

Dietary fibre intake and risk of prediabetes in China: results from the Tianjin Chronic Low-grade Systemic Inflammation and Health (TCLSIH) Cohort Study

Shunming Zhang¹, Ge Meng^{1,4}, Qing Zhang³, Li Liu³, Zhanxin Yao^{1,5}, Hongmei Wu¹, Yeqing Gu², Yawen Wang¹, Tingjing Zhang¹, Xuena Wang¹, Juanjuan Zhang¹, Shaomei Sun³, Xing Wang³, Ming Zhou³, Qiyu Jia³, Kun Song³, Lu Qi^{6,7}* and Kaijun Niu^{1,2,3,8,9}*

- ¹Nutritional Epidemiology Institute and School of Public Health, Tianjin Medical University, Tianjin 300070, People's Republic of China
- ²Nutrition and Radiation Epidemiology Research Center, Institute of Radiation Medicine, Chinese Academy of Medical Sciences & Peking Union Medical College, Tianjin, People's Republic of China
- ³Health Management Centre, Tianjin Medical University General Hospital, Tianjin, People's Republic of China
- ⁴Department of Toxicology and Sanitary Chemistry, School of Public Health, Tianjin Medical University, Tianjin, People's Republic of China
- ⁵Tianjin Institute of Environmental & Operational Medicine, Tianjin, People's Republic of China
- 6 Department of Epidemiology, School of Public Health and Tropical Medicine, Tulane University, New Orleans, LA, USA
- ⁷Department of Nutrition, Harvard T.H. Chan School of Public Health, Boston, MA, USA
- 8 Tianjin Key Laboratory of Environment, Nutrition and Public Health, Tianjin, People's Republic of China
- ⁹Center for International Collaborative Research on Environment, Nutrition and Public Health, Tianjin, People's Republic of China

(Submitted 2 April 2021 - Final revision received 2 September 2021 - Accepted 8 September 2021 - First published online 21 September 2021)

Abstract

High dietary fibre intake has been associated with a lower risk of diabetes, but the association of dietary fibre with prediabetes is only speculative, especially in China, where the supportive data from prospective studies are lacking. This study aimed to examine the association between dietary fibre intake and risk of incident prediabetes among Chinese adults. We performed a prospective analysis in 18 085 participants of the Tianjin Chronic Low-grade Systemic Inflammation and Health cohort study who were free of diabetes, prediabetes, cancer and CVD at baseline. Dietary data were collected using a validated 100-item FFQ. Prediabetes was defined based on the American Diabetes Association diagnostic criteria. Cox proportional hazard models were used to estimate hazard ratios (HR) and 95 % CI. During 63 175 person-years of follow-up, 4139 cases of incident prediabetes occurred. The multivariable HR of prediabetes for the highest v. lowest quartiles were 0-85 (95 % CI 0-75, 0-98) (P for trend = 0-02) for total dietary fibre, 0-84 (95 % CI 0-74, 0-95) (P for trend < 0-01) for soluble fibre and 1-05 (95 % CI 0-93, 1-19) (P for trend = 0-38) for insoluble fibre. Fibre from fruits but not from cereals, beans and vegetables was inversely associated with prediabetes. Our results indicate that intakes of total dietary fibre, soluble fibre and fibre derived from fruit sources were associated with a lower risk of prediabetes.

Key words: Prediabetes: Dietary fibre: Fruits: Cohort study: China

Prediabetes is an intermediate glycaemic state between normoglycaemia and diabetes. Prediabetes is characterised by impaired glucose tolerance, impaired fasting glucose or elevated glycosylated HbA1c levels⁽¹⁾. The International Diabetes Federation reported that the global prevalence in adults with prediabetes which is defined as impaired glucose tolerance was approximately 7.5 % in 2019 and will increase to 8.0 % by 2030⁽²⁾. In China, a nationally representative survey conducted

in 2013 showed that 35.7% of Chinese adults had prediabetes, which is defined as having an HbA1c level of 5.7-6.4%, a fasting plasma glucose level of 5.6-6.9 mmol/l or a 2-h plasma glucose level of 7.8-11.0 mmol/l⁽³⁾. Individuals with prediabetes have a 4–19% (varied based on different abnormal parameters) annual risk of developing type 2 diabetes (T2D)^(4,5). Furthermore, prediabetes has been associated with an increased risk of structural brain abnormalities, CVD and all-cause mortality^(6,7). Moreover,

Abbreviations: HR, hazard ratio; T2D, type 2 diabetes; WC, waist circumference.

* Corresponding authors: Dr K. Niu, email nkj0809@gmail.com or Dr L. Qi, email lqi1@tulane.edu



754 S. Zhang et al.

the control of prediabetes may play an important role in the occurrence and progression of T2D, CVD and death^(7,8). Therefore, the identification of prediabetes risk factors is crucial for the early prevention and control of these complications.

Dietary fibre is an important component of a daily diet. It can be divided into soluble and insoluble fibre types⁽⁹⁾. Generally, soluble fibre is viscous, gel-forming and highly fermentable, while insoluble fibre is non-viscous, not gel-forming and moderately fermentable⁽⁹⁾. Gut microbes can ferment some types of dietary fibre (primarily soluble fibre) to produce SCFA^(9,10). Research has suggested that SCFA are the endogenous ligands for two G protein-coupled receptors (GPR41 and GPR43)(11), which contribute to the regulation of insulin secretion through activating these receptors (12,13). Diet-derived SCFA propionate could improve β -cell function *in vivo*, and *in vitro* results have demonstrated that this beneficial effect may occur through stimulation of insulin secretion and inhibition of apoptosis(14). Dietary soluble fibre may also slow the absorption of macronutrients, thereby reducing the rate of postprandial blood glucose absorption and blood insulin level⁽¹⁵⁾. Taken together, the prior evidence suggests that dietary fibre intake may have potential protective effects on glucose metabolism disorders. Moreover, the main food sources of dietary fibre are cereals, fruits, vegetables and beans, which typically provide a distinctive mixture of both soluble and insoluble dietary fibres⁽⁹⁾. Different food sources for fibre showed different health benefits (16). We hypothesised that different dietary fibre types and different sources of dietary fibre were differentially associated with the risk of prediabetes.

Recent reviews^(9,17) and meta-analyses^(18,19) investigated the association between dietary fibre intake, including total dietary fibre, soluble fibre, insoluble fibre, cereal fibre, fruit fibre, vegetable fibre and bean fibre, and the risk of T2D, and these studies have yielded mixed results. In addition, these studies mainly consisted of American and European populations, and the findings might not be generalisable to the Chinese population with different sources of dietary fibre intake, different lifestyles, metabolic characteristics and genetic predisposition in relation to T2D⁽²⁰⁾. To date, few studies have focused on the association between dietary fibre and prediabetes in the general adult population. To fill this knowledge gap, we investigated whether dietary fibre intake and different food fibre sources were prospectively associated with the risk of prediabetes in a general Chinese population of adults.

Methods

Study population

The Tianjin Chronic Low-grade Systemic Inflammation and Health Cohort Study is an ongoing, dynamic prospective observational study with men and women aged 18–90 years, living in Tianjin, China. Details of the cohort have been published elsewhere^(21,22). Briefly, the cohort study was established in May 2013 and is ongoing. At baseline, participants received comprehensive health examinations, which included administering a questionnaire to assess diet and lifestyle factors. Follow-up visits

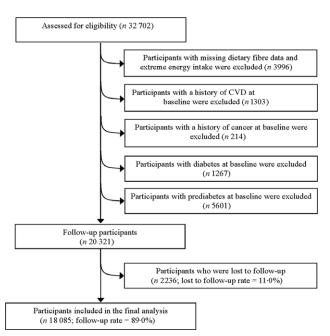


Fig. 1. Participant flow chart of the study.

were repeated annually. Written informed consent was provided by all participants. Ethical approval for this study was provided by the Institutional Review Board of Tianjin Medical University (approval number: TMUhMEC 201430).

From May 2013 to December 2019, a total of 32 702 participants in a rolling recruitment process were included in this study. Participants were excluded if they had missing data of dietary fibre or reported extreme total energy intake (defined as < 2.5% or > 97.5% percentiles of intake). Furthermore, we excluded participants who had self-reported CVD, self-reported cancer, physician-diagnosed diabetes or prediabetes at baseline. Participants were also excluded if they were lost to follow-up before December 2019 (lost to follow-up rate: 11.0%). Finally, 18085 participants (mean age: 38.5 (sp. 10.4) years; follow-up rate: 89.0%) were included in the analysis (Fig. 1).

Diagnosis of prediabetes

During annual health examinations, fasting plasma glucose was measured by the glucose hexokinase method using a blood sample after 12-h overnight fasting. Impaired glucose tolerance was determined by the 75 g oral glucose tolerance test, which was completed after an overnight fasting. HbA1c was measured using the HLC-723 G8 automated HPLC analyser (Tosoh). Prediabetes was defined as fasting plasma glucose of 5.6–6.9 mmol/l, and/or 2-h plasma glucose of 7.8–11.0 mmol/l in the oral glucose tolerance test, and/or an HbA1c of 5.7–6.4% (36–46 mmol/mol) without a history of diabetes according to the American Diabetes Association criteria⁽¹⁾.

Assessment of dietary intake

Dietary information was collected using a self-administered semi-quantitative FFQ. The FFQ assessed the usual intake of 100 food and beverage items over the last month and provided





seven frequency categories for foods ranging from 'never or hardly ever' to 'two or more times a day' and eight frequency categories for beverages ranging from 'almost never drink' to 'four or more times a day'. A typical portion size was prespecified for each food item (e.g. the standard serving size of mushrooms was 50 g for men and 30 g for women⁽²³⁾). Daily energy and nutrient intakes were estimated from the food items consumed according to the 2009 Chinese Food Composition Table (24). Due to the very low trans-fatty acid intake in our study population and lack of data on trans-fatty acid intake in the Chinese Food Composition Table, trans-fat intake was not included in the calculation of total fat intake. The FFQ has been validated using four 4-d weighed diet records (covering three non-consecutive weekdays and one weekend day) among 150 participants from the Tianjin Chronic Low-grade Systemic Inflammation and Health study⁽²⁵⁾. The Spearman correlation coefficients between FFQ and diet records were 0.49 for energy intake and 0.35-0.54 for nutrients. The energy-adjusted correlation coefficients between estimates from the FFQ and diet records ranged from 0.49 to 0.70 for dietary fibre (total fibre, soluble fibre, insoluble fibre, cereal fibre, bean fibre, vegetable fibre and fruit fibre). To correct for potential measurement error, each nutrient was expressed as intake per 4184 KJ (1000 kcal) by the nutrient density method⁽²⁶⁾.

Assessment of covariates

Information on age, sex, smoking status (current smoker, exsmoker and non-smoker), alcohol drinking status (everyday drinker, sometime drinker, ex-drinker and non-drinker), educational level, occupation, household income/month, personal and family medical history was collected from a structured questionnaire at baseline. Physical activity was assessed using the short International Physical Activity Questionnaire form⁽²⁷⁾. The short International Physical Activity Questionnaire form data were then used to estimate total weekly hours of metabolic equivalents (MET-h/week). Body height and weight of participants were measured while wearing light clothing and no shoes. BMI was calculated as body weight (kg) divided by height squared (m²). Waist circumference (WC) was measured to the nearest 0.1 cm at the umbilical line with participants standing and breathing normally.

Venous blood samples were collected after an overnight fast. Total cholesterol, TAG, HDL-cholesterol and LDL-cholesterol concentrations were analysed using an automatic biochemistry analyser (Roche Cobas 8000 modular analyser). Blood pressure was measured three times using the TM-2655 device (A&D Company Ltd) after at least 5 min of rest in a quiet room. The metabolic syndrome was defined following the criteria of the American Heart Association scientific statements of 2009⁽²⁸⁾. Information about long-term use of medications (more than 6 months) was collected at baseline using structured questionnaires.

Statistical analysis

Normality was assessed for each continuous variable by the onesample Kolmogorov–Smirnov test ($n \ge 2000$). Because the distributions of all continuous variables were non-normal, the natural logarithmic transformation was applied to normalise the data before statistical analysis. Baseline characteristics of the study participants were described using geometric means (95 % CI) for continuous variables and percentages for categorical variables. Differences in baseline characteristics between those with incident prediabetes and those without incident prediabetes were tested using ANOVA for continuous variables and logistic regression analysis for categorical variables. In addition, we compared the differences between those excluded from the study and the final study population.

The follow-up time for each participant was calculated from the date of the baseline dietary survey until the date of the first prediabetes diagnosis, the date of loss to follow-up or the last time of follow-up (31 December 2019), whichever occurred first. Cox proportional hazards regression models were used to estimate hazard ratios (HR) and 95% CI for the associations of dietary fibre intake (total fibre, soluble fibre and insoluble fibre) quartiles with the risk of prediabetes. The proportional hazards assumption was assessed using Schoenfeld residuals, and no violation was found. We fitted four statistical models. Model 1 was adjusted for age, sex and baseline BMI. Model 2 was further adjusted for smoking status, alcohol drinking status, educational level, occupation, household income per month, physical activity, family history of disease (including CVD, hypertension, hyperlipidaemia and diabetes), the metabolic syndrome, longterm use of medications and total energy intake. Model 3 was additionally adjusted for intakes of total protein, total fat, refined grains and added sugars. Moreover, analyses for soluble and insoluble fibres were mutually adjusted in model 3. Model 4 was additionally adjusted for total fruit intake. When analysing the association of sources and prediabetes, different fibre sources (cereal fibre, bean fibre, vegetable fibre and fruit fibre; modelled as quartiles) were also adjusted for each other in model 3. Tests for trend were carried out by assigning the median value to each category of fibre intake and modelling this value as a continuous variable.

As a secondary analysis, we examined the effect of substituting fruit fibre for cereal fibre, bean fibre or vegetable fibre by including all these fibres as continuous variables (5 g/1000 kcal per d) in the same multivariable model. The difference in the coefficients and variances from this multivariate model was used to estimate the HR and 95 % CI for the substitution effect (29,30).

We examined the interactions between dietary fibre intake and age, sex, BMI, smoking status, alcohol drinking status, education, occupation, income, physical activity, the metabolic syndrome and long-term medication use by including the corresponding cross-product terms in the most adjusted models and assessing the statistical significance of the log-likelihood ratios. Furthermore, multicollinearity among covariates was evaluated using the variance inflation factor.

We ran sensitivity analyses by further adjusting for WC or adjusting for WC instead of BMI. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc.). A two-sided P < 0.05 was considered statistically significant.

Results

Table 1 shows the baseline characteristics of participants according to incident prediabetes status. Participants with



756

S. Zhang et al.

Table 1. Age- and sex-adjusted baseline characteristics of the participants by incident prediabetes status (Means and 95 % confidence intervals, n 18 085)*

		Prediabe	tes status		
	No		Yes		
Characteristics	Geometric mean	95 % CI	Geometric mean	95 % CI	P†
Participants					
n	13 946		4139		_
Age (years)	35.7	35.5, 35.8	43.0	42.7, 43.3	< 0.0001
Sex (men)					
%	47.3		57⋅1		< 0.0001
BMI (kg/m ²)	23.4	23.3, 23.5	24.4	24.3, 24.5	< 0.0001
WC (cm)	79 ⋅1	79.0, 79.3	81.4	81.1, 81.7	< 0.0001
TC (mmol/l)	4.54	4.52, 4.55	4.68	4.66, 4.71	< 0.0001
TAG (mmol/l)	1.02	1.01, 1.03	1.17	1.15, 1.19	< 0.0001
LDL-cholesterol (mmol/l)	2.57	2.55, 2.58	2.70	2.68, 2.73	< 0.0001
HDL-cholesterol (mmol/l)	1.38	1.37, 1.38	1.32	1.31, 1.33	< 0.0001
SBP (mmHg)	116.9	116.6, 117.1	120.0	119.6, 120.4	< 0.0001
DBP (mmHg)	73.8	73.6, 73.9	75.6	75.3, 75.9	<0.0001
FPG (mmol/l)	4.81	4.80, 4.81	5.00	4.99, 5.01	< 0.0001
PA (MET-h/week)	9.74	9.53, 9.95	10.2	9.82, 10.7	0.04
Total energy intake (kcal/d)	2022	2013, 2032	2028	2010, 2046	0.57
Smoking status		20.0, 2002		20.0, 20.0	00.
Current smoker					
%	16.2		22.3		0.16
Ex-smoker	10.2		22.5		0.10
%	3.66		5.65		0.88
Non-smoker	3.00		5.05		0.00
	80-2		70.1		0.00
%	6U·2		72 ⋅1		0.20
Alcohol drinking status					
Everyday drinker	0.40		4.00		0.10
%	2.49		4.99		0.16
Sometime drinker	55.0		50.5		0.50
	55⋅2		58.5		0.53
Ex-drinker					
%	9.46		8.45		0.84
Non-drinker					
%	32.8		28-1		0.80
Education level (college or higher)					
%	75.0		67-2		0.27
Occupation					
Managers					
%	45.6		48-4		0.053
Professionals					
%	16.2		15.0		0.09
Other					
%	38.2		36-6		0.83
Household income (≥ 10 000 Yuan)					
%	33.5		34.3		0.89
The metabolic syndrome					
%	11.6		23.8		< 0.0001
Family history of CVD					
%	27.9		38-6		0.01
Family history of hypertension					
%	49.6		59.0		< 0.001
Family history of hyperlipidaemia					
%	0.42		0.55		0.94
Family history of diabetes					

DBP, diastolic blood pressure; FPG, fasting plasma glucose; MET, metabolic equivalent; PA, physical activity; SBP, systolic blood pressure; TC, total cholesterol; WC, waist circumference.

incident prediabetes were more likely to be older and men, had higher BMI, WC, total cholesterol, TAG, LDL-cholesterol, blood pressure, fasting plasma glucose and lower HDL-cholesterol and tended to be more physically active. They were also more likely to have the metabolic syndrome and a family history of CVD, hypertension and diabetes. The comparison

between included and excluded participants was provided in online Supplementary Table S1. Compared with those excluded, participants included in the analytical sample were younger, were more likely to be women, were more often educated and had healthier lifestyles, as well as had a better metabolic profile.



Continuous variables are expressed as geometric means (95 % CI) and categorical variables are expressed as percentages.

[†] ANOVA or logistic regression analysis adjusted for age and sex where appropriate.

Table 2. Association between dietary fibre intake and risk of prediabetes (Hazard ratios and 95 % confidence intervals, n 18 085)*

	Quartile category of intake								
	Quartile 1		Quartile 2		Quartile 3		Quartile 4		
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	P for trend†
Total fibre‡	7.48	0.02, 8.77	9.92	8.77, 11.2	12.7	11.2, 15.1	19-2	15.1, 61.7	_
Participants									
<i>n</i> Prediabetes	4522		4521		4520		4522		_
n	1015		995		1070		1059		_
Model 1§	1.00	Reference	0.95	0.87, 1.03	0.94	0.86, 1.03	0.89	0.82, 0.97	0.01
Model 2II	1.00	Reference	0.94	0.87, 1.03	0.94	0.86, 1.03	0.90	0.83, 0.98	0.02
Model 3¶	1.00	Reference	0.94	0.86, 1.02	0.93	0.85, 1.02	0.89	0.81, 0.97	0.01
Model 4**	1.00	Reference	0.93	0.85, 1.02	0.91	0.82, 1.01	0.85	0.75, 0.98	0.02
Soluble fibre‡	2.98	0.02, 3.64	4.27	3.64, 5.03	6.02	5.03, 7.50	10-6	7.50, 40.4	_
Participants	4500		4504		4500		4500		
<i>n</i> Prediabetes	4522		4521		4520		4522		_
	1041		1032		1016		1050		
n Model 1§	1.00	Reference	0.98	0.90, 1.07	0.91	0.83, 0.99	0.89	0.82, 0.97	_ < 0·01
Model 2	1.00	Reference	0.98	0.90, 1.07	0.91	0.83, 0.99	0.89	0.82, 0.98	< 0.01
Model 3¶	1.00	Reference	0.95	0.86. 1.04	0.87	0.79, 0.96	0.85	0.62, 0.96	< 0.01
Model 4**	1.00	Reference	0.94	0.86, 1.04	0.86	0.78, 0.96	0.84	0.74, 0.95	< 0.01
Insoluble fibre‡	4.16	0.11, 4.81	5.34	4.81, 5.88	6.53	5.88, 7.44	9.35	7.44, 26.3	< 0·01
Participants	4.10	0.11, 4.01	3.04	4.01, 5.00	0.55	3.00, 7.44	9.00	7.44, 20.3	
n	4522		4521		4520		4522		_
Prediabetes									
n	970		1007		1074		1088		_
Model 1§	1.00	Reference	1.01	0.93, 1.11	1.00	0.92, 1.09	0.96	0.88, 1.05	0.35
Model 2II	1.00	Reference	1.01	0.92, 1.10	1.01	0.92, 1.10	0.98	0.89, 1.07	0.59
Model 3¶	1.00	Reference	1.03	0.94, 1.13	1.06	0.96, 1.17	1.07	0.96, 1.19	0.21
Model 4**	1.00	Reference	1.03	0.94, 1.13	1.05	0.95, 1.16	1.05	0.93, 1.19	0.38

Values are hazard ratios (95 % CI) unless otherwise indicated

Table 2 presents the association between dietary fibre intake (total, soluble and insoluble) and the risk of prediabetes. Higher intakes of total and soluble fibre, but not insoluble fibre, were significantly associated with a lower risk of prediabetes in all four of the multivariable models. In the most adjusted models, the multivariable HR of prediabetes across quartiles of total dietary fibre intake were 1.00 (reference) for 1st quartile, 0.93 (95 % CI 0.85, 1.02) for 2nd quartile, 0.91 (95 % CI 0.82, 1.01) for 3rd quartile and 0.85 (95% CI 0.75, 0.98) for 4th quartile, respectively (P for trend = 0.02). Participants in the highest quartile of soluble fibre intake had a lower risk of prediabetes compared with those in the lowest quartile ($HR_{Q4v.Q1} = 0.84$, 95 % CI 0.74, 0.95; P for trend < 0.01). No significant association was observed between insoluble fibre intake and risk of prediabetes (HR_{Q4v.Q1} = 1.05, 95% CI 0.93, 1.19; P for trend = 0.38).

The mean intake of fibre from fruit, vegetable, bean and cereal sources was 12·2, 4·87, 2·42 and 2·86 g/d, respectively. Associations between dietary fibre intake from different food sources and prediabetes are presented in Fig. 2. Among the different dietary fibre sources, only fibre from fruits was significantly associated with a lower risk of prediabetes $(HR_{Q4v,Q1} = 0.89, 95 \% CI 0.81, 0.97; P \text{ for trend} < 0.01). In con$ trast, no significant association with the risk of prediabetes was observed between fibre from vegetables (HR $_{\mathrm{Q4}v.\mathrm{Q1}}$ = 1.03, 95 % CI 0.93, 1.13), beans $(HR_{O4v,O1} = 0.97, 95\% CI 0.88, 1.07)$ and cereals (HR_{O4 ν ,O1} = 0.94, 95 % CI 0.85, 1.04).

In the substitution model, the HR of substituting fruit fibre (5 g/1000 kcal per d) for 5 g/1000 kcal per d of cereal fibre, bean fibre and vegetable fibre were 0.93 (95 % CI 0.75, 0.99), 0.98 (95 % CI 0.95, 1.10) and 0.95 (95 % CI 0.86, 1.06), respectively.

No significant interactions were observed between total fibre intake and age, sex, BMI, smoking status, alcohol drinking status, education, occupation, income, physical activity, the metabolic syndrome and long-term medication use (all P for interaction > 0·10). In addition, all variance inflation factors of the covariates were less than 10, indicating that low collinearity was accepted.

When adjusting for WC + BMI or WC, the results from sensitivity analyses were comparable to those of the primary analyses (online Supplementary Table S2).

Test for trend based on variable containing median value for each quartile.

Median (range) intake, g/1000 kcal per d.

[§] Model 1: adjusted for age (continuous; years), sex (categorical; men or women) and baseline BMI (continuous; kg/m²).

Il 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), household income per month (categorical: < or ≥ 10 000 Yuan), physical activity (continuous; MET-h/week), the metabolic syndrome (yes or no), family history of disease (including CVD, hypertension, hyperlipidaemia and diabetes (each yes or no)), long-term use of medications (yes or no) and total energy intake (quartiles).

[¶] Model 3: additionally adjusted for total protein intake (quartiles), total fat intake (quartiles), refined grain intake (quartiles) and added sugar intake (quartiles). For soluble and insoluble fibres, mutual adjustment was conducted in the mode

^{*} Model 4: additionally adjusted for total fruit intake (quartiles).

Fiber sources	Median (range) intake ¹	Cases, n	HR (95% CI)	
Fruit fiber				
Quartile 1	2.02 (0.01, 2.85)	1,095	1.00 (reference)	.
Quartile 2	3.61 (2.85, 4.46)	979	0.91 (0.84, 1.00)	⊢≖ ⊢
Quartile 3	5.55 (4.46, 7.25)	1,025	0.90 (0.82, 0.98)	H ≡ H
Quartile 4	10.5 (7.25, 47.0)	1,040	0.89 (0.81, 0.97)	H ≡ H
P for trend	-	-	<0.01	
Vegetable fiber				
Quartile 1	1.21 (0.01, 1.52)	970	1.00 (reference)	•
Quartile 2	1.78 (1.52, 2.05)	1,059	1.05 (0.96, 1.15)	+=-
Quartile 3	2.36 (2.05, 2.78)	1,013	0.98 (0.90, 1.08)	+■
Quartile 4	3.53 (2.78, 15.2)	1,097	1.03 (0.93, 1.13)	⊢≖ ⊣
P for trend	-	-	0.99	
Bean fiber				
Quartile 1	0.39 (0.00, 0.56)	1,003	1.00 (reference)	•
Quartile 2	0.75 (0.56, 0.95)	1,010	0.98 (0.90, 1.07)	H ≡ H
Quartile 3	1.17 (0.95, 1.48)	1,031	0.96 (0.87, 1.05)	⊢≡ +
Quartile 4	2.03 (1.48, 7.96)	1,095	0.97 (0.88, 1.07)	H■→
P for trend	-	-	0.43	
Cereal fiber				
Quartile 1	0.75 (0.00, 0.91)	969	1.00 (reference)	•
Quartile 2	1.06 (0.91, 1.20)	987	0.96 (0.88, 1.05)	+■+

S. Zhang et al.

Fig. 2. Associations between dietary fibres from different food sources and the risk of prediabetes. Adjusted for age (continuous; years), sex (categorical; men or women), baseline BMI (continuous; kg/m²), 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), household income per month (categorical: < or ≥ 10 000 Yuan), physical activity (continuous; MET-h/week), the metabolic syndrome (yes or no), family history of disease (including CVD, hypertension, hyperlipidaemia and diabetes (each yes or no)), long-term use of medications (yes or no), total energy intake (quartiles), total protein intake (quartiles), total fat intake (quartiles), refined grain intake (quartiles), added sugar intake (quartiles) and intake (quartiles) of the other fibre sources (fruit fibre, vegetable fibre, bean fibre or cereal fibre). 1Presented as energy-adjusted intake amounts (g/1000 kcal per d) using the nutrient density method.

1,059

1,124

0.97 (0.88, 1.06)

0.94 (0.85, 1.04)

0.30

1.37 (1.20, 1.61)

2.06 (1.61, 7.95)

Discussion

In this study, we conducted a prospective assessment of the association between dietary fibre intake and the risk of prediabetes in the general population. Our results showed that total fibre and soluble fibre intakes were inversely associated with the risk of prediabetes. There was no observed association of insoluble fibre and prediabetes. Regarding food sources, only fibre from fruits was inversely associated with a lower risk of prediabetes.

Quartile 3

Quartile 4

P for trend

To the best of our knowledge, this was the first prospective cohort study from China on this topic. Two previous meta-analyses of prospective cohort studies have indicated an inverse association between total dietary fibre and fruit fibre intake and T2D^(18,19). In addition, recent findings from the NutriNet-Santé study showed that total dietary fibre intake, soluble fibre intake and fibre from fruits, but not fibre from vegetables, beans and cereals, were significantly associated with a lower risk of T2D⁽¹⁶⁾. These results are similar to those presented here. However, our results are in contrast to a previous meta-analysis that reported an inverse association between insoluble fibre, but not soluble fibre, and the risk of T2D⁽¹⁸⁾. This discrepancy may be caused by differences in study populations. In the prior meta-analysis(18), most of the studies included were conducted with American and European populations with different dietary patterns and sources of fibre compared with Chinese population. Furthermore, results from the present study were supported by the previous evidence that soluble fibre could delay gastric emptying and slow absorption of nutrients, thereby lowering postprandial glucose responses^(9,15). Indeed, a cross-sectional study conducted in 552 adult non-diabetic relatives of patients with T2D found soluble fibre intake was inversely associated with insulin resistance⁽³¹⁾. Soluble fibre is mainly from fruits in our study population (Spearman's correlation coefficient = 0.79), and we found that only fibre from fruit sources was inversely associated with the risk of prediabetes. Also, the association between soluble fibre intake and prediabetes remained statistically significant after further adjustment for total fruit intake, indicating that this relation was independent of total fruit intake. This also supports the idea that fibre rather than another component of fruit is responsible for the association. Moreover, a recent study conducted in China found that dietary fruit intake, but not vegetable intake, was prospectively associated with gut microbiota β -diversity and thirty-one microbial features (belonging to Faecalibacterium prausnitzii,



Akkermansia muciniphila, Ruminococcaceae, Clostridiales, Acidaminococcus, Prevotella stercorea, Prevotella copri, Fusobacterium and Enterobacteriaceae) $^{(32)}$. In that study, the fruit-related gut microbiota index (created from the thirty-one identified microbial features) was positively associated with fruit intake and inversely associated with T2D risk⁽³²⁾.

A recent review documented a health benefit of high dietary fibre (especially cereal fibre) intake in the prevention of diabetes⁽³³⁾. However, we found no significant inverse association between cereal fibre and prediabetes. One possible explanation for the null association is that the main source of cereal fibre in our study was refined grains, which means high consumption of grains but a very low intake of total cereal fibre. The mean intake of cereal fibre in our cohort was 2.86 g/d, lower than that of American adults (mean intake > 6 g/d) $^{(34,35)}$. In addition to the amount of cereal fibre, the primary grain consumed in our cohort was different than that of American and European cohorts. In China, cereal fibre is obtained primarily from refined rice and refined wheat flour (36). A previous study has shown that a higher intake of refined grains was associated with impaired glucose homoeostasis⁽³⁷⁾. Therefore, in our study, the possible harmful effect of refined grains on prediabetes may have offset the possible protective effect of cereal fibre on prediabetes.

In the present study, no significant association between vegetable fibre intake and prediabetes was observed, which is in line with a previous meta-analysis of seventeen prospective cohort studies on T2D⁽¹⁸⁾. Likewise, another prospective cohort study of French adults (median follow-up: 5.0 years) showed that vegetable fibre intake was not associated with the risk of T2D(16). However, a previous meta-analysis of prospective cohort studies mostly conducted in the USA found that vegetable fibre intake was inversely associated with the risk of T2D only in studies with a follow-up period of 10 years or more⁽¹⁹⁾. Therefore, in our study, this null association between vegetable fibre intake and prediabetes could be partly attributed to a relatively short follow-up period. Moreover, the dietary fibre content varies considerably among vegetable varieties and species, and thus differences in diets between China and the USA may explain this discrepancy. In addition, our results are supported by the findings from Chinese adults showed that vegetable intake was not associated with T2D⁽³²⁾.

Furthermore, we did not observe a significant association between bean fibre and prediabetes. This might be related to the insufficient intake of bean fibre in our study cohort (mean: 2.42 g/d) as well as the relatively moderate effect of bean fibre on prediabetes. A prospective cohort study in French adults, whose mean intake of bean fibre was 0.7 g/d, indicated that there is no significant association between bean fibre and T2D⁽¹⁶⁾. Although bean fibre intake was relatively high in our study cohort compared with those of Western cohorts, bean consumption appears to be falling in China.

Several potential mechanisms may explain the inverse associations between soluble, bean, and fruit fibres and prediabetes. First, fermentation of soluble dietary fibre by gut microbiota could produce SCFA, thereby improving HbA1c levels partly via increased glucagon-like peptide-1 production⁽³⁸⁾. Especially, viscous soluble fibre (e.g. pectin contained in fruits) may be more quickly fermented into SCFA and is recognised for their blood glucose-lowering effects (39). Moreover, in vitro studies have shown that SCFA could stimulate insulin secretion through activating free fatty acid receptor 2 (GPR43)⁽¹²⁾. Second, soluble fibre (can form a viscous solution in the small intestine) has been shown to increase digestion time, delay gastric emptying and enhance satiety, thereby improving insulin sensitivity and postprandial glucose^(15,40). Finally, dietary fibreinduced SCFA could reduce pro-inflammatory cytokine expression by inhibiting NF-xB activation and enhancing anti-microbial peptide secretion⁽⁴¹⁾, whereas inflammation plays a pivotal role in the pathogenesis of prediabetes⁽⁴²⁾.

There are several strengths to this study. First, this is the first large prospective cohort study among all the populations to investigate the association of dietary fibre intake and the risk of prediabetes. Second, detailed data on potential confounders allowed us to minimise potential bias. Third, there is a paucity of evidence from China associating dietary fibre and prediabetes. Our study provides an opportunity to investigate the effects of diet on human health in China, extending our understanding of the association between dietary fibre and prediabetes in China. Nonetheless, our study has potential limitations. First, diet information was self-reported, which could result in measurement errors. However, the measurement errors are most likely to be random and might bias true associations towards the null⁽²⁶⁾. Further, diet information was collected once at baseline. It is likely that dietary habits might have changed during followup. Therefore, further studies should examine the associations between changes in dietary fibre intake and subsequent prediabetes risk. Second, although we carefully adjusted for potential confounders, residual confounding could not be completely ruled out⁽⁴³⁾. For example, information on trans-fat intake was not included in the study. However, there is a very low intake of trans-fat in the Chinese population(44), and our findings were less likely to be influenced by the lack of trans-fatty acid intake. Third, this is an observational study, thus the causality of the observed associations cannot be inferred. Fourth, participants included in the present study were younger and tended to be healthier than those excluded, similar to the NutriNet-Santé cohort⁽¹⁶⁾ and the Whitehall II prospective cohort⁽⁴⁵⁾. While representative samples are necessary for estimating prevalence and incidence of disease, this is not the case when the study aims to examine the association between an exposure and an outcome⁽⁴⁶⁾, as shown by the association between dietary fibre intake and risk of prediabetes in the present study. Finally, our participants are exclusively Chinese, which limits the generalisability of the findings to other populations.

Conclusions

In conclusion, we found that higher intakes of total dietary fibre, soluble fibre and fibre from fruits were associated with a lower risk of prediabetes in Chinese adults. The results of this study suggest that high dietary fibre intake may protect against the development of prediabetes.



760 S. Zhang et al.

Acknowledgements

The authors gratefully acknowledge all the people that have made this study.

This study was supported by grants from the National Natural Science Foundation of China (No. 81872611 and 81941024), Tianjin Major Public Health Science and Technology Project (No. 21ZXGWSY00090), National Health Commission of China (No. SPSYYC 2020015), Food Science and Technology Foundation of Chinese Institute of Food Science and Technology (No. 2019-12), 2014 and 2016 Chinese Nutrition Society (CNS) Nutrition Research Foundation—DSM Research Fund (Nos. 2016-046, 2014-071 and 2016-023), China.

S. Z. analysed the data and wrote the paper. S. Z., G. M., Q. Z., L. L., Z. Y., H. W., Y. G., Y. W., T. Z., X. W., J. Z., S. S., X. W., M. Z., Q. J. and K. S. conducted the research. L. Q. and K. N. designed the research and had primary responsibility for the final content. All authors had full access to all the data in the study and read and approved the final manuscript.

The authors declared they have no conflicts of interest.

Supplementary material

For supplementary materials referred to in this article, please visit https://doi.org/10.1017/S0007114521003779

References

- American Diabetes Association (2017) 2. Classification and diagnosis of diabetes. *Diabetes Care* 40, S11–S24.
- International Diabetes Federation (2019) IDF Diabetes Atlas. https://diabetesatlas.org/en/resources/ (accessed July 2021).
- 3. Wang L, Gao P, Zhang M, *et al.* (2017) Prevalence and ethnic pattern of diabetes and prediabetes in China in 2013. *JAMA* **317**, 2515–2523.
- Gerstein HC, Santaguida P, Raina P, et al. (2007) Annual incidence and relative risk of diabetes in people with various categories of dysglycemia: a systematic overview and meta-analysis of prospective studies. Diabetes Res Clin Pract 78, 305–312.
- Bansal N (2015) Prediabetes diagnosis and treatment: a review. World J Diabetes 6, 296–303.
- van Agtmaal MJM, Houben A, de Wit V, et al. (2018) Prediabetes is associated with structural brain abnormalities: the Maastricht study. Diabetes Care 41, 2535–2543.
- Cai X, Zhang Y, Li M, et al. (2020) Association between prediabetes and risk of all cause mortality and cardiovascular disease: updated meta-analysis. BMJ 370, m2297.
- Evert AB, Dennison M, Gardner CD, et al. (2019) Nutrition therapy for adults with diabetes or prediabetes: a consensus report. Diabetes Care 42, 731–754.
- Weickert MO & Pfeiffer AFH (2018) Impact of dietary fiber consumption on insulin resistance and the prevention of type 2 diabetes. J Nutr 148, 7–12.
- Koh A, De Vadder F, Kovatcheva-Datchary P, et al. (2016) From dietary fiber to host physiology: short-chain fatty acids as key bacterial metabolites. Cell 165, 1332–1345.
- Brown AJ, Goldsworthy SM, Barnes AA, et al. (2003) The Orphan G protein-coupled receptors GPR41 and GPR43 are

- activated by propionate and other short chain carboxylic acids. *J Biol Chem* **278**, 11312–11319.
- Pingitore A, Gonzalez-Abuin N, Ruz-Maldonado I, et al. (2019) Short chain fatty acids stimulate insulin secretion and reduce apoptosis in mouse and human islets in vitro: role of free fatty acid receptor 2. Diabetes Obes Metab 21, 330–339.
- Kimura I, Ozawa K, Inoue D, et al. (2013) The gut microbiota suppresses insulin-mediated fat accumulation via the shortchain fatty acid receptor GPR43. Nat Commun 4, 1829.
- 14. Pingitore A, Chambers ES, Hill T, *et al.* (2017) The diet-derived short chain fatty acid propionate improves β -cell function in humans and stimulates insulin secretion from human islets *in vitro*. *Diabetes Obes Metab* **19**, 257–265.
- Lattimer JM & Haub MD (2010) Effects of dietary fiber and its components on metabolic health. *Nutrients* 2, 1266–1289.
- Partula V, Deschasaux M, Druesne-Pecollo N, et al. (2020)
 Associations between consumption of dietary fibers and the risk of cardiovascular diseases, cancers, type 2 diabetes, and mortality in the prospective NutriNet-Sante cohort. Am J Clin Nutr 112, 195–207.
- Gowd V, Xie L, Zheng X, et al. (2019) Dietary fibers as emerging nutritional factors against diabetes: focus on the involvement of gut microbiota. Crit Rev Biotechnol 39, 524–540.
- 18. Yao B, Fang H, Xu W, *et al.* (2014) Dietary fiber intake and risk of type 2 diabetes: a dose-response analysis of prospective studies. *Eur J Epidemiol* **29**, 79–88.
- Wang PY, Fang JC, Gao ZH, et al. (2016) Higher intake of fruits, vegetables or their fiber reduces the risk of type 2 diabetes: a meta-analysis. J Diabetes Investig 7, 56–69.
- Chan JC, Malik V, Jia W, et al. (2009) Diabetes in Asia: epidemiology, risk factors, and pathophysiology. JAMA 301, 2129–2140.
- Hu S, Gu Y, Lu Z, et al. (2019) Relationship between grip strength and prediabetes in a large-scale adult population. Am J Prev Med 56, 844–851.
- Zhang S, Kumari S, Gu Y, et al. (2020) Soy food intake is inversely associated with newly diagnosed nonalcoholic fatty liver disease in the TCLSIH cohort study. J Nutr 150, 3280–3287.
- Zhang S, Gu Y, Lu M, et al. (2020) Association between edible mushroom intake and the prevalence of newly diagnosed nonalcoholic fatty liver disease: results from the TCLSIH cohort study in China. Br J Nutr 123, 104–112.
- Yang Y (2009) China Food Composition Table, 2nd ed. Beijing: Peking University Medical Press.
- 25. Zhang S, Kumari S, Gu Y, *et al.* (2020) Honey consumption is inversely associated with prediabetes among Chinese adults: results from the Tianjin chronic low-grade systemic inflammation and health (TCLSIH) cohort study. *Br J Nutr*, 1–8 (Epublication ahead of print version).
- Walter W (2013) Nutritional Epidemiology, 3rd ed. New York: Oxford University Press.
- Craig CL, Marshall AL, Sjostrom M, et al. (2003) International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 35, 1381–1395.
- 28. Alberti KG, Eckel RH, Grundy SM, et al. (2009) Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. Circulation 120, 1640–1645.



- 29. Halton TL, Willett WC, Liu S, et al. (2006) Potato and French fry consumption and risk of type 2 diabetes in women. Am J Clin Nutr 83, 284-290.
- Song M & Giovannucci E (2018) Substitution analysis in nutritional epidemiology: proceed with caution. Eur J Epidemiol 33, 137-140.
- Ylonen K, Saloranta C, Kronberg-Kippila C, et al. (2003) Associations of dietary fiber with glucose metabolism in nondiabetic relatives of subjects with type 2 diabetes: the Botnia dietary study. Diabetes Care 26, 1979-1985.
- 32. Jiang Z, Sun TY, He Y, et al. (2020) Dietary fruit and vegetable intake, gut microbiota, and type 2 diabetes: results from two large human cohort studies. BMC Med 18, 371.
- McRae MP (2018) Dietary fiber intake and type 2 diabetes mellitus: an umbrella review of meta-analyses. J Chiropr Med 17, 44-53.
- AlEssa HB, Cohen R, Malik VS, et al. (2018) Carbohydrate quality and quantity and risk of coronary heart disease among US women and men. Am J Clin Nutr 107, 257–267
- 35. Ma W, Nguyen LH, Song M, et al. (2021) Dietary fiber intake, the gut microbiome, and chronic systemic inflammation in a cohort of adult men. Genome Med 13, 102.
- Yu D, Zhao L & Zhao W (2020) Status and trends in consumption of grains and dietary fiber among Chinese adults (1982-2015). Nutr Rev 78, 43-53.
- Song S, Lee JE, Song WO, et al. (2014) Carbohydrate intake and refined-grain consumption are associated with metabolic syndrome in the Korean adult population. J Acad Nutr Diet 114, 54-62.

- 38. Zhao L, Zhang F, Ding X, et al. (2018) Gut bacteria selectively promoted by dietary fibers alleviate type 2 diabetes. Science 359, 1151-1156.
- 39. Stephen AM, Champ MM, Cloran SJ, et al. (2017) Dietary fibre in Europe: current state of knowledge on definitions, sources, recommendations, intakes and relationships to health. Nutr Res Rev 30, 149-190.
- 40. Bernstein AM, Titgemeier B, Kirkpatrick K, et al. (2013) Major cereal grain fibers and psyllium in relation to cardiovascular health. Nutrients 5, 1471-1487.
- 41. McNabney SM & Henagan TM (2017) Short chain fatty acids in the colon and peripheral tissues: a focus on butyrate, colon cancer, obesity and insulin resistance. Nutrients 9, 1348.
- 42. Akash MS, Rehman K & Chen S (2013) Role of inflammatory mechanisms in pathogenesis of type 2 diabetes mellitus. J Cell Biochem 114, 525–531.
- 43. Agoritsas T, Merglen A, Shah ND, et al. (2017) Adjusted analyses in studies addressing therapy and harm: users' guides to the medical literature. JAMA 317, 748-759.
- 44. Jiang L, Shen J, Zhao Y, et al. (2020) Trans fatty acid intake among Chinese population: a longitudinal study from 1991 to 2011. Lipids Health Dis 19, 80.
- 45. Barbiellini Amidei C, Fayosse A, Dumurgier J, et al. (2021) Association between age at diabetes onset and subsequent risk of dementia. JAMA 325, 1640-1649.
- 46. Rothman KJ, Gallacher JE & Hatch EE (2013) Why representativeness should be avoided. Int J Epidemiol 42, 1012-1014.

