number of cases in both men and women (1). The RR estimates did not appreciably change; in fact, they increased slightly for some of the observed associations.

A significantly positive association between added sugars and CVD mortality risk was also found in a recent prospective analysis of a nationally representative sample of US adults from NHANES III (1988–2006) (6). Compared with persons who consumed ≤8% of energy from added sugars, persons with 17–21% and >21% of energy from added sugars had multivariate HRs for CVD mortality of 1.38 and 2.03, respectively. However, no significant association between added sugars and total mortality was observed. This study population had a wider range of added sugars intake (10th–90th percentile: 7.5–25% of energy intake) than our study sample of educated 50- to 69-y-old adults (10th–90th percentile: 4–18%). Had this intake been higher, we may have more conclusively found higher risks with respect to added sugars and CVD risk.

With regard to Ha et al’s discussion on the role of energy as the main mediator in the detrimental effect of fructose, we would like to emphasize that our models investigated the substitution effect of sugars, therefore simulating an isocaloric substitution of individual sugars for other energy-contributing macronutrients. Across all sugars we investigated, the strongest associations with mortality risk were found for total fructose, observed in both men and women. Our analysis thus suggests that the effect of sugars on mortality risk, and our previous investigations of the measurement error structure in self-reported sugars and energy based on predictive and recovery biomarkers, and our sensitivity analyses that excluded energy underreporters, it is unlikely that energy underreporting would have led to overestimation of the association between sugars and mortality risk in our analysis.

To conclude, even though the associations found between sugars and mortality risk were stronger and apparent across different types of sugars in women, we also observed positive associations in men. On the basis of our previous investigations of the measurement error structure in self-reported sugars and energy based on predictive and recovery biomarkers, and our sensitivity analyses that excluded energy underreporters, it is unlikely that energy underreporting would have led to overestimation of the association between sugars and mortality risk in our analysis.

Supported by the Intramural Research Program of the National Cancer Institute, NIH, US Department of Health and Human Services.

None of the authors had a conflict of interest.

Natasha Tasevska
Nutrition Program
School of Nutrition and Health Promotion
Arizona State University
500 North Third Street
Phoenix, AZ 85004-0698
E-mail: natasha.tasevska@asu.edu

Yikyung Park
Nutritional Epidemiology Branch
Division of Cancer Epidemiology and Genetics
National Cancer Institute
NIH
Bethesda, MD

Amy F Subar
Nancy Potischman
Applied Research Program
Division of Cancer Control and Population Sciences
National Cancer Institute

REFERENCES


Is nut consumption associated with decreased risk of type 2 diabetes?

Dear Sir:

We read with interest 3 recent meta-analyses of nut consumption and risk of cardiovascular disease, type 2 diabetes, and all-cause mortality (1–3). Findings from all 3 meta-analyses suggested that higher intake of nuts decreased the risk of coronary artery disease, whereas it was not associated with risk of stroke. However, there were inconsistent conclusions on the association between nut consumption and risk of type 2 diabetes. The 2 meta-analyses by Zhou et al (1) and Luo et al (2) showed no association between nut consumption and risk of type 2 diabetes, whereas the meta-analysis by Afshin et al (3) showed that nut consumption decreased the risk of type 2 diabetes. We checked the included studies by Afshin et al (3) and found some problems in their meta-analysis.

First, the meta-analysis by Afshin et al included one ineligible study (4) that examined the association of nuts and peas in combination with risk of type 2 diabetes but not the nuts-specific effect. Second, the meta-analysis omitted one important study (5) that reported a positive association between nut consumption and risk of type 2 diabetes (≥5 servings/wk compared with <1 serving/mo—RR: 1.51; 95% CI: 1.13, 2.04). Third, the meta-analysis extracted RRs and 95% CIs without adjustment for BMI according to Pan et al (6). In our opinion, this might be inappropriate because BMI is the main confounding factor influencing the association between nut intake and the risk of type 2 diabetes.

Given the problems in the meta-analysis by Afshin et al (3), it is not surprising that the authors found a significantly inverse association between nut intake and risk of type 2 diabetes but the other 2 similar meta-analyses (1, 2) reported no association. In particular, the meta-analysis by Luo et al (2) performed subgroup analyses with adjustment for BMI. In the model adjusted for BMI,
there was no association, although an inverse association was found in the model without adjustment for BMI on the basis of only 2 studies. Given the findings above, limited evidence supports the inverse association between nut consumption and risk of type 2 diabetes.

None of the authors had a conflict of interest.

Zhihao Liu

Jiangsu Provincial Center for Disease Prevention and Control
172 Jiangsu Road
Nanjing
China
E-mail: jscdliuzhihao@163.com

Pingmin Wei

Southeast University of China
Nanjing
China

Xiaoning Li

Jiangsu Provincial Center for Disease Prevention and Control
172 Jiangsu Road
Nanjing
China

Note: Afshin et al chose not to submit a reply.

REFERENCES


Sleep duration and energy intake: timing matters

Dear Sir:

It was with great interest that we read the article by Kant and Graubard (1). The authors examined both self-reported sleep duration and eating patterns of ~15,000 adult Americans of the NHANES cohort. The main finding was that short sleepers, ie, those reporting sleeping ≤6 h/night, were found to consume breakfast earlier and consume fewer main meals but more snacks compared with average sleepers (habitual sleep duration between 7 and 8 h). In contrast, self-reported eating behavior did not differ between average and long sleepers (ie, ≥9 h). Finally, the overall self-reported 24-h energy intake was not different between short, average, and long sleepers.

Notwithstanding their elegant demonstration of the association between short sleep and altered eating patterns, Kant and Graubard did not investigate whether short sleepers also eat at times of the day when the circadian system is not metabolically adjusted to process ingested nutrients or stimulants such as caffeine (ie, primarily during the night). Indeed, their article does not report how many of those who were self-reported short sleepers were also shift workers. This is an important aspect of the analysis of food intake in relation to sleep and circadian timing, because shift workers are often forced to eat, and not only sleep, at odd times of their 24-h day, including during the night (2), times during which the body is more insulin resistant and generally disadvantageously adapted to handling food intake. Not only did previous studies link shift work with the development of obesity but they also showed that under conditions of experimental circadian disruption, in which sleep is misaligned in much the same way as experienced by many shift workers, this alters the hormonal profile, increases inflammation, and reduces insulin sensitivity (3, 4). Hormones responsible for determining the appetitive and metabolic response to food intake, such as the hunger-promoting hormone ghrelin and the satiety-enhancing adipokine leptin, are known to be perturbed by circadian misalignment (4, 5). Although with ad libitum food intake such paradigms can lead to increased food intake, circadian misalignment can even promote weight loss under apparently isocaloric conditions, ie, if food intake is equal between groups, matched to the calculated 24-h energy expenditure (5). In an intervention aiming for weight loss, the timing at which food intake occurs was also linked to the success of weight loss (6), such that late lunch eaters lost less weight than did early lunch eaters during the 20-wk intervention.

At the molecular level, when the circadian machinery was disrupted in mice due to genetic mutation of the gene Clock, this resulted in obesity (7). Forcing wild-type mice under ad libitum high-fat diet conditions to flip their circadian eating time by 12 h, effectively eating during their “physiological” night, led to a 48% increase in body weight, as opposed to a 20% increase for the mice with a normal meal pattern (8). Importantly, these differences were noted despite no significant differences in energy intake between the 2 groups of mice.

Importantly, if food is provided at the incorrect time of day, this may in the long run not only cause an increase in body weight but also predispose individuals to develop type 2 diabetes—the risk of which a recent meta-analysis once more confirmed to be elevated for individuals who perform shift work (9). The importance of circadian misalignment for such ultimate consequences of shift work was highlighted by the fact that workers with rotating shifts, in which the timing of both sleep and food intake will keep occurring at time points to which the body cannot adapt to quickly enough from a chronobiological viewpoint, had the highest risk of developing obesity but they also showed that under conditions of experimental circadian disruption, in which sleep is misaligned in much the same way as experienced by many shift workers, this alters the hormonal profile, increases inflammation, and reduces insulin sensitivity (3, 4). Hormones responsible for determining the appetitive and metabolic response to food intake, such as the hunger-promoting hormone ghrelin and the satiety-enhancing adipokine leptin, are known to be perturbed by circadian misalignment (4, 5). Although with ad libitum food intake such paradigms can lead to increased food intake, circadian misalignment can even promote weight loss under apparently isocaloric conditions, ie, if food intake is equal between groups, matched to the calculated 24-h energy expenditure (5). In an intervention aiming for weight loss, the timing at which food intake occurs was also linked to the success of weight loss (6), such that late lunch eaters lost less weight than did early lunch eaters during the 20-wk intervention.

Finally, the overall self-reported 24-h energy intake was not different between short, average, and long sleepers.