A Prospective Study of Sugar Intake and Risk of Type 2 Diabetes in Women

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OBJECTIVE — To investigate prospectively whether intake of total or type of sugar is associated with the risk of developing type 2 diabetes. The contribution of sugar intake to the pathogenesis of type 2 diabetes has not been settled in the context of primary prevention because of limited prospective data.

RESEARCH DESIGN AND METHODS — The Women's Health Study is a randomized controlled trial of aspirin and vitamin E in the prevention of cardiovascular disease and cancer. A validated semiquantitative food frequency questionnaire was completed by 39,345 women aged 45 years and older. The main outcome was the incidence of type 2 diabetes. The predictor was sugar intake, including sucrose, glucose, fructose, and lactose. Using Cox proportional hazard models, multivariate RRs of type 2 diabetes for increasing quintiles of sugar intake compared with the lowest quintile were estimated.

RESULTS — Compared with the lowest quintile of sugar intake, the RRs and 95% CIs for the highest quintiles were 0.84 (0.67–1.04) for sucrose, 0.96 (0.78–1.19) for fructose, 1.04 (0.85–1.28) for glucose, and 0.99 (0.80–1.22) for lactose, after adjustment for known risk factors for type 2 diabetes. Similar findings of no association were obtained in subgroup analyses stratified by BMI.

CONCLUSIONS — Intake of sugars does not appear to play a deleterious role in primary prevention of type 2 diabetes. These prospective data support the recent American Diabetes Association's guideline that a moderate amount of sugar can be incorporated in a healthy diet.

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Prevailing beliefs over the past 20 years regarding sugars and diabetes admonished that added sugar, primarily sucrose, should be avoided and that naturally occurring sugars should be restricted in the diabetic diet (1,2). Support for these beliefs was based largely on results from animal and human studies suggesting that simple sugars would confer a higher postprandial glycemia than starch (3). Consequently, diets for diabetic patients have been sugar restricted for fear of stimulating hyperglycemia (1), exaggerating insulin response to carbohydrates (4,5), and causing possible cardiomyocyte dysfunction (6) and/or accelerated loss of β-cells (7).

However, several metabolic studies have reported that inclusion of a moderate amount of dietary sucrose within a balanced diabetic diet did not elicit subsequent deleterious effects on glycemic control (2,8–12). Different types of sugars may have variable metabolic effects on glycemia or lipemia (13–15). After fructose ingestion, several researchers observed blood glucose levels that were reduced compared with levels after starch or sucrose ingestion in diabetic patients (10,15–18). Additionally, studies conducted in healthy subjects noted that different amounts of fructose intake did not change HbA_{1c} levels (19), yet they significantly elevated plasma triglycerides (20).

The risks and benefits of sugar ingestion in metabolic studies of diabetes have been controversial, and the data on primary prevention, namely, on long-term effects of sugar intake on risk of type 2 diabetes in healthy individuals, are sparse. The need for scientific bases on primary prevention have been addressed by several researchers (2,21). The Women's Health Study (WHS) prospective cohort offered an opportunity to investigate the relation of sugar consumption and subsequent development of type 2 diabetes in a group of initially healthy women with homogeneous demography.

RESEARCH DESIGN AND METHODS

Ethical and human research considerations

The study protocol was approved by the Brigham and Women's Hospital institutional review board, and the protocol adhered to the guidelines put forth in the Helsinki declaration and Belmont Accord for the duration of the study.

Participants

WHS is a randomized, double-blind, placebo-controlled trial designed to evaluate the balance of benefits and risks of low-dose aspirin and vitamin E in the primary prevention of cardiovascular disease and cancer (22). A total of 39,876 female health professionals aged ≥45 years who were free of self-reported coronary heart disease, stroke, and cancer (other than nonmelanoma skin cancer) were randomized. Of these subjects, 39,345 (98%) provided detailed information about their diet, completing a 131-item semiquantitative food frequency questionnaire (SFFQ). We excluded those who left >70

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Abbreviations: GI, glycemic index; SFFQ, semiquantitative food frequency questionnaire; WHS, Women's Health Study.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

spaces blank in their SFFQ or reported unreasonable energy intakes of <600 kcal (2,514 kJ) or >3,500 kcal (14,665 kJ), and we excluded prevalent diabetes cases at baseline. As a result, the final sample for analyses consisted of 38,480 women.

Assessment of sugar and other dietary intake

For each food, a commonly used unit or portion size (e.g., one slice of bread, half a cup of broccoli) was specified on the SFFQ, and each participant was asked how often she had consumed that amount, on average, during the previous year. Nine possible responses ranging from "never" to "six or more times a day" were recorded. Nutrient scores were computed by multiplying the frequency of consumption of each unit of food from the SFFQ by the nutrient content of the specified portion size according to food-composition tables from the U.S. Department of Agriculture (23), the Harvard Food Composition Database, and other sources. The validity and reproducibility of the SFFQ in a similar cohort of male health professionals were reported elsewhere (24). The correlation coefficient for energy-adjusted carbohydrate intake between the SFFQ and diet record ranged from 0.59 to 0.73 in women (25). An additional validity study conducted in the Nurses' Health Study reported that the correlation coefficient of the SFFQ with two 1-week diet records for various foods ranged from 0.56 (for noncarbonated fruit drinks) to 0.84 (for orange or grapefruit juice) (26). The correlation coefficient of sucrose intake estimated by SFFQ with the average of four diet records ranged from 0.52 to 0.60 (25). Intakes of sucrose, fructose, glucose, and lactose for each participant were calculated and categorized in quintiles.

Ascertainment of outcome

The status of type 2 diabetes was evaluated at baseline, and women with a history of diagnosed diabetes were excluded. Thereafter, all of the participants were asked annually whether and when they had been diagnosed with type 2 diabetes since completing the previous questionnaire. To confirm self-reported diagnoses, we mailed a supplemental questionnaire inquiring about the onset of disease, symptoms, diagnostic tests, and hypoglycemic treatment to all respondents reporting a diagnosis of type 2 diabetes. From the supplemental questionnaire, type 2 diabetes was confirmed according to the guidelines proposed by the American Diabetes Association (27). If a participant was receiving treatment with hypoglycemic medications (insulin or oral hypoglycemic agents), a confirmed diagnosis was presumed.

We have conducted a validation study documenting the validity of our diagnostic algorithm for type 2 diabetes from the most recent cycle of data-gathering (1999–2000) in the WHS. The validity was excellent, with 97.5% (78 of 80) of self-reported cases confirmed by medical records. Because all of the participants in this cohort are >45 years of age, and the cases reported at baseline were excluded from the analysis, the self-reported incident cases thereafter were considered type 2 diabetes.

Ascertainment of confounding factors

Potential confounding factors for diabetes included age and BMI as continuous variables (kg/m^2), frequency of vigorous exercise in four levels (rarely/never, <1/week, 1–3 times/week, and ≥4 times/week), cigarette smoking status in three categories (current, past, and never), history of hypertension (yes/no), history of elevated cholesterol level (yes/no), alcohol consumption in four categories (rarely/never, 1–3 drinks/month, 1–6 drinks/week, ≥1 drinks/day), and parental history of type 2 diabetes (yes/no). Women were considered to have a history of hypertension if they reported a previous diagnosis or blood pressure ≥140/90 mmHg. Women were classified as having an elevated cholesterol level if they reported this diagnosis or cholesterol levels ≥240 mg/dl.

Statistical analyses

Using SAS statistical software, we tested for normality and calculated the means and standard deviations of all continuous variables. If normality could not be assumed, data were transformed into categorical variables. Sugar intake was categorized by quintiles, and the incidence rates of type 2 diabetes were calculated in each quintile of sugar consumption by dividing the number of cases by the number of person-years. After testing the proportional hazards assumption, the RR of developing type 2 diabetes for each quintile of sugar intake, compared with the lowest quintile, was estimated via Cox proportional hazards modeling.

The initial models were adjusted for age and smoking, and the models were then adjusted for multiple covariates including age, smoking, BMI, vigorous exercise, alcohol use, history of hypertension, history of high cholesterol, postmenopausal hormone use, vitamin use, and family history of type 2 diabetes as defined above.

Because participants with a history of hypertension or with elevated cholesterol levels might have changed their dietary intake, we carried out similar analyses excluding these women with history at baseline. In addition, because the effect of sucrose on the risk of type 2 diabetes, if any, may be mediated via cumulative effects of overweight and obesity, we examined the sugar intake–diabetes relation stratified by BMI status (BMI <25 and ≥25 kg/m^2 based on World Health Organization criteria). We also performed additional analyses excluding cases of type 2 diabetes that occurred in the first 4 years of follow-up. Because individual sugars often coexist with other sugars in diets, we examined whether total sugars, including sucrose, fructose, glucose, and lactose, would confer stronger effects related to the risk of type 2 diabetes. We also examined the independent role of starch, excluding sugars, in the incidence of type 2 diabetes.

RESULTS — The distribution of baseline risk factors across the quintiles of sugar intake is presented in Table 1. Most risk factors were distributed similarly across quintiles of sugar intake. At baseline in 1993, women who consumed more sugars were slightly older, smoked less, were thinner, and drank less, although these differences were not statistically significant. Low consumers of sugar in our cohort ingested slightly higher levels of total fat and cholesterol, both of which have been postulated to contribute to insulin resistance (28,29). High consumers of sugar in this cohort appeared to consume less protein and more carbohydrates, and exercised more.

A total of 918 incident cases of type 2 diabetes occurred during 222,521 person-years of follow-up. The RRs of type 2 diabetes with increasing quintiles compared with the lowest quintile of total

Table 1—*Baseline distributions of other risk factors for type 2 diabetes according to quintiles of sucrose intake*

	Quintiles of sucrose intake				
	1 (lowest)	2	3	4	5 (highest)
Median intake (g/day)	25.8	33.6	39.3	45.8	57.2
Age	53.3 ± 6.6	53.6 ± 6.8	53.9 ± 7.0	54.2 ± 7.1	54.4 ± 7.4
Smoking (%)					
Current	17.6	12.1	10.9	10.5	14.0
Past	41.5	37.5	34.5	34.2	32.0
Never	41.0	50.4	54.6	55.4	54.0
Exercise (%)					
Rarely/never	39.7	36.7	35.6	37.0	40.5
<1 time/week	19.8	20.1	20.0	20.0	19.8
1–3 times/week	30.5	32.4	33.6	31.4	29.3
≥4 times/week	9.9	10.8	10.7	11.6	10.7
Alcohol (%)					
Rarely/never	32.0	39.8	43.0	48.6	56.7
1–3 drinks/month	10.4	12.6	14.4	14.4	14.4
1–6 drinks/week	34.8	35.8	34.5	31.2	25.1
≥1 drinks/day	22.8	11.9	8.2	5.8	3.8
Postmenopausal (%)	51.9	53.7	53.9	56.3	56.8
Hormone replacement treatment (%)					
Never	48.6	46.6	48.1	47.7	47.5
Past	9.9	10.6	9.6	9.6	10.7
Current	41.6	42.8	42.3	42.7	41.8
Mean BMI (kg/m^2)	26.2	26.0	25.8	25.8	25.5
Multivitamin use (%)	27.7	29.4	30.0	29.7	29.8
History of hypertension	25.4	25.0	24.3	25.0	25.4
History of high cholesterol	24.7	25.7	25.6	28.1	29.1
Family History of diabetes	24.8	25.4	24.8	24.3	24.3
Total energy (kcal)	1,696 ± 527	1,750 ± 519	1,760 ± 526	1,739 ± 538	1,687 ± 558
Total fat (g)	61.5 ± 12.4	58.8 ± 11.4	57.4 ± 11.1	56.4 ± 11.0	54.0 ± 11.6
Saturated fat (g)	21.2 ± 5.3	20.0 ± 4.6	19.5 ± 4.5	19.2 ± 4.5	18.4 ± 4.8
Carbohydrate (g)	194.1 ± 32.2	213.2 ± 28.1	223.2 ± 27.8	231.6 ± 28.1	247.5 ± 31.1
Dietary GI	74.1 ± 5.2	74.7 ± 4.4	75.0 ± 4.3	75.4 ± 4.3	76.5 ± 4.7
Proteins (g)	89.4 ± 15.0	85.6 ± 12.6	81.9 ± 11.8	77.9 ± 11.6	70.4 ± 12.1
Dietary cholesterol (mg)	255.9 ± 82.2	236.0 ± 67.5	224.3 ± 63.8	213.1 ± 62.8	194.9 ± 63.5
Dietary folate (mcg)	419.6 ± 227.2	435.4 ± 219.6	436.7 ± 217.6	433.0 ± 225.1	417.6 ± 231.5

Data are means ± SD, unless otherwise indicated. All covariate values are according to the quintiles of sucrose intake. All the means of nutrients are energy adjusted. History of hypertension was defined as ever diagnosed by physician or self-reported blood pressure >140/90; history of high cholesterol and family history of diabetes were self-reported and validated in a subsample. All the means of nutrients are energy adjusted. Model 1: age and smoking adjusted. Model 2: age, smoking, BMI, vigorous exercise, alcohol use, postmenopausal hormone use, multivitamin use, history of hypertension, high cholesterol, and family history of diabetes.

sugar intake were 1.0, 0.94, 0.88, 0.92, and 0.86 (*P* value for linear trend = 0.17), and with sucrose they were 1.0, 0.98, 1.00, and 0.84 (*P* for trend <0.16), adjusting for all pertinent confounding variables. In this cohort, as expected, sucrose comprised ~75% of total sugar intake, similar to what was reported in an Iowa women's study. A similar absence of significant trend was observed for fructose, glucose, and lactose. Several initial models adjusted for age and smoking indicated a strong inverse linear trend of association between sugar intake and the risk of type 2 diabetes (*P* = 0.0007 for total sugar, 0.006 for sucrose, 0.002 for fructose, 0.04 for glucose, and 0.02 for lactose). When a full set of covariates were included in the model, none of the RRs was statistically significant. The multivariate-adjusted RRs for the highest category of sugar intake compared with the lowest were 0.86 (95% CI 0.69–1.06) for total sugar, 0.84 (0.67–1.04) for sucrose, 0.96 (0.78–1.19) for fructose, 1.04 (0.85–1.28) for glucose, and 0.99 (0.80–1.22) for lactose (Table 2).

In a subcohort excluding subjects with hypertension or elevated cholesterol level at baseline (271 incident cases of type 2 diabetes and 131,025 person-years of follow-up), sucrose and lactose appeared to suggest an inverse association with type 2 diabetes in initial models, with RRs for increasing quintiles of intake at 1.0, 0.83, 0.84. 0.78, and 0.60 (*P* for trend = 0.03) for sucrose and 1.0, 0.69, 1.03, 0.94, and 0.76 (*P* for trend <0.06) for lactose, but only sucrose intake remained inversely associated after full adjustment for other risk factors. Corresponding RRs for ascending quintiles of sucrose in the multivariate model were 1.0, 0.84, 0.85, 0.73, and 0.59 (*P* value for linear trend = 0.05) (see Table 3). In

Table 2—*RR of type 2 diabetes according to quintiles of sugar intake in the whole cohort of the WHS*

	Quintiles of sugar intake					
	1 (lowest)	2	3	4	5 (highest)	*P* for trend
Total sugar						
Case subjects	215	190	183	167	163	
Person-years	44,414	44,580	44,464	44,607	44,457	
Model 1	1.0	0.87 (0.72–0.84)	0.84 (0.68–1.02)	0.75 (0.61–0.92)	0.73 (0.59–0.89)	0.0007
Model 2	1.0	0.94 (0.77–1.15)	0.88 (0.72–1.08)	0.92 (0.74–1.14)	0.86 (0.69–1.06)	0.17
Sucrose						
Case subjects	196	194	175	188	165	
Person-years	44,362	44,298	44,549	44,567	44,746	
Model 1	1.0	0.99 (0.81–1.21)	0.89 (0.72–1.09)	0.95 (0.77–1.16)	0.82 (0.66–1.01)	0.06
Model 2	1.0	1.00 (0.81–1.23)	0.98 (0.79–1.22)	1.00 (0.81–1.24)	0.84 (0.67–1.04)	0.16
Fructose						
Case subjects	208	189	175	177	169	
Person-years	44,564	44,515	44,479	44,587	44,379	
Model 1	1.0	0.90 (0.74–1.1)	0.83 (0.68–1.02)	0.83 (0.68–1.02)	0.79 (0.65–0.97)	0.02
Model 2	1.0	0.99 (0.81–1.22)	1.04 (0.85–1.29)	1.03 (0.83–1.27)	0.96 (0.78–1.19)	0.86
Glucose						
Case subjects	203	192	178	168	177	
Person-years	44,693	44,426	44,470	44,626	44,308	
Model 1	1.0	0.95 (0.78–1.16)	0.87 (0.71–1.06)	0.81 (0.66–0.99)	0.85 (0.70–1.05)	0.04
Model 2	1.0	1.08 (0.88–1.33)	1.02 (0.82–1.26)	0.96 (0.77–1.19)	1.04 (0.85–1.28)	0.91
Lactose						
Case subjects	198	205	186	157	172	
Person-years	44,671	44,458	44,545	44,528	44,321	
Model 1	1.0	1.05 (0.86–1.27)	0.94 (0.77–1.15)	0.79 (0.64–0.97)	0.86 (0.70–1.06)	0.02
Model 2	1.0	1.08 (0.88–1.32)	1.03 (0.83–1.26)	0.86 (0.69–1.07)	0.99 (0.8–1.22)	0.33
Starch						
Case subjects	199	179	200	185	155	
Person-years	44,477	44,655	44,580	44,517	44,292	
Model 1	1.0	0.91 (0.76–1.11)	1.03 (0.85–1.26)	0.96 (0.49–1.18)	0.83 (0.67–1.02)	0.19
Model 2	1.0	0.95 (0.77–1.17)	1.05 (0.85–1.28)	1.06 (0.86–1.30)	0.88 (0.71–1.09)	0.61

Data are RR and RR (95% CI). All covariate values are according to the quintiles of sucrose intake.

neither stratified analyses by BMI <25 and BMI ≥25 kg/m^2 (Table 4) nor analyses excluding cases of type 2 diabetes that occurred in the first 4 years of follow-up (Table 3) did sugar intake exhibit any consistent trend in relation to the incidence of type 2 diabetes. There was only a weak positive relationship between glucose intake and the incidence of type 2 diabetes in the subgroup excluding cases of type 2 diabetes that occurred in the first 4 years of follow-up. The RRs were 1.0, 1.03, 1.03, 1.15, and 1.34 for increasing quintiles in a fully adjusted model, a trend that was not significant ($P = 0.09$) (data not shown). Finally, the intake of starch, excluding total sugar, was not associated with increased risk type 2 diabetes, and the adjustment for glycemic index (GI) did not change the relation between sugar intake and risk of type 2 diabetes.

CONCLUSIONS — In our large cohort of 38,480 initially healthy postmenopausal women followed for an average of 6 years, we accrued 918 incident cases of type 2 diabetes and found no definitive influence of sugar intake on the risk of developing type 2 diabetes. In the subcohort excluding subjects with hypertension and elevated cholesterol level at baseline, sucrose intake was inversely associated with the risk of type 2 diabetes with marginal significance ($P = 0.05$), whereas fructose, glucose, and lactose did not appear to be significantly associated with the risk of type 2 diabetes. It is possible that those who were diagnosed with hypertension and high cholesterol at baseline might have changed their dietary intakes from their long-term dietary pattern. Excluding those who might have changed their dietary intake because of hypertension and high cholesterol elicited a less-biased association. Although our results concur with the results from several randomized metabolic trials (8–10,12,30) investigating the acute responses to sugar intake among diabetic patients, our prospective study further extends these findings to the risk of developing type 2 diabetes in a cohort of initially healthy women, offering scientific bases for primary prevention.

Since the introduction of the GI paradigm by Jenkins et al. in 1981 (31), the rationale that the contribution of carbohydrates to postprandial glycemia depends on their glucogenic ability, not on the size of carbohydrate molecules, has been gaining acceptance in the context of pathogenesis of diabetes (32,33). The glucogenic ability, measured as GI, of carbohydrates has been implicated in the development of atherosclerotic processes considered "the common base" for type 2

Table 3—*RR of type 2 diabetes according to quintiles of sugar intake in a subcohort of women (n = 22,243) without history of hypertension and high cholesterol levels at baseline*

	Quintiles of sugar intake					
	1 (lowest)	2	3	4	5 (highest)	*P* for trend
Total sugar						
Case subjects	70	51	64	45	41	
Person-years	26,133	26,293	26,148	26,270	26,182	
Model 1	1.0	0.75 (0.52–1.07)	0.95 (0.67–1.33)	0.66 (0.45–0.96)	0.59 (0.40–0.88)	0.009
Model 2	1.0	0.86 (0.59–1.24)	1.10 (0.77–1.57)	0.85 (0.57–1.25)	0.77 (0.52–1.15)	0.26
Sucrose						
Case subjects	68	52	55	55	41	
Person-years	26,045	26,169	26,204	26,225	26,382	
Model 1	1.0	0.83 (0.58–1.19)	0.84 (0.58–1.19)	0.78 (0.55–1.13)	0.60 (0.41–0.88)	0.03
Model 2	1.0	0.84 (0.58–1.21)	0.85 (0.59–1.22)	0.73 (0.50–1.05)	0.59 (0.39–0.88)	0.05
Fructose						
Case subjects	55	56	66	44	50	
Person-years	26,262	26,251	26,186	26,144	26,182	
Model 1	1.0	0.85 (0.57–1.26)	1.27 (0.89–1.83)	1.07 (0.74–1.56)	0.95 (0.64–1.40)	0.47
Model 2	1.0	1.16 (0.77–1.74)	1.61 (1.11–2.33)	1.17 (0.79–1.71)	1.24 (0.84–1.85)	0.30
Glucose						
Case subjects	60	54	61	48	48	
Person-years	26,296	26,166	26,270	26,224	26,069	
Model 1	1.0	0.84 (0.57–1.23)	1.06 (0.74–1.52)	0.95 (0.65–1.37)	0.83 (0.57–1.22)	0.27
Model 2	1.0	1.05 (0.71–1.55)	1.30 (0.89–1.87)	1.02 (0.70–1.49)	1.12 (0.76–1.65)	0.55
Lactose						
Case subjects	63	58	62	42	46	
Person-years	26,291	26,211	26,244	26,212	26,068	
Model 1	1.0	0.69 (0.47–1.03)	1.03 (0.72–1.45)	0.94 (0.66–1.35)	0.76 (0.52–1.12)	0.06
Model 2	1.0	0.77 (0.51–1.14)	1.17 (0.81–1.68)	1.03 (0.72–1.49)	0.93 (0.62–1.38)	0.34
Starch						
Case subjects	55	58	62	61	35	
Person-years	26,218	26,282	26,252	26,204	26,070	
Model 1	1.0	1.11 (0.77–1.60)	1.21 (0.84–1.74)	1.20 (0.83–1.74)	0.72 (0.47–1.10)	0.34
Model 2	1.0	1.17 (0.81–1.71)	1.31 (0.90–1.90)	1.26 (0.87–1.83)	0.78 (0.50–1.21)	0.59

Data are RR or RR (95% CI). All covariate values are according to the quintiles of sucrose intake. All the means of nutrients are energy-adjusted. Model 1: age and smoking adjusted. Model 2: age, smoking, BMI, vigorous exercise, alcohol use, postmenopausal hormone use, multivitamin use, history of hypertension, high cholesterol, and family history of diabetes.

diabetes and coronary heart disease (34–36).

Meyer et al. (37) observed no association between GI/load and type 2 diabetes, but they found significant inverse association between sugar intake and type 2 diabetes in their study. In contrast, we observed no quantifiable association with either GI or sugar intake and risk of type 2 diabetes. GI, in the present analyses, was positively associated with type 2 diabetes in a model adjusted for age, randomization, and smoking (RR 1.46, 95% CI 1.10–1.79, *P* for trend <0.001). However, this relationship was attenuated in a multivariate-adjusted model (1.10, 0.87–1.38, *P* for trend = 0.22). Our reports are consistent with the rationale that the contribution of sucrose and other sugars to blood glucose level depends on which carbohydrate they replace (38,39). Because sucrose by itself has a glycemic response similar to or less than that of starchy foods such as bread, rice, and potatoes, sugars that replaced starch of equal GI value would not raise the glucogenicity of the meal. However, if sugars substitute for low-GI food such as legumes, then the blood glucose level would be elevated (40).

We also observed parallel findings between our results and the results by Meyer et al. (37), whose RR of type 2 diabetes for the highest versus the lowest quintile of sucrose intake was 0.81, compared with our RR of 0.84. Moreover, sucrose intake from our subgroup analyses excluding the participants with hypertension and elevated cholesterol was inversely associated with type 2 diabetes, with marginal significance ($P < 0.05$) (data not shown), an observation consistent with the report by Meyer et al. (37). Our RR for glucose intake suggests a nonsignificant positive association with the incidence of diabetes (*P* for trend <0.09) (data not shown), consistent with the notion that among sugars, glucose best predicted the insulin response (41). According to our data, sugar intake does not appear to increase significantly the risk of developing type 2 diabetes. The homogeneity of our cohort may provide a more precise estimate of the association between sugar intake and risk of type 2 diabetes, although generalizability of our results is limited.

The finding that higher sugar consumption corresponds to higher total carbohydrate intake in our cohort is in

Table 4—*RR of type 2 diabetes according to quintiles of sugar intake in the WHS stratified by BMI*

	BMI <25 kg/m^2		BMI ≥25 kg/m^2	
	Case subjects/person-years	Multivariate RR* (95% CI)	Case subjects/person-years	Multivariate RR* (95% CI)
Total sugars				
Q1	21/20,942	1.0	189/22,512	1.0
Q2	25/21,664	1.18 (0.65–2014)	158/22,030	0.91 (0.73–1.13)
Q3	20/22,926	0.84 (0.44–1.57)	156/20,637	0.91 (0.73–1.13)
Q4	25/24,124	0.86 (0.46–1.59)	136/19,676	0.94 (0.74–1.18)
Q5	26/24,877	0.86 (0.47–1.58)	137/18,647	0.88 (0.70–1.11)
P for trend	—	*P* = 0.36	—	*P* = 0.38
Sucrose				
Q1 (lowest)	25/21,653	1.00	164/21,830	1.00
Q2	19/22,322	0.69 (0.37–1.29)	170/21,060	1.10 (0.88–1.35)
Q3	17/23,031	0.62 (0.33–1.16)	157/20,648	1.02 (0.82–1.27)
Q4	28/23,230	0.87 (0.49–1.54)	154/20,388	1.00 (0.81–1.26)
Q5 (highest)	28/24,296	0.77 (0.44–1.36)	131/19,579	0.87 (0.70–1.12)
P for trend	—	*P* = 0.70	—	*P* = 0.25
Fructose				
Q1	24/20,493	1.00	178/23,135	1.00
Q2	16/21,693	0.69 (0.36–1.31)	167/21,930	1.05 (0.84–1.30)
Q3	25/23,097	1.04 (0.58–1.86)	145/20,423	1.05 (0.84–1.32)
Q4	22/24,141	0.83 (0.45–1.0)	149/19,499	1.09 (0.87–1.36)
Q5	30/25,107	0.90 (0.51–1.59)	137/18,517	1.00 (0.79–1.26)
P for trend		*P* = 0.94		*P* = 0.87
Glucose				
Q1	22/20,562	1.00	176/23,142	1.00
Q2	17/21,878	0.78 (0.41–1.49)	170/21,696	1.13 (0.91–1.40)
Q3	27/23,017	1.15 (0.64–2.05)	141/20,576	1.00 (0.80–1.26)
Q4	20/23,969	0.77 (0.41–1.45)	143/19,696	1.02 (0.81–1.28)
Q5	31/25,105	1.04 (0.59–1.85)	146/18,394	1.08 (0.86–1.35)
P for trend		*P* = 0.87		*P* = 0.85
Lactose				
Q1	31/23,175	1.00	161/20,510	1.00
Q2	18/22,703	0.63 (0.35–1.13)	178/20,833	1.17 (0.94–1.45)
Q3	27/22,946	0.87 (0.51–1.48)	154/20,640	1.05 (0.83–1.31)
Q4	22/22,586	0.67 (0.38–1.18)	131/21,172	0.88 (0.70–1.13)
Q5	19/23,122	0.60 (0.34–1.08)	152/20,349	1.06 (0.84–1.33)
P for trend	—	*P* = 0.13	—	*P* = 0.57
Starch				
Q1	25/22,759	1.0	170/20,604	1.0
Q2	20/22,513	0.75 (0.42–1.37)	155/21,367	0.96 (0.77–1.20)
Q3	20/22,288	0.91 (0.50–1.64)	174/21,535	1.06 (0.85–1.32)
Q4	25/22,932	1.10 (0.63–1.92)	157/20,665	1.03 (0.83–1.29)
Q5	27/24,039	1.03 (0.59–1.81)	120/19,331	0.85 (0.67–1.08)
P for trend	—	*P* = 0.54	—	*P* = 0.98

Multivariate RR was adjusted for smoking, BMI, exercise, alcohol use, history of hypertension, high cholesterol, and family history of diabetes.

agreement with reports showing that individuals who consume high amounts of added sugars eat more total carbohydrate than those who consume lesser amounts of sugars (42–44). Wolever and Miller (40) reported that the glycemic response of sugar followed a logarithmic curve dependent on concomitant carbohydrate ingestion, and said curve leveled off at ~100 g of carbohydrate. Thus, the impact of sugar ingestion is greatly attenuated when individuals consume >100 g of carbohydrates. Our findings are consistent with this report by Wolever and Miller (40) because our recorded mean intake of carbohydrates was 194.1 g in the lowest quintile and 247.5 g in the highest, and the impact of sugars on plasma glucose levels may be insignificant in the context of such high carbohydrate intake.

Limitations

We have adjusted for all known covariates, but it is possible that some residual confounding covariates may remain. Additionally, the number of diabetes events

(918) might not have provided sufficient statistical power to detect the observed moderate RRs. The median follow-up time of 6 years might not have been long enough to detect a very subtle relationship between sugar intake and incidence of type 2 diabetes. It is also possible that measurement errors associated with dietary assessment might have attenuated an otherwise inverse or positive association between sugar intake and risk of type 2 diabetes.

A more definitive answer to this question of whether sugars contribute to the pathogenesis of type 2 diabetes may emerge with further research efforts that include long-term metabolic trials and other large prospective studies.

In summary, the intake of sugars does not play a detrimental role in primary prevention of type 2 diabetes. However, the results from this study should not be interpreted as an endorsement for unlimited sugar intake. Rather, it should be emphasized that only moderate sugar intake should be incorporated within the boundaries of acceptable energy intake in a well-balanced diet. This moderate sugar allowance may promote better compliance with the diet regimen among diabetic patients (12).

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