Protein

Effects of Substituting Eggs for High-Carbohydrate Breakfast Foods on the Cardiometabolic Risk-Factor Profile in Adults at Risk for Type 2 Diabetes Mellitus

Maki KC, Palacios OM, Kramer MW, Trivedi R, Dicklin MR, Wilcox M, et al. Eur J Clin Nutr. 2020 Mar 9. doi: 10.1038/s41430-020-0599-2. Article Link

Significance: Compared with the baseline diet, eating 12 eggs/week for 4 weeks at breakfast was associated with less reduction in LDL cholesterol, and more lowering of systolic blood pressure, than observed with non-egg-based foods rich in carbohydrates.

To assess effects of egg-based versus non-egg, higher-carbohydrate (CHO) breakfast meals on cardiometabolic health markers in overweight or obese adults with prediabetes and/or metabolic syndrome. This randomized, crossover study included two 4-week dietary interventions, separated by a ≥4-week washout. Subjects incorporated into their habitual diets breakfast meals containing either 2 eggs/day for 6 days/week (Egg condition), or energy-matched, non-egg, higher-CHO-based foods (Non-Egg condition). Dietary intakes, insulin sensitivity, and other CHO metabolism indices, lipid biomarkers, high-sensitivity C-reactive protein, and blood pressures were measured. Thirty men and women with mean age 54.1 ± 1.9 years and body mass index 31.9 ± 0.7 kg/m² provided data. Neither diet condition significantly altered insulin sensitivity indices, but the homeostasis model assessment for insulin resistance was significantly (p = 0.028) higher after the Non-Egg vs. the Egg condition. Low-density lipoprotein cholesterol (LDL-C) was decreased from baseline (119 mg/dL) by 2.9 and 6.0% with Egg and Non-Egg breakfasts, respectively (p = 0.023). Systolic blood pressure was reduced from baseline (127 mm Hg) by 2.7 and 0.0% with Egg and Non-Egg, respectively (p = 0.018). Diet records indicated 149 kcal/day higher (p = 0.008) energy intake from non-study foods during the Egg condition; however, weight change from baseline did not differ between conditions. Compared with the baseline diet, consumption of 12 eggs/week for 4 weeks at breakfast was associated with less reduction in LDL-C, and more lowering of systolic blood pressure, than observed with non-egg-based, energy-matched, control foods higher in CHO.

Lipids

Single Nucleotide Polymorphisms Related to Lipoprotein Metabolism Are Associated With Blood Lipid Changes Following Regular Avocado Intake in a Randomized Control Trial Among Adults With Overweight and Obesity

Hannon BA, Edwards CG, Thompson SV, Reeser GE, Burd NA, Holscher HD, et al. J Nutr. 2020 Mar 20. pii: nxaa054. doi: 10.1093/jn/nxaa054. Article Link

Significance: Results from this analysis show that avocado consumption may help manage dyslipidemia in adults with overweight and obesity, and that SNPs related to lipoprotein metabolism may play a role in this relationship.

Avocados are rich in unsaturated fat and fiber; clinical trials have investigated their effects on metabolic disease. There is high variability in individual changes following avocado consumption, which may be in part due to individual genetic differences. Secondary analyses of the Persea americana for Total Health (PATH) Study were used to examine how single nucleotide polymorphisms (SNPs) impact blood lipid changes following a daily meal containing avocado compared with control. Adults (n = 115, 37% male)
aged 25–45 y with overweight and obesity were randomly assigned to receive a daily isocaloric meal with (intervention) or without (control) a standardized amount (males: 175 g; females: 140 g) of avocado for 12 wk. Control meals were higher in saturated fat (17% of energy compared with 7%) and lower in fiber (4 g compared with 16 g) than intervention meals. Whole venous blood was taken at baseline and 12 wk to determine total cholesterol (TC), high-density lipoprotein (HDL) cholesterol, and triglyceride (TG) concentrations. Seventeen SNPs in 10 genes related to lipoprotein metabolism were genotyped. Effects of SNP, diet, and SNP–diet interactions were determined using general linear models. No group-by-time effects were detected for changes in TC (P = 0.96), HDL cholesterol (P = 0.28), or TG (P = 0.06) over 12 wk. Three SNP–diet interactions were associated with final TC concentrations: ANGPTL3-rs10889337 (P = 0.01), ANGPTL4-rs2278236 (P = 0.02), and CD36-rs10499859 (P = 0.01). SNPs in GCKR and LPL were associated with TC changes (P = 0.01). The interaction between GCKR-rs1260326 and diet was such that C-homozygotes receiving avocado (n = 23) had final TC concentrations that were significantly lower than the C-homozygotes in the control group (n = 20) (P = 0.02). Results from these exploratory analyses indicate that avocado consumption may help manage dyslipidemia in adults with overweight and obesity; however, effectiveness may differ by genetic profile. Understanding the role of genetic variation in variability following dietary intervention can potentially inform personalized nutrition recommendations.

Long-Term Dietary Intervention Reveals Resilience of the Gut Microbiota Despite Changes in Diet and Weight
Frangiadakis GK, Wastyk HC, Robinson JL, Sonnenburg ED, Sonnenburg JL, Gardner CD. Am J Clin Nutr. 2020 Mar 18. pii: nqaa046. doi: 10.1093/ajcn/nqaa046. Article Link

Significance: A year-long profile of microbiota composition in 49 participants suggests that diet-induced perturbations to gut microbiota composition are typically followed by reversion to the microbiota’s starting profile.

With the rising rates of obesity and associated metabolic disorders, there is a growing need for effective long-term weight-loss strategies, coupled with an understanding of how they interface with human physiology. Interest is growing in the potential role of gut microbes as they pertain to different weight-loss diets; however, the ways that diet, the gut microbiota, and long-term weight loss influence one another is not well understood. Our primary objective was to determine if baseline microbiota composition or diversity was associated with weight-loss success. A secondary objective was to track the longitudinal associations of changes to lower-carbohydrate or lower-fat diets and concomitant weight loss with the composition and diversity of the gut microbiota. We used 16S ribosomal RNA gene amplicon sequencing to profile microbiota composition over a 12-mo period in 49 participants as part of a larger randomized dietary intervention study of participants consuming either a healthy low-carbohydrate or a healthy low-fat diet. While baseline microbiota composition was not predictive of weight loss, each diet resulted in substantial changes in the microbiota 3-mo after the start of the intervention; some of these changes were diet-specific (14 taxonomic changes specific to the healthy low-carbohydrate diet, 12 taxonomic changes specific to the healthy low-fat diet) and others tracked with weight loss (7 taxonomic changes in both diets). After these initial shifts, the microbiota returned near its original baseline state for the remainder of the intervention, despite participants maintaining their diet and weight loss for the entire study. These results suggest a resilience to perturbation of the microbiota’s starting profile. When considering the established contribution of obesity-associated microbiotas to weight gain in animal models, microbiota resilience may need to be overcome for long-term alterations to human physiology.

Carbohydrates
Effects of High-Fiber Diets Enriched With Carbohydrate, Protein, or Unsaturated Fat on Circulating Short Chain Fatty Acids: Results From the OmniHeart Randomized Trial
Mueller NT, Zhang M, Juraschek SP, Miller ER, Appel LJ. Am J Clin Nutr. 2020 Mar 1;111(3):545–554. doi: 10.1093/ajcn/nqz322. Article Link

Significance: Macronutrient composition in high-fiber diets affect circulating short-chain fatty-acids which are associated with measures of appetite and cardiometabolic health.

Short chain fatty acids (SCFAs; e.g., acetate, propionate, and butyrate) are produced by microbial fermentation of fiber in the colon. Evidence is lacking on how high-fiber diets that differ in macronutrient composition affect circulating SCFAs. We aimed to compare the effects of 3 high-fiber isocaloric diets differing in %kcal of carbohydrate, protein, or unsaturated fat on circulating SCFAs. Based on previous literature, we hypothesized that serum acetate, the main SCFA in circulation, increases on all high-fiber diets, but differently by macronutrient composition of the diet. OmniHeart is a randomized crossover trial of 164 men and women (≥30 y old); 163 participants with SCFA data were included in this analysis. We provided participants 3 isocaloric high-fiber (~30 g/2100 kcal) diets, each for 6 wk, in random order: a carbohydrate-rich (Carb) diet, a protein-rich (Prot) diet (protein predominantly from plant sources), and an unsaturated fat–rich (Unsat) diet. We used LC-MS to quantify SCFA concentrations in fasting serum, collected at baseline and the end of each diet period. We fitted linear regression models with generalized estimating equations to examine change in In-transformed SCFAs from baseline to the end of each diet; differences between diets; and associations of changes in SCFAs with cardiometabolic parameters. From baseline, serum acetate concentrations were
increased by the Prot (β: 0.24; 95% CI: 0.12, 0.35), Unsat (β: 0.21; 95% CI: 0.10, 0.33), and Carb (β: 0.12; 95% CI: 0.01, 0.24) diets; between diets, only Prot compared with Carb was significant (P = 0.02). Propionate was decreased by the Carb (β: −0.10; 95% CI: −0.16, −0.03) and Unsat (β: −0.10; 95% CI: −0.16, −0.04) diets, not the Prot diet; between diet comparisons of Carb vs. Prot (P = 0.006) and Unsat vs. Prot (P = 0.002) were significant. The Prot diet increased butyrate (β: 0.05; 95% CI: 0.00, 0.09) compared with baseline, but not compared with the other diets. Increases in acetate were associated with decreases in insulin and glucose; increases in propionate with increases in leptin, LDL cholesterol, and blood pressure; and increases in butyrate with increases in insulin and glucose and decreases in HDL cholesterol and ghrelin (Ps < 0.05). Macronutrient composition of high-fiber diets affects circulating SCFAs, which are associated with measures of appetite and cardiometabolic health.

**Low-Calorie Sweeteners**

**Short-Term Consumption of Sucralose With, But Not Without, Carbohydrate Impairs Neural and Metabolic Sensitivity to Sugar in Humans**

Dalenberg JR, Patel BP, Denis R, Veldhuizen MG, Nakamura Y, Vinke PC. *Cell Metab*. 2020 Mar 3;31(3):493–502.e7. doi: 10.1016/j.cmet.2020.01.014. [Article Link]

**Significance:** The results from this study suggest that consuming low-calorie sweeteners may decrease metabolic and neural responses to sugar when consumed with foods or drinks containing sugar, but not without.

Low-calorie sweeteners (LCSs) were developed to provide sweet taste without the calories. LCSs are present in thousands of food products despite a lack of consensus from the scientific community on their potential for causing negative effects on health. Here, investigators at Yale and their collaborators assessed brain activity, taste perception, and metabolic function before and after healthy volunteers consumed seven 355 mL beverages containing an LCS, a sugar, or the combination of LCS plus a sugar over a series of days. They discovered that consuming the LCS in combination with, but not without, the sugar decreased metabolic and neural responses to sugar, suggesting that consuming LCSs with foods or drinks containing real sugar (or carbohydrate) may negatively impact metabolic health.

**Bioactives**

**Can Dietary Self-Reports Usefully Complement Blood Concentrations for Estimation of Micronutrient Intake and Chronic Disease Associations?**

Prentice RL, Pettinger M, Neuhouse ML, Tinker LF, Huang Y, Zheng C. *Am J Clin Nutr*. 2020 Mar 4. pii: nqaa034. doi: 10.1093/ajcn/nqaa034. [Article Link]

**Significance:** Food frequency surveys may complement the interpretation of blood concentration data in estimating the intake of micronutrients from carotenoids (canned pumpkin, carrots) and tocopherols (found in vegetables, eggs and wheat germ).

We recently presented associations between serum-based biomarkers of carotenoid and tocopherol intake and chronic disease risk in a Women’s Health Initiative (WHI) Measurement Precision subcohort (n = 5488). Questions remain as to whether self-reported dietary data can usefully augment such biomarkers or can be calibrated using biomarkers for reliable disease association estimation in larger WHI cohorts. The aims were to examine the potential of FFQ data to explain intake variation in a WHI Feeding Study and to compare association parameter estimates and their precision from studies based on biomarker-calibrated FFQ intake in larger WHI cohorts, with those previously presented. Serum-based intake measures were augmented by using FFQ data in a WHI Feeding Study (n = 153). Corresponding calibration equations were generated, both in a companion Nutritional Biomarker Study (n = 436) and in the previously mentioned subcohort (n = 5488), by regressing these intake measures on dietary data and participant characteristics, for α- and β-carotene, lutein plus zeaxanthin, and α-tocopherol. The supplemental value of FFQ data was considered by examining the fraction of feeding study intake variation explained by these regression models. Calibrated intake and disease association analyses were evaluated by comparisons with previously reported subcohort results. The inclusion of FFQ data led to some increases in feeding study intake variation explained (total R² of ~50%). Calibrated intake estimates explained 25–75% of serum-based intake variation, whether developed using either of the 2 cohort subsamples. Related disease associations for micronutrients were precisely estimated in larger WHI cohorts (n = 76,691) but were often closer to the null compared with previously reported associations. FFQ data may usefully augment blood concentrations in estimating the intake of carotenoids and tocopherols. Calibrated intake estimates using FFQ, dietary supplement, and participant characteristics only may require further justification to ensure reliable estimation of related disease associations.
Sodium

Interim Effects of Salt Substitution on Urinary Electrolytes and Blood Pressure in the China Salt Substitute and Stroke Study (SSaSS)
Huang L, Tian M, Yu J, Li Q, Liu Y, Yin X. Am Heart J. 2020 Mar;221:136-145. doi: 10.1016/j.ahj.2019.12.020. Article Link

Significance: Preliminary results from a large-scale cluster randomized trial investigating the effects of salt substitute versus usual salt on stroke risk are presented. The overall estimated annual event rate for fatal and non-fatal stroke was 3.2% in this research.

The Salt Substitute and Stroke Study is an ongoing 5-year large-scale cluster randomized trial investigating the effects of potassium-enriched salt substitute compared to usual salt on the risk of stroke. The study involves 600 villages and 20,996 individuals in rural China. Intermediate risk markers were measured in a random subsample of villages every 12 months over 3 years to track progress against key assumptions underlying study design. Measures of 24-hour urinary sodium, 24-hour urinary potassium, blood pressure and participants’ use of salt substitute were recorded, with differences between intervention and control groups estimated using generalized linear mixed models. The primary outcome of annual event rate in the two groups combined was determined by dividing confirmed fatal and non-fatal strokes by total follow-up time in the first 2 years. The mean differences (95% CI) were -0.32 g (-0.68 to 0.05) for 24-hour urinary sodium, +0.77 g (+0.60 to +0.93) for 24-hour urinary potassium, -2.65 mmHg (-4.32 to -0.97) for systolic blood pressure and +0.30 mmHg (-0.72 to +1.32) for diastolic blood pressure. Use of salt substitute was reported by 97.5% in the intervention group versus 4.2% in the control group (P<.0001). The overall estimated annual event rate for fatal and non-fatal stroke was 3.2%. The systolic blood pressure difference and the annual stroke rate were both in line with the statistical assumptions underlying study design. The trial should be well placed to address the primary hypothesis at completion of follow-up.

Gut Microbiome

Current Explorations of Nutrition and the Gut Microbiome: A Comprehensive Evaluation of the Review Literature
Frame LA, Costa E, Jackson SA. Nutr Rev. 2020 Mar 25. pii: nuz106. doi: 10.1093/nutrit/nuz106. Article Link

Significance: This review aims to assess the understanding of the interactions between nutrition and the gut microbiome in healthy adults.

The ability to measure the gut microbiome led to a surge in understanding and knowledge of its role in health and disease. The diet is a source of fuel for and influencer of composition of the microbiome. To assess the understanding of the interactions between nutrition and the gut microbiome in healthy adults is the objective. PubMed and Google Scholar searches were conducted in March and August 2018 and were limited to the following: English, 2010–2018, healthy adults, and reviews. A total of 86 articles were independently screened for duplicates and relevance, based on preidentified inclusion criteria. Research has focused on dietary fiber – microbiota fuel. The benefits of fiber center on short-chain fatty acids, which are required by colonocytes, improve absorption, and reduce intestinal transit time. Contrastingly, protein promotes microbial protein metabolism and potentially harmful by-products that can stagnate in the gut. The microbiota utilize and produce micronutrients; the bidirectional relationship between micronutrition and the gut microbiome is emerging. Nutrition has profound effects on microbial composition, in turn affecting wide-ranging metabolic, hormonal, and neurological processes. There is no consensus on what defines a “healthy” gut microbiome. Future research must consider individual responses to diet.