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Biomarkers

25-Hydroxyvitamin D as a Biomarker of Vitamin D Status and Its Modeling to Inform Strategies for Prevention of Vitamin D Deficiency Within the Population

Cashman KD, van den Heuvel EG, Schoemaker RJ, Prévéraud DP, Macdonald HM, Arcot J. *Adv Nutr.* 2017 Nov 15;8(6):947–957. [Article Link](#)

Significance: This article provides a state-of-the-art summary of how vitamin D modeling can be used to predict population serum 25(OH)D and inform strategies to address low vitamin D status.

There is substantial evidence that the prevalence of vitamin D deficiency is unacceptably high in the population, and this requires action from a public health perspective. Circulating 25-hydroxyvitamin D [25(OH)D] is a robust and reliable marker of vitamin D status and has been used by numerous agencies in the establishment of vitamin D dietary requirements and for population surveillance of vitamin D deficiency or inadequacy. In a wider context, modeling of serum 25(OH)D data and its contributory sources, namely dietary vitamin D supply and UVB availability, can inform our understanding of population vitamin D status. The aim of this review is to provide the current status of knowledge in relation to modeling of such vitamin D-relevant data. We begin by highlighting the importance of the measurement of 25(OH)D and its standardization, both of which have led to new key data on the prevalence of vitamin D deficiency and inadequacy in North America and Europe. We then overview how state-of-the-art modeling can be used to inform our understanding of the potential effect of ergocalciferol and 25(OH)D on vitamin D intake estimates and how meteorological data on UVB availability, when coupled with other key data, can help predict population serum 25(OH)D concentration, even accounting for seasonal fluctuations, and lastly, how these *in silico* approaches can help inform policymakers on strategic options on addressing low vitamin D status through food-based approaches and supplementation. The potential of exemplar food-based solutions will be highlighted, as will the possibility of synergies between vitamin D and other dairy food-based micronutrients, in relation to vitamin D status and bone health. Lastly, we will briefly consider the interactions between season and vitamin D supplements on vitamin D status and health.

Bioactives

The Nitrate-Independent Blood Pressure-Lowering Effect of Beetroot Juice: A Systematic Review and Meta-Analysis

Bahadoran Z, Mirmiran P, Kabir A, Azizi F, Ghasemi A. *Adv Nutr.* 2017 Nov 15;8(6):830–838. [Article Link](#)

Significance: This systematic review of RCTs indicated that beetroot juice (and potentially NO₃ independently) may lower blood pressure.



Beetroot is considered a complementary treatment for hypertension because of its high content of inorganic NO₃. This systematic review and meta-analysis aimed to clarify several aspects of beetroot juice supplementation on systolic blood pressure (SBP) and diastolic blood pressure (DBP). We searched PubMed, Scopus, and Embase databases, and the reference lists of previous reviews. Randomized clinical trials that investigated the effects of beetroot juice on resting blood pressure in humans were recruited for quality assessment, meta-analyses, subgroup analyses, and meta-regressions; of these, 22 were conducted between 2009 and 2017 and included a total of 47 intervention (n = 650) and 43 control (n = 598) groups. Overall, SBP (-3.55 mm Hg; 95% CI: -4.55, -2.54 mm Hg) and DBP (-1.32 mm Hg; 95% CI: -1.97, -0.68 mm Hg) were significantly lower in the beetroot juice-supplemented groups than in the control groups. The mean difference of SBP was larger between beetroot juice-supplemented and control groups in the longer than in the shorter (≥ 14 compared with < 14 d) study durations (-5.11 compared with -2.67 mm Hg) and the highest compared with the lowest (500 compared with 70 and 140 mL/d) doses of beetroot juice (-4.78 compared with -2.37 mm Hg). A positive correlation was observed between beetroot juice doses and the mean differences of blood pressures. In contrast, a smaller effect size of blood pressures was observed after supplementation with higher NO₃

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(milligrams per 100 mL beetroot juice). A weak effect size was observed in a meta-analysis of trials that used NO₃-depleted beetroot juice as a placebo compared with other interventions (-3.09 compared with -4.51 mm Hg for SBP and -0.81 compared with -2.01 mm Hg for DBP). Our results demonstrate the blood pressure-lowering effects of beetroot juice and highlight its potential NO₃-independent effects.

Dietary Guidance for Lutein: Consideration for Intake Recommendations Is Scientifically Supported

Ranard KM, Jeon S, Mohn ES, Griffiths JC, Johnson EJ, Erdman JW Jr. *Eur J Nutr*. 2017 Nov 17. doi: 10.1007/s00394-017-1580-2. [Article Link](#)

Significance: The authors conclude that available data for lutein meet the 9 criteria for pursuit of a bioactive DRI, as outlined previously by Lupton et al.

Lutein, a yellow xanthophyll carotenoid found in egg yolks and many colorful fruits and vegetables, has gained public health interest for its putative role in visual performance and reducing the risk of age-related macular degeneration. The National Academies of Sciences, Engineering and Medicine's recommended Dietary Reference Intakes (DRIs) focus on preventing deficiency and toxicity, but there is a budding interest in establishing DRI-like guidelines for non-essential bioactives, like lutein, that promote optimal health and/or prevent chronic diseases. Lupton et al. developed a set of nine criteria to determine whether a bioactive is ready to be considered for DRI-like recommendations. These criteria include: (1) an accepted definition; (2) a reliable analysis method; (3) a food database with known amounts of the bioactive; (4) cohort studies; (5) clinical trials on metabolic processes; (6) clinical trials for dose-response and efficacy; (7) safety data; (8) systematic reviews and/or meta-analyses; (9) a plausible biological rationale. Based on a review of the literature supporting these criteria, lutein is ready to be considered for intake recommendations. Establishing dietary guidance for lutein would encourage the consumption of lutein-containing foods and raise public awareness about its potential health benefits.

Dietary Patterns and Quality

Food Groups and Risk of Hypertension: A Systematic Review and Dose-Response Meta-Analysis of Prospective Studies

Schwingshackl L, Schwedhelm C, Hoffmann G, Knüppel S, Iqbal K, Andriolo V, et al. *Adv Nutr*. 2017 Nov 15;8(6):793–803. [Article Link](#)

Significance: In this systematic review and meta-analysis, optimal intake amounts of whole grains, fruits, nuts, dairy, red meat, processed meat, and SSBs were identified as related to reducing the risk of hypertension.

The aim of this systematic review and meta-analysis was to summarize the evidence on the relation of the intakes of 12 major food groups, including whole grains, refined grains, vegetables, fruits, nuts, legumes, eggs, dairy, fish, red meat, processed meat, and sugar-sweetened beverages (SSBs) with the risk of hypertension. PubMed, Scopus, and Web of Science were searched systematically until June 2017 for prospective studies having quantitatively investigated the above-mentioned foods. We conducted meta-analysis on the highest compared with the lowest intake categories and linear and nonlinear dose-response meta-analyses to analyze the association. Summary RRs and 95% CIs were estimated by using a random-effects model. Overall, 28 reports were included in the meta-analysis. An inverse association for the risk of hypertension was observed for 30 g whole grains/d (RR: 0.92; 95% CI: 0.87, 0.98), 100 g fruits/d (RR: 0.97; 95% CI: 0.96, 0.99), 28 g nuts/d (RR: 0.70; 95% CI: 0.45, 1.08), and 200 g dairy/d (RR: 0.95; 95% CI: 0.94, 0.97), whereas a positive association for 100 g red meat/d (RR: 1.14; 95% CI: 1.02, 1.28), 50 g processed meat/d (RR: 1.12; 95% CI: 1.00, 1.26), and 250 mL SSB/d (RR: 1.07; 95% CI: 1.04, 1.10) was seen in the linear dose-response meta-analysis. Indication for nonlinear relations of the intakes of whole grains, fruits, fish, and processed meats with the risk of hypertension was detected. In summary, this comprehensive dose-response meta-analysis of 28 reports identified optimal intakes of whole grains, fruits, nuts, legumes, dairy, red and processed meats, and SSBs related to the risk of hypertension. These findings need to be seen under the light of very-low to low quality of meta-evidence. However, the findings support the current dietary guidelines in the prevention of hypertension.

Diet Quality Is Linked to Insulin Resistance Among Adults in China

Wang Z, Adair LS, Cai J, Gordon-Larsen P, Siega-Riz AM, Zhang B, et al. *J Nutr*. 2017 Nov;147(11):2102–2108. [Article Link](#)

Significance: Baseline and changes in diet quality were independently associated with lower HOMA-IR and plasma insulin but not with fasting blood glucose and HbA_{1c} in Chinese adults.

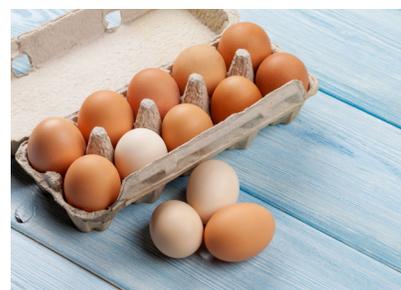
Background: Little is known about the impact of Chinese diet quality changes on diabetes-related markers. **Objective:** The present study examined the association of changes in overall diet quality with various biomarkers of diabetes among adults in China. **Methods:** The current analysis used longitudinal diet data from 1991 to 2006 and fasting blood samples from 2009 for 4734 adults aged 18–65 y from the China Health and Nutrition Survey. Dietary intake was assessed by using 3 consecutive 24-h recalls and household food weighing. The tailored Alternative Healthy Eating Index (tAHEI) was adapted from the 2010 Harvard Alternative Healthy Eating Index to measure overall diet quality. We categorized baseline tAHEI scores into tertiles and annual changes in the scores into 5 levels (high decrease, low decrease, maintain, low increase, and high increase). We performed mixed-effects regressions to assess the associations between baseline scores and changes in the tAHEI scores and diabetes or insulin markers. **Results:** Adults with high baseline tAHEI scores tended to be male, older, of lower socioeconomic status, and with higher physical activity levels. After adjustment for all of the covariates, insulin and homeostasis model assessment of insulin resistance (HOMA-IR) values were 5.1% (95% CI: -0.100, -0.002) and 5.7% (95% CI: -0.113, -0.001) lower, respectively, for adults with high compared with low baseline tAHEI scores and 8.6% (95% CI: -0.155, -0.017) and 9.8% (95% CI: -0.177, -0.018) lower, respectively, for adults with a high increase in score compared with the “maintain” category. Null associations were observed between baseline scores and changes in the scores and fasting blood glucose, glycated hemoglobin (HbA1c), and diabetes prevalence. **Conclusions:** Baseline and changes in diet quality were independently associated with lower HOMA-IR and plasma insulin but not with fasting blood glucose and HbA1c in Chinese adults. Prospective studies on overall diet quality in relation to diabetes markers and risk of diabetes are needed.

Micronutrients

Eggs Early in Complementary Feeding Increase Choline Pathway Biomarkers and DHA: A Randomized Controlled Trial in Ecuador

Iannotti LL, Lutter CK, Waters WF, Gallegos Riofrío CA, Malo C, Reinhart G, et al. *Am J Clin Nutr.* 2017 Nov 1. doi: 10.3945/ajcn.117.160515. [Article Link](#)

Significance: This RCT in infants ages 6–9 years indicated that provision of 1 egg/d for a period of 6 months significantly improved choline status and other markers of methyl group metabolism.



Background: Choline status has been associated with stunting among young children. Findings from this study showed that an egg intervention improved linear growth by a length-for-age z score of 0.63. **Objective:** We aimed to test the efficacy of eggs introduced early in complementary feeding on plasma concentrations of biomarkers in choline pathways, vitamins B-12 and A, and essential fatty acids. **Design:** A randomized controlled trial, the Lulun (“egg” in Kichwa) Project, was conducted in a rural indigenous population of Ecuador. Infants aged 6–9 mo were randomly assigned to treatment (1 egg/d for 6 mo; n = 80) and control (no intervention; n = 83) groups. Socioeconomic data, anthropometric measures, and blood samples were collected at baseline and endline. Household visits were made weekly for morbidity surveillance. We tested vitamin B-12 plasma concentrations by using chemiluminescent competitive immunoassay and plasma concentrations of choline, betaine, dimethylglycine, retinol, essential fatty acids, methionine, dimethylamine (DMA), trimethylamine, and trimethylamine-N-oxide (TMAO) with the use of liquid chromatography-tandem mass spectrometry. **Results:** Socioeconomic factors and biomarker concentrations were comparable at baseline. Of infants, 11.4% were vitamin B-12 deficient and 31.7% marginally deficient at baseline. In adjusted generalized linear regression modeling, the egg intervention increased plasma concentrations compared with control by the following effect sizes: choline, 0.35 (95% CI: 0.12, 0.57); betaine, 0.29 (95% CI: 0.01, 0.58); methionine, 0.31 (95% CI: 0.03, 0.60); docosahexaenoic acid, 0.43 (95% CI: 0.13, 0.73); DMA, 0.37 (95% CI: 0.37, 0.69); and TMAO, 0.33 (95% CI: 0.08, 0.58). No significant group differences were found for vitamin B-12, retinol, linoleic acid (LA), α -linolenic acid (ALA), or ratios of betaine to choline and LA to ALA. **Conclusion:** The findings supported our hypothesis that early introduction of eggs significantly improved choline and other markers in its methyl group metabolism pathway.

A 25-Hydroxycholecalciferol-Fortified Dairy Drink Is More Effective at Raising a Marker of Postprandial Vitamin D Status Than Cholecalciferol in Men With Suboptimal Vitamin D Status

Guo J, Jackson KG, Che Taha CSB, Li Y, Givens DI, Lovegrove JA. *J Nutr.* 2017 Nov;147(11):2076–2082. [Article Link](#)

Significance: In this randomized, controlled, 3-way crossover, double-blind, postprandial study in 17 men, a 25-hydroxycholecalciferol-fortified dairy drink was more effective at raising serum (OH)D₃ concentrations at 24 h.

Background: One strategy for improving population vitamin D status is consumption of fortified foods. However, the effects of dairy products fortified with different vitamin D isoforms on postprandial vitamin D status and metabolic outcomes have not been addressed. **Objective:** We investigated whether consumption of dairy drinks fortified with either 25-hydroxycholecalciferol [25(OH)D₃] or cholecalciferol (vitamin D₃) had differential effects on 24-h circulating plasma 25(OH)D₃ concentration (a marker of vitamin D status) and cardiometabolic risk markers. **Methods:** A randomized, controlled, 3-way crossover, double-blind, postprandial study was conducted in 17 men with suboptimal vitamin D status [mean \pm SEM age: 49 \pm 3 y; body mass index (in kg/

m2): 26.4 ± 0.6 ; and plasma 25(OH)D3 concentration: 31.7 ± 3.4 nmol/L]. They were randomly assigned to consume 3 different test meals (4.54 MJ, 51 g fat, 125 g carbohydrate, and 23 g protein), which contained either a nonfortified dairy drink (control), 20 μ g 25(OH)D3-fortified (+HyD3) dairy drink, or 20 μ g vitamin D3-fortified (+D3) dairy drink with toasted bread and jam on different occasions, separated by a 2-wk washout. Plasma 25(OH)D3 concentrations and cardiometabolic risk markers, including vascular stiffness, serum lipids, and inflammatory markers, were measured frequently within 8 h postprandially and 24 h after the dairy drink was consumed. **Results:** Plasma 25(OH)D3 concentrations (the primary outcome) were significantly higher after the +HyD3 dairy drink was consumed compared with +D3 and control ($P = 0.019$), which was reflected in the 1.5-fold and 1.8-fold greater incremental area under the curve for the 0-8 h response, respectively. The change in plasma 25(OH)D3 concentrations from baseline to 24 h for the +HyD3 dairy drink was also 0.9-fold higher than the +D3 dairy drink and 4.4-fold higher than the control ($P < 0.0001$), which were not significantly different from each other. **Conclusion:** The dairy drink fortified with 25(OH)D3 was more effective at raising plasma 25(OH)D3 concentrations postprandially than was the dairy drink fortified with vitamin D3 in men with suboptimal vitamin D status.

Carbohydrates and Fiber

Effects of Isolated Soluble Fiber Supplementation on Body Weight, Glycemia, and Insulinemia in Adults With Overweight and Obesity: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Thompson SV, Hannon BA, An R, Holscher HD. *Am J Clin Nutr.* 2017 Nov 1. pii: ajcn163246. doi: 10.3945/ajcn.117.163246. [Article Link](#)

Significance: This systematic review and meta-analysis indicated that provision of a fiber intervention for between 2 to 17 weeks resulted in significantly positive effects on markers of body weight and body composition and blood glucose metabolism.

Background: There is strong epidemiologic evidence that dietary fiber intake is protective against overweight and obesity; however, results of intervention studies have been mixed. Soluble fiber beneficially affects metabolism, and fiber supplementation may be a feasible approach to improve body composition and glycemia in adults with overweight and obesity. **Objective:** We evaluated randomized controlled trials (RCTs) of isolated soluble fiber supplementation in overweight and obese adults on outcomes related to weight management [body mass index (BMI; in kg/m^2), body weight, percentage of body fat, and waist circumference] and glucose and insulin metabolism (homeostasis model assessment of insulin resistance and fasting insulin) through a systematic review and meta-analysis. **Design:** We searched PubMed, Web of Science, Cumulative Index to Nursing and Allied Health Literature and Cochrane Library databases. Eligible studies were RCTs that compared isolated soluble fiber with placebo treatments without energy-restriction protocols. Random-effects models were used to estimate pooled effect sizes and 95% CIs. Meta-regressions were performed to assess outcomes in relation to the intervention duration, fiber dose, and fiber type. Publication bias was assessed via Begg's and Egger's tests and funnel plot inspection. **Results:** Findings from 12 RCTs ($n = 609$ participants) from 2 to 17 wk of duration are summarized in this review. Soluble fiber supplementation reduced BMI by 0.84 (95% CI: -1.35, -0.32; $P = 0.001$), body weight by 2.52 kg (95% CI: -4.25, -0.79 kg; $P = 0.004$), body fat by 0.41% (95% CI: -0.58%, -0.24%; $P < 0.001$), fasting glucose by 0.17 mmol/L (95% CI: -0.28, -0.06 mmol/L; $P = 0.002$), and fasting insulin by 15.88 pmol/L (95% CI: -29.05, -2.71 pmol/L; $P = 0.02$) compared with the effects of placebo treatments. No publication bias was identified. Considerable between-study heterogeneity was observed for most outcomes. **Conclusions:** Isolated soluble fiber supplementation improves anthropometric and metabolic outcomes in overweight and obese adults, thereby indicating that supplementation may improve fiber intake and health in these individuals. However, the interpretation of these findings warrants caution because of the considerable between-study heterogeneity.

Association of Whole Grain Intake With All-Cause, Cardiovascular, and Cancer Mortality: A Systematic Review and Dose-Response Meta-Analysis From Prospective Cohort Studies

Zhang B, Zhao Q, Guo W, Bao W, Wang X. *Eur J Clin Nutr.* 2017 Nov 1. doi: 10.1038/ejcn.2017.149. [Article Link](#)



Significance: This systematic review and meta-analysis indicated that whole grain intake was inversely associated with risk of total, CVD, and cancer mortality.

Background/Objectives: Whole grains are rich source of nutrients and have shown beneficial effects on human health. This study was designed to systematically review the existing results and quantitatively assess the dose-response relationship of whole grain intake with all-cause and cause-specific mortality. **Subjects/Methods:** We searched 'whole grain' or 'whole grains' in combination with 'mortality' or 'cardiovascular disease' or 'cancer' through the Web of Science and PubMed databases till 20 January 2016. To be eligible for inclusion, publications should be prospective cohort studies and reported the influence of whole grain intake on human mortality. Relative risks (RRs) and 95% confidence intervals (CIs) from the included studies were pooled by a random effects model or fixed effect model. **Results:** We included 19 cohort studies from 17 articles, with 1 041 692 participants and 96 710 deaths in total, in the analyses. We observed an inverse relationship of whole grain intake with risk of total, cardiovascular

disease and cancer mortality. The pooled RR was 0.84 (95% CI 0.81-0.88, n=9) for total mortality, 0.83 (95% CI 0.79-0.86, n=8) for CVD mortality and 0.94 (95% CI 0.87-1.01, n=14) for cancer mortality, comparing the highest intake of whole grain with the lowest category. For dose-response analysis, we found a nonlinear relationship of whole grain intake with risk of total, cardiovascular and cancer mortality. Each 28 g/d intake of whole grains was associated with a 9% (pooled RR: 0.91 (0.90-0.93)) lower risk for total mortality, 14% (pooled RR: 0.86 (0.83-0.89)) lower risk for CVD mortality and 3% (pooled RR: 0.97 (0.95-0.99)) lower risk for cancer mortality. **Conclusions:** Our study shows that whole grain intake was inversely associated with risk of total, CVD and cancer mortality. Our results support current dietary guidelines to increase the intake of whole grains. Government officials, scientists and medical staff should take actions to promote whole grains intake.

A High-Carbohydrate, High-Fiber, Low-Fat Diet Results in Weight Loss among Adults at High Risk of Type 2 Diabetes

Sylvetsky AC, Edelstein SL, Walford G, Boyko EJ, Horton ES, Ibebuogu UN, et al.; Diabetes Prevention Program Research Group. *J Nutr.* 2017 Nov;147(11):2060–2066. [Article Link](#)

Significance: In the Diabetes Prevention Program study, higher carbohydrate consumption, specifically high-fiber carbohydrates, and lower total and saturated fat intake best predicted weight loss when adjusted for changes in calorie intake.

Background: Weight loss is a key factor in reducing diabetes risk. The Diabetes Prevention Program (DPP) is a completed clinical trial that randomly assigned individuals at high risk of diabetes to a placebo (PLBO), metformin (MET), or intensive lifestyle intervention (ILS) group, which included physical activity (PA) and reduced dietary fat intake. **Objective:** We aimed to evaluate the associations between diet and weight at baseline and to identify specific dietary factors that predicted weight loss among DPP participants. **Methods:** Diet was assessed by a food frequency questionnaire. The associations between intakes of macronutrients and various food groups and body weight among DPP participants at baseline were assessed by linear regression, adjusted for race/ethnicity, age, sex, calorie intake, and PA. Models that predicted weight loss at year 1 were adjusted for baseline weight, change in calorie intake, and change in PA and stratified by treatment allocation (MET, ILS, and PLBO). All results are presented as estimates \pm SEs. **Results:** A total of 3234 participants were enrolled in the DPP; 2924 had completed dietary data (67.5% women; mean age: 50.6 \pm 10.7 y). Adjusted for calorie intake, baseline weight was negatively associated with carbohydrate intake (-1.14 \pm 0.18 kg body weight/100 kcal carbohydrate, $P < 0.0001$) and, specifically, dietary fiber (-1.26 \pm 0.28 kg/5 g fiber, $P < 0.0001$). Baseline weight was positively associated with total fat (1.25 \pm 0.21 kg/100 kcal, $P < 0.0001$), saturated fat (1.96 \pm 0.46 kg/100 kcal, $P < 0.0001$), and protein (0.21 \pm 0.05 kg/100 kcal, $P < 0.0001$). For all groups, weight loss after 1 y was associated with increases in carbohydrate intake, specifically dietary fiber, and decreases in total fat and saturated fat intake. **Conclusions:** Higher carbohydrate consumption among DPP participants, specifically high-fiber carbohydrates, and lower total and saturated fat intake best predicted weight loss when adjusted for changes in calorie intake. Our results support the benefits of a high-carbohydrate, high-fiber, low-fat diet in the context of overall calorie reduction leading to weight loss, which may prevent diabetes in high-risk individuals.

Plasma Glucose and Insulin Responses After Consumption of Breakfasts With Different Sources of Soluble Fiber in Type 2 Diabetes Patients: A Randomized Crossover Clinical Trial

de Carvalho CM, de Paula TP, Viana LV, Machado VM, de Almeida JC, Azevedo MJ. *Am J Clin Nutr.* 2017 Nov;106(5):1238–1245. [Article Link](#)

Significance: Higher fiber intake was associated with lower postprandial glucose at breakfast, and the intake of soluble fiber from food and supplements had a similar effect in patients with T2D.

Background: The amount and quality of carbohydrates are important determinants of plasma glucose after meals. Regarding fiber content, it is unclear whether the intake of soluble fibers from foods or supplements has an equally beneficial effect on lowering postprandial glucose. **Objective:** The aim of our study was to compare the acute effect of soluble fiber intake from foods or supplements after a common meal on postprandial plasma glucose and plasma insulin in patients with type 2 diabetes (T2D). **Design:** A randomized crossover clinical trial was conducted in patients with T2D. Patients consumed isocaloric breakfasts (mean \pm SD: 369.8 \pm 9.4 kcal) with high amounts of fiber from diet food sources (total fiber: 9.7 g; soluble fiber: 5.4 g), high amounts of soluble fiber from guar gum supplement (total fiber: 9.1 g; soluble fiber: 5.4 g), and normal amounts of fiber (total fiber: 2.4 g; soluble fiber: 0.8 g). Primary outcomes were postprandial plasma glucose and insulin (0-180 min). Data were analyzed by repeated measures ANOVA and post hoc Bonferroni test. **Results:** A total of 19 patients [aged 65.8 \pm 7.3 y; median (IQR), 10 (5-9) y of T2D duration; glycated hemoglobin 7.0% \pm 0.8%; body mass index (in kg/m²) 28.2 \pm 2.9] completed 57 meal tests. After breakfast, the incremental area under the curve (iAUC) for plasma glucose [mg/dL \cdot min; mean (95% CI)] did not differ between high fiber from diet (HFD) [7861 (6257, 9465)] and high fiber from supplement (HFS) [7847 (5605, 10,090)] ($P = 1.00$) and both were lower than usual fiber (UF) [9527 (7549, 11,504)] ($P = 0.014$ and $P = 0.037$, respectively). iAUCs [μ IU/mL \cdot min; mean (95% CI)] did not differ ($P = 0.877$): HFD [3781 (2513, 5050)], HFS [4006 (2711, 5302)], and UF [4315 (3027, 5603)]. **Conclusions:** Higher fiber intake was associated with lower postprandial glucose at breakfast, and the intake of soluble fiber from food and supplement had a similar effect in patients with T2D.

Biomarkers

Surrogate Disease Markers as Substitutes for Chronic Disease Outcomes in Studies of Diet and Chronic Disease Relations

Yetley EA, DeMets DL, Harlan WR Jr. *Am J Clin Nutr.* 2017 Nov;106(5):1175–1189. [Article Link](#)

Significance: This perspective builds upon the 2010 Institute of Medicine report on surrogate endpoints for chronic disease by folding in some of the considerations brought forth in the 2017 National Academies of Sciences, Engineering, and Medicine report on options for basing a DRI on a chronic disease endpoint.

Surrogate biomarkers for clinical outcomes afford scientific and economic efficiencies when investigating nutritional interventions in chronic diseases. However, valid scientific results are dependent on the qualification of these disease markers that are intended to be substitutes for a clinical outcome and to accurately predict benefit or harm. In this article, we examine the challenges of evaluating surrogate markers and describe the framework proposed in a 2010 Institute of Medicine report. The components of this framework are presented in the context of nutritional interventions for chronic diseases. We present case studies of 2 well-accepted surrogate markers [blood pressure within sodium intake and cardiovascular disease (CVD) context and low density lipoprotein-cholesterol concentrations within a saturated fat and CVD context]. We also describe additional cases in which the evidence is insufficient to validate their surrogate status. Guidance is offered for future research that evaluates or uses surrogate markers.

Lipids

Associations Between Fatty Acids and Low-Grade Inflammation in Children From the LISApplus Birth Cohort Study

Harris C, Demmelmair H, von Berg A, Lehmann I, Flexeder C, Koletzko B, et al. *Eur J Clin Nutr.* 2017 Nov;71(11):1303–1311. [Article Link](#)

Significance: Findings suggest that higher SFA and minor n-6 HUFA are associated with increased low-grade inflammation in children, whereas the major dietary n-6 PUFA and total PUFA are associated with reduced inflammation.

Background/Objectives: Assessing fatty acid (FA) composition in relation to inflammatory markers can shed light on the role of different FA and their metabolism in low-grade inflammation. Existing exploratory studies in children are scarce, and findings inconsistent. We hence aim to analyse associations of FA with common inflammatory markers, high-sensitivity C-reactive protein (hs-CRP) and interleukin-6 (IL-6), in 10-year-old children. **Subjects/Methods:** Complete data were available for 958 participants from the 10-year follow-up of the LISApplus (Influence of Lifestyle-Related Factors on the Immune System and the Development of Allergies in Childhood plus the Influence of Traffic Emissions and Genetics) birth cohort study. FA composition was assessed in serum glycerophospholipids. Hs-CRP and IL-6 were categorised into three levels. Associations of FA with inflammatory markers were assessed using multinomial logistic regression, adjusting for potential confounders. Additionally, sex-stratified analyses were carried out. **Results:** FA exposures associated with significantly higher low-grade inflammation, as indicated by higher hs-CRP or IL-6 levels, included: palmitic acid (PA) (IL-6: $P < 0.001$, 95% confidence interval: 1.30; 2.43), arachidonic acid (AA) (hs-CRP: $P = 0.002$, 1.07; 1.31), n-6 highly unsaturated FA (HUFA) (hs-CRP: $P = 0.002$, 1.06; 1.27), ratio of AA to linoleic acid (AA/LA) (hs-CRP: $P < 0.001$, 1.16; 1.62) and total saturated FA (SFA) (IL-6: $P < 0.001$, 1.77; 3.15). FA exposures associated with reduced levels of inflammatory markers included LA (hs-CRP: $P = 0.001$, 0.84; 0.96; IL-6: $P < 0.001$, 0.69; 0.90) and total polyunsaturated FA (PUFA) (IL-6: $P < 0.001$, 0.57; 0.78). **Conclusions:** These findings suggest that higher SFA and minor n-6 HUFA, namely PA and AA, are associated with increased low-grade inflammation in children, whereas the major dietary n-6 PUFA and total PUFA are associated with reduced inflammation. Elevated desaturase activity, estimated by the ratio AA/LA, may be associated with higher inflammation, particularly in boys.

Effect of Diets Rich in Either Saturated Fat or n-6 Polyunsaturated Fatty Acids and Supplemented With Long-Chain n-3 Polyunsaturated Fatty Acids on Plasma Lipoprotein Profiles

Dias CB, Amigo N, Wood LG, Correig X, Garg ML. *Eur J Clin Nutr.* 2017 Nov;71(11):1297–1302. [Article Link](#)

Significance: In an RCT of 26 subjects, diets rich in SFA and n-6PUFA reduced the concentration of total very-low-density lipoprotein (VLDL) particles and their subclasses and increased VLDL and LDL particle size.

Background/Objectives: Abnormalities in lipoprotein profiles (size, distribution and concentration) play an important role in the pathobiology of atherosclerosis and coronary artery disease. Dietary fat, among other factors, has been demonstrated to modulate lipoprotein profiles. We aimed to investigate if background dietary fat (saturated, SFA versus omega-6 polyunsaturated fatty acids, n-6PUFA) was a determinant of the effects of LCn-3PUFA supplementation on lipoprotein profiles. **Subjects/Methods:** A randomized controlled clinical intervention trial in a parallel design was conducted. Healthy subjects (n=26) were

supplemented with 400 mg eicosapentaenoic acid plus 2000 mg docosahexaenoic acid daily and randomized to consume diets rich in either SFA or n-6PUFA for a period of 6 weeks. Blood samples, collected at baseline and after 6 weeks of intervention, were assessed for plasma lipoprotein profiles (lipoprotein size, concentration and distribution in subclasses) determined using nuclear magnetic resonance spectroscopy. **Results:** Study participants receiving the SFA or the n-6PUFA enriched diets consumed similar percentage energy from fat (41 and 42% respectively, $P=0.681$). However, subjects on the SFA diet consumed 50% more energy as saturated fat and 77% less as linoleic acid than those consuming the n-6PUFA diet ($P<0.001$). The diets rich in SFA and n-6PUFA reduced the concentration of total very-low-density lipoprotein (VLDL) particles ($P<0.001$, both), and their subclasses and increased VLDL ($P=0.042$ and $P=0.007$, respectively) and LDL ($P=0.030$ and 0.027 , respectively) particle size. In addition, plasma triglyceride concentration was significantly reduced by LCn-3PUFA supplementation irrespective of the dietary fat.

Obesity

Simulation of Growth Trajectories of Childhood Obesity Into Adulthood

Ward ZJ, Long MW, Resch SC, Giles CM, Craddock AL, Gortmaker SL. *N Engl J Med*. 2017 Nov 30;377(22):2145–2153.

[Article Link](#)

Significance: Given the current level of childhood obesity, the models predicted that a majority of today's children (57.3%; 95% uncertainty interval [UI], 55.2 to 60.0) will be obese at the age of 35 years, and roughly half of the projected prevalence will occur during childhood.

Background: Although the current obesity epidemic has been well documented in children and adults, less is known about long-term risks of adult obesity for a given child at his or her present age and weight. We developed a simulation model to estimate the risk of adult obesity at the age of 35 years for the current population of children in the United States. **Methods:** We pooled height and weight data from five nationally representative longitudinal studies totaling 176,720 observations from 41,567 children and adults. We simulated growth trajectories across the life course and adjusted for secular trends. We created 1000 virtual populations of 1 million children through the age of 19 years that were representative of the 2016 population of the United States and projected their trajectories in height and weight up to the age of 35 years. Severe obesity was defined as a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 35 or higher in adults and 120% or more of the 95th percentile in children. **Results:** Given the current level of childhood obesity, the models predicted that a majority of today's children (57.3%; 95% uncertainty interval [UI], 55.2 to 60.0) will be obese at the age of 35 years, and roughly half of the projected prevalence will occur during childhood. Our simulations indicated that the relative risk of adult obesity increased with age and BMI, from 1.17 (95% UI, 1.09 to 1.29) for overweight 2-year-olds to 3.10 (95% UI, 2.43 to 3.65) for 19-year-olds with severe obesity. For children with severe obesity, the chance they will no longer be obese at the age of 35 years fell from 21.0% (95% UI, 7.3 to 47.3) at the age of 2 years to 6.1% (95% UI, 2.1 to 9.9) at the age of 19 years. **Conclusions:** On the basis of our simulation models, childhood obesity and overweight will continue to be a major health problem in the United States. Early development of obesity predicted obesity in adulthood, especially for children who were severely obese.

Gut Microbiome

A Human Gut Commensal Ferments Cranberry Carbohydrates to Produce Formate

Özcan E, Sun J, Rowley DC, Sela DA. *Appl Environ Microbiol*. 2017 Jun 30. doi: 10.1128/AEM.01097-17. [Article Link](#)

Significance: Specific strains of *B. longum* in the gut microbiota metabolize cranberry extract xyloglucans, indicating unknown mechanisms that are not universal in bifidobacteria.



Commensal bifidobacteria colonize the human gastrointestinal tract and catabolize glycans that are impervious to host digestion. Accordingly, *Bifidobacterium longum* typically secretes acetate and lactate as fermentative endproducts. This study tested the hypothesis that *B. longum* utilize cranberry-derived xyloglucans in a strain-dependent manner. Interestingly, the *B. longum* strain that efficiently utilizes cranberry xyloglucans secretes 2.0–2.5 moles acetate:lactate. The 1.5 ratio theoretical yield obtained in hexose fermentations shifts during xyloglucan metabolism. Accordingly, this metabolic shift is characterized by increased acetate and formate production at the expense of lactate. α -L-arabinofuranosidase, an arabinan endo-1,5- α -L-arabinosidase, and a β -xylosidase with a carbohydrate substrate-binding protein and carbohydrate ABC transporter membrane proteins are upregulated (> 2-fold change), which suggests carbon flux through this catabolic pathway. Finally, syntrophic interactions occurred with strains that utilize carbohydrate products derived from initial degradation from a heterologous bacterium. **Importance:** This is a study of bacterial metabolism of complex cranberry carbohydrates termed xyloglucans that are likely not digested prior to reaching the colon. This is significant as bifidobacteria interact with this dietary compound to potentially impact human host health through energy and metabolite production by bacterial utilization of these substrates. Specific bacterial strains utilize

cranberry xyloglucans as a nutritive source indicating unknown mechanisms that are not universal in bifidobacteria. In addition, xyloglucan metabolism proceeds using an alternative pathway could lead to further research to investigate mechanisms underlying this interaction. Finally, we observed cross-feeding between bacteria in which one strain degrades the cranberry xyloglucan to make it available to a second strain. Similar nutritive strategies are known to occur within the gut. In aggregate, this study may lead to novel foods or supplements to impact human health through rational manipulations of their microbiome.

Scientific Integrity

Disclosures in Nutrition Research: Why It Is Different

Ioannidis JPA, Trepanowski JF. *JAMA*. 2017 Dec 7. doi: 10.1001/jama.2017.18571. [Article Link](#)

Significance: This commentary discusses the bias that is unique to nutrition science.
