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Nutrition Briefs

Research Methodology

Perspective: Application of N-of-1 Methods in Personalized Nutrition Research

Potter T, Vieira R, de Roos B. *Adv Nutr.* 2021 Jan 18;nmaa173. doi: 10.1093/advances/nmaa173. [Article link](#)

Significance: N-of-1 study designs can be used to monitor a participant's usual health or behavior in a naturalistic setting, with repeated measurements conducted in real time. These designs may be useful in investigating complex research questions and studying underrepresented groups.

Personalized and precision nutrition aim to examine and improve health on an individual level, and this requires reconsideration of traditional dietary interventions or behavioral study designs. The limited frequency of measurements in group-level human nutrition trials cannot be used to infer individual responses to interventions, while in behavioral studies, retrospective data collection does not provide an accurate measure of how everyday behaviors affect individual health. This review introduces the concept of N-of-1 study designs, which involve the repeated measurement of a health outcome or behavior on an individual level. Observational designs can be used to monitor a participant's usual health or behavior in a naturalistic setting, with repeated measurements conducted in real time using an Ecological Momentary Assessment. Interventional designs can introduce a dietary or behavioral intervention with predictors and outcomes of interest measured repeatedly either during or after 1 or more intervention and control periods. Due to their flexibility, N-of-1 designs can be applied to both short-term physiological studies and longer-term studies of eating behaviors. As a growing number of disease markers can be measured outside of the clinic, with self-reported data delivered via electronic devices, it is now easier than ever to generate large amounts of data on an individual level. Statistical techniques can be utilized to analyze changes in an individual or to aggregate data from sets of N-of-1 trials, enabling hypotheses to be tested on a small number of heterogeneous individuals. Although their designs necessitate extra methodological and statistical considerations, N-of-1 studies could be used to investigate complex research questions and to study underrepresented groups. This may help to reveal novel associations between participant characteristics and health outcomes, with repeated measures providing power and precision to accurately determine an individual's health status.

Meal Pattern Analysis in Nutritional Science: Recent Methods and Findings

O'Hara C, Gibney ER. *Adv Nutr.* 2021 Jan 18:nmaa175. doi: 10.1093/advances/nmaa175. [Article link](#)

Significance: Research on intakes of whole meals is limited, but a growing area of research has recently begun to utilize advanced statistical techniques to manage the large number of variables and permutations associated with these complex meal patterns. The aim of this narrative review was to evaluate those techniques and the meal patterns they detect.



There is a scarcity of dietary intake research focusing on the intake of whole meals rather than on the nutrients and foods of which those meals are composed. This growing area of research has recently begun to utilize advanced statistical techniques to manage the large number of variables and permutations associated with these complex meal patterns. The aim of this narrative review was to evaluate those techniques and the meal patterns they detect. The 10 observational studies identified used techniques such as principal components analysis, clustering, latent class analysis, and decision trees. They examined meal patterns under 3 categories: temporal patterns (relating to the timing and distribution of meals), content patterns (relating to combinations of foods within a meal and combinations of those meals over a day), and context patterns (relating to external elements of the meal, such as location, activities while eating, and the presence



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or absence of others). The most common temporal meal patterns were the 3 meals/d pattern, the skipped breakfast pattern, and a grazing pattern consisting of smaller but more frequent meals. The 3 meals/d pattern was associated with increased diet quality compared with the other 2 patterns. Studies identified between 7 and 12 content patterns with limited similarities between studies and no clear associations between the patterns and diet quality or health. One study simultaneously examined temporal and context meal patterns, finding limited associations with diet quality. No study simultaneously examined other combinations of meal patterns. Future research that further develops the statistical techniques required for meal pattern analysis is necessary to clarify the relations between meal patterns and diet quality and health.

Dietary Patterns

Western Dietary Pattern Antioxidant Intakes and Oxidative Stress: Importance During the SARS-CoV-2/COVID-19 Pandemic

Trujillo-Mayol I, Guerra-Valle M, Casas-Forero N, Sobral MMC, Viegas O, Alarcón-Enos J, et al. *Adv Nutr.* 2021 Jan 13:nmaa171. doi: 10.1093/advances/nmaa171. [Article link](#)

Significance: Viral pandemics like the COVID-19 crisis involve high oxidative damage caused by both the infection and the resultant social stresses, which increases the probability and severity of infection. Although firm evidence is lacking, vulnerable populations such as elders and obese individuals could benefit from antioxidant supplementation to improve their antioxidant response.

The importance of balanced dietary habits, which include appropriate amounts of antioxidants to maintain the immune system, has become increasingly relevant during the current SARS-CoV-2/COVID-19 pandemic, because viral infections are characterized by high oxidative stress. Furthermore, the measures taken by governments to control the pandemic have led to increased anxiety, stress, and depression, which affect physical and mental health, all of which are influenced by nutritional status, diet, and lifestyle. The Mediterranean diet (MD), Atlantic diet (AD), and the Dietary Guidelines for Americans all provide the essential vitamins, minerals, and phenolic compounds needed to activate enzymatic and nonenzymatic antioxidant responses. However, viral pandemics such as the current COVID-19 crisis entail high oxidative damage caused by both the infection and the resultant social stresses within populations, which increases the probability and severity of infection. Balanced dietary patterns such as the MD and the AD are characterized by the consumption of fruit, vegetables, legumes, olive oil, and whole grains with low intakes of processed foods and red meat. For a healthy lifestyle in young adults, the MD in particular provides the required amount of antioxidants per day for vitamins D (0.3-3.8 µg), E (17.0 mg), C (137.2-269.8 mg), A (1273.3 µg), B-12 (1.5-2.0 µg), and folate (455.1-561.3 µg), the minerals Se (120.0 µg), Zn (11.0 mg), Fe (15.0-18.8 mg), and Mn (5.2-12.5 mg), and polyphenols (1171.00 mg) needed to maintain an active immune response. However, all of these diets are deficient in the recommended amount of vitamin D (20 µg/d). Therefore, vulnerable populations such as elders and obese individuals could benefit from antioxidant supplementation to improve their antioxidant response. Although evidence remains scarce, there is some indication that a healthy diet, along with supplemental antioxidant intake, is beneficial to COVID-19 patients.

Protein

Partial Replacement of Animal Proteins with Plant Proteins for 12 Weeks Accelerates Bone Turnover Among Healthy Adults: A Randomized Clinical Trial

Itkonen ST, Päivärinta E, Pellinen T, Viitakangas H, Risteli J, Erkkola M, et al. *J Nutr.* 2021 Jan 4;151(1):11-19. doi: 10.1093/jn/nxaa264. [Article link](#)

Significance: Partial replacement of animal proteins with plant-based proteins for 3 months increased the markers of bone resorption and formation among adults, indicating a possible risk for bone health. However, it is unclear whether differences in protein intake or quality play a major role.

Background: Plant-based diets may reduce the risk of chronic diseases, but can also lead to low calcium and vitamin D intakes, posing a risk for bone health. **Objectives:** We investigated whether partial replacement of animal proteins with plant-based proteins using a whole-diet approach affects bone and mineral metabolism in healthy adults in 3 groups fed diets differing in protein composition. **Methods:** This 12-week clinical trial was comprised of 107 women and 29 men (20–69 years old; BMI mean \pm SD, 24.8 \pm 3.9) randomly assigned to consume 1 of 3 diets designed to provide 17 energy percent (E%) protein: “animal” (70% animal protein, 30% plant protein of total protein intake), “50/50” (50% animal, 50% plant), and “plant” (30% animal, 70% plant) diets. We examined differences in bone formation [serum intact procollagen type I amino-terminal propeptide (S-iPINP)], bone resorption [serum collagen type 1 cross-linked C-terminal telopeptide (S-CTX)], mineral metabolism markers (primary outcomes), and nutrient intakes (secondary outcomes) by ANOVA/ANCOVA. **Results:** S-CTX was significantly higher in the plant group (mean \pm SEM, 0.44 \pm 0.02 ng/mL) than in the other

groups (P values < 0.001 for both), and differed also between the animal (mean \pm SEM, 0.29 ± 0.02 ng/mL) and 50/50 groups (mean \pm SEM, 0.34 ± 0.02 ng/mL; $P = 0.018$). S-iPINP was significantly higher in the plant group (mean \pm SEM, 63.9 ± 1.91 ng/mL) than in the animal group (mean \pm SEM, 55.0 ± 1.82 ng/mL; $P = 0.006$). In a subgroup without a history of vitamin D supplement use, plasma parathyroid hormone was significantly higher in the plant than in the animal group ($P = 0.018$). Vitamin D and calcium intakes were below recommended levels in the plant group (mean \pm SEM, 6.2 ± 3.7 µg/d and 733 ± 164 mg/d, respectively). **Conclusions:** Partial replacement of animal proteins with plant-based proteins for 12 weeks increased the markers of bone resorption and formation among healthy adults, indicating a possible risk for bone health. This is probably caused by lower vitamin D and calcium intakes from diets containing more plant-based proteins, but it is unclear whether differences in protein intake or quality play a major role.

Lipids

Associations of Serum Fatty Acid Proportions with Obesity, Insulin Resistance, Blood Pressure, and Fatty Liver: The Cardiovascular Risk in Young Finns Study

Kaikkonen JE, Jula A, Viikari JSA, Juonala M, Hutri-Kähönen N, Kähönen M, et al. *J Nutr.* 2021 Feb 9:nxaa409. doi: 10.1093/jn/nxaa409. [Article link](#)

Significance: A study of the associations between serum standardized fatty acid percentages and cardiometabolic outcomes in Finnish adults found that total SFAs and MUFAAs and low PUFAAs—along with several FAs—predict future adverse cardiometabolic outcomes.

Background: The links between fatty acids (FAs) and cardiometabolic outcomes are topics of debate. **Objective:** Our aim was to investigate the associations between serum standardized FA percentages and cardiometabolic outcomes. **Methods:** We used cross-sectional ($n = 2187$ - 2200 subjects, age 24-39 y, women 54%) and 10-year prospective data ($n = 975$ - 1414 subjects) from the Young Finns Study. Outcomes included prevalent and incident obesity, insulin resistance (HOMA-IR index in the upper quintile), elevated blood pressure (BP; taking medication, or diastolic or systolic BP in the upper quintile), and incident nonalcoholic fatty liver. Logistic regression models were used to calculate ORs per SD increase in fatty acids (FAs). The models were adjusted for age and sex, and additionally for other potential confounders. **Results:** Several cross-sectional findings were also statistically significant in prospective models (Bonferroni corrected $P < 0.003$). In fully-adjusted models for obesity, these consisted of SFAs (OR: 1.28) and MUFAAs (OR: 1.38), including palmitoleic (OR: 1.39) and oleic acids (OR: 1.37). Furthermore, PUFAAs (OR: 0.70), including linoleic (OR: 0.67) and docosahexaenoic acids (OR: 0.75), were inversely related with obesity, whereas γ -linolenic acid (OR: 1.32) was positively associated with obesity. In age- and sex-adjusted models for insulin resistance, MUFAAs (OR: 1.26) and oleic acid (OR: 1.25) were positively, and PUFAAs (OR: 0.81), particularly linoleic acid (OR: 0.78), were inversely associated with HOMA-IR. Similarly with elevated BP, palmitic acid (OR: 1.22), MUFAAs (OR: 1.28), and oleic acid (OR: 1.28) were positively associated with elevated BP, whereas PUFAAs (OR: 0.77), n-6 (omega-6) PUFAAs (OR: 0.79), and linoleic acid (OR: 0.77) were inversely associated. In fully-adjusted models for incident fatty liver, the most consistent predictors were high palmitic (OR: 1.61) and low linoleic acid (OR: 0.63) percentages. The n-6/n-3 (omega-3) PUFA ratio was not linked with any adverse outcomes. **Conclusions:** High serum percentages of total SFAs and MUFAAs and low PUFAAs, but also several specific FAs, predict future unfavorable cardiometabolic outcomes in Finnish adults.

Carbohydrates

Effect of Fructose Instead of Glucose or Sucrose on Cardiometabolic Markers: A Systematic Review and Meta-Analysis of Isoenergetic Intervention Trials

Fattore E, Botta F, Bosetti C. *Nutr Rev.* 2021 Jan 9;79(2):209-226. doi: 10.1093/nutrit/nuaa077. [Article link](#)

Significance: Isoenergetic substitution of fructose or high-fructose corn syrup for glucose or sucrose has no significant effect on most of the cardiometabolic outcomes investigated. However, some results of the review were affected by studies with high or unclear risk of bias.



Context: Free, or added, sugars are considered important determinants in the pandemics of obesity and associated chronic diseases, and fructose has emerged as the sugar of main concern. **Objective:** The aim of this review was to assess the evidence of the effects of isoenergetic replacement of fructose or high-fructose corn syrup (HFCS) for glucose or sucrose on cardiometabolic markers in controlled dietary intervention trials. **Data sources:** The electronic databases PubMed/MEDLINE, the Cochrane Library, and Embase were searched from 1980 to May 5, 2020. **Study selection:** Studies

were eligible if they measured at least one of the following outcomes: total cholesterol, low- and high-density lipoprotein cholesterol, triacylglycerols, apolipoprotein A1, apolipoprotein B, systolic blood pressure, diastolic blood pressure, fasting glucose, and body weight. **Data extraction:** For each outcome, the mean values and the corresponding measure of dispersion were extracted after the intervention or control diet. **Data analysis:** Fixed-effects and random-effects models were used to pool study-specific estimates. Between-study heterogeneity was assessed by the χ^2 test and the I₂ statistic and publication bias by the Egger test and funnel plots. **Results:** Twenty-five studies involving 1744 volunteers were identified. No significant effects were found when fructose or HFCS was substituted for glucose, except for a slight decrease in diastolic blood pressure when fructose was substituted for glucose. Similarly, no effects were found when fructose or HFCS was substituted for sucrose, except for a small increase, of uncertain clinical significance, of apolipoprotein B when HFCS was substituted for sucrose. **Conclusions:** Isoenergetic substitution of fructose or HFCS for glucose or sucrose has no significant effect on most of the cardiometabolic markers investigated; however, some results were affected by residual between-study heterogeneity and studies with high or unclear risk of bias.

The Breath Carbon Isotope Ratio Reflects Short-term Added-Sugar Intake in a Dose-Response, Crossover Feeding Study of 12 Healthy Adults

O'Brien DM, Niles KR, Black J, Schoeller DA. *J Nutr.* 2021 Jan 12:nxaa352. doi: 10.1093/jn/nxaa352. [Article link](#)

Significance: This study found support for using breath carbon isotope ratios as a biomarker of short-term added sugar (AS) intake in healthy US adults.

Background: Objective dietary biomarkers are urgently needed for a wider range of foods and nutrients. The breath carbon isotope ratio (CIR; measured as $\delta^{13}\text{C}$ values) has potential as a noninvasive measure of short-term added sugar (AS) intake but has not been evaluated in a controlled-feeding study. **Objective:** The aim was to evaluate the effect of short-term AS intake on breath CIR in a dose-response, randomized, crossover feeding study. **Methods:** Six men and 6 women, aged 25 to 60 y, were randomly assigned to a balanced sequence of 5 dietary treatments. Three treatments delivered low (0 g/d), medium (75 g/d), or high (150 g/d) amounts of AS over the course of a single day's breakfast and lunch and 2 switched high and low intake amounts between breakfast and lunch. Experimental meals delivered 60% of daily energy and added-sugar targets. There was a washout period of 1-2 wk between treatments. Breath was collected at 2-h intervals from 08:00 (fasting) to 16:00 h. Breath CIR was measured using cavity ring-down spectroscopy, and the effects of dietary treatments and baseline were evaluated using multivariate linear regression. **Results:** Breath CIR showed a significant response to increasing AS intake at all sampling time points (all $P < 0.0001$), with a dose-response of 0.030 (95% CI: 0.024, 0.037) ‰/g. Fasting breath CIR (baseline) influenced post-feeding breath CIR at all sampling time points ($P < 0.0001$); however, effect sizes were largest in the morning. For afternoon-collected samples (14:00 and 16:00), the effect of recent AS intake (lunch) was 4-fold greater than the effect of previous added-sugar intake (breakfast). **Conclusions:** These findings support the potential of the breath CIR as a biomarker of short-term AS intake in healthy US adults. More work is needed to evaluate other potential dietary effects and whether multiple breath collections could capture daily AS intake.

Low-Calorie Sweeteners

Effects of Unsweetened Preloads and Preloads Sweetened with Caloric or Low-/No-Calorie Sweeteners on Subsequent Energy Intakes: A Systematic Review and Meta-Analysis of Controlled Human Intervention Studies

Lee HY, Jack M, Poon T, Noori D, Venditti C, Hamamji S, et al. *Adv Nutr.* 2021 Jan 13:nmaa157. doi: 10.1093/advances/nmaa157. [Article link](#)

Significance: Unsweetened or low-/no-calorie sweetener-sweetened preloads appear to have similar effects on subsequent energy intakes when compared with one another or with CS-sweetened preloads. These findings suggest low- or no-calorie-sweetened foods and beverages are viable alternatives to caloric-sweetened foods and beverages to manage short-term energy intake.

Effects of isocaloric (sweetness differences but constant calories) preloads and isosweet (caloric differences but constant sweetness) preloads, as well as preloads that were neither isosweet nor isocaloric (sweetness and caloric differences) on subsequent ad libitum meal and total (preload + ad libitum) energy intakes were investigated. Thirty-five crossover studies were eligible for inclusion, representing 116 comparisons (41, isocaloric; 41, isosweet; and 34, neither isosweet nor isocaloric). References of existing reviews and literature from 4 databases were searched. The calculated raw mean differences in ad libitum and total energy intakes were pooled in meta-analyses using a random-effects model and the inverse of the variance as the weighting factor. Energy intakes at an ad libitum meal were significantly lower for low-/no-calorie sweetener (LNCS)-sweetened compared with unsweetened preloads in the isocaloric comparison (-55.5 kcal; 95% CI: -82.9, -28.0 kcal; $P < 0.001$); however, the difference in energy intake was not significant in additional sensitivity analyses (i.e.,

removal of comparisons where the matrix was a capsule and when xylitol was the LNCS). For the isosweet comparison, although the pooled energy intake at the ad libitum meal was significantly greater with the LNCS-sweetened preload compared with the caloric sweetener (CS)-sweetened preload (58.5 kcal; 95% CI: 35.4, 81.7 kcal; $P < 0.001$), the pattern was reversed when total energy intake was considered (-132.4 kcal; 95% CI: -163.2, -101.6 kcal; $P < 0.001$), explained by only partial compensation from the CS-sweetened preload. The results were similar when assessing ad libitum and total energy intakes when unsweetened compared with CS-sweetened preloads were consumed. Unsweetened or LNCS-sweetened preloads appear to have similar effects on intakes when compared with one another or with CS-sweetened preloads. These findings suggest that LNCS-sweetened foods and beverages are viable alternatives to CS-sweetened foods and beverages to manage short-term energy intake.

Bioactives

Dietary Lutein Plus Zeaxanthin and Choline Intake is Interactively Associated with Cognitive Flexibility in Middle-Adulthood in Adults with Overweight and Obesity

Edwards CG, Walk AM, Thompson SV, Reeser GE, Dilger RN, Erdman JW Jr, et al. *Nutr Neurosci*. 2021 Jan 15: 1-16. doi: 10.1080/1028415X.2020.1866867. [Article link](#)

Significance: Among a group of adults with overweight and obesity, increased intake of choline and lutein+zeaxanthin was associated with faster performance on a cognitive flexibility task.



The xanthophyll carotenoids lutein+zeaxanthin and the dietary component choline have been linked to benefits in cognition. However, knowledge on the interactive influence of these dietary components on cognitive function is sparse. **Design:** 80 middle-aged adults with overweight and obesity (Body Mass Index: (BMI) $\geq 25.0 \text{ kg/m}^2$), completed 7-day diet records, venous blood draws, heterochromatic flicker photometry, assessment of intelligence quotient (IQ), and a cognitive flexibility task while undergoing electroencephalographic recording for event-related potential (ERP) extraction. Multiplicative interaction terms and hierarchical linear regressions, controlling for age, BMI, sex, annual household income, and IQ were utilized to assess independent and interactive contributions of dietary and biomarker data on Switch task outcomes. **Results:** Higher intake of lutein+zeaxanthin and choline was associated interactively, but not independently, with faster reaction time (RT), after controlling for pertinent covariates. Dietary intake of lutein+zeaxanthin and choline was associated with serum lutein concentrations, but not with plasma choline metabolites nor macular pigmentation. Plasma phosphatidylcholine (PC) concentrations were associated with higher accuracy in Switch trials, while no other biomarkers were associated with cognitive outcomes. Dietary intake and biomarker data were not related to the N2 nor P3 ERP component. **Conclusions:** Among a sample of adults with overweight and obesity, greater intake of choline and lutein+zeaxanthin was associated with faster performance on a cognitive flexibility task. Future work examining methods of increasing consumption of both of these dietary components as a possible means of improving or maintaining cognitive flexibility among adults with overweight and obesity is therefore warranted.

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Sodium

Effects of the Dietary Approaches to Stop Hypertension Diet and Sodium Reduction on Blood Pressure in Persons With Diabetes

Tseng E, Appel LJ, Yeh HC, Pilla SJ, Miller ER, Juraschek SP, et al. *Hypertension*. 2021 Feb;77(2):265-274. doi: 10.1161/HYPERTENSIONAHA.120.14584. [Article link](#)

Significance: The DASH dietary pattern and dietary sodium reduction are recommended as lifestyle interventions in individuals with diabetes, even though these recommendations are largely based on studies conducted in persons without diabetes. This study highlights a substantial need for additional research on the blood pressure lowering effects of these interventions in people with diabetes and hypertension.

Elevated blood pressure and blood pressure-related morbidity are extraordinarily common in persons with diabetes. The Dietary Approaches to Stop Hypertension dietary pattern and dietary sodium reduction are recommended as lifestyle interventions in individuals with diabetes. However, these recommendations have largely been based on studies conducted in persons without diabetes. In this review, we summarize available evidence from trials that tested the effects of these 2 dietary interventions on blood pressure in people with diabetes. Overall, of the 3 trials (total n=151) that tested the effects of the Dietary Approaches to Stop Hypertension dietary pattern in persons with diabetes, 2 trials documented that the Dietary

Approaches to Stop Hypertension dietary pattern lowered blood pressure. While 16 trials (total n=445) tested the effects of sodium reduction in persons with diabetes, results were inconsistent, likely because of design limitations, for example, brief duration, small sample size, and low baseline blood pressure levels, as well as differences in the mode of intervention delivery (behavioral interventions, feeding studies, and sodium supplements). In conclusion, there is a substantial need for additional research on the blood pressure lowering effects of the Dietary Approaches to Stop Hypertension diet and sodium reduction in people with diabetes and hypertension, given the high prevalence of hypertension and the dearth of high-quality trials in this population.

Gut Microbiome

Long-Term Dietary Intake From Infancy to Late Adolescence is Associated with Gut Microbiota Composition in Young Adulthood

Oluwagbemigun K, O'Donovan AN, Berding K, Lyons K, Alexy U, Schmid M, et al. *Am J Clin Nutr.* 2021 Jan 20:nqaa340. doi: 10.1093/ajcn/nqaa340. [Article link](#)

Significance: The links between long-term carbohydrate intake to microbiota composition is a growing area of enquiry. Given that high carbohydrate intake and microbiota composition are associated with some diseases, this research could lead to gut microbiota-targeted dietary recommendations for disease prevention.

Background: Gut microbiota composition as influenced by long-term diet may be associated with the risk of adult chronic diseases. Thus, establishing the relation of long-term diet, particularly starting from early life, with adult microbiota composition would be an important research advance. **Objective:** We aimed to investigate the association of long-term intake of energy, carbohydrate, fiber, protein, and fat from infancy to late adolescence with microbiota composition in adulthood. **Methods:** Within the prospective DOrtmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study, we sampled stool 1 or 2 times within 1 y from 128 adults (median age: 29 y). Microbiota composition was profiled by 16S ribosomal RNA sequencing. Annual dietary records from age 1 to 18 y were retrieved. We estimated trajectories of energy, energy-adjusted carbohydrate, fiber, protein, and fat intake with multilevel models, producing predicted intake at age 1 y and rates of change in intake. A multivariate, zero-inflated, logistic-normal model was used to model the association between intake trajectories and the composition of 158 genera in single-sampled individuals. Associations found in this model were confirmed in double-sampled individuals using a zero-inflated Beta regression model.

Results: Adjusting for covariates and temporal differences in microbiota composition, long-term carbohydrate intake was associated with 3 genera. Specifically, carbohydrate intake at age 1 y was negatively associated with *Phascolarctobacterium* [coefficient = -4.31; false discovery rate (FDR)-adjusted P = 0.006] and positively associated with *Dialister* (coefficient = 3.06; FDR-adjusted P = 0.003), and the rate of change in carbohydrate intake was positively associated with *Desulfovibrio* (coefficient = 13.16; FDR-adjusted P = 0.00039). Energy and other macronutrients were not associated with any genus.

Conclusions: This work links long-term carbohydrate intake to microbiota composition. Considering the associations of high carbohydrate intake and microbiota composition with some diseases, these findings could inform the development of gut microbiota-targeted dietary recommendations for disease prevention.