Nutrition Briefs

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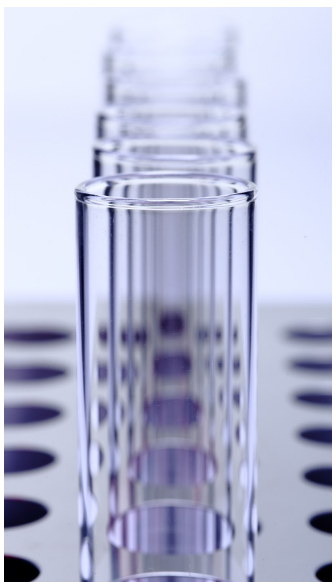
Scientific Integrity

Scientific Integrity Principles and Best Practices: Recommendations from a Scientific Integrity Consortium

Kretser A, Murphy D, Bertuzzi S, Abraham T, Allison DB, Boor KJ, et al. *Sci Eng Ethics*. 2019 Feb 27. doi: 10.1007/s11948-019-00094-3. Article Link

Significance: The Scientific Integrity Consortium developed a set of recommended principles and best practices for scientific integrity that can be used broadly across scientific disciplines and will better equip scientists to operate in a rapidly changing research environment.



A Scientific Integrity Consortium developed a set of recommended principles and best practices that can be used broadly across scientific disciplines as a mechanism for consensus on scientific integrity standards and to better equip scientists to operate in a rapidly changing research environment. The two principles that represent the umbrella under which scientific processes should operate are as follows: (1) Foster a culture of integrity in the scientific process. (2) Evidence-based policy interests may have legitimate roles to play in influencing aspects of the research process, but those roles should not interfere with scientific integrity. The nine best practices for instilling scientific integrity in the implementation of these two overarching principles are (1) Require universal training in robust scientific methods, in the use of appropriate experimental design and statistics, and in responsible research practices for scientists at all levels, with the training content regularly updated and presented by qualified scientists. (2) Strengthen scientific integrity oversight and processes throughout the research continuum with a focus on training in ethics and conduct. (3) Encourage reproducibility of research through transparency. (4) Strive to establish open science as the standard operating procedure throughout the scientific enterprise. (5) Develop and implement educational tools to teach communication skills that uphold scientific integrity. (6) Strive to identify ways to further strengthen the peer review process. (7) Encourage scientific journals to publish unanticipated findings that meet standards of quality and scientific integrity. (8) Seek harmonization and implementation among journals of rapid, consistent, and transparent processes for correction and/or retraction of published papers. (9) Design rigorous and comprehensive evaluation criteria that recognize and reward the highest standards of integrity in scientific research.

This work was conducted by the Scientific Integrity Consortium, which comprises 4 U.S. government agencies, 3 Canadian government agencies, 11 professional societies, 6 universities and 3 non-profit organizations. ILSI North America is a member of the Consortium.

Dietary Reference Intakes

Dietary Reference Intakes for Sodium and Potassium

National Academies of Sciences, Engineering, and Medicine. 2019. *Dietary Reference Intakes for Sodium and Potassium*. Washington, DC: The National Academies Press. doi: 10.17226/25353. Article Link

Significance: This report reaffirms the sodium AI for individuals ages 14-50, decreases the sodium AIs for children age 1-13, increases the sodium AIs for adults ages 51 and older, and decreases the potassium AIs for individuals age 1 and older.

As essential nutrients, sodium and potassium contribute to the fundamentals of physiology and pathology of human health and disease. In clinical settings, these are two important blood electrolytes, are frequently measured and influence care decisions. Yet, blood electrolyte concentrations are usually not influenced by dietary intake, as kidney and hormone systems carefully regulate blood values. Over the years, increasing evidence suggests that sodium and potassium intake patterns of children

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and adults influence long-term population health mostly through complex relationships among dietary intake, blood pressure and cardiovascular health. The public health importance of understanding these relationships, based upon the best available evidence and establishing recommendations to support the development of population clinical practice guidelines and medical care of patients is clear. This report reviews evidence on the relationship between sodium and potassium intakes and indicators of adequacy, toxicity, and chronic disease. It updates the Dietary Reference Intakes (DRIs) using an expanded DRI model that includes consideration of chronic disease endpoints, and outlines research gaps to address the uncertainties identified in the process of deriving the reference values and evaluating public health implications.

Dietary Supplement Assessment

Best Practices for Dietary Supplement Assessment and Estimation of Total Usual Nutrient Intakes in Population-Level Research and Monitoring

Bailey RL, Dodd KW, Gahche JJ, Dwyer JT, Cowan AE, Jun S, et al. *J Nutr*. 2019 Feb 8. doi: 10.1093/jn/nxy264. Article Link

Significance: This review describes the available methods and analytical strategies for incorporating nutrient intakes from dietary supplements to usual intakes from foods to address research questions.

The use of dietary supplements (DS) is pervasive and can provide substantial amounts of micronutrients to those who use them. Therefore when characterizing dietary intakes, describing the prevalence of inadequacy or excess, or assessing relations between nutrients and health outcomes, it is critical to incorporate DS intakes to improve exposure estimates. Unfortunately, little is known about the best methods to assess DS, and the structure of measurement error in DS reporting. Several characteristics of nutrients from DS are salient to understand when comparing to those in foods. First, DS can be consumed daily or episodically, in bolus form and can deliver discrete and often very high doses of nutrients that are not limited by energy intakes. These characteristics contribute to bimodal distributions and distributions severely skewed to the right. Labels on DS often provide nutrient forms that differ from those found in conventional foods, and underestimate analytically derived values. Finally, the bioavailability of many nutrient-containing DS is not known and it may not be the same as the nutrients in a food matrix. Current methods to estimate usual intakes are not designed specifically to handle DS. Two temporal procedures are described to refer to the order that nutrient intakes are combined relative to usual intake procedures, referred to as a "shrinking" the distribution to remove random error. The "shrink then add" approach is preferable to the "add then shrink" approach when users and nonusers are combined for most research questions. Stratifying by DS before usual intake methods is another defensible option. This review describes how to incorporate nutrient intakes from DS to usual intakes from foods, and describes the available methods and fit-for-purpose of different analytical strategies to address research questions where total usual intakes are of interest at the group level for use in nutrition research and to inform policy decisions. Clinical Trial Registry: NCT03400436.

Dietary Patterns

Fast-Food Offerings in the United States in 1986, 1991, and 2016 Show Large Increases in Food Variety, Portion Size, Dietary Energy, and Selected Micronutrients

McCrory MA, Harbaugh AG, Appeadu S, Roberts SB. *J Acad Nutr Diet*. 2019 Feb 22. pii: S2212-2672(18)32383-9. doi: 10.1016/j.jand.2018.12.004. Article Link

Significance: Offerings at fast-food restaurants have increased in variety, portion size, energy and sodium content over the last 30 years.

Background: US national survey data shows fast food accounted for 11% of daily caloric intake in 2007-2010. *Objective:* To provide a detailed assessment of changes over time in fast-food menu offerings over 30 years, including food variety (number of items as a proxy), portion size, energy, energy density, and selected micronutrients (sodium, calcium, and iron as percent daily value [%DV]), and to compare changes over time across menu categories (entrées, sides, and desserts). *Design:* Fast-food entrées, sides, and dessert menu item data for 1986, 1991, and 2016 were compiled from primary and secondary sources for 10 popular fast-food restaurants. *Statistical Analysis:* Descriptive statistics were calculated. Linear mixed-effects analysis of variance was performed to examine changes over time by menu category. *Results:* From 1986 to 2016, the number of entrées, sides, and desserts for all restaurants combined increased by 226%. Portion sizes of entrées (13 g/decade) and desserts (24 g/decade), but not sides, increased significantly, and the energy (kilocalories) and sodium of items in all three menu categories increased significantly. Desserts showed the largest increase in energy (62 kcal/decade), and entrées had the largest increase in sodium (4.6% DV/decade). Calcium increased significantly in entrées (1.2%DV/decade) and to a greater extent in desserts (3.9% DV/decade), but not sides, and iron increased significantly only in desserts (1.4% DV/decade). *Conclusions:* These results demonstrate broadly detrimental changes in fast-food restaurant offerings over a 30-year span including increasing variety, portion size, energy, and sodium content. Research is needed to identify effective strategies that may help consumers reduce energy intake from fast-food restaurants as part of measures to improve dietary-related health issues in the United States.

Obesity

Food Groups and Risk of Overweight, Obesity, and Weight Gain: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies

Schlesinger S, Neuenschwander M, Schwedhelm C, Hoffmann G, Bechthold A, Boeing H, et al. *Adv Nutr*. 2019 Feb 25. pii: nmy092. doi: 10.1093/advances/nmy092. Article Link

Significance: This meta-analysis found low to very low quality of evidence that certain food groups have an impact on measures of adiposity.

This meta-analysis summarizes the evidence of a prospective association between the intake of foods [whole grains, refined grains, vegetables, fruit, nuts, legumes, eggs, dairy, fish, red meat, processed meat, and sugar-sweetened beverages (SSBs)] and risk of general overweight/obesity, abdominal obesity, and weight gain. PubMed and Web of Science were searched for prospective observational studies until August 2018. Summary RRs and 95% CIs were estimated from 43 reports for the highest compared with the lowest intake categories, as well as for linear and nonlinear relations focusing on each outcome separately: overweight/obesity, abdominal obesity, and weight gain. The quality of evidence was evaluated with use of the NutriGrade tool. In the dose-response meta-analysis, inverse associations were found for whole-grain (RRoverweight/obesity: 0.93; 95% CI: 0.89, 0.96), fruit (RRoverweight/obesity: 0.93; 95% CI: 0.86, 1.00; RRweight gain: 0.91; 95% CI: 0.86, 0.97), nut (RRabdominal obesity: 0.42; 95% CI: 0.31, 0.57), legume (RRoverweight/obesity: 0.88; 95% CI: 0.84, 0.93), and fish (RRabdominal obesity: 0.83; 95% CI: 0.71, 0.97) consumption and positive associations were found for refined grains (RRoverweight/obesity: 1.05; 95% CI: 1.00, 1.10), red meat (RRabdominal obesity: 1.10; 95% CI: 1.04, 1.16; RRweight gain: 1.14; 95% CI: 1.03, 1.26), and SSBs (RRoverweight/obesity: 1.05; 95% CI: 1.00, 1.11; RRabdominal obesity: 1.12; 95% CI: 1.04, 1.20). The dose-response meta-analytical findings provided very low to low quality of evidence that certain food groups have an impact on different measurements of adiposity risk. To improve the quality of evidence, better-designed observational studies, inclusion of intervention trials, and use of novel statistical methods (e.g., substitution analyses or network meta-analyses) are needed.

Protein

Effect of a Hypocaloric, Nutritionally Complete, Higher-Protein Meal Plan on Bone Density and Quality in Older Adults With Obesity: A Randomized Trial

Weaver AA, Houston DK, Shapses SA, Lyles MF, Henderson RM, Beavers DP, et al. *Am J Clin Nutr*. 2019 Feb 1;109(2):478-486. doi: 10.1093/ajcn/nqy237. Article Link

Significance: In this study, older adults on a hypocaloric, higher-protein nutritionally complete diet maintained similar bone density as weight-stable controls.

Background: Dietary protein and micronutrients are important to the maintenance of bone health and may be an effective countermeasure to weight-loss–associated bone loss. *Objectives:* We aimed to determine the effect of a 6-mo hypocaloric, nutritionally complete, higher-protein meal plan on change in bone density and quality as compared with weight stability in older adults using a randomized post-test design. We hypothesized that participants randomly assigned to this meal plan would maintain similar bone density and quality to weight-stable controls, despite significant reductions in body mass. *Methods:* Ninety-six older adults (aged 70.3 ± 3.7 y, 74% women, 27% African American) with obesity [body mass index (kg/m2): 35.4 ± 3.3] were randomly assigned to a 6-mo hypocaloric, nutritionally complete, higher-protein meal plan targeting ≥1.0 g protein · kg body weight^{-1} · d^{-1} [weight-loss (WL) group; n = 47] or to a weight-stability (WS) group targeting 0.8 g protein · kg body weight^{-1} · d^{-1}, the current Recommended Dietary Allowance (n = 49). The primary outcome was total hip bone mineral density (BMD), with femoral neck BMD, lumbar spine BMD, and lumbar spine trabecular bone score (TBS) as secondary outcomes, all assessed at baseline and 3 and 6 mo with dual-energy X-ray absorptiometry. *Results:* Baseline total hip, femoral neck, and lumbar spine BMDs were 1.016 ± 0.160, 0.941 ± 0.142, and 1.287 ± 0.246 g/cm2, respectively; lumbar TBS was 1.398 ± 0.109. Despite significant weight loss achieved in the WL group (6.6 ± 0.4 kg; 8.6% ± 0.4% of baseline weight), 6-mo regional BMD estimates were similar to those in the WS group (all P > 0.05). Lumbar spine TBS significantly increased at 6 mo in the WL group (mean: 1.421; 95% CI: 1.401, 1.441) compared with the WS group (1.390: 95% CI: 1.370, 1.409; P = 0.02). *Conclusions:* Older adults following a hypocaloric, nutritionally complete, higher-protein meal plan maintained similar bone density and quality to weight-stable controls. Our data suggest that adherence to this diet does not produce loss of hip and spine bone density in older adults and may improve bone quality. This trial was registered at clinicaltrials.gov as NCT02730988.

Carbohydrates

Association Between Added Sugar Intake and Mortality Is Nonlinear and Dependent on Sugar Source in 2 Swedish Population-Based Prospective Cohorts

Ramne S, Alves Dias J, González-Padilla E, Olsson K, Lindahl B, Engström G, et al. *Am J Clin Nutr.* 2019 Feb 1;109(2):411-423. doi: 10.1093/ajcn/nqy268. Article Link

Significance: The results from this study suggest that both high (>20% of energy) and low (<5% of energy) intakes of sugar are associated with increased mortality risk, but this association is dependent on type of sugar source.

Background: Although sugar consumption has been associated with several risk factors for cardiometabolic diseases, evidence for harmful long-term effects is lacking. In addition, most studies have focused on sugar-sweetened beverages (SSBs), not sugar per se. *Objective:* The aim of this study was to examine the associations between added and free sugar intake, intake of different sugar sources, and mortality risk. *Methods:* Two prospective population-based cohorts were examined: the Malmö Diet and Cancer Study (MDCS; n = 24,272), which collected dietary data by combining a food diary, interview, and food-frequency questionnaire (FFQ), and the Northern Swedish Health and Disease Study (NSHDS; n = 24,475), which assessed diet with an FFQ. Sugar intakes defined as both added and free sugar and different sugar sources were examined. The associations with mortality were examined using a multivariable Cox proportional hazards regression. *Results:* Higher sugar consumption was associated with a less favorable lifestyle in general. The lowest mortality risk was found with added sugar intakes between 7.5% and 10% of energy (E%) intake in both cohorts. Intakes >20E% were associated with a 30% increased mortality risk, but increased risks were also found at intakes <5E% [23% in the MDCS and 9% (nonsignificant) in the NSHDS]. Similar U-shaped associations were found for both cardiovascular and cancer mortality in the MDCS. By separately analyzing the different sugar sources, the intake of SSBs was positively associated with mortality, whereas the intake of treats was inversely associated. *Conclusions:* Our findings indicate that a high sugar intake is associated with an increased mortality risk. However, the risk is also increased among low sugar consumers, although they have a more favorable lifestyle in general. In addition, the associations are dependent on the type of sugar source.

Bioactives

Plasma, Urine, and Adipose Tissue Biomarkers of Dietary Intake Differ Between Vegetarian and Non-Vegetarian Diet Groups in the Adventist Health Study-2

Miles FL, Lloren JIC, Haddad E, Jaceldo-Siegl K, Knutsen S, Sabate J, et al. *J Nutr*. 2019 Feb 15. pii: nxy292. doi: 10.1093/jn/nxy292. Article Link

Significance: Diet-related biomarkers including carotenoids, isoflavones, enterolactone, saturated and polyunsaturated fatty acids differ significantly between individuals consuming a vegetarian versus a non-vegetarian diet pattern.

Background: Differences in food composition, nutrient intake, and various health outcomes have been reported for vegetarians and non-vegetarians in the Adventist Health Study-2 (AHS-2) cohort. *Objective:* We sought to determine whether biomarkers of dietary intake also differed between individuals classified as vegetarian (vegan, lacto-ovo-vegetarian, pesco-vegetarian, semi-vegetarian) and non-vegetarians based on patterns of consumption of meat, dairy, and eggs. *Methods:* Fasting plasma, overnight urine, and adipose tissue samples were collected from a representative subset of AHS-2 participants classified into 5 diet groups (vegan, lacto-ovo-vegetarian, pesco-vegetarian, semi-vegetarian, non-vegetarian) who also completed food-frequency questionnaires. Diet-related biomarkers including carotenoids, isoflavones, enterolactone, saturated and polyunsaturated fatty acids, and vitamins were analyzed in 840 male and female participants. Multiple linear regression was used to examine the association between diet pattern and biomarker abundance, comparing each of 4 vegetarian dietary groups to non-vegetarians, and adjusted mean values were calculated. Bonferroni correction was applied to control for multiple testing. *Results:* Vegans had higher plasma total carotenoid concentrations (1.6-fold, $P < 0.0001$), and higher excretion of urinary isoflavones (6-fold, $P < 0.0001$) and enterolactone (4.4-fold) compared with non-vegetarians. Vegans had lower relative abundance of saturated fatty acids including myristic, pentadecanoic, palmitic, and stearic acids ($P < 0.0001$). Vegans had higher linoleic acid (18:2ω-6) relative to non-vegetarians (23.3% compared with 19.1%) ($P < 0.0001$), and a higher proportion of total ω-3 fatty acids (2.1% compared with 1.6%) ($P < 0.0001$). Results overall were similar but less robust for lacto-ovo- and pesco-vegetarians. 1-Methylhistidine was 92% lower in vegans, and lower in lacto-ovo- and pesco-vegetarians by 90% and 80%, respectively, relative to non-vegetarians ($P < 0.0001$). *Conclusion:* AHS-2 participants following vegan, and lacto-ovo- or pesco-vegetarian diet patterns have significant differences in plasma, urine, and adipose tissue biomarkers associated with dietary intakes compared with those who consume a non-vegetarian diet. These findings provide some validation for the prior classification of dietary groups within the AHS-2 cohort.

Sodium

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

Ahuja JKC, Li Y, Nickle MS, Haytowitz DB, Roseland J, Nguyen Q, et al. *J Acad Nutr Diet*. 2019 Feb;119(2):293-300.e17. doi: 10.1016/j.jand.2018.08.155. Article Link

Significance: A majority of label and laboratory sodium values are in agreement, and underdeclaration of sodium values is limited in US foods.

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

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

Raeisi-Dehkordi H, Amiri M, Humphries KH, Salehi-Abargouei A. *Adv Nutr*. 2019 Feb 27. pii: nmy108. doi: 10.1093/advances/nmy108. Article Link

Significance: This systematic review and meta-analysis found that while canola oil consumption reduces body weight, it does not alter other markers of adiposity such as waist or hip circumference or body fat mass.

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.

Microbiome

High Dietary Fat Intake Induces a Microbiota Signature That Promotes Food Allergy

Hussain M, Bonilla-Rosso G, Kwong Chung CK, Bäriswyl L, Rodriguez MP, Kim BS, et al. *J Allergy Clin Immunol*. 2019 Feb 12. pii: S0091-6749(19)30205-2. doi: 10.1016/j.jaci.2019.01.043. Article Link

Significance: In mice, a high-fat diet induced changes to the gut microbiome that increase susceptibility to food allergy.

Background: Diet-induced obesity and food allergies rise in tandem, but a potential cause-and-effect relationship between these diseases of affluence remains to be tested. *Objective:* To test the role of high dietary fat intake, diet-induced obesity and associated changes in gut microbial community structure on food allergy pathogenesis. *Methods:* Mice were fed a high fat diet (HFD) for 12 weeks prior to food allergen sensitization on an atopic dermatitis-like skin lesion followed by intra-gastric allergen challenge to induce experimental food allergy. Germ-free animals were colonized with a signature HFD- or lean microbiota for 8 weeks prior to induction of food allergy. Food allergic responses were quantified using a clinical allergy score, serum IgE levels, serum MMCP-1 concentrations and type-2 cytokine responses. Accumulation of intestinal mast cells was examined by flow cytometry and chloroacetate esterase tissue staining. Changes in the gut microbial community structure were assessed by high-throughput 16S ribosomal DNA gene sequencing. *Results:* HFD-induced obesity potentiates food allergic responses associated with dysregulated intestinal effector mast cell responses, increased intestinal permeability and gut dysbiosis. A HFD-associated microbiome was transmissible to germ-free mice with the gut microbial community structure of recipients segregating according to the microbiota input source. Independent of an obese state, a HFD-associated gut microbiome was sufficient to confer enhanced susceptibility to food allergy. *Conclusion:* These findings identify HFD-induced microbial alterations as risk factor for experimental food allergy and uncouple a pathogenic role of a HFD-associated microbiome from obesity. Post-dieting microbiome alterations due to over indulgence of dietary fat may increase susceptibility to food allergy.