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# Nutrition Briefs

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## Dietary Patterns

### Eating Timing: Associations with Dietary Intake and Metabolic Health

Taetzsch A, Roberts SB, Bukhari A, Lichtenstein AH, Gilhooly CH, Martin E, et al. *J Acad Nutr Diet*. 2021 Apr; 121(4):738-748. doi: 10.1016/j.jand.2020.10.001. [Article link](#).

**Significance:** In a population of overweight and obese women, eating timing and time-restricted feeding can be effective behavioral modification tools to improve diet. Future studies with varying combinations of eating timing and time-restricted feeding may be helpful to investigate weight gain in children and men.

**Background:** Emerging research indicates that eating timing may influence dietary intake and metabolic health. However, studies to date have not examined the association of multiple measures of eating timing with both dietary intake and metabolic health in adults with overweight and obesity. **Objective:** To examine the association of multiple measures of eating timing with dietary intake (ie, dietary composition, diet quality, and eating frequency) and metabolic health (ie, body composition and cardiometabolic risk). **Design:** This is a cross-sectional analysis of baseline data from a weight loss and maintenance intervention collected from May 2015 to January 2018. **Participants/setting:** Participants were women with overweight or obesity who were dependents of active duty and retired military personnel (N = 229; mean  $\pm$  standard error, BMI = 34.7  $\pm$  0.4 kg/m<sup>2</sup>, age = 40.9  $\pm$  0.7 years). The study was conducted at military installations in Massachusetts, Connecticut, New York, Colorado, and Kentucky. **Main outcome measures:** Eating timing variables examined included daily eating interval (time between first and last eating occasion), time-restricted eating ( $\leq$ 11 hours daily eating interval), early energy eaters (eating  $\geq$ 60% of energy during the first half of time awake), and bedtime eaters (eating within 2 hours of bedtime). **Statistical analysis:** The main analysis was limited to those reporting plausible energy intake (64% of total sample [n = 146]). Linear, quantile, or logistic regression models were used to determine the association of eating timing with measures of dietary intake and metabolic health. **Results:** In individuals reporting plausible energy intake, each additional 1 hour in daily eating interval was associated with 53 kcal higher energy intake, higher glycemic load, eating frequency, and waist circumference (P < 0.05 for all). Significant associations were observed for: time-restricted eating and a lower energy intake, glycemic load, and eating frequency; early energy eating and higher carbohydrate intake; bedtime eating and a higher energy intake, glycemic load, and eating frequency. **Conclusions:** These findings lend support for the mechanistic targeting of eating timing in behavioral interventions aimed at improving dietary intake and body composition.



## Protein

### Low Protein Intake, Physical Activity, and Physical Function in European and North American Community-Dwelling Older Adults: A Pooled Analysis of Four Longitudinal Aging Cohorts

Mendonça N, Hengeveld LM, Visser M, Presse N, Canhão H, Simonsick EM, et al. *Am J Clin Nutr*. 2021 Apr 7: nqab051. doi: 10.1093/ajcn/nqab051. [Article link](#).

**Significance:** Cohort studies of older adults in community living facilities found a dose-dependent correlation between protein intake and walking speed. Higher protein intake (1.2 g/kg bw/d) reduces walking decline, even for those at or below the recommended intake (0.8 g/kg bw/d).

**Background:** Dietary protein may slow the decline in muscle mass and function with aging, making it a sensible candidate to prevent or modulate disability progression. At present, studies providing reliable estimates of the association



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between protein intake and physical function, and its interaction with physical activity (PA), in community-dwelling older adults are lacking. **Objectives:** We investigated the longitudinal relation between protein intake and physical function, and the interaction with PA. **Methods:** We undertook a pooled analysis of individual participant data from cohorts in the PROMISS (Prevention Of Malnutrition In Senior Subjects in the European Union) consortium (the Health Aging and Body Composition Study, Quebec Longitudinal Study on Nutrition and Successful Aging, Longitudinal Aging Study Amsterdam, and Newcastle 85+) in which 5725 community-dwelling older adults were followed up to 8.5 y. The relation between protein intake and walking speed was determined using joint models (linear mixed-effects and Cox proportional hazards models) and the relation with mobility limitation was investigated using multistate models. **Results:** Higher protein intake was modestly protective of decline in walking speed in a dose-dependent manner [e.g., protein intake  $\geq 1.2$  compared with 0.8 g/kg adjusted body weight (aBW)/d:  $\beta = 0.024$ , 95% CI: 0.009, 0.032 SD/y], with no clear indication of interaction with PA. Participants with protein intake  $\geq 0.8$  g/kg aBW/d had also a lower likelihood of incident mobility limitation, which was observed for each level of PA. This association seemed to be dose-dependent for difficulty walking but not for difficulty climbing stairs. No associations between protein intake and other mobility limitations transitions were observed. **Conclusions:** Higher daily protein intake can reduce physical function decline not only in older adults with protein intake below the current RDA of 0.8 g/kg BW/d, but also in those with a protein intake that is already considered sufficient. This dose-dependent association was observed for each level of PA, suggesting no clear synergistic association between protein intake and PA in relation to physical function.

## Lipids

### A Combination of Single Nucleotide Polymorphisms Is Associated With the Interindividual Variability in the Blood Lipid Response to Dietary Fatty Acid Consumption in a Randomized Clinical Trial

Rajendiran E, Lamarche B, She Y, Ramprasath V, Eck P, Brassard D, et al. *Am J Clin Nutr.* 2021 Apr 19:nqab064. doi: 10.1093/ajcn/nqab064. [Article link.](#)

**Significance:** Individual variability in LCL cholesterol and TG levels can be explained by different SNP combinations generated following intakes of different fatty acids profiles. Generated multivariate models explained from 16.0 to 33.6% of the interindividual variability in LDL cholesterol concentration changes.

**Background:** Blood lipid concentrations display high interindividual variability in response to dietary interventions, partly due to genetic factors. Existing studies have focused on single nucleotide polymorphisms (SNPs) analyzed individually, which only explain a limited fraction of the variability of these complex phenotypes. **Objective:** We aimed to identify combinations of SNPs associated with the variability in LDL cholesterol and triglyceride (TG) concentration changes following 5 dietary interventions. **Design:** In a multicenter randomized crossover trial, 92 participants with elevated waist circumference and low HDL cholesterol concentrations consumed 5 isoenergetic diets for 4 wk: a diet rich in saturated fatty acids (SFAs) from cheese, SFA from butter, monounsaturated fatty acids (MUFAs), n-6 polyunsaturated fatty acids (PUFAs), and a diet higher in carbohydrates (CHO). The association between 22 candidate SNPs in genes involved in lipid and bile acid metabolism and transport and changes in LDL cholesterol and TG concentrations was assessed with univariate statistics followed by partial least squares regression. **Results:** Endpoint LDL cholesterol concentrations were significantly different (cheese:  $3.18 \pm 0.04$ , butter:  $3.31 \pm 0.04$ , MUFA:  $3.00 \pm 0.04$ , PUFA:  $2.81 \pm 0.04$ , CHO:  $3.11 \pm 0.04$  mmol/L;  $P < 0.001$ ) while endpoint TG concentrations were not ( $P = 0.117$ ). Both displayed consistently elevated interindividual variability following the dietary interventions (CVs of  $34.5 \pm 2.2\%$  and  $55.8 \pm 1.8\%$ , respectively). Among the 22 candidate SNPs, only ABCA1-rs2066714 and apolipoprotein E (APOE) isoforms exhibited consistent significant effects, namely on LDL cholesterol concentrations. However, several SNPs were significantly associated with changes in LDL cholesterol and TG concentrations in a diet-specific fashion. Generated multivariate models explained from 16.0 to 33.6% of the interindividual variability in LDL cholesterol concentration changes and from 17.5 to 32.0% of that in TG concentration changes. **Conclusions:** We report combinations of SNPs associated with a significant part of the variability in LDL cholesterol and TG concentrations following dietary interventions differing in their fatty acid profiles.

## Carbohydrates

### Diets Varying in Carbohydrate Content Differentially Alter Brain Activity in Homeostatic and Reward Regions in Adults

Holsen LM, Hoge WS, Lennerz BS, Cerit H, Hye T, Moondra P, et al. *J Nutr.* 2021 Apr 14:nxab090. doi: 10.1093/jn/nxab090. [Article link.](#)

**Significance:** Different intake levels of dietary carbohydrate differentially alter brain rCBFs in overweight adults. These changes may be due to insulin secretion. Chronic intake of a higher carbohydrate diet may affect brain reward centers and impede weight-loss maintenance.



**Background:** Obesity has one of the highest refractory rates of all chronic diseases, in part because weight loss induced by calorie restriction, the first-line treatment for obesity, elicits biological adaptations that promote weight regain. Although acute feeding trials suggest a role for macronutrient composition in modifying brain activity related to hunger and satiety, relevance of these findings to weight-loss maintenance has not been studied. **Objectives:** We investigated effects of weight-loss maintenance diets varying in macronutrient content on regional cerebral blood flow (rCBF) in brain regions involved in hunger and reward. **Methods:** In conjunction with a randomized controlled feeding trial, we investigated the effects of weight-loss maintenance diets varying in carbohydrate content [high, 60% of total energy: n = 20; 6 men/14 women; mean age: 32.5 y; mean BMI (in kg/m<sup>2</sup>): 27.4; moderate, 40% of total energy: n = 22; 10 men/12 women; mean age: 32.5

y; mean BMI: 29.0; low, 20% of total energy: n = 28; 12 men/16 women; mean age: 33.2 y; mean BMI: 27.7] on rCBF in brain regions involved in hunger and reward preprandial and 4 h postprandial after 14–20 wk on the diets. The primary outcome was rCBF in the nucleus accumbens (NAcc) at 4 h postprandial; the secondary outcome was preprandial rCBF in the hypothalamus. **Results:** Consistent with a priori hypothesis, at 4 h postprandial, NAcc rCBF was 43% higher in adults assigned to the high- compared with low-carbohydrate diet {P[family-wise error (FWE)-corrected] < 0.05}. Preprandial hypothalamus rCBF was 41% higher on high-carbohydrate diet [P(FWE-corrected) < 0.001]. Exploratory analyses revealed that elevated rCBF on high-carbohydrate diet was not specific to prandial state: preprandial NAcc rCBF [P(FWE-corrected) < 0.001] and 4 h postprandial rCBF in hypothalamus [P(FWE-corrected) < 0.001]. Insulin secretion predicted differential postprandial activation of the NAcc by diet. **Conclusions:** We report significant differences in rCBF in adults assigned to diets varying in carbohydrate content for several months, which appear to be partially associated with insulin secretion. These findings suggest that chronic intake of a high-carbohydrate diet may affect brain reward and homeostatic activity in ways that could impede weight-loss maintenance.

## Low- and No-Calorie Sweeteners

### D-Tagatose Feeding Reduces the Risk of Sugar-Induced Exacerbation of Myocardial I/R Injury When Compared to Its Isomer Fructose

Durante M, Sgambellone S, Lucarini L, Failli P, Laurino A, Collotta D, et al. *Front Mol Biosci.* 2021 Apr 13;8:650962. doi: 10.3389/fmolb.2021.650962. [Article link.](#)

**Significance:** In a 12-week study with rats fed diet with 30% D-tagatose or fructose, D-tagatose offered a better alternative to its fructose isomer, presenting lower risk of adverse effects on metabolic profile and related heart I/R injury.

It is known that fructose may contribute to myocardial vulnerability to ischemia/reperfusion (I/R) injury. D-tagatose is a fructose isomer with less caloric value and used as low-calorie sweetener. Here we compared the metabolic impact of fructose or D-tagatose enriched diets on potential exacerbation of myocardial I/R injury. Wistar rats were randomly allocated in the experimental groups and fed with one of the following diets: control (CTRL), 30% fructose-enriched (FRU 30%) or 30% D-tagatose-enriched (TAG 30%). After 24 weeks of dietary manipulation, rats underwent myocardial injury caused by 30 min ligation of the left anterior descending (LAD) coronary artery followed by 24 h' reperfusion. Fructose consumption resulted in body weight increase (49%) as well as altered glucose, insulin and lipid profiles. These effects were associated with increased I/R-induced myocardial damage, oxidative stress (36.5%) and inflammation marker expression. TAG 30%-fed rats showed lower oxidative stress (21%) and inflammation in comparison with FRU-fed rats. Besides, TAG diet significantly reduced plasmatic inflammatory cytokines and GDF8 expression (50%), while increased myocardial endothelial nitric oxide synthase (eNOS) expression (59%). Overall, we demonstrated that D-tagatose represents an interesting sugar alternative when compared to its isomer fructose with reduced deleterious impact not only on the metabolic profile but also on the related heart susceptibility to I/R injury.

## Bioactives

### Micronutrients and Bioactive Substances: Their Potential Roles in Combating COVID-19

Keflie TS, Biesalski HK. *Nutrition.* 2021 Apr;84:111103. doi: 10.1016/j.nut.2020.111103. [Article link.](#)

**Significance:** The role of micronutrients and bioactives in the immune response to prevent or combat the effect of COVID-19 infection remains understudied and limited. Future research should focus on immunomodulatory, anti-inflammatory, antioxidant, and antiviral properties of these nutrients.

**Objectives:** The coronavirus disease 2019 (COVID-19) pandemic is seriously threatening public health and setting off huge economic crises across the world. In the absence of specific drugs for COVID-19, there is an urgent need to look for alternative approaches. Therefore, the aim of this paper was to review the roles of micronutrients and bioactive substances as potential alternative approaches in combating COVID-19. **Methods:** This review was based on the literature identified using electronic searches in different databases. **Results:** Vitamins (A, B, C, D, and E), minerals (selenium and zinc), and bioactive substances from curcumin, echinacea, propolis, garlic, soybean, green tea, and other polyphenols were identified as having potential roles in interfering with spike glycoproteins, angiotensin converting enzyme 2, and transmembrane protease serine 2 at the entry site, and inhibiting activities of papain-like protease, 3 chymotrypsin-like protease, and RNA-dependent RNA polymerase in the replication cycle of severe acute respiratory syndrome coronavirus 2. Having immunomodulating, anti-inflammatory, antioxidant, and antiviral properties, such micronutrients and bioactive substances are consequently promising alternative nutritional approaches to combat COVID-19. **Conclusions:** The roles of micronutrients and bioactive substances in the fight against COVID-19 are exciting areas of research. This review may suggest directions for further study.

## Sodium

### Differences in Hypertension Prevalence and Hypertension Control by Urbanization Among Adults in the United States, 2013-2018

Osthegea Y, Hughes JP, Zhang G, Nwankwo T, Graber J, Nguyen DT. *Am J Hypertens*. 2021 Apr 28;hpabo67. doi: 10.1093/ajh/hpabo67. [Article link](#).

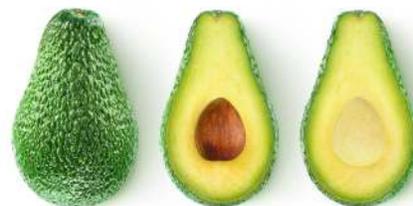
**Significance:** Dietary sodium reduction has been recommended for all Americans to reduce high blood pressure. NHANES data from 2013 to 2018 found that the prevalence of hypertension (stage II) increases with urbanization. Such information could enhance the design of interventions to reduce dietary sodium.

**Objective:** To examine the associations between urbanization and hypertension, stage II hypertension, and hypertension control. **Methods:** Data on 16,360 U.S. adults aged 18 years or older from the 2013-2018 National Health and Nutrition Examination Survey (NHANES) were used to estimate the prevalence of hypertension (blood pressure (BP)  $\geq 130/80$  mm Hg or use of medication for hypertension), stage II hypertension (BP  $\geq 140/90$  mm Hg), and hypertension control (BP  $< 130/80$  mm Hg among hypertensives) by urbanization, classified by levels of metropolitan statistical areas as large MSAs (population  $\geq 1,000,000$ ), medium to small MSAs (population 50,000-999,999), and non-MSAs (population  $< 50,000$ ). **Results:** All prevalence ratios (PRs) were compared with large MSAs and adjusted for demographics and risk factors. The PRs of hypertension were 1.07 (95% CI= 0.99-1.14) for adults residing in medium to small MSAs and 1.06 (95% CI=0.99-1.13) for adults residing in non-MSAs, For stage II hypertension, the PRs were higher for adults residing in medium to small MSAs 1.21 (95% CI =1.06-1.36) but not for adults residing in non-MSAs 1.06 (95% CI= 0.88-1.29). For hypertension control, the PRs were 0.96 (95% CI=0.91-1.01) for adults residing in medium to small MSAs and 1.00 (95% CI=0.93-1.06) for adults residing in non-MSAs. **Conclusion:** Among U.S. adults, urbanization was associated with stage II hypertension.

## Gut Microbiome

### Avocado Consumption Alters Gastrointestinal Bacteria Abundance and Microbial Metabolite Concentrations among Adults with Overweight or Obesity: A Randomized Controlled Trial

Thompson SV, Bailey MA, Taylor AM, Kaczmarek JL, Mysonhimer AR, Edwards CG, et al. *J Nutr*. 2021 Apr 8;151(4):753-762. doi: 10.1093/jn/nxaa219. [Article link](#).



**Significance:** A small 12-week RCT study with overweight and obese subjects reported that daily intake of avocado (140-170 g/d) led to a decrease in intestinal bile acid, increase in SCFAs, and greater abundance/diversity of fermenting bacteria.

**Background:** Avocados are rich in dietary fiber and monounsaturated fatty acids (MUFAs), nutrients that have been independently connected to metabolic health benefits and the gastrointestinal microbiota. **Objectives:** We aimed to evaluate

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the impact of avocado consumption on the gastrointestinal microbiota and microbial metabolites, secondary outcomes of the *Persea americana* for Total Health (PATH) study, and conduct exploratory analyses to assess relations between the fecal microbiota, fecal metabolites, and health markers. **Methods:** Adults [n = 163, 25-45 y, BMI (kg/m<sup>2</sup>) ≥ 25.0] were enrolled in the PATH study, a 12-wk investigator-blinded trial where participants were batch randomized to match the 2 groups by age, sex, visceral adiposity, and fasting glucose concentrations. Participants consumed isocaloric meals with or without avocado (175 g, men; 140 g, women) once daily for 12 wk. The fecal microbiota was assessed with 16S ribosomal RNA gene (V4 region) sequencing and analysis using DADA2 and QIIME2. Fecal fatty acid and bile acid concentrations were quantified using GC and LC-MS. Per-protocol (≥80% meal consumption) and intent-to-treat analyses were conducted using univariate ANOVA and Mann-Whitney U tests. Bivariate correlations were conducted between fecal microbiota, fecal metabolites, and health measures. **Results:** The avocado treatment increased a diversity and enriched *Faecalibacterium*, *Lachnospira*, and *Alistipes* between 26% and 65% compared with the control group. The avocado group had 18% greater fecal acetate, 70% greater stearic acid, and 98% greater palmitic acid concentrations than the control group, while the concentrations of the bile acids cholic and chenodeoxycholic acid were 91% and 57% lower, respectively. **Conclusions:** Daily avocado consumption resulted in lower fecal bile acid concentrations, greater fecal fatty acid and SCFAs, and greater relative abundances of bacteria capable of fiber fermentation, providing evidence that this nutrient-dense food affects digestive physiology, as well as the composition and metabolic functions of the intestinal microbiota.