true associations of sodium and potassium intake with health outcomes in observational studies.

Background: Understanding measurement error in sodium and potassium intake is essential for assessing population intake and studying associations with health outcomes. Objective: The aim of this study was to compare sodium and potassium intake derived from 24-h dietary recall (24HDR) with intake derived from 24-h urinary excretion (24HUE). Design: Data were analyzed from 776 nonpregnant, noninstitutionalized US adults aged 20–69 y who completed 1-to-2 24HUE and 24HDR measures in the 2014 NHANES. A total of 1190 urine specimens and 1414 dietary recalls were analyzed. Mean bias was estimated as mean of the differences between individual mean 24HDR and 24HUE measurements. Correlations and attenuation factors were estimated using the Kipnis joint-mixed effects model accounting for within-person day-to-day variability in sodium excretion. The attenuation factor reflects the degree to which true associations between long-term intake (estimated using 24HUEs) and a hypothetical health outcome would be approximated using a single 24HDR: values near 1 indicate close approximation and near 0 indicate bias toward null. Estimates are reported for sodium, potassium, and the sodium:potassium (Na/K) ratio. Model parameters can be used to estimate correlations/attenuation factors when multiple 24HRSs are available. Results: Overall, mean bias for sodium was −452 mg (95% CI: −646, −259), for potassium −315 mg (CI: −450, −179), and for the Na/K ratio −0.04 (CI: −0.15, 0.07, NS). Using 1 24HDR, the attenuation factor for sodium was 0.16 (CI: 0.09, 0.21), for potassium 0.25 (CI:0.16, 0.36), and for the Na/K ratio 0.20 (CI: 0.10, 0.25). The correlation for sodium was 0.27 (CI: 0.16, 0.37), for potassium 0.35 (CI: 0.26, 0.55),
and for the Na/K ratio 0.27 (CI: 0.13, 0.32). **Conclusions:** Compared with 24HUE, using 24HDR underestimates mean sodium and potassium intake but is unbiased for the Na/K ratio. Additionally, using 24HDR as a measure of exposure in observational studies attenuates the true associations of sodium and potassium intake with health outcomes.

**Gut Microbiome**

**The Role of the Gut Microbiome in Predicting Response to Diet and the Development of Precision Nutrition Models. Part I: Overview of Current Methods**


**Significance:** This article is the first in a two-part series intended to summarize current science, knowledge gaps, and future directions related to the contribution of gut microbiota to interindividual variability in diet response.

Health care is increasingly focused on health at the individual level. In the rapidly evolving field of precision nutrition, researchers aim to identify how genetics, epigenetics, and the microbiome interact to shape an individual’s response to diet. With this understanding, personalized responses can be predicted and dietary advice can be tailored to the individual. With the integration of these complex sources of data, an important aspect of precision nutrition research is the methodology used for studying interindividual variability in response to diet. This article stands as the first in a 2-part review of current research investigating the contribution of the gut microbiota to interindividual variability in response to diet. Part I reviews the methods used by researchers to design and carry out such studies as well as the statistical and bioinformatic methods used to analyze results. Part II reviews the findings of these studies, discusses gaps in our current knowledge, and summarizes directions for future research. Taken together, these reviews summarize the current state of knowledge and provide a foundation for future research on the role of the gut microbiome in precision nutrition.

**The Role of the Gut Microbiome in Predicting Response to Diet and the Development of Precision Nutrition Models. Part II: Results**


**Significance:** This article is the second in a two-part series intended to summarize current science, knowledge gaps, and future directions related to the contribution of gut microbiota to interindividual variability in diet response.

The gut microbiota is increasingly implicated in the health and metabolism of its human host. The host’s diet is a major component influencing the composition and function of the gut microbiota, and mounting evidence suggests that the composition and function of the gut microbiota influence the host’s metabolic response to diet. This effect of the gut microbiota on personalized dietary response is a growing focus of precision nutrition research and may inform the effort to tailor dietary advice to the individual. Because the gut microbiota has been shown to be malleable to some extent, it may also allow for therapeutic alterations of the gut microbiota in order to alter response to certain dietary components. This article is the second in a 2-part review of the current research in the field of precision nutrition incorporating the gut microbiota into studies investigating interindividual variability in response to diet. Part I reviews the methods used by researchers to design and carry out such studies as well as analyze the results subsequently obtained. Part II reviews the findings of these studies and discusses the gaps in our current knowledge and directions for future research. The studies reviewed provide the current understanding in this field of research and a foundation from which we may build, utilizing and expanding upon the methods and results they present to inform future studies.
Taste

New Insight Into Human Sweet Taste: A Genome-Wide Association Study of the Perception and Intake of Sweet Substances

Significance: This study found limited support for associations between the TAS1R2, TAS1R3, and GNAT3 genes and perception and sweet taste perception and intake of sweet-tasting foods, suggesting that genes additional to those related to the peripheral receptor system are involved.

Background: Individual differences in human perception of sweetness are partly due to genetics; however, which genes are associated with the perception and the consumption of sweet substances remains unclear. Objective: The aim of this study was to verify previous reported associations within genes involved in the peripheral receptor systems (i.e., TAS1R2, TAS1R3, and GNAT3) and reveal novel loci. Methods: We performed genome-wide association scans (GWASs) of the perceived intensity of 2 sugars (glucose and fructose) and 2 high-potency sweeteners (neohesperidin dihydrochalcone and aspartame) in an Australian adolescent twin sample (n = 1757), and the perceived intensity and sweetness and the liking of sucrose in a US adult twin sample (n = 686). We further performed GWASs of the intake of total sugars (i.e., total grams of all dietary mono- and disaccharides per day) and sweets (i.e., handfuls of candies per day) in the UK Biobank sample (n = ≤174,424 white-British individuals). All participants from the 3 independent samples were of European ancestry. Results: We found a strong association between the intake of total sugars and the single nucleotide polymorphism rs11642841 within the FTO gene on chromosome 16 (P = 3.8 × 10−8) and many suggestive associations (P < 1.0 × 10−5) for each of the sweet perception and intake phenotypes. We showed genetic evidence for the involvement of the brain in both sweet taste perception and sugar intake. There was limited support for the associations with TAS1R2, TAS1R3, and GNAT3 in all 3 European samples. Conclusions: Our findings indicate that genes additional to those involved in the peripheral receptor system are also associated with the sweet taste perception and intake of sweet-tasting foods. The functional potency of the genetic variants within TAS1R2, TAS1R3, and GNAT3 may be different between ethnic groups and this warrants further investigations.