

Online Supplementary Material for Imamura *et al*, ‘Confounding by Dietary Patterns of the Inverse Association between Alcohol Consumption and Type 2 Diabetes Risk’

The study addressed the question whether the association between alcoholic beverage consumption and risk of type 2 diabetes mellitus (T2DM) was confounded by dietary patterns derived from factor analysis or partial least squares techniques. Confounding arises if a certain factor is associated with both an exposure and an outcome of interest. Therefore, the supplementary analyses were performed to test whether dietary pattern variables were associated with T2DM risk with or without adjustment for alcoholic beverage consumption.

Using the same data from the Framingham Offspring Study cohort (N=2,879), as presented in the main article, Cox-proportional hazard regression analyses were performed to test whether dietary patterns were associated with incident T2DM. The analyses simultaneously included the three dietary pattern variables derived from factor analysis or partial least square technique as continuous variables (see the method section of the main article). The analyses involved statistical adjustment for the same covariates as those for the main analyses (see the footnote of Table 3). In addition, we tested whether the additional adjustment for alcoholic beverages consumption (five categories) changed the association or not, by estimating the ratio of hazard ratios (HRs) with and without adjustment for alcoholic beverage consumption.

The results are presented in the supplementary table 1. The associations between dietary pattern variables and T2DM risk were observed, indicating the potential to confound the association between alcoholic beverage drinking and T2DM risk. For the analyses without adjustment for alcoholic beverage consumption, all dietary patterns derived from factor analysis

were found positively associated with T2DM risk, and patterns of ‘beer drinkers’ and ‘wine drinkers’ were positively associated with T2DM risk.

As expected, adjustment for alcohol consumption shifted the estimates of HRs. Because ‘western’ diet was positively associated with alcohol and T2DM risk and because alcohol was inversely associated with T2DM risk, the adjustment for alcohol consumption strengthened the positive association between the pattern and T2DM risk, removing the protective association by alcohol consumption within the pattern. In the same way, depending on the direction of associations between alcohol consumption and dietary patterns, the HR estimates for dietary pattern variables behaved reasonably; the changes of the HRs were statistically significant, according to the ratios of the two HRs. The strength and the behaviors support the hypothesis that dietary patterns are confounders for the association between alcohol consumption and T2DM risk.

Supplementary Table 1. Results from Cox-Proportional Hazard Model to Examine Association Between Dietary Pattern Variables and Incident Type 2 Diabetes Mellitus in the Framingham Offspring Study Cohort (N=2,879)[†].

Estimates	Factor Analysis			Partial Least Squares		
	Western	Prudent	Alcohol	Beer Drinkers	Wine Drinkers	Liquor Drinkers
HR _{unadj} [‡]	1.38	1.23	1.32	1.09	1.11	0.95
95% CI	1.10, 1.75	0.98, 1.53	1.08, 1.61	0.99, 1.21	1.00, 1.23	0.84, 1.07
HR _{adj} [‡]	1.45	1.01	1.55	1.14	1.18	0.99
95% CI	1.15, 1.82	0.78, 1.30	1.24, 1.92	1.03, 1.26	1.05, 1.31	0.87, 1.12
HR _{adj} /HR _{unadj} [‡]	1.05	0.82	1.17	1.05	1.06	1.04
95% CI	1.01, 1.09	0.74, 0.92	1.07, 1.29	1.02, 1.08	1.02, 1.10	1.01, 1.07

CI, confidence interval; HR, hazard ratio

[†] All estimates were adjusted for the covariates: age (<50, 50-64, or ≥65 years of age), parental history of diabetes (yes/no), body mass index (<25.0, 25.0-29.9, or ≥30.0 kg/m²), hypertension (yes/no, yes if >130/85 mm Hg or receiving therapy), hyperglycemia (<100 or 100-126 mg/dL), triglyceride concentration (≥150 mg/dL or else), low high-density lipoprotein cholesterol concentration (yes/no, yes if <40 mg/dL for men and <50 mg/dL for women), sex, weight change over the follow-up period (quintiles), and total caloric intake (quintiles).

[‡] HR_{unadj} stands for hazard ratio unadjusted for alcoholic beverage consumption (five categories);

HR_{adj} stands for hazard ratio additionally adjusted for alcoholic beverage consumption;

HR_{adj}/HR_{unadj} is the ratio of the two HRs.