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Dietary Patterns

Global Coverage of Mandatory Large-Scale Food Fortification Programs: A Systematic Review and Meta-Analysis

Fabian Rohner, James P Wirth, Wu Zeng, Nicolai Petry, William E S Donkor, Lynnette M Neufeld, Penjani Mkambula, et. al. *Adv Nutr*. 2023 Sep;14(5):1197-1210. doi.org/10.1016/j.advnut.2023.07.004. Article link

Significance: This review of global fortification practices between 2010-2012 found considerable data gaps except for salt. Data was limited for fortified wheat flour, vegetable oil, maize flour, rice and sugar. Future work includes better data collection on these foods to reduce micronutrient deficiencies.

Food fortification with micronutrients is widely implemented to reduce micronutrient deficiencies and related outcomes. Although many factors affect the success of fortification programs, high population coverage is needed to have a public health impact. We aimed to provide recent global coverage estimates of salt, wheat flour, vegetable oil, maize flour, rice, and sugar among countries with mandatory fortification legislation. The indicators were the proportion of households consuming the: food, fortifiable food (that is, industrially processed), fortified food (to any extent), and adequately fortified food (according to national or international standards). We estimated the number of individuals reached with fortified foods. We systematically retrieved and reviewed all applicable evidence from: published reports and articles from January 2010 to August 2021, survey lists/databases from key organizations, and reports/literature received from key informants. We analyzed data with R statistical package using random-effects meta-analysis models. An estimated 94.4% of households consumed salt, 78.4% consumed fortified salt (4.2 billion people), and 48.6% consumed adequately fortified salt in 64, 84, and 31 countries, respectively. Additionally, 77.4% of households consumed wheat flour, 61.6% consumed fortifiable wheat flour, and 47.1% consumed fortified wheat flour (66.2 million people) in 15, 8, and 10 countries, respectively, and 87.0% consumed vegetable oil, 86.7% consumed fortifiable oil, and 40.1% consumed fortified oil (123.9 million people) in 10, 7, and 5 countries, respectively. Data on adequately fortified wheat flour and vegetable oil and coverage indicators for maize flour, rice, and sugar were limited. There are major data gaps on fortification coverage for most foods except salt. All countries with mandatory fortification programs should generate and use more coverage data to assess program performance and adjust programs as needed to realize their potential to reduce micronutrient deficiencies.

Carbohydrates

Associations of Dietary Sugar Types with Coronary Heart Disease Risk: A Prospective Cohort Study

Significance: A higher heart disease risk was associated with carbohydrate and sugar intake reported in a prospective cohort study of 76,815 women and 38,878 men. Conversely fructose from fruits and vegetables not associated with heart disease.

Background: Higher intake of total sugar has been linked with coronary heart disease (CHD) risk, but the role of individual sugars, particularly fructose, is uncertain. **Objectives:** This study aimed to investigate the associations of individual dietary sugars with CHD risk. **Methods:** In prospective cohort studies, we followed 76,815 women (Nurses' Health Study, 1980-2020) and 38,878 men (Health Professionals Follow-up Study, 1986-2016). Sugar and carbohydrate intake, including total fructose equivalents ([TFE] from fructose monosaccharides and sucrose), total glucose equivalents ([TGE] from glucose monosaccharides, disaccharides, and starch), and other sugar types, was measured every 2 to 4 y by semiquantitative food frequency questionnaires. **Results:** We documented 9,723 incident CHD cases over 40 years. In isocaloric substitution models with total fat as a comparison nutrient, comparing extreme quintiles of intake, hazard ratios (HRs), 95% confidence interval [CI]) for CHD risk were 1.31 (1.20 to 1.42; Ptrend < 0.001) for TGE and 1.03 (0.94 to 1.11; Ptrend = 0.25) for TFE. TFE from fruits and vegetables was not associated with CHD risk (Ptrend = 0.70), but TFE from added sugar and juice was associated with CHD risk (HR: 1.12, 95% CI: 1.04 to 1.20; Ptrend < 0.01). Intakes of total sugars and added sugar were positively associated with CHD risk (HRs: 1.16, 95% CI: 1.07 to 1.26, Ptrend < 0.001; 1.08, 95% CI: 0.99 to 1.16, Ptrend = 0.04). **Conclusions:** Intakes of TGE, total sugar, added sugar, and fructose from added sugar and juice were associated with higher CHD risk, but TFE and fructose from fruits and vegetables were not.

Protein

Whole-Milk Dairy Foods: Biological Mechanisms Underlying Beneficial Effects on Risk Markers for Cardiometabolic Health

Significance: Current evidence suggests dairy foods should be considered as complex food matrices and not just as delivery systems for isolated nutrients, such as saturated fatty acids.

Lifestyle modifications that include adherence to healthy dietary patterns that are low in saturated fat have been associated with reduced risk for cardiovascular disease, the leading cause of death globally. Whole-milk dairy foods, including milk, cheese, and yogurt, are leading sources of saturated fat in the diet. Dietary guidelines around the world recommend the consumption of low-fat and fat-free dairy foods to obtain overall healthy dietary patterns that help meet nutrient recommendations while keeping within recommended calorie and saturated fat limitations. A body of observational and clinical evidence indicates, however, that whole-milk dairy food consumption, despite saturated fat content, does not increase the risk for cardiovascular disease. This review describes the proposed biological mechanisms underlying inverse associations between whole-milk dairy food consumption and risk markers for cardiometabolic health, such as altered lipid digestion, absorption, and metabolism; influence on the gut microflora; and regulation of oxidative stress and inflammatory responses. The dairy food matrix, a term used to describe how the macronutrients and micronutrients and other bioactive components of dairy foods are differentially packaged and compartmentalized among fluid milk, cheese, and yogurt, may dictate how each affects cardiovascular risk. Current evidence indicates consideration of dairy foods as complex food matrices, rather than delivery systems for isolated nutrients, such as saturated fatty acids, is warranted.

Low- and No-Calorie Sweeteners

Elevated Erythritol: A Marker of Metabolic Dysregulation or Contributor to the Pathogenesis of Cardiometabolic Disease?

Significance: Elevated circulating erythritol is linked to higher platelet aggregation and adverse cardiovascular events. However, data on long-term effects of erythritol intakes on cardiometabolic outcomes are lacking. Clinical trials are needed on the causal effects of dietary erythritol on platelet activation, thrombosis and cardiometabolic risk.

Erythritol is a non-nutritive sugar replacement that can be endogenously produced by humans. Witkowski et al. reported that elevated circulating erythritol is associated with adverse cardiovascular events in three independent cohorts, demonstrated in vitro and ex vivo that erythritol promotes platelet activation, and showed faster clotting time in mice injected with erythritol. It was concluded that erythritol fosters enhanced thrombosis. This narrative review presents additional evidence that needs to be considered when evaluating these data and conclusions. We conducted a search of all studies related to erythritol exposure with focus on those that reported vascular health outcomes. Patients with chronically elevated erythritol levels due to inborn errors of metabolism do not exhibit higher platelet activation or thrombosis risk. Most long-term studies in which animals consumed high levels of erythritol do not support its role in platelet activation and thrombosis formation. Clinical data on the effects of chronic intake of erythritol are limited. Erythritol may be merely a marker of dysregulation in the Pentose Phosphate Pathway caused by impaired glycemia. However, this suggestion and the findings of Witkowski et al. need to be further examined. Clinical trials examining the long-term effects of erythritol consumption on cardiometabolic outcomes are required to test the causality between dietary erythritol and cardiometabolic risk. Until supportive data from these trials are available, it cannot be concluded that dietary erythritol promotes platelet activation, thrombosis, and cardiometabolic risk.

Cognitive Health

APOE-Genotype and Insulin Modulate Estimated Effect of Dietary Macronutrients on Cognitive Performance: Panel Analyses in Non-Diabetic Older Adults at Risk for Dementia

Significance: An APOE-based precision nutrition approach is promising for cognitive performance based on a 2-year study with older adults with no diabetes. Both relative hyper- and hypo-insulinemia modulates the effect of diet on cognition.

Background: The APOE-gene (ε-2/3/4, combined as six different genotypes: ε-22/23/24/33/34/44) and insulin status modulate dementia risk and play a role in the metabolism of macronutrients. **Objective:** Our aim was to examine APOE-genotype and fasting insulin as effect-modifiers of the slopes between dietary macronutrients and cognitive performance among older adults at risk for dementia. **Method:** Panel analyses-with diet and cognition measured at baseline and follow-up at year 1 and 2-were performed in a sub-sample from the FINGER trial (n=676, 60-77 years, 46% females, all non-diabetics). The associations between macronutrients (3-day food records, z-scores) and global cognition (modified Neuropsychological Test Battery, z-score) were analyzed in mixed regression models adjusted for confounders selected a priori. After a gradient was implied by the point estimates in categorical APOE-analyses, we investigated a continuous APOE variable [APOE-gradient, coded -1 (for ε-23), -0.5 (ε-24), 0 (ε-33), 1 (ε-34), 2 (ε-44)] as an effect-modifier. **Results:** At increasing levels of the APOE-gradient a relatively more favorable slope between diet and cognition was observed for a lower carbohydrate/fat-ratio (β=-0.040, 95% CI -0.074, -0.006, P=0.020 for interaction diet x APOE-gradient), and higher protein (β=0.075, CI 0.042, 0.109, P=9.4x10-6). Insulin concentration (log-linear) modulated the association between CFr and cognition by a quadratic interaction (β=-0.016, P=0.039). Coherent findings for exploratory predictors (fiber, fat-subtypes, composite score, metabolic biomarkers) were compatible with published hypotheses of differential dietary adaptation by APOE, with cognition among ε-33 being relatively independent of dietary parameters-implying "metabolic flexibility". Antagonistic slopes to cognition for ε-23 (positive) versus ε-34 and ε-44 (negative) were found for a Higher-carbohydrates-fiber-Lower-fat-protein composite score, even as within-subjects effects. **Conclusions:** APOE-based precision nutrition appears conceptually promising but replications in wider samples are warranted, as well as support from trials. Both relative hyper- and hypo-insulinemia might modulate the effect of diet on cognition.

Lipids

Cheese Consumption and Multiple Health Outcomes: An Umbrella Review and Updated Meta-Analysis of Prospective Studies

Significance: An umbrella review suggests that cheese intake has neutral to moderate benefits for human health. An inverse association of cheese consumption with all-cause and cardiovascular mortality, incident disease, coronary heart disease and stroke was found.

This umbrella review aims to provide a systematic and comprehensive overview of current evidence from prospective studies on the diverse health effects of cheese consumption. We searched PubMed, Embase, and Cochrane Library to identify meta-analyses/pooled analyses of prospective studies examining the association between cheese consumption and major health outcomes from inception to August 31, 2022. We reanalyzed and updated previous meta-analyses and performed de novo meta-analyses with recently published prospective studies, where appropriate. We calculated the summary effect size, 95% prediction confidence intervals, between-study heterogeneity, small-study effects, and excess significance bias for each health outcome. We identified 54 eligible articles of meta-analyses/pooled analyses. After adding newly published original articles, we performed 35 updated meta-analyses and 4 de novo meta-analyses. Together with 8 previous meta-analyses, we finally included 47 unique health outcomes. Cheese consumption was inversely associated with all-cause mortality (highest compared with lowest category: RR = 0.95; 95% CI: 0.92, 0.99), cardiovascular mortality (RR = 0.93; 95% CI: 0.88, 0.99), incident cardiovascular disease (CVD) (RR = 0.92; 95% CI: 0.89, 0.96), coronary heart disease (CHD) (RR = 0.92; 95% CI: 0.86, 0.98), stroke (RR = 0.93; 95% CI: 0.89, 0.98), estrogen receptor-negative (ER-) breast cancer (RR = 0.89; 95% CI: 0.82, 0.97), type 2 diabetes (RR = 0.93; 95% CI: 0.88, 0.98), total fracture (RR = 0.90; 95% CI: 0.86, 0.95), and dementia (RR = 0.81; 95% CI: 0.66, 0.99). Null associations were found for other outcomes. According to the NutriGrade scoring system, moderate quality of evidence was observed for inverse associations of cheese consumption with all-cause and cardiovascular mortality, incident CVD, CHD, and stroke, and for null associations with cancer mortality, incident hypertension, and prostate cancer. Our findings suggest that cheese consumption has neutral to moderate benefits for human health.

Sodium

Effective and Scalable Interventions to Reduce Sodium Intake: a Systematic Review and Meta-Analysis

Significance: Global sodium intakes exceed World Health Organization recommendations. Combination strategies including mandatory food reformulation, food labeling, taxes/subsidies, and social marketing and communication are most effective in reducing population sodium intake.

Purpose of review: High-sodium intake is a main risk factor for increased blood pressure and cardiovascular disease, the leading cause of death worldwide. Reducing sodium intake at the population level is one of the most cost-effective strategies to address this. The aim of the present systematic review and meta-analysis are to examine data from recent studies that measure the effectiveness and scalability of interventions aimed at reducing sodium intake at both the population and individual level. **Recent findings**: Worldwide, sodium intake is higher than the World Health Organization recommendations. Structural interventions such as mandatory reformulation of foods, food labeling, taxes or subsidies, and communication campaigns have shown to be the most effective in reducing the population's sodium consumption. Interventions in education, particularly those that use a social marketing framework with short duration, food reformulation, and combined strategies, have the potential to decrease sodium intake.

Gut Health
Synthesis and Functions of Resistant Starch

Significance: This review provides a current state of knowledge on resistance starch (RS) and perspectives on classification, synthesis and efficacy and serves to guide future development and applications.

Resistant starch (RS) has become a popular topic of research in recent years. Most scholars believe that there are 5 types of RS. However, accumulating evidence indicates that in addition to starch-lipid complexes, which are the fifth type of RS,

complexes containing starch and other substances can also be generated. The physicochemical properties and physiologic functions of these complexes are worth exploring. New physiologic functions of several original RSs are constantly being discovered. Research shows that RS can provide health improvements in many patients with chronic diseases, including diabetes and obesity, and even has potential benefits for kidney disease and colorectal cancer. Moreover, RS can alter the short-chain fatty acids and microorganisms in the gut, positively regulating the body's internal environment. Despite the increase in its market demand, RS production remains limited. Upscaling RS production is thus an urgent requirement. This paper provides detailed insights into the classification, synthesis, and efficacy of RS, serving as a starting point for the future development and applications of RS based on the current status quo.

Emerging Science Areas

Emerging Areas: Time of Exercise and Obesity

The Diurnal Pattern of Moderate-to-Vigorous Physical Activity and Obesity: A Cross-Sectional Analysis

Tongyu Ma, Thomas Bennett, Chong-Do Lee, Mairead Wicklow. *Obesity.* 04 Sept. 2023. Doi.org/10.1002.oby.23851. [Article link](#)

Significance: A NHANES analysis from 2003-2006 found that diurnal pattern of moderate to vigorous exercise impacts obesity. Early morning physical activity is the optimal time to enhance the beneficial association between activity and lower obesity.

Objective: Moderate-to-vigorous physical activity (MVPA) is obesity-protective. However, the optimal time of the day to engage in MVPA for weight management is controversial. This study is designed to investigate the influence of the diurnal pattern of MVPA on the association between MVPA and obesity. **Methods:** A total of 5285 participants in the 2003 to 2006 National Health and Nutrition Examination Survey (NHANES) were cross-sectionally analyzed. The diurnal pattern of objectively measured MVPA was classified into three clusters by K-means clustering analysis: morning (n = 642); midday (n = 2456); and evening (n = 2187). The associations of MVPA level and the diurnal pattern with obesity were tested. **Results:** A strong linear association between MVPA and obesity was found in the morning group, whereas a weaker curvilinear association between MVPA and obesity was observed in the midday and evening groups, respectively. Among those who met the physical activity guidelines, the adjusted means for BMI were 25.9 (95% CI: 25.2–26.6), 27.6 (95% CI: 27.1–28.1), and 27.2 (95% CI: 26.8–27.7) kg/m2 in the morning, midday, and evening groups, respectively, and for waist circumference were 91.5 (95% CI: 89.4–93.6), 95.8 (95% CI: 94.7–96.9), and 95.0 (95% CI: 93.9–96.1) cm, respectively. **Conclusions:** The diurnal pattern of MVPA influences the association between MVPA and obesity. The promising role of morning MVPA for weight management warrants further investigation.

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