



News and Views

1. Long-term coffee consumption is non-linearly associated with cardiovascular disease risk

Globally, coffee is an extensively consumed stimulant and is considered to be safe. However, there have been contradictory reports on the health benefits as well as risks of coffee. Moreover, caffeine metabolism is less effective in individuals carrying a functional variant at cytochrome P450 1A2 (CYP1A2), which may lead to increased risk of myocardial infarction and hypertension in them. A recent study published in the American Journal of Clinical Nutrition examined whether the CYP1A2 genotype or a genetic score for caffeine metabolism (caffeine-GS) affects the association between habitual coffee consumption and risk of cardiovascular disease (CVD). Data on genetics, habitual coffee intake and relevant covariates were obtained from the UK Biobank for 347,077 individuals, including 8368 incident CVD cases. The association between coffee intake and CVD risk and whether it varies with CYP1A2 genotype or caffeine-GS were examined using logistic regression. Of note, a higher caffeine-GS score indicates a slower caffeine metabolism.

The study reported a non-linear relationship between habitual coffee intake and CVD risk. In addition, the risk of CVD was higher among participants who did not drink coffee, who drank decaffeinated coffee and who reported drinking >6 cups/day than those who drank 1–2 cups/day. Therefore, CYP1A2 genotype and caffeine-GS were not statistically associated with CVD, and the study found no evidence for an interaction between the CYP1A2 genotype or caffeine-GS and coffee intake with respect to risk of CVD. Heavy coffee consumption was associated with a modest increase in CVD risk, but this association was unaffected by genetic variants influencing caffeine metabolism.

Zhou A, Hyppönen E. Long-term coffee consumption, caffeine metabolism genetics, and risk of cardiovascular disease: A prospective analysis of up to 347,077 individuals and 8368 cases. *Am J Clin Nutr*. 2019; 109(3):509–16.

2. Cashew nuts do not influence cardiovascular disease markers in humans

Previous studies suggest an association between the consumption of tree nuts and a decrease in risk factors for and incidence of CVD. Although the US Food and Drug Administration (FDA) has approved a qualified health claim for tree nuts and reduction of cardiovascular disease, cashews are excluded from this claim because of the saturated fats, predominantly stearic acid in cashews. Stearic acid is neutral with respect to blood lipids, and the results of studies examining the effect of cashew nuts on blood lipids are contradictory. A recent controlled-feeding randomized crossover trial with two treatment phases, published in the American Journal of Clinical Nutrition, determined the effect of cashews fed at the amount specified in the health claim on risk factors for cardiovascular disease. Participants were 42 individuals who were given the same base diet in both treatment phases. In the cashew nut phase, an additional 42 grams (1.5 servings) of cashews/day was administered (and the amount of all foods was proportionally decreased to achieve isocaloric overall diets).

After an intervention of 4 weeks, no significant differences were found in blood lipids, blood pressure, augmentation index, blood glucose, endothelin, adhesion molecules or clotting factors. Although no change in LDL cholesterol was reported, PCSK9 enzyme levels were significantly decreased after cashew consumption. Consumption of the amount of cashew nuts the FDA qualified health claim for tree nuts and cardiovascular disease, i.e., 42 grams, did not have any influence the aforementioned primary risk factors for cardiovascular disease.

Baer DJ, Novotny JA. Consumption of cashew nuts does not influence blood lipids or other markers of cardiovascular disease in humans: A randomized controlled trial. *Am J Clin Nutr*. 2019;109(2):269–75.

3. Eating one egg daily is not associated with increase in cardiovascular disease risk or all-cause mortality

Although eggs are known to be highly nutritious, there are concerns over their cholesterol content, due to which many people avoid eggs in their diet. Additionally, there are important international differences in reliable dietary guidance. A study published in the *European Journal of Nutrition* is the first prospective study in China investigating the association between egg consumption and cardiovascular disease (CVD) mortality. Participants were 28,024 individuals without CVD at baseline in Guangzhou Biobank Cohort Study recruited during 2003–2008. All-cause and CVD mortality were identified using record linkage, Cox proportional hazards regression was used and the meta-analysis Of Observational Studies in Epidemiology reporting guidelines were followed.

During the mean follow-up of 9.8 years, no significant difference was reported in all-cause mortality between higher (>7 eggs/week) and low consumption (<1 egg/week) and mortality from CVD, ischemic heart disease (IHD) or stroke. This updated meta-analyses including the aforementioned results revealed that >7 eggs/week is not associated with all-cause mortality or IHD but is associated with a small reduction in stroke.

Therefore, this study indicated that eating one egg daily is not associated with increase in CVD or all-cause mortality. The finding of this study support current guidelines recommending eggs as part of a healthy diet and, therefore, should be considered in other dietary recommendations.

Xu L, Lam TH, Jiang CQ, Zhang WS, Zhu F, Jin YL, et al. Egg consumption and the risk of cardiovascular disease and all-cause mortality: Guangzhou Biobank Cohort Study and meta-analyses. Eur J Nutr. 2019;58(2):785–96.

4. Excessive consumption of energy drinks induce acute cardiovascular and metabolic changes

Energy drinks are popular nonalcoholic beverages, and case reports have indicated a possible link between them and adverse events, including deaths. A recent study published in the *Journal of Nutrition* investigated the cardiovascular and metabolic effects of energy drinks and mixtures providing relevant ingredients of energy drinks as well as compared them to a similarly composed control product without these components. This randomized, crossover trial included 38 adults (mean age, 22 years) and examined the effects of a single administration of a commercial energy drink, the control product, and the

control product supplemented with major energy drink-ingredients at the same concentrations.

The results revealed that both volumes (750 mL and 1000 mL) were acceptably tolerated with no dose-dependent effects on the primary outcome blood pressure (BP) as well as heart rate, heart rate corrected duration of QT-segment in electrocardiography (QTc interval) and glucose metabolism. Notably, 11% and 0%–3% of the participants reported symptoms after the consumption of energy drink and after consumption of other study products. One hour after the consumption of energy drink showed an increase in systolic BP and a QTc prolongation. Caffeine, but not taurine or glucuronolactone, was shown to lead to an increase in BP but no QTc prolongation. Additionally, the BP effects were the most evident after 1 hour and returned to normal after a few hours. All study products showed a decrease in serum glucose and an increase in insulin levels 1 hour after consumption compared to baseline values, corresponding to an elevation in the HOMA-IR.

Therefore, a single high-volume intake of energy drink was reported to have adverse changes in BP, QTc and insulin sensitivity in young, healthy individuals. However, of note, these effects cannot be easily accredited to the single components caffeine, taurine or glucuronolactone.

Basrai M, Schweinlin A, Menzel J, Mielke H, Weikert C, Dusemund B, et al. Energy Drinks Induce Acute Cardiovascular and Metabolic Changes Pointing to Potential Risks for Young Adults: A Randomized Controlled Trial. J Nutr. 2019;149(3):441–50.

5. Vitamin D supplements do not lower incidence of invasive cancer or cardiovascular events

Whether vitamin D- supplementation decreases the risk of cancer or cardiovascular disease is unclear and, so far, randomized trials have given inadequate data. A nationwide, randomized, placebo-controlled trial with a two-by-two factorial design that examined the benefits and risks of vitamin D₃ (cholecalciferol) at a dose of 2000 IU/day and marine n-3 (also called omega-3) fatty acids at a dose of 1 g/day for the prevention of cancer and cardiovascular disease was recently published in the *New England Journal of Medicine*. Participants were men aged ≥50 years and women aged ≥55 years in the United States. Any type of invasive cancer and major cardiovascular events (a composite of myocardial infarction, stroke or death from cardiovascular causes) were the primary endpoints. Site-specific cancers, death from cancer and additional cardiovascular events were included as secondary endpoints.

The report comparing vitamin D with placebo showed that supplementation with vitamin D was not linked to a lower risk of either of the primary endpoints. During the study

period (median follow-up, 5.3 years), cancer was diagnosed in 1617 participants (hazard ratio, 0.96) and a major cardiovascular event occurred in 805 participants (hazard ratio, 0.97). With regard to the secondary end points, the hazard ratios were as follows: for death from cancer, 0.83; for breast cancer, 1.02 for prostate cancer, 0.88; for colorectal cancer, 1.09; for the expanded composite end point of major cardiovascular events plus coronary revascularization, 0.96; for myocardial infarction, 0.96; for stroke, 0.95 and for death from cardiovascular causes, 1.11. Furthermore, excess risks of hypercalcemia or other adverse events were not identified.

To conclude, supplementation with vitamin D did not lead to a lower incidence of invasive cancer or cardiovascular events than placebo.

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Manson JE, Cook NR, Lee IM, Christen W, Bassuk SS, Mora S, Gibson H, Gordon D, Copeland T, D'Agostino D, Friedenberg G. Vitamin D supplements and prevention of cancer and cardiovascular disease. New England Journal of Medicine. 2019;380(1):33–44.