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Added sugar intake and its forms and sources in relation to risk of non-alcoholic fatty liver disease: results from the Tianjin Chronic Low-grade Systemic Inflammation and Health cohort study

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Abstract

It has been suggested that added sugar intake is associated with non-alcoholic fatty liver disease (NAFLD). However, previous studies only focused on sugar-sweetened beverages; the evidence for associations with total added sugars and their sources is scarce. This study aimed to examine the associations of total added sugars, their physical forms (liquid *v.* solid) and food sources with risk of NAFLD among adults in Tianjin, China. We used data from 15 538 participants, free of NAFLD, other liver diseases, CVD, cancer or diabetes at baseline (2013–2018 years). Added sugar intake was estimated from a validated 100-item FFQ. NAFLD was diagnosed by ultrasonography after exclusion of other causes of liver diseases. Multivariable Cox proportional hazards models were fitted to calculate hazard ratios (HR) and corresponding 95 % CI for NAFLD risk with added sugar intake. During a median follow-up of 4·2 years, 3476 incident NAFLD cases were documented. After adjusting for age, sex, BMI and its change from baseline to follow-up, lifestyle factors, personal and family medical history and overall diet quality, the multivariable HR of NAFLD risk were 1·18 (95 % CI 1·06, 1·32) for total added sugars, 1·20 (95 % CI 1·08, 1·33) for liquid added sugars and 0·96 (95 % CI 0·86, 1·07) for solid added sugars when comparing the highest quartiles of intake with the lowest quartiles of intake. In this prospective cohort of Chinese adults, higher intakes of total added sugars and liquid added sugars, but not solid added sugars, were associated with a higher risk of NAFLD.

Key words: **Added sugar: Non-alcoholic fatty liver disease: Epidemiology: Cohort study: China**

Non-alcoholic fatty liver disease (NAFLD) is emerging as the leading chronic liver disease worldwide with an estimated prevalence of 25–30 % of adults in many countries[1,2]. The prevalence of NAFLD was estimated to be 29·8 % in China[3]. NAFLD has traditionally been viewed as a liver disease with a high risk of developing liver-related disorders such as liver fibrosis, cirrhosis and hepatocellular carcinoma. However, convincing evidence indicates that NAFLD is a multisystem disease[4], related to increased risks of CVD, type 2 diabetes and all-cause mortality[4]. Currently, there are no approved pharmacotherapies for the management of NAFLD[5]. Thus, the identification of potentially modifiable risk factors (e.g. diet) for NAFLD

Abbreviations: HR, hazard ratio; NAFLD, non-alcoholic fatty liver disease.

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becomes highly relevant for prevention and management of this condition.

Recently, the influence of sugar intake on human health has attracted growing scientific and media attention[6]. Sugars naturally exist in foods in low amounts, such as fruit and vegetables, and are usually consumed with dietary fibre and other healthy nutrients. Therefore, these types of sugars are not a major concern because they are within the food matrix. However, concerns arise with added sugars, which are defined as all sugars used in prepared or processed foods or added at the table[7]. While added sugars have been consistently related to the detrimental effects on liver health[8,9], the previous studies primarily focused on NAFLD and sugar-sweetened beverages[10–13], rather than added sugars *per se*. The study of added sugar intake and NAFLD may help to understand the role of added sugars in contributing to the epidemic of NAFLD. In addition, different food sources of added sugars may vary in composition, energy density and absorption. Thus, it is important to distinguish between different sources of added sugars when studying their associations with NAFLD. Further, considering the sources of added sugars is meaningful to inform dietary guidance. On the other hand, emerging evidence has suggested that liquid and solid sugars are metabolised differently, and thus they might have a distinct effect on the risk of NAFLD[14]. However, to our knowledge, evidence on the association between added sugar intake *per se* and the risk of NAFLD is lacking.

To address this research gap, we prospectively investigated the associations of added sugars, their physical forms (liquid and solid) and food sources with the risk of NAFLD in a general Chinese adult population.

Methods

Study population

The Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) cohort study is a prospective dynamic cohort study established in Tianjin, China. Details of the study design have been published previously[15]. In brief, participants (aged ≥ 18 years) were randomly selected since May 2013 from the general population residing in Tianjin. All participants were invited to undergo in-person examinations and a detailed interview on diet and lifestyle factors at baseline. Follow-up information was obtained from annual health examinations and periodical re-interviews. This cohort study was approved by the Institutional Review Board of Tianjin Medical University (approval number: TMUhMEC 201430), and written informed consent was obtained from all participants prior to participation. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients.

The current study included participants who were recruited from May 2013 to December 2018 (baseline) and followed up until 31 December 2019. Of 28 445 individuals eligible for participation, we excluded participants with CVD, cancer or diabetes at baseline. Participants were defined as having diabetes if they had a fasting blood glucose ≥ 7·0 mmol/l or self-reported history of diabetes. In addition, we excluded those with alcoholic fatty liver disease, NAFLD or other liver diseases at baseline. Ultimately, a total of 15 538 participants were included in this analysis (Fig. 1).

Ascertainment of outcome

At both baseline and subsequent follow-up examinations, hepatic steatosis was tested by abdominal ultrasonography, which was carried out by experienced sonographers using a TOSHIBA SSA-660A ultrasound machine (Toshiba), with a 2–5 MHz curved array probe. Fatty liver disease was defined as having two or more of the following abnormal findings of liver ultrasonography: 'bright liver', vascular blurring and deep attenuation of the ultrasound signal[16]. NAFLD was defined as the presence of fatty liver disease without significant alcohol consumption (≥ 210 g/week for men and ≥ 140 g/week for women) and/or any other causes for secondary hepatic fat accumulation[17]. The outcome was a first-time NAFLD that occurred during the follow-up period, as described previously[18].

Assessments of dietary intake and added sugar intake

At the baseline visit, dietary intake was collected using a validated 100-item self-administered FFQ[12]. Participants were inquired how often, on average, they consumed a standard portion of foods in the previous month. There were seven response categories ranged from 'never eating' to 'more than two times per day' for foods and eight choices ranged from 'never drinking' to 'more than four times per day' for beverages. Daily intakes of total energy and nutrients were calculated based on the 2009 Chinese Food Composition Table. Since added sugar value was not available in the Chinese Food Composition Table database, estimates of the added sugar content of each sugary food and beverage in the FFQ were derived from the US Department of Agriculture nutrient database[19]. The reproducibility and validity of the FFQ have been described in detail elsewhere[20]. Briefly, Spearman rank correlation coefficients between the two FFQ collected approximately 3 months apart were 0·68 for energy intake and 0·62–0·79 for added sugars, fruits, vegetables and beverages. Spearman's rank correlations between the FFQ and four non-consecutive 4-d weighed dietary records, also known as the FFQ validity correlation coefficients, were 0·49 for energy intake and 0·35–0·54 for nutrients. We created a healthy diet score by combining five common elements of healthy dietary patterns, which included vegetables, fruits, fish, unprocessed red meat and processed meat[12,21]. The score ranged from 0 to 5, with a higher score indicating a healthier diet. To characterise overall dietary patterns, we employed exploratory factor analysis to derive three main dietary patterns: sugar rich dietary pattern, vegetable rich dietary pattern and animal food dietary pattern, as described in our recent study[22].

In the present study, exposure variables included total added sugars, liquid added sugar, solid added sugar and added sugars from different foods. We classified sugary foods and beverages on the FFQ into seven subgroups: bread, yogurt, desserts (including cakes, cookies, pastries, ice cream and other Chinese desserts), candies/jam, soft drinks, fruit/vegetable drinks and coffee. The relative contribution of each food source to added sugar intake is presented in online Supplementary Fig. 1.

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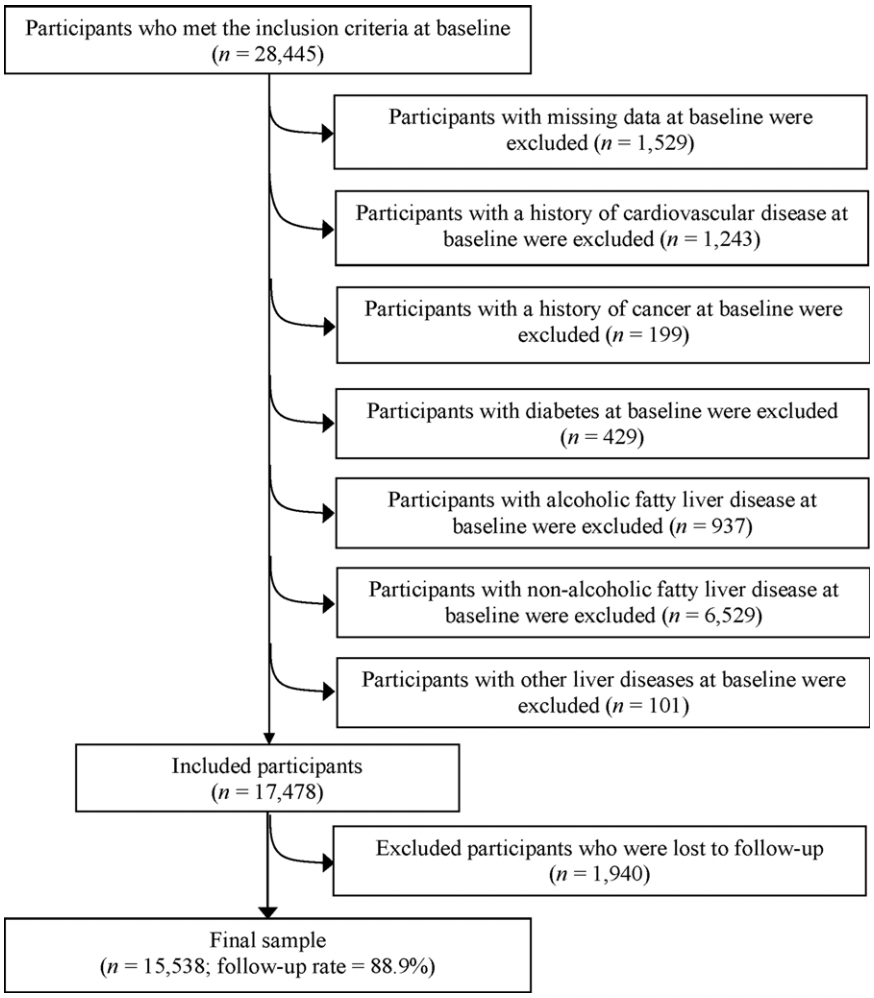

Fig. 1. Flow chart for analysis cohort study creation.

Assessment of covariates

Information on age, sex, educational level, occupation, monthly family income, smoking status and alcohol drinking status was obtained from structured questionnaires completed by participants upon enrolment in the study. Personal and family medical history was determined by self-reported survey responses at baseline. Height and waist circumference were measured to the nearest 0·1 cm, while body weight was measured to the nearest 0·1 kg. BMI was calculated as weight (kg) divided by height (m) squared. Physical activity in the most recent week and sedentary time per day were measured using the International Physical Activity Questionnaire short version[23]. Physical activity then was calculated as the weekly metabolic equivalent hours.

Fasting blood glucose and lipid profiles were analysed using standardised laboratory procedures. Participants were defined as hyperlipidaemia if they met any of the following conditions: total cholesterol ≥ 5·17 mmol/l, TAG ≥ 1·7 mmol/l, LDL-cholesterol ≥ 3·37 mmol/l or taking lipid-lowering drugs. Blood pressure was measured at least twice using an electronic sphygmomanometer (TM-2655, A&D), and the mean of the last two measurements was calculated. Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or having a history of hypertension. Depressive symptoms were determined by the Chinese version of the Zung Self-Rating Depression Scale[24], and the scale scores ≥ 45 were considered to have depressive symptoms.

Statistical analysis

The quantile–quantile plot was used to examine the normal distribution of continuous variables. Baseline characteristics were presented as medians (interquartile ranges) for all continuous variables due to their non-normal distributions and as percentages for categorical variables. Differences in the distribution of baseline covariates according to NAFLD status were assessed using Wilcoxon rank sum test for continuous variables and χ^2 test for categorical variables. To assess bias from loss to follow-up, we compared the difference between the final analytic sample and those who were lost to follow-up.

Person time for follow-up was computed from the baseline survey to the date of the first occurrence of NAFLD or the end of follow-up (31 December 2019), whichever occurred first. The crude NAFLD incidence rates were calculated by taking the number of NAFLD cases and that by the sum of the

person-years and were expressed as incidence per 1000 person-years. Cox proportional hazards regression models with follow-up as time scale were performed to estimate hazard ratios (HR) and their 95 % CI for the association between quartile of added sugar intake and risk of NAFLD. The proportional hazards assumption was checked by including time-by-covariate interaction terms in the Cox proportional hazards model, and all variables satisfied the conditions (all $P > 0{\cdot}05$). Model adjustments were done in three sets. Model 1 was adjusted for age, sex and BMI. Model 2 was additionally adjusted for education, occupation, monthly family income, smoking status, alcohol drinking status, family medical history (including CVD, hypertension, hyperlipidaemia and diabetes), hypertension, hyperlipidaemia, depressive symptoms, physical activity, sedentary time, total energy intake and healthy diet score. Model 3 was identical to model 2, except that it was adjusted for BMI change from baseline to follow-up to correct for the possible effect of weight change on the risk of developing NAFLD.

In sensitivity analyses, we adjusted for sugar rich dietary pattern, vegetable rich dietary pattern and animal food dietary pattern instead of the self-calculated healthy diet score. Furthermore, to reduce the possibility of reverse causality, we excluded incident NAFLD cases that occurred within the first 2 years of follow-up.

All statistical analyses were performed using SAS statistical software, version 9.4 (SAS Institute Inc.). The significance level was set at a two-sided 0·05.

Results

The mean added sugar intake was 20·8 g/d for all participants. Among the added sugar sources, desserts (48 %) and yogurt (19 %) contributed the largest share, followed by soft drinks (12 %) and fruit/vegetable drinks (12 %).

Table 1 shows the baseline characteristics of the study population. Participants with incident NAFLD were older, were more likely to be men and have metabolic risk factors, such as higher baseline BMI, waist circumference and fasting blood glucose, than those without incident NAFLD. Furthermore, those with incident NAFLD were more likely to drink alcohol and smoke and had a higher proportion of personal and family history of disease. Moreover, participants included in this study were more likely to be younger, tended to be men, had a better metabolic profile and were more likely to have healthier lifestyles and higher socio-economic status than those who were lost to follow-up (online Supplementary Table 1).

During the 54 081 person-years of follow-up (median follow-up time: 4·2 years), 3476 participants received a diagnosis of NAFLD (incident rate 64 per 1000 person-years). Table 2 displays the HR (95 % CI) of the association between added sugar intake and risk of NAFLD. Total added sugar intake and liquid added sugar intake were significantly and positively associated with the risk of NAFLD. After adjusting for age, sex and baseline BMI, the multivariable HR of NAFLD risk for the highest compared with the lowest quartile of intakes were 1·15 (95 % CI 1·05, 1·27) for total added sugar intake and 1·19 (95 % CI 1·09, 1·31) for liquid added sugar intake, respectively. By contrast, solid added sugar intake was not associated with the risk of NAFLD (Q4 *v.* Q1 HR = 0·98; 95 % CI 0·89, 1·08). Additional adjustment for socio-economic status, lifestyle factors, medical history, diet quality and BMI change did not appreciably change the association estimates. In the fully adjusted models, comparing the upper quartiles to the lower quartiles of exposure, the increased relative risks of NAFLD were 18 % for total added sugar intake (HR = 1·18; 95 % CI 1·06, 1·32) and 20 % for liquid added sugar intake (HR = 1·20; 95 % CI 1·08, 1·33), respectively. In contrast, there was no significant association between solid added sugar intake and the risk of NAFLD (HR = 0·96; 95 % CI 0·86, 1·07).

Figure 2 presents the associations between added sugar intake from food sources and risk of NAFLD. Only added sugar from soft drinks was significantly associated with the risk of NAFLD, with an HR of 1·05 (95 % CI 1·03, 1·08) for each additional 5 g daily, $P < 0{\cdot}0001$. Added sugars from bread, yogurt, desserts, candies, fruit/vegetable drinks and coffee were not significantly associated with the risk of NAFLD ($P \geq 0{\cdot}09$).

In sensitivity analyses, adjustment for sugar rich dietary pattern, vegetable rich dietary pattern and animal food dietary pattern produced comparable results with those obtained from the primary analyses (data not shown). In addition, the exclusion of NAFLD cases that occurred within the first 2 years of follow-up did not materially change the associations of added sugars with risk of NAFLD (online Supplementary Table 2).

Discussion

In this large-scale prospective cohort study, we found that intakes of total added sugars and liquid added sugars were significantly associated with an increased risk of NAFLD. There was no association observed between solid added sugar intake and the risk of NAFLD. In addition, only added sugar from soft drinks was associated with an increased risk of NAFLD. No association was observed for other sources of added sugars.

In our study population, the mean intake of added sugars was 20·8 g/d, which was similar to the estimate of 18·8 g/d from the Chinese Nutrition and Health Surveillance in 2012[25]. The 2016 Chinese Dietary Guidelines recommended that added sugar intake should be less than 50 g/d and preferably less than 25 g/d. Our findings indicated that added sugar intake in this population was below the Chinese Dietary Guidelines. Further, the added sugar intake level in our study was much lower than those of the Western countries. For example, the mean intake of added sugars in the US population was 67·8 g/d in 2017–2018[26], while the mean added sugar intake in the Australian population was 60·3 g/d in 2011–2012[27].

Regarding sources of added sugars, we found that the top sources of added sugars were desserts and yogurt, and followed by soft drinks and fruit/vegetable drinks, consistent with China National survey data[28]. In contrast, added sugars in the USA[26] and other Western countries[27] primarily came from soft drinks. Collectively, these findings indicate that our study population (adult Chinese population) and Western populations have different food sources for added sugar intake.

Table 1. Baseline characteristics of the study participants by incident NAFLD status (*n* 15 538)*
(Percentages; medians and interquartile ranges)

	Incident NAFLD status						
	No			Yes			
Characteristics	%	Median	IQR	%	Median	IQR	*P*†
No. of participants		12 062			3476		–
Age (years)		35·5	30·2, 44·7		38·7	31·6, 49·0	< 0·0001
Sex (men, %)	36·1			61·8			< 0·0001
BMI (kg/m^2)		22·2	20·3, 24·2		24·8	23·1, 26·7	< 0·0001
WC (cm)		75·0	69·0, 82·0		84·0	78·0, 90·0	< 0·0001
TC (mmol/l)		4·49	3·99, 5·06		4·69	4·13, 5·28	< 0·0001
TAG (mmol/l)		0·84	0·64, 1·13		1·19	0·88, 1·63	< 0·0001
LDL-cholesterol (mmol/l)		2·55	2·09, 3·06		2·80	2·33, 3·31	< 0·0001
HDL-cholesterol (mmol/l)		1·50	1·27, 1·76		1·28	1·09, 1·50	< 0·0001
SBP (mmHg)		115	105, 125		120	110, 130	< 0·0001
DBP (mmHg)		70	65, 80		75	70, 85	< 0·0001
FPG (mmol/l)		4·80	4·60, 5·10		5·00	4·70, 5·30	< 0·0001
ALT (U/L)		12·0	10·0, 17·0		17·0	12·0, 24·0	< 0·0001
PA (MET-h/week)		11·6	3·85, 23·1		11·7	4·13, 24·8	< 0·0001
Total energy intake (kcal/d)		2258	1761, 2883		2355	1809, 3036	< 0·0001
Smoking status (%)							
Current smoker	11·9			22·2			< 0·0001
Ex-smoker	3·08			5·40			< 0·0001
Non-smoker	85·0			72·5			< 0·0001
Alcohol drinking status (%)							
Everyday drinker	2·78			4·38			< 0·0001
Sometime drinker	51·6			58·5			< 0·0001
Ex-drinker	8·96			8·99			0·95
Non-drinker	36·7			28·2			< 0·0001
Education level (college or higher, %)	77·2			74·0			< 0·001
Occupation (%)							
Managers	47·4			46·8			0·56
Professionals	16·3			16·8			0·45
Other	36·4			36·4			0·98
Household income (≥ 10 000 Yuan, %)	39·6			38·5			0·26
Hyperlipidaemia (%)	28·9			46·6			< 0·0001
Hypertension (%)	10·4			21·9			< 0·0001
Depressive symptoms (%)	15·4			14·1			0·06
Family history of disease (%)							
CVD	29·0			34·8			< 0·0001
Hypertension	49·4			55·1			< 0·0001
Hyperlipidaemia	0·38			0·53			0·23
Diabetes	22·9			27·2			< 0·0001

ALT, alanine aminotransferase; DBP, diastolic blood pressure; FPG, fasting plasma glucose; MET, metabolic equivalent; NAFLD, non-alcoholic fatty liver disease; PA, physical activity; SBP, systolic blood pressure; TC, total cholesterol; WC, waist circumference.
* Continuous variables are presented as medians (interquartile ranges) and categorical variables as percentages.
† Wilcoxon rank sum tests for continuous variables or χ^2 tests for categorical variables.

Our study is the first to investigate the association between added sugar intake *per se* and the risk of NAFLD. The results showed a positive association between total added sugar intake and the risk of NAFLD. This finding was supported by data from the US National Health and Nutrition Examination Survey that indicated the parallel rise in NAFLD prevalence and added sugar consumption in the periods from 1988 to 2012[8,29]. However, the consumption of added sugars was very low in China when compared with the US population[26]. Indeed, only 7·7 % of individuals consumed more than 50 g/d of added sugars in our study population. Thus, our study provides novel evidence that total added sugar intake is positively associated with incident NAFLD among adults with low consumption of added sugars.

Furthermore, added sugars in the liquid form were associated with an increased risk of NAFLD, whereas added sugars in the solid form were not. This discrepancy between physical forms of added sugars has been found in previous studies on sugar and health outcomes. For example, a cross-sectional study of adults in the East of England showed that added sugar intake in a liquid form was associated with higher levels of chronic inflammation, one of the potential mechanisms associated with NAFLD, but sugars from solids were not associated[30]. In addition, a cohort study found that liquid sugar intake was associated with an increased risk of overall cancer incidence and mortality and all-cause mortality, but intake of sugars in solid form was unrelated to these outcomes[31]. Likewise, results from two Swedish population-based prospective cohorts also indicated that liquid added sugars in sweetened beverages were positively associated with mortality, whereas solid added sugars in treats were inversely associated[32]. Taken together, these findings highlight that added sugars in liquid *v.* solid forms may impact metabolic diseases differently[33]. One possible explanation for

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Table 2. Association between added sugar intake and risk of non-alcoholic fatty liver disease (*n* 15 538)*
(Hazard ratios and 95 % confidence intervals)

	Quartile category of intake								
	Quartile 1		Quartile 2		Quartile 3		Quartile 4		
	Hazard ratios	95 % CI	Hazard ratios	95 % CI	Hazard ratios	95 % CI	Hazard ratios	95 % CI	$P_{for\ trend}$†
Total added sugar intake (g/d)‡									
Median	4·28		12·5		22·0		41·0		–
Range	0·00, 8·60		8·60, 16·7		16·7, 28·8		28·8, 258·4		
Number of participants	3885		3884		3884		3885		–
Number of cases	933		863		778		902		–
Person-years	13 298		13 474		13 712		13 598		–
Incidence per 1000 person-years	70		64		57		66		–
Model 1	1·00 (reference)		1·07	0·98, 1·18	1·00	0·91, 1·11	1·15	1·05, 1·27	< 0·01
Model 2	1·00 (reference)		1·10	1·00, 1·21	1·04	0·94, 1·15	1·20	1·07, 1·33	< 0·01
Model 3	1·00 (reference)		1·11	1·01, 1·23	1·04	0·94, 1·16	1·18	1·06, 1·32	< 0·01
Liquid added sugar intake (g/d)‡									
Median	0·85		4·41		9·96		19·6		–
Range	0·00, 2·62		2·67, 6·97		6·98, 13·4		13·4, 175·3		
Number of participants	3925		3956		3745		3912		–
Number of cases	932		807		758		979		–
Person-years	13 359		13 847		13 342		13 534		–
Incidence per 1000 person-years	70		58		57		72		–
Model 1	1·00 (reference)		1·02	0·93, 1·13	1·00	0·91, 1·10	1·19	1·09, 1·31	< 0·0001
Model 2	1·00 (reference)		1·03	0·94, 1·14	1·02	0·92, 1·13	1·22	1·10, 1·34	< 0·0001
Model 3	1·00 (reference)		1·04	0·94, 1·14	1·02	0·92, 1·14	1·20	1·08, 1·33	< 0·001
Solid added sugar intake (g/d)‡									
Median	0·58		5·73		11·0		23·9		–
Range	0·00, 3·41		3·43, 7·94		7·94, 16·3		16·3, 184·2		
Number of participants	3904		3876		3870		3888		–
Number of cases	986		852		837		801		–
Person-years	13 421		13 456		13 438		13 767		–
Incidence per 1000 person-years	73		63		62		58		–
Model 1	1·00 (reference)		0·98	0·90, 1·08	1·00	0·91, 1·10	0·98	0·89, 1·08	0·81
Model 2	1·00 (reference)		1·01	0·92, 1·10	1·03	0·93, 1·13	0·99	0·90, 1·10	0·91
Model 3	1·00 (reference)		1·00	0·91, 1·10	1·01	0·91, 1·11	0·96	0·86, 1·07	0·40

Model 1: adjusted for age (continuous; years), sex (categorical; men or women) and baseline BMI (continuous; kg/m^2).
Model 2: additionally adjusted for smoking status (categorical; current smoker, ex-smoker or non-smoker), alcohol drinking status (categorical; everyday drinker, sometime drinker, ex-drinker or non-drinker), educational level (categorical: < or ≥ college graduate), occupation (categorical; managers, professionals and other), annual family income (categorical: < or ≥ 10 000 Yuan), physical activity (continuous; MET-h/week), family history of disease (including CVD, hypertension, hyperlipidaemia and diabetes (each yes or no)), hypertension (yes or no), hyperlipidaemia (yes or no), depressive symptoms (score < or ≥ 45), sedentary time (hour/d), total energy intake (kcal/d) and healthy diet score (0, 1, 2, 3, 4 or 5).
Model 3: additionally adjusted for BMI change from baseline to follow-up (continuous; kg/m^2). For liquid and solid added sugars, mutual adjustment was conducted in model 3.
* Values are hazard ratios (95 % CI) unless otherwise indicated.
† Test for trend based on variable containing median value for each quartile.
‡ Median (range) intake.

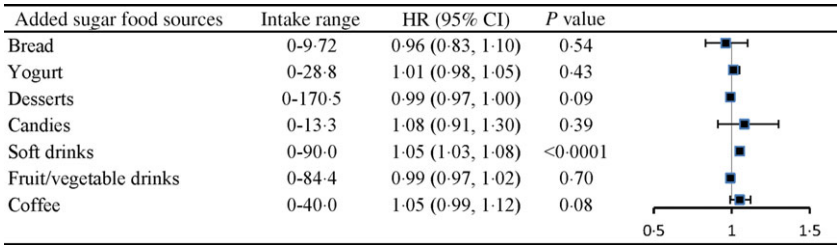

Fig. 2. Associations between added sugars from different food sources and the risk of non-alcoholic fatty liver disease. The multivariable Cox model included age, sex, baseline BMI, smoking status, alcohol drinking status, educational level, occupation, annual family income, physical activity, family history of disease (including CVD, hypertension, hyperlipidaemia and diabetes), hypertension, hyperlipidaemia, depressive symptoms, sedentary time, total energy intake, healthy diet score, BMI change from baseline to follow-up and intake of the other added sugar sources.

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this difference may be that added sugars in liquid form are digested more rapidly than added sugars in solid foods; thus, quickly absorbable added sugars in liquid form increase the rate of hepatic extraction of fructose, *de novo* lipogenesis and production of lipids[33]. Another possible explanation may be that liquid added sugars lead to less satiety than added sugars from solid foods[34]. This may give rise to a positive energy balance and subsequent hepatic fat accumulation[14,34].

Our study for the first time investigated the associations between different food sources of added sugars and risk of NAFLD. The results indicated that only added sugars from soft drinks were significantly associated with the risk of NAFLD. In line with our study, previous studies consistently showed that sugar-sweetened soft drink consumption was associated with a higher risk of NAFLD[10–13]. Furthermore, we did not observe significant associations between other food sources of added sugars and risk of NAFLD. Such findings suggested that different food sources of added sugars were differently associated with the risk of NAFLD. Further, our findings support the benefits of public health campaigns to reduce soft drink intake. At the same time, this also highlights that dietary recommendations without considering specific sources of added sugars may be simplistic and insufficient.

Consistent with our previous study[35], the current study showed that those with incident NAFLD were more physically active (Table 1). The reason is that men (geometric mean of physical activity was 12·0 (95 % CI 11·7, 12·4)) were more physically active than women (geometric mean of physical activity was 8·58 (95 % CI 8·35, 8·81)), and NAFLD patients were more likely to be men; thus, sex is an important factor that explains the fact that NAFLD patients are more physically active than controls. Indeed, the sex-adjusted geometric means of physical activity were 9·87 (95 % CI 9·65, 10·1) in controls and 9·94 (95 % CI 9·51, 10·4) in NAFLD patients, respectively (P value = 0·79).

The strengths of the present study include the large sample size, prospective design, objective assessment of NAFLD and careful adjustments for a wide range of lifestyle factors. In addition, the current study for the first time prospectively investigated the associations between added sugars and their forms/sources and the risk of NAFLD.

There are also several limitations to our study. First, the added sugar intake in this study was estimated using the US Department of Agriculture database due to the lack of sugar data in the Chinese Food Composition Tables. However, the estimated intakes were similar to those reported in the Chinese Nutrition and Health Survey[25,28]. Second, dietary intake was measured only at baseline. However, we had excluded participants with CVD, cancer and diabetes at baseline from the current study because these diseases could result in significant dietary changes[36]. Thus, the vast majority of participants would not have changed their diet intake in such a relatively short follow-up period (median 4·2 years). Third, the diagnosis of NAFLD was conducted by abdominal ultrasound instead of liver biopsy, which is the gold diagnostic standard for NAFLD. However, abdominal ultrasound is not invasive and easy to accept by participants. Moreover, this non-invasive method is widely used in large-scale population-based studies due to its high sensitivity and specificity[37]. Fourth, although we adjusted for a long list of risk factors including sedentary time, depressive symptoms and BMI change, unmeasured or residual confounding cannot be entirely ruled out. Finally, as our cohort is comprised of relatively healthy Chinese adults with low added sugar consumption, our results may not be generalisable to other ethnic populations. In addition, more than 10 % of participants lost to follow-up might bias our results.

Conclusions

In conclusion, this large prospective cohort study indicates that total added sugars and liquid added sugars, especially added sugars from soft drinks, were associated with an increased risk of NAFLD. Our findings suggest that reducing the consumption of added sugars, mainly from soft drinks, could be an effective preventive measure to prevent NAFLD.

Supplementary material

For supplementary material accompanying this paper visit https://doi.org/10.1017/S000711452200277X

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S. Z., L. Q. and K. N. conceptualised and designed the study. S. Z. performed the data analysis and drafted the manuscript. S. Z., G. M., Q. Z., L. H., H. W., Y. G., T. Z., X. W., J. Z., J. D., X. Z., Z. C., X. Z., X. D., S. S., X. W., M. Z., Q. J., K. S., Y. B., E. S., L. Q. and K. N. contributed to analysis and interpretation of data. L. Q. and K. N. contributed to the revision of the manuscript and approved the final draft. K. N. and S. Z obtained funding for the study. L. Q. and K. N. were involved in study supervision. All authors contributed to the intellectual content, critical revisions to the drafts of the paper and approved the final version.

The authors declared they have no conflicts of interest.

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