# Associations of Intake of Free and Naturally Occurring Sugars from Solid Foods and Drinks with Cardiometabolic Risk Factors in a Quebec Adult Population: The PREDISE (PRÉDicteurs Individuels, Sociaux et Environnementaux) Study

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### **ABSTRACT**

**Background:** Associations between sugar consumption and cardiometabolic health, taking into account the physical form of sugar-containing foods (liquid vs. solid) and the type of sugars consumed [free sugars (FSs) vs. naturally occurring sugars (NOSs)], remain to be thoroughly documented.

**Objective:** The objective was to examine whether FS and NOS intakes from drinks and solid foods are associated with cardiometabolic risk factors in a sample of French-speaking adults from the province of Quebec, Canada.

**Methods:** Data were collected as part of the cross-sectional PREDISE (PRÉDicteurs Individuels, Sociaux et Environnementaux) study (n = 1019, 18–65 y old; 50% women). FS and NOS intakes were assessed by three 24-h dietary recalls using a self-administered, web-based application. Diet quality was assessed using the Alternative Healthy Eating Index–2010. Participants underwent on-site clinical assessment of cardiometabolic risk factors, including blood pressure, waist circumference, BMI, and fasting blood sampling (glucose, insulin, C-reactive protein, blood lipids). Multivariable linear regression models were performed to examine the associations between sugar intake and cardiometabolic risk factors with sociodemographic characteristics, lifestyle variables, and diet quality entered as covariates.

**Results:** In fully adjusted models, FS intake from drinks was associated with fasting insulin (1.06%; 95% CI: 0.30%, 1.84%; P = 0.006) and with insulin resistance as estimated using the HOMA model (1.01%; 95% CI: 0.19%, 1.84%; P = 0.02). All metabolic variables that were significantly associated with NOS intake from solid foods in minimally adjusted models were no longer significant after entering sociodemographic and lifestyle variables (e.g., educational and income levels, smoking, physical activity, daily energy intake) and diet quality in the models.

**Conclusions:** Our data from an adult sample showed that unfavorable and favorable associations with cardiometabolic risk factors observed, respectively, for FS intake from drinks and NOS intake from foods are mostly explained by sociodemographic and lifestyle variables, as well as by diet quality. *J Nutr* 2021;151:1561–1571.

**Keywords:** sugar intakes, free sugars, naturally occurring sugars, drinks, solid foods, diet quality, sociodemographic characteristics, lifestyle variables, cardiometabolic health, adults

### Introduction

Recently, sugars have attracted growing scientific and media attention (1). Countries and health organizations have set recommendations for added, free, or total sugar intake (2). Chemically, the sugar molecules may be the same but the state they are in foods (added, free, or naturally occurring) changes

the definition we give them. As defined by the USDA, added sugars are "caloric sweeteners that are added to foods as ingredients during food processing, during food preparation, or at the table" (3). According to the WHO, the definition of free sugars (FSs) includes all added sugars plus sugars in fruit juices (4). Total sugars, in turn, correspond to the sum of FSs and

sugars that are naturally present in foods [naturally occurring sugars (NOSs)] such as fruit or milk.

The WHO recommends limiting FS intake to a maximum of 10% of daily energy (%E) and even proposes to aim at a 5%E limit as a conditional recommendation, particularly to prevent dental caries (4). The Scientific Advisory Committee on Nutrition advising the UK government organizations also recommends a maximum of 5%E as FSs in order to limit total energy intake and the risk of dental caries (5). Health Canada, through the Canada's dietary guidelines for health professionals and policy makers issued along with the 2019 version of the Canada's food guide, endorses the WHO recommendations (6). In order to limit FS intake, Health Canada recommends reducing consumption of highly processed food and sugary drinks and consuming nutritious food containing little to no FSs (6).

For over a decade, an increasing number of studies on sugars and their effects on cardiometabolic outcomes and risk factors have been published in the literature (1). However, most studies were on sugar-sweetened beverages (SSBs) (7), whose consumption is clearly linked with adverse health outcomes (8, 9) and which is sometimes used as a proxy for total sugar consumption (10). The impact of some aspects of sugar consumption, such as the type of sugars (total, added, free, or naturally occurring) consumed (8) and the physical form of foods in which they are consumed (liquid vs. solid; i.e., drinks vs. solid foods) (11), has not been as thoroughly studied (7). This literature gap impedes the comprehensive understanding of the complex associations between sugar intake and health outcomes. Furthermore, associations observed between diet and health may be far more complex than strictly based on the effect of single nutrients (12). The fact that sugar intake can be a marker of diet quality suggests that the associations between sugars and health may be mediated, at least in part, by diet quality (13). In fact, a high intake of added or free sugars may be the reflection of a poorer diet quality—namely, through nutrient dilution if nutrient-dense foods are replaced with foods rich in added or free sugars (14, 15).

Tybor et al. (1) systematically reviewed all published studies on dietary sugars and identified knowledge gaps in the complex relation between sugar intake and health outcomes. In designing the present study, we considered some of the research questions related to sugar and health that were identified by Tybor et al. as not yet having clear answers, such as "What factors modify the effects of sugars intake on cardiovascular disease outcomes?"

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Supplemental Tables 1–4 are available from the "Supplementary data" link in the online posting of the article and from the same link in the online table of contents at https://academic.oup.com/jn/.

Address correspondence to SL (e-mail: Simone.Lemieux@fsaa.ulaval.ca). Abbreviations used: AHEI, Alternative Healthy Eating Index–2010; CRP, C-reactive protein; DBP, diastolic blood pressure; FS, free sugar; MS z score, continuous metabolic syndrome risk score; NOS, naturally occurring sugar; PREDISE, PRÉDicteurs Individuels, Sociaux et Environnementaux; SBP, systolic blood pressure; SSB, sugar-sweetened beverage; TC, total cholesterol; TG, triglyceride; WC, waist circumference; %E, percentage of daily energy.

and "Does type, form, source, or timing of dietary sugars have different effects on cardiovascular disease outcomes?"

(1). More precisely, the objective of the present study was to cross-sectionally examine the associations of the intake of FSs and NOSs from drinks and solid foods with cardiometabolic risk factors in an age- and sex-representative sample of French-speaking adults from the province of Quebec, Canada. We hypothesized that the type of sugars (free vs. naturally occurring) and the physical form of foods in which they are consumed (solid foods vs. drinks) are differently associated with cardiometabolic risk factors and that these associations are largely explained by sociodemographic characteristics, lifestyle variables, and diet quality.

### **Methods**

### Participants and procedures

The PREDISE (PRÉDicteurs Individuels, Sociaux et Environnementaux) study is a cross-sectional, web-based, multicentered study that was designed to assess how individual, social, and perceived environmental factors are associated with adherence to dietary guidelines (16). Participants were recruited between August 2015 and April 2017 using random-digit dialing in 5 different administrative regions of the province of Quebec, Canada: Capitale-Nationale/Chaudière-Appalaches, Estrie, Mauricie, Montréal, and Saguenay-Lac-St-Jean. A total of 76 728 individuals were contacted and 1849 eligible individuals accepted to participate. Participants were asked to fill out online questionnaires and to complete three 24-h dietary recalls (1149 completed at least one 24-h dietary recall). Pregnant women (n = 2) were excluded. The final sample is representative based on sex and predetermined age groups (18-34, 35-49, and 50-65 y) of the 5 administrative regions and includes 1147 participants (50.2% women). Participants were mostly White (94.3%) and 44.5% had a university degree. Following completion of the questionnaires, participants were subsequently invited to a research center partner of the project for the measurement of cardiometabolic risk factors: blood pressure [systolic blood pressure (SBP) and diastolic blood pressure (DBP)] assessment (sitting, after 10-min rest, mean of 3 measures taken 3 min apart; Digital BPM HEM-907XL model; Omron), anthropometric measurements [height, weight, waist circumference (WC) (standardized protocol)], fasting blood sampling 12-h fast; serum; [blood glucose (Hexokinase method; Roche Modular P System), insulin (Cobas 6000; Roche Diagnostics), C-reactive protein (CRP; serum, ELISA; High Sensitivity C-Reactive Protein Enzyme Immunoassay Test Kit, model BC-1119; Biocheck, Inc.), triglycerides (TGs), total cholesterol (TC), and HDL cholesterol (Roche Modular P System; Roche Diagnostics) and LDL cholesterol (calculated with the use of the Friedewald equation)]. The detailed methodology is described elsewhere (17). For the present study, participants who did not come to their research center visit (n = 123) and who were not fasted before blood sampling (n = 5) were excluded. Therefore, this study sample includes 1019 participants (50.9% women, 92.2% White, 45.1% with a university degree). Written informed consent was obtained from all participants. The project was conducted in accordance with the Declaration of Helsinki and was approved by the Research Ethics Committees of Université Laval (ethics number: 2014-271), Centre Hospitalier Universitaire de Sherbrooke (ethics number: MP-31–2015-997), Montreal Clinical Research Institute (ethics number: 2015–02), and Université du Québec à Trois-Rivières (ethics number: 15-2009-07.13).

### **Dietary assessment**

On 3 unannounced randomly allocated days during a period of 21 d, participants had to complete a 24-h dietary recall, in which they were asked to indicate what they had eaten the day before. The number of completed recalls was evenly distributed across the 7 d of the week (17). The 24-h dietary recalls were completed using an automated, self-administered, web-based 24-h dietary recall instrument (R24W).

In our sample, 98.9% of participants completed 3 web-based 24-h dietary recalls and all participants completed at least 2 web-based 24-h

The R24W has been previously shown to be a valid tool for measuring the intakes of energy and macro- and micronutrients as well as for assessing diet quality in our population (18-20). The nutritional value of foods declared by participants is automatically calculated by the R24W using data from the Canadian Nutrient File (21). For each individual, dietary intake data used in this study are based on the average of all available recalls. Total sugar content of each food item was differentiated into FS and NOS in the R24W database using a step-by-step systematic methodology (22) inspired by an algorithm developed by Louie et al. (23) and thereafter modified by Bernstein et al. (24), and using the WHO's FS definition: "Free sugars include monosaccharides and disaccharides added to foods and beverages by the manufacturer, cook or consumer, and sugars naturally present in honey, syrups, fruit juices and fruit juice concentrates" (4). The complete sugar differentiation methodology used is presented elsewhere (22). Main food sources of sugars were based on food categories determined by the Canadian Bureau of Nutritional Sciences and used to assess main sources of total sugars in the 2015 Canadian Community Health Surveys (25). The drinks category included alcoholic beverages, hot drinks (coffee, hot chocolate, tea), energy drinks, soft drinks, sports drinks, plant-based beverages, water, fruit juices, fruit drinks, vegetable juices, milk, milkshakes, smoothies, and powders and concentrates used to reconstitute those drinks. Solid foods were all foods not included in the drinks category.

### Diet quality

A higher Alternative Healthy Eating Index-2010 (AHEI) score (maximum: 110) indicates a diet that is associated with a significant reduction in chronic disease risk (cardiovascular disease, type 2 diabetes, cancer, and neurodegenerative disease) and all-cause mortality (26, 27). For the purpose of this study, a partial AHEI score was used to assess diet quality and was entered as a covariate in linear regression models. To avoid overadjustment for %E as FS from liquid sources and %E as NOS from solid sources, "sugar-sweetened beverages and fruit juice" and "whole fruits" subscores were removed from the original score. Thus, a partial score (maximum: 90) was calculated for each participant based on their intakes of various food groups (vegetables, whole grains, nuts and legumes, red/processed meat, and alcohol) and specific nutrients [trans fat, long-chain (n-3) fats (EPA + DHA), (n-3) PUFAs, and sodium] (27).

### Plausibility of self-reported energy intakes

The plausibility of self-reported energy intakes was determined using a method described by Huang et al. (28). Reported energy intake was compared with predicted energy requirements calculated with the equations from the Institute of Medicine (29). A ratio of self-reported energy intake over predicted energy requirements < 0.78 implied underreporting of energy intake, whereas a ratio >1.22 suggested overreporting of energy intake.

### **HOMA-IR**

The HOMA-IR was calculated by multiplying fasting glucose (millimoles/liter) by fasting insulin (picomoles/liter) and dividing the product by 135, as proposed by Matthews et al. (30).

### Continuous metabolic syndrome risk score (z score)

To assess a continuous metabolic syndrome risk score (MS z score), we used formulas that were previously documented (31) in which each component was normalized at the reference threshold of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) for men and women separately (32). More precisely, normalized, continuous MS z scores were calculated as follows:

Women: 
$$[(1.53 - HDL-C)/0.46] + [(TG - 1.35)/0.93]$$
  
+  $[(FG - 5.20)/0.83] + [(WC - 87.8)/15.8]$   
+  $[MAP - 88.3)/10.8]$  (1)

Men: 
$$[1.33 - HDL-C)/0.37] + [(TG - 1.35)/0.93]$$
  
+  $[(FG - 5.20)/0.83] + [(WC - 97.0)/15.6]$   
+  $[(MAP - 88.3)/10.8](31)$  (2)

where HDL-C = HDL cholesterol (millimoles/liter); FG = fasting glucose (millimoles/liter); MAP = mean arterial pressure [DBP (mm Hg) multiplied by 2 + SBP (mm Hg)/3; denominators are finite population SDs of the corresponding variables specific to the PREDISE sample and were calculated while taking into consideration the stratified sampling methods of the PREDISE study.

### Statistical analyses

To account for the stratified design of the study, analyses were performed using SURVEY procedures in SAS Studio (version 3.6; SAS Institute). Because the sample size was slightly larger than anticipated, sampling weights were used in order to ensure that our sample remains age- and sex-representative of each region of the province of Quebec included in the study. Missing sociodemographic characteristics, used as covariates, were imputed using the fully efficient fractional imputation method [household income level (n = 94), educational level (n = 6), and physical activity level (either low, moderate, or high; n = 119)], as presented elsewhere (17). Descriptive analyses were used to present population characteristics and to determine food sources of all types of sugars. Sugar intakes were expressed as percentages of daily energy intake (%E). Associations of %E as FSs and NOSs for the overall diet, solid foods, and drinks with AHEI score (total and partial) and AHEI individual components were assessed by univariable correlation analyses. Participants with reported type 1 diabetes (n = 5) were excluded from analyses involving fasting glucose and insulin, HOMA-IR, and MS z score. Participants with CRP concentrations of  $\geq 10$  mg/L (n = 60), which indicates acute inflammation process (33), were excluded from analyses involving CRP. Participants taking medication that could affect the studied outcome were removed from specific analyses [WC and BMI: no exclusion; glucose, insulin, and HOMA-IR: exclusion of participants taking antidiabetic medication (n = 41); CRP: exclusion of women taking systemic hormonal contraceptives (n = 79); TGs, LDL cholesterol, HDL cholesterol, and TC:HDL cholesterol: exclusion of participants taking lipid-lowering medication (n = 98); SBP and DBP: exclusion of participants taking antihypertensive medication (n = 116); MS z score: exclusion of participants taking antidiabetic, antihypertensive, lipid-lowering, or heart disease medication (n = 185)].

Multivariable linear regressions were performed to assess the associations between %E as FSs and NOSs and cardiometabolic risk factors (WC, BMI, fasting glucose and insulin, HOMA-IR, CRP, TGs, LDL cholesterol and HDL cholesterol, ratio of TC to HDL cholesterol, SBP and DBP, and MS z score). Fasting glucose, fasting insulin, HOMA-IR, CRP, and TG variables were log-transformed due to the linear regression model residuals not being normally distributed. Different regression models were tested. Model 1 was adjusted for sex, continuous age, and administrative region (Capitale-Nationale/Chaudière-Appalaches, Estrie, Mauricie, Montreal, and Saguenay-Lac-St-Jean). In addition to the variables included in model 1, the following variables were also included in model 2: continuous WC (except when WC or BMI is the studied outcome), educational level [high school or no diploma, Colle'ge d'Enseignement Ge'ne'ral et Professionnel (pre-university and technical college institution particular to the province of Quebec educational system, which is considered higher than high school and lower than university), university], household income level in Canadian dollars  $(<30,000, \ge 30,000 \text{ to } <60,000, \ge 60,000 \text{ to } <90,000, \ge 90,000),$ smoking (yes, no, former smoker), physical activity [low, moderate, high, based on the 2005 International Physical Activity Questionnaire (IPAQ) categorical scoring rules (34)], mean daily energy intake, plausibility of self-reported energy intake (underreporters, plausible reporters, overreporters of energy intake), and the number of 24-h dietary recalls completed on weekend days (0, 1, 2, 3). Model 3 included all covariates from models 1 and 2 and the AHEI partial score. Estimates were also rescaled to represent a change equivalent to the interquartile range of %E from each type and physical form of sugar (Supplemental Tables 1 and 2). Finally, multivariable linear regressions (model 3) were also performed to assess the associations between each of the top 3

sources of FSs (sugars, syrups and confectionary, fruit juices, and baked products) and NOSs (whole fruits, milk, and vegetables) [expressed as daily portions calculated by dividing the daily quantity consumed by the reference amount determined by Health Canada for each category of foods) (35)] and cardiometabolic risk factors. Associations at P < 0.05 were considered significant.

### **Results**

### **Population characteristics**

Characteristics of study participants and intakes of key nutrients are presented by quartiles of %E as FSs and NOSs in Tables 1 and 2. Men and women are represented equally across quartiles of %E from FS intake, whereas women represent a lower proportion (35.5%) of the lowest quartile of %E from NOS intake and a higher proportion (65.3%) of the highest quartile of %E from NOS intake. The lowest quartile of %E from FS intake is characterized by a higher proportion of potential energy underreporters (22.9%) and a lower proportion of potential energy overreporters (9.6%) compared with the highest quartile of %E from FS intake. Mean %E from FSs is above the maximum intake of 10%E from FSs recommended by WHO (ISBN: 9789241549028) in the third and fourth quartiles (mean  $\pm$  SE; quartile  $1 = 5.3\%E \pm 0.1\%E$ ; quartile  $2 = 9.5\%E \pm 0.1\%E$ ; quartile  $3 = 13.1\%E \pm 0.1\%E$ ; quartile  $4 = 19.3\%E \pm 0.2\%E$ ).

### Food sources of sugars

In our sample, sugars, syrups, and confectionary (20.4%); fruit juices (17.6%); baked products (17.2%); and soft drinks (8.5%) were the main sources of FSs. Top food sources of NOSs were whole fruits (34.7%), milk (24.2%), vegetables (14.6%), and yogurt (4.3%). Top food sources of total sugars, FSs, and NOSs are presented in **Supplemental Table 3**.

## Correlations between the different types of sugars and subscores of the AHEI

Supplemental Table 4 shows correlation coefficients between the different types of sugars and AHEI total score and AHEI partial score and subscores. %E as FS from foods was inversely associated with AHEI total (r = -0.10, P = 0.001) and partial (r = -0.07, P = 0.03) scores. %E as FS from drinks was also inversely associated with AHEI total (r = -0.50, P < 0.0001) and partial (r = -0.23, P < 0.0001) scores and with most of the AHEI subscores. %E as NOS from foods was positively associated with AHEI total (r = 0.59, P < 0.0001) and partial (r = 0.44, P < 0.0001) scores and with nearly all AHEI subscores.

# Multivariable linear associations of sugar intake (%E as FS and NOS, from foods and drinks) with cardiometabolic risk factors

Table 3 shows results of the multivariable linear regression analyses assessing the associations between FS intake and cardiometabolic risk factors. In fully adjusted models, %E as FSs from foods was associated positively with LDL cholesterol. For %E as FSs from drinks, positive associations with fasting insulin and HOMA-IR were found in fully adjusted models. Although %E as FSs from drinks was significantly associated with TGs, HDL cholesterol, TC:HDL cholesterol, SBP, DBP, and MS z score in model 1 (which includes only sex, age, and administrative region), these associations were no longer significant in model 2 (all covariates included except for diet

quality) and model 3 (fully adjusted). %E as FSs from drinks was positively associated with CRP in model 1 and model 2, but the association was no longer significant in model 3, with further adjustment for diet quality.

**Table 4** shows results of the multivariable linear regression analyses assessing the associations between NOS intake and cardiometabolic risk factors. Although %E as NOSs from foods was inversely associated with fasting insulin, HOMA-IR, CRP, TGs, TC:HDL cholesterol, DBP and MS z score in Model 1, these associations were no longer significant in model 2 and model 3. For WC and BMI, the inverse association observed in model 1 and model 2 was no longer significant in model 3. %E as NOSs from drinks was associated only with fasting insulin (positive association observed in all models).

# Multivariable linear associations of mean daily portions of top 3 sources of FSs and NOSs with cardiometabolic risk factors

Main sources of FSs were 1) sugars, syrups, and confectionary; 2) juice; and 3) baked products. Only a few significant associations were observed in fully adjusted models. Mean daily portions of juice were inversely associated with HDL cholesterol (-0.04 mmol/L; 95% CI: -0.07, -0.01 mmol/L; P=0.01). Main sources of NOSs were 1) whole fruits, 2) milk, and 3) vegetables. As with main sources of FSs, only a few associations were observed in fully adjusted models. Mean daily intake of milk was positively associated with fasting insulin (3.26%; 95% CI: 0.10%, 6.53%; P=0.04). Mean daily intake of vegetables was inversely associated with fasting insulin (-2.01%; 95% CI: -3.67%, -0.34%; P=0.02) and HOMA-IR (-2.05%; 95% CI: -3.76%, -0.31%; P=0.02) (results not shown).

### **Discussion**

Results from multivariable linear regression models assessing the associations between sugar intakes and cardiometabolic risk factors showed that, after adjustment for confounding variables, FS intake, especially from drinks, was associated with some impaired cardiometabolic risk factors related to insulin homeostasis, whereas NOS intake from solid foods was no longer associated with a favorable cardiometabolic risk profile. This suggests that both the state of the sugars (either free or naturally occurring) and their physical form in foods (either liquid or solid; i.e., drinks or solid foods) partly influence the association between sugars and cardiometabolic risk factors.

The only metabolic variables that were significantly associated with FSs from drinks in fully adjusted models were fasting insulin and insulin resistance (HOMA-IR). It has been suggested that FS molecules in drinks, which are rapidly absorbed in the bloodstream, may affect directly glucose-insulin metabolism (36). Some authors came to the conclusion that deleterious effects of FSs (or added sugars) on health markers could be mostly driven by beverages (11, 37-39). Compared with liquid sources of FSs, solid-food sources require chewing and a greater amount of time to be consumed and may thus engage a more efficient energy compensation mechanism, meaning that subsequent intakes are better adjusted to reach a state of energy balance which might contribute to a better insulin homeostasis (40, 41). This may partly explain why %E as FS from solid foods was not associated with elevated insulin concentrations in the present study. Our results showing that NOS intake from drinks as well as milk intake are associated with a higher fasting

TABLE 1 Descriptive characteristics of the study sample of 1019 adults from the province of Quebec, Canada, according to quartiles of FS and NOS intake<sup>1</sup>

		Quartiles of F	Quartiles of FS intake, %E			Quartiles of NOS intake, %E	intake, %E	
	0.1	0.2	0.3	0.4	0.1	0.2	03	0.4
%Е	<7.8	7.8 to <11.3	11.3 to <15.2	≥15.2	<4.9	4.9 to <7.0	7.0 to <9.7	>9.7
Unweighted <i>n</i>	254	255	253	257	258	253	256	252
Sex								
Women	128 (50.0)	138 (53.9)	130 (50.8)	126 (49.2)	92 (35.5)	120 (47.1)	144 (55.9)	167 (65.3)
Men	128 (50.0)	118 (46.1)	126 (49.2)	131 (50.8)	166 (64.5)	135 (52.9)	113 (44.1)	89 (34.7)
Administrative region								
Capitale-Nationale/Chaudière-Appalaches	102 (39.7)	104 (40.7)	104 (40.5)	89 (34.8)	96 (37.0)	107 (42.1)	102 (39.6)	95 (37.1)
Estrie	30 (11.6)	25 (9.9)	23 (8.9)	22 (8.5)	29 (11.1)	25 (9.7)	22 (8.7)	24 (9.5)
Mauricie	19 (7.5)	22 (8.6)	28 (11.1)	23 (8.9)	30 (11.6)	27 (10.4)	20 (7.9)	16 (6.1)
Montreal	90 (35.0)	83 (32.5)	76 (29.6)	83 (32.5)	80 (31.0)	66 (25.9)	87 (33.7)	100 (39.0)
Saguenay-Lac-St-Jean	16 (6.1)	21 (8.3)	25 (9.8)	39 (15.3)	24 (9.3)	30 (12.0)	26 (10.1)	21 (8.2)
Educational level								
High school or no diploma	63 (24.5)	48 (18.8)	63 (24.7)	70 (27.1)	82 (31.6)	64 (24.9)	53 (20.6)	46 (17.9)
CEGEP2	73 (28.4)	86 (33.4)	84 (32.8)	75 (29.1)	95 (36.9)	76 (30.0)	82 (31.7)	64 (25.0)
University	121 (47.1)	123 (47.8)	109 (42.5)	113 (43.8)	81 (31.5)	115 (45.1)	122 (47.6)	146 (57.0)
Household income level (\$CAD)								
<30,000	36 (13.9)	34 (13.2)	43 (16.8)	51 (20.0)	52 (20.2)	39 (15.3)	32 (12.4)	41 (16.1)
$\geq$ 30,000 to <60,000	81 (31.7)	67 (26.0)	66 (25.9)	82 (31.9)	85 (32.9)	68 (26.8)	70 (27.1)	73 (28.6)
$\geq$ 60,000 to <90,000	64 (25.0)	51 (19.8)	48 (18.9)	38 (15.0)	42 (16.3)	56 (22.0)	54 (21.1)	50 (19.4)
> 000,000	75 (29.4)	105 (40.9)	99 (38.4)	85 (33.2)	79 (30.7)	92 (36.0)	101 (39.4)	92 (35.9)
Smoking								
Yes	39 (15.4)	27 (10.6)	29 (11.5)	31 (12.1)	59 (22.8)	31 (12.4)	20 (7.7)	17 (6.6)
No	111 (43.5)	137 (53.6)	148 (57.6)	159 (61.9)	115 (44.7)	130 (51.0)	156 (60.6)	154 (60.4)
Former smokers	105 (41.1)	92 (35.8)	79 (30.9)	67 (26.0)	84 (32.5)	93 (36.6)	81 (31.7)	84 (33.0)
Physical activity level <sup>3</sup>								
Low	49 (19.0)	40 (15.5)	55 (21.6)	55 (21.4)	56 (21.5)	59 (23.0)	44 (17.2)	40 (15.7)
Moderate	106 (41.4)	89 (34.7)	105 (40.9)	98 (38.0)	115 (44.4)	96 (37.7)	102 (39.6)	85 (33.4)
High	101 (39.6)	128 (49.8)	96 (37.5)	104 (40.6)	88 (34.1)	100 (39.4)	111 (43.2)	130 (50.9)
Plausibility of self-reported energy intakes								
Potential energy underreporters	59 (22.9)	42 (16.6)	29 (11.3)	25 (9.6)	38 (14.7)	44 (17.2)	29 (11.3)	44 (17.1)
Potential energy plausible reporters	138 (53.7)	133 (52.0)	139 (54.2)	141 (55.0)	145 (56.0)	126 (49.3)	143 (55.6)	138 (54.0)
Potential energy overreporters	60 (23.4)	80 (31.4)	88 (34.5)	91 (35.4)	76 (29.3)	86 (33.6)	85 (33.1)	74 (28.8)
Number of 24-h dietary recalls completed on weekend days								
0	49 (19.3)	45 (17.7)	37 (14.5)	44 (17.3)	36 (14.1)	35 (13.6)	44 (17.1)	61 (24.0)
	118 (46.2)	113 (44.0)	121 (47.3)	124 (48.4)	117 (45.2)	125 (49.2)	127 (49.4)	107 (42.0)
2	78 (30.6)	85 (33.1)	86 (33.4)	75 (29.1)	94 (36.4)	80 (31.4)	72 (28.0)	78 (30.4)
က	10 (4.0)	13 (5.1)	12 (4.8)	14 (5.3)	11 (4.3)	15 (5.8)	14 (5.5)	9 (3.6)
								(Continued)

FABLE 1 (Continued)

		Quartiles of F	Quartiles of FS intake, %E			Quartiles of NOS intake, %E	intake, %E	
	01	0.2	03	0.4	01	02	03	04
Medication usage <sup>4</sup>								
Antidiabetic	11 (4.4)	12 (4.9)	11 (4.3)	7 (2.8)	16 (6.3)	7 (2.8)	8 (3.2)	10 (4.0)
Antihypertensive	30 (11.7)	33 (13.0)	21 (8.3)	35 (13.6)	36 (14.0)	35 (13.7)	21 (8.3)	27 (10.6)
Lipid-lowering	23 (8.9)	33 (12.8)	27 (10.6)	20 (7.6)	28 (10.9)	32 (12.7)	26 (10.1)	16 (6.1)
Heart disease	12 (4.5)	4 (1.6)	7 (2.8)	7 (2.8)	9 (3.6)	10 (4.1)	8 (3.3)	2 (0.8)
Systemic hormonal contraceptives <sup>5</sup>	16 (6.1)	22 (8.7)	21 (8.3)	20 (7.9)	18 (7.0)	17 (6.6)	31 (12.1)	14 (5.3)
No	199 (77.8)	183 (71.4)	195 (76.0)	191 (74.1)	190 (73.5)	185 (72.7)	188 (73.2)	204 (80.0)

CEGEP is a pre-university and technical college institution particular to the province of Quebec educational system, which is considered higher than high school and lower than university ntake; \$CAD, Canadian dollars.

Values are weighted n (%), which might have caused the sample size to be unequal to 1019. CEGEP Colle'ge d'Enseignement Ge'ne'ral et Professionnel; FS, free sugar; NOS, naturally occurring sugar; O, quartile; %E, percentage of daily energy

categorical 2005 International Physical Activity Questionnaire (IPAQ) <sup>4</sup>Medication usage that may affect relevant outcomes studied <sup>3</sup> Physical activity level is based on the

insulin concentration are also consistent with this potential explanation.

In minimally adjusted models, FSs and NOSs displayed opposite associations with the cardiometabolic risk factors studied. However, results from moderately and fully adjusted models suggest that most of the associations observed between intakes of FSs or NOSs and cardiometabolic risk factors were largely attenuated when including sociodemographic characteristics, markers of adiposity, smoking, physical activity, plausibility of self-reported energy intake, the number of recalls completed on weekend days (model 2), and diet quality (model 3). This was especially true for the intake of NOSs, for which none of the beneficial associations observed with cardiometabolic variables in minimally adjusted models remained significant in fully adjusted models. Our results emphasize that the consumption of sugars might be a marker of a constellation of sociodemographic and lifestyle variables and diet quality known to be associated with cardiometabolic risk (26, 27, 42-47), which, in turn, may greatly influence the association between sugars and health. Indeed, in many studies, fruit intake (which is the main source of NOS in our sample) has been associated with higher socioeconomic status, educational levels, and physical activity, and was higher among nonsmokers (42, 43, 48, 49). In contrast, a higher consumption of SSBs has been frequently associated with lower educational and income levels, inactivity, and smoking (50-52). In a Portuguese sample, NOS and FS intakes showed similar associations with sociodemographic variables than those mentioned above for fruit and SSB intakes, respectively (53).

We cannot exclude that other factors currently unknown or whose scientific interest is growing may also have an impact on the diet-disease and the sugar-disease associations. For example, the gut microbiota, which is itself impacted by the composition of the diet, has been shown to be associated with inflammatory and metabolic disorders, cardiovascular diseases, obesity, and the risk of type 2 diabetes (54).

Our results support the idea that sugar intake is part of a complex dietary scheme. In that context, it becomes difficult to isolate its specific contribution to cardiometabolic risk from that of the overall diet quality and its determinants. Accordingly, some authors have argued that it is preferable to study the link between diet and disease with the perspective of overall diet quality instead of focusing only on 1 single nutrient such as sugar (13, 55). Overall, our results also suggest that sugar intakes are not strongly associated with cardiometabolic risk factors when diet quality and other biological, sociodemographic, and lifestyle factors are taken into account, as suggested by other authors (10, 56).

The strengths of our study were that participants were recruited with random-digit dialing in order to be representative in terms of age and sex of the adult French-speaking population of the province of Quebec and that they completed 3 selfadministered, web-based, validated 24-h dietary recalls on randomly allocated days. Also, FSs and NOSs were rigorously differentiated using a systematic algorithm (22).

Our study also has some limitations. Due to its crosssectional design, causality cannot be established and caution must be used in the interpretation of the results. Results could be different in an older sample or in a sample defined by different sociodemographic characteristics. The fact that our sample was slightly more educated than the general Quebec population might have influenced the results [in our sample, 45% of the participants hold a university degree vs. 33% in the general population of the province of Quebec (57)].

TABLE 2 Characteristics and key nutrient intakes of the study sample of 1019 adults from the province of Quebec, Canada, according to quartiles of FS and NOS intake

		Quartiles of F	Quartiles of FS intake, %E			Quartiles of NOS intake, %E	S intake, %E	
	01 (n = 254)	$\Omega 2 (n = 255)$	03 (n = 253)	04 (n = 257)	01 (n = 258)	02 (n = 253)	03 (n = 256)	04 ( $n = 252$ )
Age, y	44.7 ± 0.8	44.0 ± 0.7	43.7 ± 0.8	41.4 ± 0.8	41.4 ± 0.7	43.3 ± 0.7	43.5 ± 0.7	45.7 ± 0.7
WC, cm	$91.9 \pm 1.0$	$92.0 \pm 1.0$	$92.1 \pm 1.0$	93.1 ± 1.1	$95.9 \pm 1.0$	94.2 ± 1.1	$90.3 \pm 1.0$	$88.7 \pm 0.9$
BMI, kg/m²	$27.5 \pm 0.4$	$27.4 \pm 0.4$	$27.4 \pm 0.4$	$27.6 \pm 0.4$	$28.4 \pm 0.4$	$28.1 \pm 0.4$	26.9 ± 0.4	$26.6 \pm 0.3$
Fasting glucose, <sup>2</sup> mmol/L	$5.2 \pm 0.0$	$5.3 \pm 0.1$	$5.1 \pm 0.0$	$5.2 \pm 0.0$	$5.3 \pm 0.0$	$5.2 \pm 0.1$	$5.1 \pm 0.0$	$5.2 \pm 0.1$
Fasting insulin, <sup>2</sup> pmol/L	$91.1 \pm 2.9$	$93.0 \pm 3.1$	$105.3 \pm 5.0$	$106.2 \pm 5.2$	$109.0 \pm 4.8$	$103.7 \pm 4.2$	89.8 ± 4.1	$93.2 \pm 3.5$
HOMA-IR	$3.6 \pm 0.2$	$3.8 \pm 0.2$	$4.1 \pm 0.2$	$4.2 \pm 0.2$	$4.4 \pm 0.2$	$4.2 \pm 0.2$	$3.5 \pm 0.2$	$3.7 \pm 0.2$
CRP,2 mg/L	$2.1 \pm 0.2$	$2.1 \pm 0.1$	$2.3 \pm 0.1$	$2.3 \pm 0.2$	$2.3 \pm 0.1$	$2.4 \pm 0.2$	$2.0 \pm 0.1$	$2.2 \pm 0.2$
TGs, <sup>2</sup> mmol/L	$1.3 \pm 0.1$	$1.3 \pm 0.0$	1.4 ± 0.1	$1.4 \pm 0.0$	$1.6 \pm 0.1$	$1.3 \pm 0.0$	$1.2 \pm 0.0$	$1.2 \pm 0.0$
LDL-C, <sup>2</sup> mmol/L	2.8 ± 0.1	2.8 ± 0.1	$2.9 \pm 0.1$	$2.8 \pm 0.1$	$2.9 \pm 0.1$	$2.7 \pm 0.1$	$2.8 \pm 0.1$	$2.9 \pm 0.1$
HDL-C, <sup>2</sup> mmol/L	$1.5 \pm 0.0$	$1.5 \pm 0.0$	$1.4 \pm 0.0$	$1.4 \pm 0.0$	$1.4 \pm 0.0$	$1.4 \pm 0.0$	$1.4 \pm 0.0$	$1.5 \pm 0.0$
TC:HDL-C, <sup>2</sup> mmol/L	3.6 ± 0.1	3.6 ± 0.1	$3.7 \pm 0.1$	3.8 ± 0.1	$4.0 \pm 0.1$	$3.6 \pm 0.1$	$3.5 \pm 0.1$	$3.5 \pm 0.1$
SBP, mm Hg	$117.3 \pm 0.9$	$116.4 \pm 0.9$	$118.3 \pm 0.8$	$119.2 \pm 0.9$	$120.0 \pm 0.8$	$118.4 \pm 0.9$	$116.0 \pm 0.8$	$116.7 \pm 0.9$
DBP, mm Hg	72.6 ± 0.6	$72.6 \pm 0.6$	73.9 ± 0.6	$75.0 \pm 0.6$	$74.8 \pm 0.7$	$73.9 \pm 0.6$	$72.6 \pm 0.6$	$72.8 \pm 0.6$
MS z score <sup>3</sup>	$-0.1 \pm 0.2$	$0.0 \pm 0.2$	$0.0 \pm 0.2$	$0.3 \pm 0.2$	$2.0 \pm 0.0$	$12.5 \pm 0.0$	$-0.4 \pm 0.2$	$-0.5 \pm 0.2$
Daily energy intake, 4 kcal	2228 ± 42	$2341 \pm 42$	2469 ± 44	2602 ± 52	2542 ± 48	2484 ± 49	2416 ± 45	2199 ± 39
%E as total sugars <sup>4</sup>	$13.8 \pm 0.3$	$17.4 \pm 0.2$	$20.3 \pm 0.2$	$25.8 \pm 0.3$	$16.5 \pm 0.4$	$18.6 \pm 0.3$	$20.1 \pm 0.3$	$22.1 \pm 0.4$
%E as FS	$5.3 \pm 0.1$	$9.5 \pm 0.1$	$13.1 \pm 0.1$	$19.3 \pm 0.2$	$13.0 \pm 0.4$	$12.7 \pm 0.3$	$11.8 \pm 0.3$	$9.7 \pm 0.3$
%E FS, drinks	0.9 ± 0.1	$2.6 \pm 0.1$	4.4 ± 0.2	$8.7 \pm 0.3$	$5.6 \pm 0.3$	$4.6 \pm 0.3$	$3.7 \pm 0.2$	$2.8 \pm 0.2$
%E FS, solid foods	$4.3 \pm 0.1$	6.8 ± 0.1	$8.7 \pm 0.2$	$10.6 \pm 0.2$	$7.3 \pm 0.2$	$8.1 \pm 0.2$	$8.1 \pm 0.2$	$6.9 \pm 0.2$
%E as NOS	8.6 ± 0.3	$8.0 \pm 0.2$	$7.2 \pm 0.2$	$6.6 \pm 0.2$	$3.6 \pm 0.1$	$6.0 \pm 0.0$	$8.3 \pm 0.0$	$12.5 \pm 0.2$
%E NOS, drinks	1.8 ± 0.1	$2.0 \pm 0.1$	$2.0 \pm 0.1$	1.8 ± 0.1	$0.7 \pm 0.0$	$1.4 \pm 0.1$	$2.4 \pm 0.1$	$3.2 \pm 0.2$
%E NOS, solid foods	$6.7 \pm 0.3$	$6.0 \pm 0.2$	$5.2 \pm 0.2$	4.8 ± 0.2	$2.9 \pm 0.1$	$4.6 \pm 0.1$	$6.0 \pm 0.1$	$9.3 \pm 0.3$
AHEI score <sup>4,5</sup>	$59.7 \pm 0.7$	$56.4 \pm 0.7$	$51.8 \pm 0.7$	$47.2 \pm 0.6$	$46.0 \pm 0.6$	$51.5 \pm 0.6$	$56.0 \pm 0.7$	$61.5 \pm 0.6$
HEI partial score <sup>4.6</sup>	$47.1 \pm 0.6$	$46.3 \pm 0.5$	$44.7 \pm 0.5$	$41.9 \pm 0.5$	$40.1 \pm 0.5$	$43.9 \pm 0.5$	$46.9 \pm 0.5$	$49.1 \pm 0.5$

'Values are means ± SEs. n is unweighted. n values are listed for each variable: age (n = 1019); WC and BMI (n = 1017); fasting glucose, fasting insulin, and HOMA-IR (n = 1004); CRP (n = 947); TGs, LDL-C, and TC:HDL (n = 1009); SBP and DBP (n = 1018); MS z score (n = 1001); energy and sugar intakes and AHEI (n = 1019). AHEI, Alternative Healthy Eating Index-2010; CRP C-reactive protein; DBP diastolic blood pressure; FS, free sugar; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MS z Score, continuous metabolic syndrome risk score; NOS, naturally occurring sugar; Q, quartile; SBP systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; %E, percentage of daily energy.

<sup>&</sup>lt;sup>t</sup>For each participant, energy intake, sugar intake, AHEI score, and AHEI partial score are based on the average of all available dietary recalls. <sup>3</sup>A higher MS z score indicates a stronger presence of the metabolic syndrome.

A higher AHEI score (maximum: 110) indicates a diet that is associated with a significant reduction in chronic disease risk and all-cause mortality. AHEI score (maximum: 90): whole fruits and sugar-sweetened beverages and fruit juice subscores were removed from the AHEI score.

**TABLE 3** Multivariable linear associations of %E as FS from solid foods and drinks with cardiometabolic risk factors in an adult sample (n = 1019) from the province of Quebec, Canada<sup>1</sup>

	Model 1 <sup>2</sup>		Model 2 <sup>3</sup>		Model 3 <sup>4</sup>	
	β (95% CI)	P	β (95% CI)	Р	β (95% CI)	Р
WC, cm						
%E FS, solid foods	-0.064 (-0.324, 0.197)	0.63	0.026 (-0.203, 0.255)	0.83	-0.042 (-0.268, 0.183)	0.71
%E FS, drinks	0.219 (-0.004, 0.441)	0.05	0.154 (-0.041, 0.350)	0.12	0.032 (-0.163, 0.228)	0.75
BMI, kg/m <sup>2</sup>						
%E FS, solid foods	-0.015 (-0.126, 0.097)	0.80	0.015 (-0.082, 0.113)	0.76	-0.008 (-0.105, 0.090)	0.88
%E FS, drinks	0.043 (-0.049, 0.135)	0.36	0.015 (-0.064, 0.095)	0.71	-0.027 (-0.106, 0.051)	0.50
Fasting glucose, 5,6 %						
%E FS, solid foods	-0.08 (-0.34, 0.19)	0.57	-0.04 (-0.32, 0.25)	0.81	-0.03 (-0.31, 0.26)	0.86
%E FS, drinks	-0.03 (-0.22, 0.16)	0.78	-0.07 (-0.26, 0.12)	0.46	-0.05 (-0.25, 0.14)	0.58
Fasting insulin, <sup>5,6</sup> %						
%E FS, solid foods	-0.53 (-1.52, 0.48)	0.30	-0.38 (-1.38, 0.62)	0.45	-0.42 (-1.41, 0.59)	0.41
%E FS, drinks	1.39 (0.58, 2.21)	0.0008	1.08 (0.33, 1.83)	0.005	1.06 (0.30, 1.84)	0.006
HOMA-IR,6 %						
%E FS, solid foods	-0.60 (-1.58, 0.39)	0.23	-0.42 (-1.34, 0.51)	0.37	-0.44 (-1.37, 0.49)	0.35
%E FS, drinks	1.36 (0.50, 2.23)	0.002	1.01 (0.20, 1.82)	0.01	1.01 (0.19, 1.84)	0.02
CRP, <sup>5,6</sup> %						
%E FS, solid foods	-0.51 (-2.31, 1.32)	0.58	0.09 (-1.50, 1.70)	0.92	-0.04 (-1.65, 1.60)	0.96
%E FS, drinks	2.49 (0.77, 4.25)	0.005	1.59 (0.14, 3.05)	0.03	1.42 (-0.05, 2.90)	0.06
TGs, <sup>5,6</sup> %						
%E FS, solid foods	-0.10 (-1.00, 0.82)	0.83	0.02 (-0.85, 0.89)	0.97	-0.06 (-0.94, 0.83)	0.89
%E FS, drinks	0.87 (0.12, 1.63)	0.02	0.63 (-0.13, 1.40)	0.10	0.50 (-0.26, 1.27)	0.20
LDL-C,5 mmol/L						
%E FS, solid foods	0.0144 (-0.0004, 0.0292)	0.06	0.0176 (0.0025, 0.0327)	0.02	0.0174 (0.0022, 0.0327)	0.02
%E FS, drinks	0.0033 (-0.0093, 0.0160)	0.61	0.0027 (-0.0102, 0.0156)	0.68	0.0022 (-0.0111, 0.0154)	0.75
HDL-C, <sup>5</sup> mmol/L						
%E FS, solid foods	-0.0048 (-0.0120, 0.0024)	0.19	-0.0055 (-0.0127, 0.0016)	0.13	-0.0053 (-0.0125, 0.0020)	0.15
%E FS, drinks	-0.0080 (-0.0141, -0.0019)	0.01	-0.0054 (-0.0113, 0.0005)	0.07	-0.0051 (-0.0110, 0.0008)	0.09
TC:HDL-C,5 mmol/L						
%E FS, solid foods	0.012 (-0.013, 0.034)	0.35	0.016 (-0.008, 0.040)	0.19	0.014 (-0.011, 0.038)	0.26
%E FS, drinks	0.023 (0.004, 0.042)	0.02	0.018 (-0.002, 0.038)	0.07	0.014 (-0.005, 0.034)	0.15
SBP, mm Hg						
%E FS, solid foods	0.14 (-0.09, 0.36)	0.24	0.08 (-0.14, 0.30)	0.48	0.08 (-0.14, 0.30)	0.47
%E FS, drinks	0.23 (0.03, 0.43)	0.02	0.11 (-0.08, 0.31)	0.25	0.12 (-0.08, 0.32)	0.23
DBP, mm Hg						
%E FS, solid foods	0.07 (-0.11, 0.24)	0.44	0.02 (-0.14, 0.19)	0.77	0.01 (-0.15, 0.18)	0.88
%E FS, drinks	0.21 (0.06, 0.36)	0.01	0.13 (-0.01, 0.28)	0.08	0.11 (-0.04, 0.26)	0.14
MS z score <sup>7</sup>						
%E FS, solid foods	0.014 (-0.044 , 0.071)	0.65	0.014 (-0.033, 0.062)	0.56	0.012 (-0.037, 0.061)	0.63
%E FS, drinks	0.053 (0.010 , 0.097)	0.02	0.028 (-0.004, 0.060)	0.09	0.024 (-0.010, 0.057)	0.17

 $^1$ Values are estimates of the change in the outcome (95% CI) for every unit of %E FS from solid foods or drinks. Individuals taking medication that could affect the studied outcome were removed from analyses. See the Methods section for details. n is listed for each variable: WC and BMI (n = 1017); fasting glucose, fasting insulin, and HOMA-IR (n = 963); CRP (n = 868); TGs, LDL-C, HDL-C, and TC:HDL-C (n = 911); SBP and DBP (n = 902); and MS z score (n = 816). AHEI, Alternative Healthy Eating Index–2010; CRP, C-reactive protein; DBP, diastolic blood pressure; FS, free sugar; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MS z score, continuous metabolic syndrome risk score; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; %E, percentage of daily energy.

However, it has to be emphasized that the educational level was a covariate in regression models tested. We also have to keep in mind that reverse causation is possible. As such, some participants at risk of chronic diseases may have improved their eating habits, which may possibly influence or hide cross-sectional associations. Also, as in any other observational study examining the association between diet and health risk factors,

residual confounding due to factors and variables not measured in this study is possible. Furthermore, despite using repeated 24-h dietary recalls, within-person random error may have biased associations observed. Finally, even if it was suggested that the web-based nature of the 24-h dietary recall tool may reduce the risk of social desirability bias compared with inperson completion (18), it is possible that underreporting of

<sup>&</sup>lt;sup>2</sup>Model 1 is adjusted for sex, age, and administrative region.

<sup>&</sup>lt;sup>3</sup>Model 2 is adjusted for model 1 + WC (except when WC or BMI is the studied outcome), educational and household income levels, smoking, physical activity [based on the 2005 International Physical Activity Questionnaire (IPAQ) categorical scoring rules], mean daily energy intake, plausibility of self-reported energy intake, and the number of 24-h dietary recalls completed on weekend days.

<sup>4</sup>Model 3 is adjusted for model 2 + AHEI partial score (AHEI score from which whole fruits and sugar-sweetened beverages and fruit juice subscores were removed).

<sup>&</sup>lt;sup>5</sup>Blood tests were performed on serum.

 $<sup>^6</sup>$ Log-transformed data;  $\beta$  values (95% CI) are expressed as % change upon back-transformation calculated as 100 imes exponential (logB) - 100.

 $<sup>^{7}</sup>$ A higher MS z score indicates a stronger presence of the metabolic syndrome.

TABLE 4 Multivariable linear associations of %E as NOS from solid foods and drinks with cardiometabolic risk factors and in an adult sample (n = 1019) from the province of Quebec, Canada<sup>1</sup>

	Model 1 <sup>2</sup>		Model 2 <sup>3</sup>		Model 3 <sup>4</sup>	
	β (95%CI)	P	β (95%CI)	Р	β (95%CI)	Р
WC, cm						
%E NOS, solid foods	-0.63 (-0.96, -0.29)	0.0002	-0.43 (-0.78, -0.08)	0.01	-0.22 (-0.50, 0.06)	0.13
%E NOS, drinks	0.04 (-0.46, 0.54)	0.88	0.20 (-0.25, 0.64)	0.38	0.16 (-0.27, 0.59)	0.47
BMI, kg/m <sup>2</sup>						
%E NOS, solid foods	-0.226 (-0.369, -0.083)	0.002	-0.152 (-0.298, -0.006)	0.04	-0.080 (-0.205, 0.045)	0.21
%E NOS, drinks	0.037 (-0.162, 0.236)	0.71	0.088 (-0.083, 0.259)	0.31	0.076 (-0.090, 0.242)	0.37
Fasting glucose, 5,6 %						
%E NOS, solid foods	-0.061 (-0.268, 0.146)	0.56	0.057 (-0.128, 0.243)	0.55	0.026 (-0.182, 0.235)	0.81
%E NOS, drinks	-0.371 (-0.743, 0.003)	0.05	-0.360 (-0.742, 0.024)	0.07	-0.355 (-0.737, 0.029)	0.07
Fasting insulin, 5,6 %						
%E NOS, solid foods	-1.46 (-2.70, -0.20)	0.02	-0.67 (-1.70, 0.36)	0.20	-0.63 (-1.72, 0.49)	0.27
%E NOS, drinks	1.78 (0.18, 3.41)	0.03	1.86 (0.36, 3.38)	0.02	1.84 (0.34, 3.36)	0.02
HOMA-IR, <sup>6</sup> %						
%E NOS, solid foods	-1.52 (-2.89, -0.13)	0.03	-0.62 (-1.73, 0.50)	0.28	-0.60 (-1.81, 0.62)	0.33
%E NOS, drinks	1.40 (-0.31, 3.15)	0.11	1.49 (-0.13, 3.14)	0.07	1.48 (-0.14, 3.13)	0.07
CRP, <sup>5,6</sup> %						
%E NOS, solid foods	-3.09 (-4.77, -1.39)	0.0004	-1.43 (-2.94, 0.10)	0.07	-1.14 (-2.76, 0.52)	0.18
%E NOS, drinks	-0.10 (-3.51, 3.42)	0.95	1.42 (-1.62, 4.56)	0.36	1.34 (-1.68, 4.44)	0.39
TGs, <sup>5,6</sup> %						
%E NOS, solid foods	-1.91 (-3.71, -0.08)	0.04	-1.14 (-2.71, 0.44)	0.16	-0.95 (-2.56, 0.68)	0.25
%E NOS, drinks	-0.66 (-2.33, 1.04)	0.44	-0.33 (-1.91, 1.28)	0.69	-0.37 (-1.95, 1.23)	0.65
LDL-C <sup>5</sup> , mmol/L						
%E NOS, solid foods	-0.010 (-0.025, 0.005)	0.17	-0.004 (-0.018, 0.011)	0.63	-0.003 (-0.017, 0.012)	0.72
%E NOS, drinks	-0.009 (-0.037, 0.020)	0.55	-0.006 (-0.036, 0.023)	0.68	-0.006 (-0.036, 0.023)	0.67
HDL-C,5 mmol/L						
%E NOS, solid foods	0.0083 (-0.0028, 0.0193)	0.14	0.0011 (-0.0079, 0.0101)	0.81	0.0003 (-0.0089, 0.0095)	0.95
%E NOS, drinks	-0.0101 (-0.0229, 0.0028)	0.12	-0.0107 (-0.0225, 0.0011)	0.08	-0.0105 (-0.0224, 0.0013)	0.08
TC:HDL-C,5 mmol/L						
%E NOS, solid foods	-0.036 (-0.069, -0.003)	0.03	-0.016 (-0.044, 0.012)	0.25	-0.010 (-0.036, 0.016)	0.46
%E NOS, drinks	-0.013 (-0.056, 0.030)	0.55	-0.008 (-0.050, 0.033)	0.69	-0.010 (-0.051, 0.032)	0.65
SBP, mm Hg						
%E NOS, solid foods	-0.12 (-0.38, 0.13)	0.35	0.09 (-0.17, 0.36)	0.50	0.10 (-0.19, 0.38)	0.50
%E NOS, drinks	0.18 (-0.22, 0.57)	0.39	0.21 (-0.18, 0.60)	0.29	0.21 (-0.18, 0.61)	0.29
DBP, mm Hg						
%E NOS, solid foods	-0.25 (-0.42, -0.09)	0.003	-0.11 (-0.27, 0.06)	0.21	-0.07 (-0.25, 0.12)	0.47
%E NOS, drinks	0.21 (-0.07, 0.50)	0.13	0.22 (-0.04, 0.48)	0.10	0.21 (-0.05, 0.46)	0.12
MS z score <sup>7</sup>						
%E NOS, solid foods	-0.106 (-0.189, -0.022)	0.01	-0.021 (-0.071, 0.029)	0.40	-0.014 (-0.064, 0.036)	0.59
%E NOS, drinks	-0.034 (-0.133, 0.064)	0.49	-0.005 (-0.074, 0.065)	0.89	-0.007 (-0.077, 0.063)	0.85

<sup>1</sup> Values are estimates of the change in the outcome (95% CI) for every unit of %E NOS from solid foods or drinks. Individuals taking medication that could affect the studied outcome were removed from analyses. See the Methods section for details. n is listed for each variable: WC and BMI (n = 1017); fasting glucose, fasting insulin, and HOMA-IR (n = 963); CRP (n = 868); TGs, LDL-C, HDL-C, and TC:HDL-C (n = 911); SBP and DBP (n = 902); and MS z score (n = 816). AHEI, Alternative Healthy Eating Index–2010; CRP, C-reactive protein; DBP, diastolic blood pressure; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; MS z score, continuous metabolic syndrome risk score; NOS; naturally occurring sugar; SBP, systolic blood pressure; TC, total cholesterol; TG, triglyceride; WC, waist circumference; %E, percentage of daily energy.

FS intake is more prevalent in people suffering from chronic diseases typically associated with obesity, which may also have biased the results. Plausibility of self-reported energy intakes was, however, added as a covariate in multivariable linear regression models to mitigate this issue.

In conclusion, in addition to being the first study on the topic in Canada, to the best of our knowledge, this study is the first to

assess how FSs and NOSs from solid- and liquid-food sources are related to multiple cardiometabolic risk factors, and how sociodemographic characteristics, lifestyle variables, and diet quality affect these associations in an adult sample.

Our results revealed that many of the associations between sugar intake and cardiometabolic variables were attenuated or were no longer significant when considering overall diet

<sup>&</sup>lt;sup>2</sup>Model 1 is adjusted for sex, age, and administrative region.

<sup>3</sup> Model 2 is adjusted for model 1 + WC (except when WC or BMI is the studied outcome), educational and household income levels, smoking, physical activity (based on the 2005 International Physical Activity Questionnaire (IPAQ) categorical scoring rules], mean daily energy intake, plausibility of self-reported energy intake, and the number of 24-h dietary recalls completed on weekend days.

<sup>&</sup>lt;sup>4</sup>Model 3 is adjusted for model 2 + AHEI partial score (AHEI score from which whole fruits and sugar-sweetened beverages and fruit juice subscores were removed).

<sup>&</sup>lt;sup>5</sup>Blood tests were performed on serum.

<sup>&</sup>lt;sup>6</sup>Log-transformed data; β values (95% CI) are expressed as % change upon back-transformation calculated as 100 × exponential (log*B*) – 100.

<sup>&</sup>lt;sup>7</sup>A higher MS z score indicates a stronger presence of the metabolic syndrome.

quality and other relevant covariates, such as sociodemographic variables. This was true for both the unfavorable associations implicating FSs from drinks and the favorable ones implicating NOSs from solid foods. Other authors also concluded that associations between sugar intakes and cardiometabolic health are either inconsistent, not systematically observed, small, or absent (5, 39, 55, 58-62). In future studies, it would be interesting to study the impact of free and naturally occurring sugar intakes from solid- and liquid-food sources on cardiometabolic health outcomes in a controlled interventional context to be able to draw causal relations. Finally, and more importantly, our results, supported by conclusions from other authors (13, 55), suggest that caution must be taken not to overestimate the sole impact of sugar intake on health outcomes without considering other health determinants (44) and the overall quality of eating habits (63).

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