Dear Sir:

We thank Ha et al for their comments on our findings from the analysis of dietary sugars and mortality risk in a large US cohort study (1). In their letter, Ha et al claim that the positive associations for sugars and cardiovascular vascular disease (CVD) mortality risk in women observed in our study may have been overestimated due to energy underreporting, which is more common in women. First, we would like to clarify that although we did not find added or total sugars from beverages to be positively associated with CVD mortality risk in men, there was a significant increase in risk with greater intake of fructose from beverages in both men (HR for quartile 5 compared with quartile 1: 1.13; 95% CI: 1.05, 1.22; P-trend = 0.001) and women (HR for quartile 5 compared with quartile 1: 1.14; 95% CI: 1.02, 1.28; P-trend = 0.002). Furthermore, in both men and women, there was a borderline increased risk for CVD mortality with high total sugars and fructose intake (P-trend = 0.08–0.09) (Table 2 in reference 1).

Ha et al argue that adjusting for energy intake “reduces the effect of potential confounding variables but does not address the underlying limitation of energy intake measurements: underreporting, which may lead to overestimation of the association between exposure and outcome.” In fact, adjusting for energy intake has been recommended in analyses of nutritional cohort studies as an approach to alleviate measurement error and attenuation of RR estimate in multivariable outcome. In fact, adjusting for energy intake has been recommended in analyses of nutritional cohort studies as an approach to alleviate measurement error and attenuation of RR estimate in multivariable models. In the Observing Protein and Energy Nutrition (OPEN) study, using the predictive biomarker for total sugars intake, we showed that the disease risk attenuation would be much less severe, albeit still present, when using total sugars density (g/1000 kcal) rather than absolute intake (g/d), as measured by the Diet History Questionnaire (4). Similar to findings for self-reported energy with the use of doubly labeled water (5), we also found that measurement error in self-reported sugars and predicted risk attenuation was greater in women than in men (4). We would, therefore, expect that the risk estimates for sugars observed in our article may have been attenuated and thus underestimated, rather than being overestimated as claimed by Ha et al. More important, to further investigate the Observing Protein and Energy Nutrition possible effect of energy underreporting, the main analyses were re-run after excluding potential energy underreporters identified by the Goldberg cutoffs, which more than halved the sample size and the

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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 fructose in particular, extends beyond energy and may be explained by other mechanisms discussed in our article (1).

To conclude, even though the associations found between sugars and mortality risk were stronger and apparent across different types of 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 fructose in particular, extends beyond energy and may be explained by other mechanisms discussed in our article (1).

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.

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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,