

Tea consumption and risk of diabetes in the Chinese population: a multi-centre, cross-sectional study

Yaling Chen¹, Wei Li¹, Shanhu Qiu¹, Carvalho Vladimir¹, Xiaohan Xu¹, Xinling Wang², Xin Nian³, Qingyun Chen⁴, Qing Wang⁵, Ping Tu⁶, Lihui Zhang⁷, Sunjie Yan⁸, Kaili Li⁹, Juan Chen¹, Hang Wu¹, Xuyi Wang¹, Xiaohang Wang¹, Jingbao Liu¹, Min Cai¹, Zhiyao Wang¹⁰, Bei Wang¹¹ and Zilin Sun^{1*}

¹Department of Endocrinology, Zhongda Hospital, Institute of Diabetes, School of Medicine, Southeast University, Nanjing 210009, People's Republic of China

²Department of Endocrinology, People's Hospital of Xinjiang Uyghur Autonomous Region, Urumqi 830001, People's Republic of China

³Department of Endocrinology, First Affiliated Hospital of Kunming Medical University, Kunming 650032, People's Republic of China

⁴Department of Endocrinology, The First Affiliated Hospital of Guangxi Medical University, Nanning 530021, People's Republic of China

⁵Department of Endocrinology, China-Japan Union Hospital of Jilin University, Changchun 130031, People's Republic of China

⁶Department of Endocrinology, The Third Hospital of Nanchang, Nanchang 330009, People's Republic of China

⁷Department of Endocrinology, The Second Hospital of Hebei Medical University, Shijiazhuang 050035, People's Republic of China

⁸Department of Endocrinology, The First Affiliated Hospital of Fujian Medical University, Diabetes Research Institute of Fujian Province, Fuzhou 350005, People's Republic of China

⁹Department of Endocrinology, Xinjiang Uygur Autonomous Region Hospital of Traditional Chinese Medicine, Urumqi 830006, People's Republic of China

¹⁰Suzhou MetroHealth Medical Technology Co. Ltd, Suzhou 215101, People's Republic of China

¹¹School of Public Health, Southeast University, Nanjing 210009, People's Republic of China

(Submitted 25 July 2019 – Final revision received 16 October 2019 – Accepted 30 October 2019 – First published online 25 November 2019)

Abstract

The aim of the present study was to explore the influence of tea consumption on diabetes mellitus in the Chinese population. This multi-centre, cross-sectional study was conducted in eight sites from south, east, north, west and middle regions in China by enrolling 12 017 subjects aged 20–70 years. Socio-demographic and general information was collected by a standardised questionnaire. A standard procedure was used to measure anthropometric characteristics and to obtain blood samples. The diagnosis of diabetes was determined using a standard 75-g oral glucose tolerance test. In the final analysis, 10 825 participants were included and multiple logistic models and interaction effect analysis were applied for assessing the association between tea drinking with diabetes. Compared with non-tea drinkers, the multivariable-adjusted OR for newly diagnosed diabetes were 0.80 (95 % CI 0.67, 0.97), 0.88 (95 % CI 0.71, 1.09) and 0.86 (95 % CI 0.67, 1.11) for daily tea drinkers, occasional tea drinkers and seldom tea drinkers, respectively. Furthermore, drinking tea daily was related to decreased risk of diabetes in females by 32 %, elderly (>45 years) by 24 % and obese (BMI > 30 kg/m²) by 34 %. Moreover, drinking dark tea was associated with reduced risk of diabetes by 45 % (OR 0.55; 95 % CI 0.42, 0.72; *P* < 0.01). The results imply that drinking tea daily was negatively related to risk of diabetes in female, elderly and obese people. In addition, drinking dark tea was associated with decreased risk of type 2 diabetes mellitus.

Key words: Tea consumption: Lifestyle: Diabetes mellitus: Risk

Diabetes mellitus is a complex metabolic syndrome and has been cited by the WHO as the third most serious non-communicable disease that threatens people's health, following cancer and CVD. It was reported that the prevalence of diabetes in China has reached a staggering 10.9 %; what is more, it was estimated that 388.1 million Chinese adults (200.4 million men and

187.7 million women) may have suffered from pre-diabetes in 2013⁽¹⁾. Furthermore, according to the eighth IDF Diabetes Atlas in 2017, the cost of diabetes reached \$727 billion, of which China's medical expenses for diabetes reached \$110 billion⁽²⁾. Former studies have demonstrated that diabetes is caused by the combination of genetic, environmental and modifiable

Abbreviation: T2DM, type 2 diabetes mellitus.

* **Corresponding author:** Zilin Sun, email sunzilin1963@126.com

lifestyle factors which are considered extremely significant in the prevention of type 2 diabetes mellitus (T2DM)⁽³⁻⁵⁾.

After water, tea is the second most consumed beverages in many parts of the world and has been regularly consumed for centuries in China. Tea is generally divided into five categories based on how it is processed⁽⁶⁾: unfermented tea (green tea), 10–20% fermented tea (white tea), semi-fermented tea (oolong tea) and fully fermented tea (black tea and dark tea)⁽⁷⁾. Black tea is made by using endogenous enzymes (polyphenol oxidase) to promote fermentation, whereas dark tea is developed through a series of processes and fermented completely, also with the help of exogenous enzymes. Finally, the differences in the fermentation process may lead to different effects on diabetes with these diverse phytochemicals⁽⁸⁾.

The predominant bioactive substance contained in tea, for example, catechin, caffeine, thearubigins and polyphenols, has been suggested to have anti-diabetic effects in diabetic mice⁽⁹⁾. In addition, researches^(10,11) reported that tea consumption could prevent the development of obesity, T2DM and cancer. In recent years, population-based studies about association between tea consumption and diabetes have received significant attention. A survey conducted in Poland showed that tea consumption was negatively correlated with central obesity and fasting plasma glucose in adults⁽¹²⁾. The Singapore Chinese Health Study aged 45–74 years reported that consuming ≥ 1 cup of black tea/d had a potential 14% reduction in risk of T2DM (risk ratio 0.86; 95% CI 0.74, 1.00) compared with non-consumers and reported no association with green tea⁽¹³⁾. Nevertheless, studies in Japan found that oolong tea may increase the risk of T2DM in Japanese women adults, but there was no correlation of green tea and black tea with the risk of diabetes⁽¹⁴⁾. A cross-sectional study conducted in a community-based specialised care centre in Pakistan observed that higher consumption of tea was independently associated with uncontrolled T2DM, as OR 1.5 (95% CI 1.0, 2.2)⁽¹⁵⁾. In short, inconsistent results have been reported in different subjects;

it seems to be prudent for tea drinkers to acquire effective prevention. The aim of the present study was to investigate the connection of tea consumption with T2DM within a large representative sample in the Chinese population.

Methods

Study design and population

This multi-centre, cross-sectional study, based on the ‘Non-lab and semi-lab algorithms for screening undiagnosed diabetes’ study⁽¹⁶⁾, was conducted in eight centres including seven provinces in China from November 2016 to June 2017. A multi-stage cluster and simple randomisation method was applied to recruit subjects aged 20–70 years in 1–2 provinces that were randomly selected in east, south, west, north and central regions across China. Finally, a total of 12 017 participants completed the investigation, including three parts: face-to-face questionnaire, physical examination and laboratory examination, in which fasting blood (at least 8 h) in the morning and postprandial blood (after oral administration of 75 g glucose) were drawn.

After excluding 100 subjects with missing data on socio-demographic information (e.g. age, sex and nationality), 649 with self-reported diabetes, thirty-two with defined other nationality, 355 with missing important laboratory indexes (including fasting plasma glucose, 2-h plasma glucose) or seven common lifestyle characteristics (such as diet habits, physical exercise, alcohol drinking, tea consumption and smoking status) and substituting the mean and the median for empty data (containing TAG, total cholesterol, HDL, LDL, waist circumference, height, weight, systolic blood pressure, diastolic blood pressure), outliers with waist circumference and BMI > 95.5 percentile or < 0.5 percentile, a total of 10 825 participants were included in the final data analysis (Fig. 1).

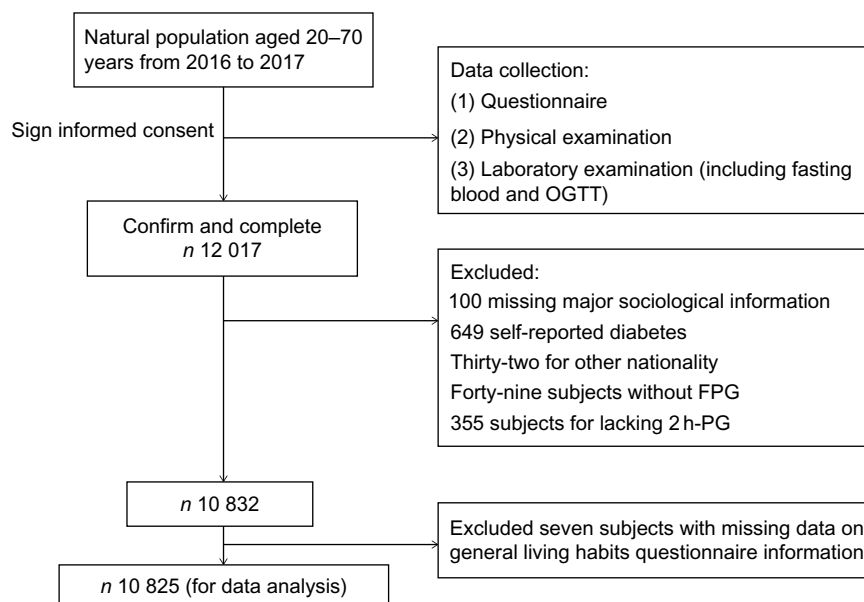


Fig. 1. Flow chart of the study population. OGTT, oral glucose tolerance test; FPG, fasting plasma glucose; PG, plasma glucose.

The present study protocols were approved by the ethics committee of Zhongda Hospital, School of Medicine, Southeast University and other sub-centre hospitals involved, and written informed consent were signed from each participant before the study.

Descriptive data collection

A standardised questionnaire was used to collect demographic characteristics (sex, age, ethnicity, education level, annual household income and family history of diabetes) and lifestyle factors (diet habit, vegetable and fruit consumption, smoking, alcohol consumption, tea consumption, regular exercise participation and sedentary work) by trained doctors and nurses during the face-to-face interview.

Clinical measurements

All measurement instruments were conformed to the national metrological certification requirements, and all measurement methods met the industrial standard of the People's Republic of China human measurement methods (WS/t424-2013). Waist circumference was measured from the costal margin along the mid-axillary line to the iliac crest level at the horizontal plane. BMI was calculated as weight (kg) divided by height (m) squared. Blood pressure was measured three times at 2-min intervals by a sphygmomanometer, and then the average of three measurements was taken. Fasting venous blood samples from the antecubital vein were obtained, and participants without T2DM conducted a 75-g oral glucose tolerance test performed by a trained staff. All blood samples stayed at room temperature for no more than 4 h and within the prescribed time limit for cold-chain transport (2–8°C) to central laboratory for testing total cholesterol, TAG, HDL-cholesterol and LDL-cholesterol and blood glucose.

Assessments

Newly diagnosed diabetes were defined as fasting plasma glucose ≥ 7.0 mmol/l or 2-h plasma glucose ≥ 11.1 mmol/l according to diagnostic criteria published by the WHO in 1999⁽¹⁷⁾, without a history of diabetes. BMI was categorised for common obesity based on WHO suggestion: <25 , 25–30 and >30 kg/m². We define 'drinking tea every day' as daily tea drinkers, 'drinking tea at least once a week' as occasional tea drinkers, 'drinking tea at least once a month' as seldom tea drinkers. Smoking status and alcohol intake were assessed by using a structured questionnaire. Tea types in questionnaire are classified as green tea, white tea, oolong tea, black tea, dark tea, bottled tea beverage and other tea. To improve statistical power, white tea, oolong tea and bottled tea are combined with other types in the following analyses considering the small sample size.

Statistical analyses

First, 10 825 participants' characteristics were assessed by diabetic status. The difference among newly diagnosed diabetes, pre-diabetes mellitus and non-diabetics was assessed with the χ^2 and Kruskal–Wallis test, respectively. Second, hierarchical logistic regression was used to examine the association of tea

consumption with newly diagnosed diabetes. Third, the interactive effect between tea consumption and sex/age/BMI on diabetes was explored by using Stata MP version 15.0. Statistical significance was defined as a *P* value of < 0.05 and based on two-sided probability.

Results

Characteristics of study population

Baseline characteristics of the 10 825 participants according to diabetic status are presented in Table 1. Compared with non-diabetic group, the proportion of newly diagnosed diabetes in men was higher (41.6% *v.* 29.1%). Furthermore, these newly diagnosed diabetics were more likely to smoke cigarettes or drink alcohol, less likely to consume vegetables or fruit and had higher BMI, LDL, TAG, total cholesterol and systolic blood pressure. Of particular interest, the percentage of daily tea drinkers in diabetic patients was significantly lower than that of non-diabetic group (28.7% *v.* 35.4%).

OR for type 2 diabetes mellitus according to tea-drinking status

Table 2 shows the unadjusted prevalence of newly diagnosed diabetes: 9.8, 7.4, 7.7 and 7.2% in the four groups. The crude OR of seldom tea drinkers, occasional tea drinkers and daily tea drinkers were 0.74 (95% CI 0.59, 0.94), 0.77 (95% CI 0.63, 0.94) and 0.72 (95% CI 0.61, 0.85), respectively, compared with non-tea drinkers. In model 4, after multiple adjustments, the prominent prevention impact of daily tea drinkers on T2DM declined slightly, but remained significant (OR 0.78; 95% CI 0.65, 0.94; *P* = 0.01).

Interactive effect of tea drinking with sex, age and BMI on type 2 diabetes mellitus

To improve statistical power, we merged 'non-tea drinkers', 'seldom tea drinkers' and 'occasional tea drinkers' as 'non-daily tea drinkers'. As shown in Table 3, daily tea drinking was associated with a decreased risk of diabetes in female, elderly and obese subjects, with the adjusted OR of 0.68 (95% CI 0.54, 0.87), 0.77 (95% CI 0.64, 0.93) and 0.66 (95% CI 0.47, 0.94), respectively. These results demonstrate a significant interactive effect of tea drinking with sex, age and BMI on T2DM ($P_{\text{interaction1}} = 0.014$, $P_{\text{interaction2}} = 0.043$ and $P_{\text{interaction3}} = 0.038$).

The impact of tea types on type 2 diabetes mellitus

To investigate the impact of tea types on the prevalence of undiagnosed T2DM, subgroup analyses were performed and are shown in Table 4. Those who consume dark tea (Pu'er) revealed the lowest newly diagnosed prevalence (5%). After adjustments for covariates, including age, sex, BMI, systolic blood pressure, TAG, education level, family history of DM (yes or no), smoking status, alcohol consumption, vegetable consumption, food consumption, fruit consumption, sedentary work (yes or no) and regular physical exercise (yes or no), subjects consuming dark tea had a 46% decreased risk of T2DM,



Table 1. Baseline characteristics of 10 825 study participants according to the status of diabetes mellitus (Medians and interquartile ranges (IQR); numbers and percentages)

Variables	Total population		Non-diabetics		Pre-diabetes*		Newly diagnosed diabetes		P†
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
<i>n</i>	10 825		7401		2526		898		
%			68.4		23.3		8.3		
Demographic data									
Age	51	40, 60	48	37, 57	55	47, 63	58	51, 64	<0.01
Sex (<i>n</i> and %)									
Male	3400	31.4	2150	29.1	876	34.7	374	41.6	<0.01
Female	7425	68.6	5251	70.9	1650	65.3	524	58.4	
Educated level (<i>n</i> and %)									
Middle school or lower	3993	36.9	2739	37.0	924	36.6	330	36.7	0.03
High school	3514	32.5	2460	33.2	784	31.0	270	30.1	
College or higher	3318	30.7	2202	29.8	818	32.4	298	33.2	
Annual household income (<i>n</i> and %)									
Less	6010	55.5	4097	55.4	1417	56.1	496	55.2	0.90
Moderate	2567	23.7	1773	24.0	585	23.2	209	23.3	
More	2248	20.8	1531	20.7	524	20.7	193	21.5	
Family history of diabetes (<i>n</i> and %)									
Yes	1444	13.3	884	11.9	379	15.0	181	20.2	<0.01
No	9381	86.7	6517	88.1	2147	85.0	717	79.8	
Lifestyle information									
Smoking status (<i>n</i> and %)									
Current smokers	1526	14.1	970	13.1	391	15.5	165	18.4	<0.01
Ex-smokers	324	3.0	177	2.4	113	4.5	34	3.8	
Never smokers	8975	82.9	6254	84.5	2022	80.0	699	77.8	
Alcohol consumption status (<i>n</i> and %)									
Current drinkers	2213	20.4	1393	18.8	566	22.4	254	28.3	<0.01
Ex-drinkers	423	3.9	260	3.5	122	4.8	41	4.6	
Never drinkers	8189	75.6	5748	77.7	1838	72.8	603	67.1	
Food consuming amount (<i>n</i> and %)									
Excess	1201	11.1	786	10.6	284	11.2	131	14.6	<0.01
Normal	8983	83.0	6206	83.9	2079	82.3	698	77.7	
Less	641	5.9	409	5.5	163	6.5	69	7.7	
Vegetable consuming amount (<i>n</i> and %)									
Excess	3222	29.8	2190	29.6	759	30.0	273	30.4	0.01
Normal	7009	64.7	4823	65.2	1633	64.6	553	61.6	
Less	594	5.5	388	5.2	134	5.3	72	8.0	
Fruit consuming amount (<i>n</i> and %)									
Excess	1678	15.5	1198	16.2	366	14.5	114	12.7	<0.01
Normal	6701	61.9	4657	62.9	1541	61.0	503	56.0	
Less	2446	22.6	1546	20.9	619	24.5	281	31.3	
Sedentary work (<i>n</i> and %)									
Yes	3234	29.9	2157	29.1	796	31.5	281	31.3	0.14
No	7058	65.2	4885	66.0	1599	63.3	574	63.9	
Unclear	533	4.9	359	4.9	131	5.2	43	4.8	

Effect of tea consumption on type 2 diabetes

Table 1. (Continued)

Variables	Total population		Non-diabetics		Pre-diabetes*		Newly diagnosed diabetes		P†
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	
Physical exercise regularly (<i>n</i> and %)									
Yes	4192	38.7	2780	37.6	1026	40.6	386	43.0	0.01
No	6633	61.3	4621	62.4	1500	59.4	512	57.0	
Tea-drinking status (<i>n</i> and %)									
Never drink tea	4118	38.0	2602	35.2	1114	44.1	402	44.8	<0.01
Tea-drinking seldom	1254	11.6	881	11.9	280	11.1	93	10.4	
Tea-drinking occasionally	1887	17.4	1301	17.6	441	17.5	145	16.1	
Tea-drinking daily	3566	32.9	2617	35.4	691	27.4	258	28.7	
Laboratory examination									
BMI (kg/m ²)	24	22, 27	24	22, 27	25	23, 28	26	24, 29	<0.01
TAG (mmol/l)	1.18	0.81, 1.78	1.07	0.75, 1.56	1.42	0.96, 2.13	1.72	1.14, 2.68	<0.01
TC (mmol/l)	5.07	4.35, 5.87	4.93	4.24, 5.71	5.33	4.59, 6.08	5.52	4.76, 6.33	<0.01
HDL (mmol/l)	1.54	1.30, 1.81	1.56	1.33, 1.82	1.51	1.27, 1.78	1.47	1.25, 1.73	<0.01
LDL (mmol/l)	2.90	2.36, 3.49	2.79	2.28, 3.37	3.08	2.55, 3.64	3.21	2.68, 3.79	<0.01
DBP (mmHg)	80	72, 88	78	70, 86	83	76, 91	86	78, 95	<0.01
SBP (mmHg)	127	115, 143	124	112, 138	134	122, 150	142	129, 156	<0.01

TC, total cholesterol; DBP, diastolic blood pressure; SBP, systolic blood pressure.

* Pre-diabetes: impaired fasting glucose (6.1–7.0 mmol/l), impaired glucose tolerance (7.8–11.1 mmol/l) or both exist, according to diagnostic criteria published by the WHO in 1999⁽¹⁷⁾.

† For continuous data with skewed distribution, the data are presented as medians and IQR and analysed by the Kruskal–Wallis test. Categorical data are presented as *n* and % and analysed by the χ^2 test. Significant level, $\alpha = 0.05$.

Table 2. Newly diagnosed incidence rates and risk for type 2 diabetes mellitus according to tea drinking status (Odds ratios and 95% confidence intervals)

	Never drink tea (<i>n</i> 4118): OR	Tea-drinking seldom (<i>n</i> 1254)		Tea-drinking occasionally (<i>n</i> 1887)		Tea-drinking daily (<i>n</i> 3566)		<i>P</i> _{for trend}
		OR	95% CI	OR	95% CI	OR	95% CI	
Cases	402		93		145		258	
Rate (%)	9.8		7.4		7.7		7.2	
Model 1*	1 (Ref)	0.74	0.59, 0.94	0.77	0.63, 0.94	0.72	0.61, 0.85	<0.001
Model 2†	1 (Ref)	0.86	0.67, 1.09	0.87	0.71, 1.07	0.68	0.57, 0.81	<0.001
Model 3‡	1 (Ref)	0.80	0.62, 1.02	0.82	0.67, 1.02	0.73	0.61, 0.87	0.006
Model 4§	1 (Ref)	0.83	0.65, 1.07	0.86	0.69, 1.06	0.78	0.65, 0.94	0.010

Ref, reference.

* Model 4: adjusted for all factors in model 3 plus smoking status, alcohol consumption status, vegetable consumption, food consumption, fruit consumption, sedentary work (yes or no), physical exercise regularly (yes or no).

† Model 1: crude.

‡ Model 2: adjusted for factors in model 1 plus age, sex and BMI.

§ Model 3: adjusted for all factors in model 2 plus systolic blood pressure, TAG, education level, family history of diabetes mellitus (yes or no).

Table 3. Interactive effect of tea consumption on the risk of diabetes (Odds ratios and 95 % confidence intervals)

Variables	Tea-drinking non-daily		Tea-drinking daily		Effect of tea*		
	DM	%	DM	%	OR	95 % CI	P*
Sex							
Male	220	11.2	154	10.8	1.03	0.82, 1.31	0.794
Female	420	7.9	104	4.9	0.68	0.54, 0.87	0.002
<i>P</i> _{interaction1}							0.014
Age (years)							
20–44	60	2.8	52	3.2	1.21	0.81, 1.78	0.356
45–70	580	11.3	206	10.5	0.77	0.64, 0.93	0.005
<i>P</i> _{interaction2}							0.043
BMI (kg/m ²)							
≤30	545	8.1	189	6.4	1.00	0.84, 1.21	0.837
>30	95	19.1	69	11.1	0.66	0.47, 0.94	0.018
<i>P</i> _{interaction3}							0.038

* Adjusted for other confounding factors other than interaction variables.

Table 4. Newly diagnosed incidence rates and risk for type 2 diabetes mellitus according to tea types (Odds ratios and 95 % confidence intervals)

	n	%	Cases	Prevalence	Adjusted for sex, age and BMI		Multivariate adjustment*		P*
					OR	95 % CI	OR	95 % CI	
Never drink tea	4118	38.0	402	9.8	1	Ref	1	Ref	0.001
Green tea	1310	12.1	125	9.5	0.96	0.77, 1.20	0.93	0.74, 1.17	0.556
Black tea	1443	13.3	84	5.8	0.65	0.50, 0.84	0.85	0.65, 1.11	0.226
Dark tea	1543	14.3	77	5.0	0.46	0.35, 0.60	0.54	0.41, 0.72	<0.001
Other tea	1307	12.1	116	8.9	0.97	0.77, 1.21	0.96	0.76, 1.21	0.702
More than one type	1104	10.2	94	8.5	0.80	0.63, 1.02	0.79	0.61, 1.02	0.072

Ref, reference.

* Adjusted for sex, age, BMI, systolic blood pressure, TAG, education level, family history of diabetes mellitus (yes or no), smoking status, alcohol consumption status, vegetable consumption, food consuming, fruit, sedentary work (yes or no), physical exercise regularly (yes or no).

compared with non-tea drinkers. However, subjects drinking green tea and black tea did not show significant reduction, with adjusted OR of 0.93 (0.74, 1.17) and 0.85 (0.65, 1.11), respectively.

Discussion

According to our knowledge, this is the first national observational study addressing the relationship of tea-drinking status and various tea types with T2DM in China. In our study, about 62 % of Chinese is drinking tea, mainly dark tea, black tea and green tea, accounting for 14.3, 13.3 and 12.1 %, respectively. Moreover, 32.9 % of subjects have the habit of drinking tea daily. It is fully confirmed that it is necessary to study the impact of tea drinking on the risk of diabetes in the Chinese population. According to the research, the total food consumption, alcohol consumption and physical exercise regularly of daily tea drinkers were lower than those of non-daily tea drinkers; however, vegetable consumption and fruit consumption of them were more than those of non-daily tea drinkers in men and women ($P < 0.05$) (data not shown). It could be speculated that dietary and living habits of tea drinkers daily are significantly different from those of non-daily tea drinkers in China. The interaction between diet habits

and tea drinking, which has been not reported by previous researchers, requires further exploration in the future. Furthermore, the diet and living habits have been adjusted to increase the credibility of those results in these following results.

Our results observed a negative association between tea consumption and risk of T2DM. These findings are inconsistent with several previous studies^(15,18,19), which observed a higher risk of T2DM in tea consumers, but consistent with several previous studies^(13,20–22) and meta-analyses^(23,24), in which a negative association was discovered. This discrepancy could be due to subjects, types or frequency of tea drinking. Additionally, a positive association between pesticides and T2DM has also been found in several studies^(25–27). Liu *et al.*'s study in Shanghai also proposed that more pesticide exposures among tea drinkers may be associated with an increased risk of T2DM⁽¹⁸⁾. Besides, drinking tea daily is more beneficial to prevent T2DM than seldom or occasional tea drinking in this research. Our result is in accordance with a meta-analysis⁽²³⁾ in which drinking more than three cups of tea per d was associated with a lower risk of T2DM. Additionally, Jing *et al.*⁽²⁴⁾ also found that consuming more than four cups per d may reduce the risk of T2DM by approximately 20 % (risk ratio 0.80; 95 % CI 0.70, 0.93). Furthermore, experimental studies have discovered that several bioactive

components, including catechins, gallic acid, polysaccharides and epigallocatechin-3-gallate, within tea show antioxidant activity^(28,29) and improve insulin sensitivity⁽³⁰⁾. The polysaccharides extracted from fully fermented black tea and dark tea contain a higher percentage of low molecular weight portions (antioxidants) than those extracted from green tea and oolong tea, resulting in more benefits to T2DM⁽⁹⁾. According to Bhupathiraju *et al.*, the effect of tea on diabetes might be attributed to caffeine. The study demonstrated that caffeinated tea could lower the risk of T2DM among women⁽³¹⁾. To sum up, these effects and mechanisms mentioned above are discrepant, possibly caused by different subjects, various tea types or tea drinking frequencies in previous researches; therefore, further evidence of the impact of tea drinking on Chinese is required in the future.

In our study, the negative correlation of daily tea drinking with the risk of T2DM is likely influenced by sex, age and BMI, which was determined by the significant interaction effect. Our results suggest that daily tea drinking may diminish the risk of diabetes in female by 32%, elderly by 23% and obese subjects by 34%. Yang *et al.*'s finding also demonstrated that drinking tea was associated with a reduced risk of diabetes in women and no significant effect in men was found⁽²³⁾; this disparity may be related to more men smoking than women, and a linear positive correlation between the amount of smoking and the risk of diabetes has previously been acknowledged⁽³²⁾. Additionally, the significant interaction effect between daily tea drinking and smoking is also found ($P_{\text{interaction}} = 0.015$) (data not shown), which demonstrates that daily tea drinking is associated with lowering the risk of diabetes in non-smokers, not significant effective on smokers. Therefore, smoking (mostly male) would counteract the protective effect of daily tea drinking on diabetes, which is consistent with the above result. Moreover, in our study, daily tea consumption was not significantly associated with weight loss, which is supported by Greenberg *et al.*'s cohort study⁽³³⁾. Therefore, we can speculate that the negative association between drinking tea daily and the risk of T2DM in obese may be achieved through increasing insulin sensitivity of obese patients, but more research on the mechanisms is needed in the future. In addition, we showed a decreased risk of diabetes in the elderly, which coincide with that of the Singapore Chinese Health Study⁽¹³⁾. This difference could be due to young people's preference for bottled or sugary beverage, which has been demonstrated to increase the risk of T2DM⁽³⁴⁾. In our study, the proportion of young people drinking bottled tea (2.3%) was three times that of the elderly (0.7%). However, because of the small sample of subjects who drink bottled tea, larger sample studies are needed to verify this speculation. In addition, the shorter duration of tea drinking by young people may also be a factor of the results, long-term follow-up studies are necessary.

As for tea types, the diabetes-related research on rats⁽³⁵⁾ has suggested potential benefits of green and black teas in insulin and glucose metabolism. Mahmoud's cohort work discovered that administering three cups per d of black tea can ameliorate the progression of T2DM in adults⁽³⁶⁾. The Singapore Chinese study had a suggestive 14% (risk ratio 0.86; 95% CI 0.74, 1.00) reduction in risk of diabetes within participants drinking black tea more than one cup per d compared with

non-consumers, but there was no association observed concerning green tea⁽¹³⁾. Additionally, daily consumption of black tea has been confirmed to increase the level of plasma antioxidants such as glutathione and decrease serum C-reactive protein level in diabetic populations^(37,38). Moreover, Deng *et al.*⁽²⁰⁾ observed, *in vitro* and *in vivo*, that Pu'er (dark tea) could suppress blood sugar in diabetes by inhibiting α -glucosidase activity. In our study, both black tea and dark tea were related to reducing the risk of diabetes after adjusting for sex, age and BMI; however, after adjusting for other confounding factors, the effect of dark tea remained significant (OR 0.54; 95% CI 0.41, 0.72; $P < 0.001$), while no significance was observed in black and green tea, consistent with the study in Japan⁽¹⁴⁾.

To our knowledge, as fully fermented tea, dark tea is a unique tea type in China and population-based research about dark tea is lacking. Our results showed that whole fermented tea, especially dark tea, is associated with a reduced risk of diabetes. Nevertheless, the disagreements with some of the previous studies about green or black tea could most likely be influenced by research population (ethnics), tea preparation methods, concentration of tea, level of pesticides exposure in tea or other unadjusted incorporated lifestyles.

These findings convey a potential high significance for public health because tea is the second most consumed beverages worldwide after water. Though China has a long history of tea drinking, former cohort studies on this topic had been limited to western populations. The highlights of the present study are summarised as follows: (1) The present study includes a large sample population from eight different sites in five areas in China, and the questionnaire information was comprehensive. (2) This is the first time to explore the interaction between sex, age and BMI with daily tea drinking on diabetes risk, and the result plays an instructive role in personalised prevention of diabetes. (3) The types of tea are classified in detail, whereas previous studies were mostly limited to green tea, black tea or oolong tea, solely. (4) The oral glucose tolerance test was tested for diagnosis of diabetes in the present study, and bias related to self-reports was avoided. (5) The present study did not contain already diagnosed patients, whose lifestyles had been influenced by medical intervention (data not shown).

However, several limitations of the present study should be considered: (1) This is a cross-sectional study that can only explain correlation and not causality. (2) The data related to lifestyles were obtained from the self-reported questionnaire, likely containing memory and self-reported bias. (3) The category of tea consumption status was not quantified (specific to frequency), possibly resulting in understanding bias. (4) Other unknown confounders potentially exist, such as milk, sweet foods and beverages consumption status, despite adjustments for multiple confounding factors. For example, Kazakhs and Uyghurs in China drink salty tea with mare milk at meal time, especially breakfast. It is not clear whether the effect of tea is affected by milk or salt, and the interaction of different micronutrients also needs to be clarified in the future. (5) The results of the present study are limited to the Chinese population and may be ineffective against other ethnic groups, such as Caucasians, with characteristic genes or habits.

In summary, our study suggests that daily tea consumption is negatively associated with the risk of T2DM among female,



elderly and obese people. Furthermore, consuming dark tea in particular showed the greatest association with reduced risk of diabetes in the Chinese population. Further cohorts studies should be conducted to elucidate the effect of tea on T2DM.

Acknowledgements

We thank all the participants, cooperative hospitals and investigators who contributed their precious time in this research.

The present study was supported by the National Key R&D Program of China (no. 2016YFC1305700), the National Key Scientific Instrument and Equipment Development Project of China (no. 51627808) and the grants from the Excellence Project of Southeast University (no. SJCX17_0072).

Z. S., Y. C. and W. L. were responsible for the study design. Y. C., W. L., S. Q. and B. W. were responsible for data collection, data analysis, interpretation and writing of the manuscript. Z. S., S. H., X. X., C. V., X. W., X. N., Q. C., Q. W., P. T., L. Z., S. Y., K. L., J. C., H. W., X. W., X. W., J. L., M. C. and Z. W. assisted with the data collection and manuscript modification. All authors have read the manuscript critically and approved the submitted version.

The authors declare no conflicts of interest of any commercial or financial relationships.

References

- Wang L, Gao P, Zhang M, *et al.* (2017) Prevalence and ethnic pattern of diabetes and prediabetes in China in 2013. *JAMA* **317**, 2515.
- Farag YM & Gaballa MR (2011) Diabetes: an overview of a rising epidemic. Nephrology, dialysis, transplantation: official publication of the European dialysis and transplant association. *Eur Renal Assoc* **26**, 28–35.
- Kolb H & Martin S (2017) Environmental/lifestyle factors in the pathogenesis and prevention of type 2 diabetes. *BMC Med* **15**, 131.
- Pan XR, Li GW, Hu YH, *et al.* (1997) Effect of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. *Diab Care* **20**, 537.
- Golozar A, Khademi H, Kamangar F, *et al.* (2011) Diabetes mellitus and its correlates in an Iranian adult population. *PLoS ONE* **6**, e26725.
- Yajima H (2014) Prevention of diet-induced obesity by dietary polyphenols derived from *Nelumbo nucifera* and black tea. *Polyphenols Hum Health Dis* **15**, 135–142.
- Chan EWC, Soh EY, Pei PT, *et al.* (2011) Antioxidant and antibacterial properties of green, black, and herbal teas of *Camellia sinensis*. *Pharmacogn Res* **3**, 266–272.
- Sanlier N, Gokcen BB & Altug M (2018) Tea consumption and disease correlations. *Trends Food Sci Technol* **78**, 95–106.
- Fu QY, Li QS, Lin XM, *et al.* (2017) Antidiabetic effects of tea. *Molecules* **22**, 849.
- Gondoin A, Grussu D, Stewart D, *et al.* (2010) White and green tea polyphenols inhibit pancreatic lipase *in vitro*. *Food Res Int* **43**, 1537–1544.
- Mao JT (2013) Chapter 3. White tea: the plants, processing, manufacturing, and potential health benefits. In *Tea in Health and Disease Prevention*, pp. 33–40 [VR Preedy, editor]. London: Academic Press.
- Grosso G, Stepaniak U, Micek A, *et al.* (2015) Association of daily coffee and tea consumption and metabolic syndrome: results from the Polish arm of the HAPIEE study. *Eur J Nutr* **54**, 1129–1137.
- Odegaard AO, Pereira MA, Koh WP, *et al.* (2008) Coffee, tea, and incident type 2 diabetes: the Singapore Chinese health study. *Am J Clin Nutr* **88**, 979–985.
- Oba S, Nagata C, Nakamura K, *et al.* (2010) Consumption of coffee, green tea, oolong tea, black tea, chocolate snacks and the caffeine content in relation to risk of diabetes in Japanese men and women. *Br J Nutr* **103**, 453–459.
- Siddiqui FJ, Avan BI, Mahmud S, *et al.* (2015) Uncontrolled diabetes mellitus: prevalence and risk factors among people with type 2 diabetes mellitus in an Urban District of Karachi, Pakistan. *Diab Res Clin Prac* **107**, 148–156.
- Li W, Xie B, Qiu S, *et al.* (2018) Non-lab and semi-lab algorithms for screening undiagnosed diabetes: a cross-sectional study. *EBioMed* **35**, 307–316.
- Drouin P, Blicke JF & Charbonnel B (1999) Diagnosis and classification of diabetes mellitus: the new criteria. *Diab Metabol* **25**, 72–83.
- Liu X, Xu W, Cai H, *et al.* (2018) Green tea consumption and risk of type 2 diabetes in Chinese adults: the Shanghai Women's Health Study and the Shanghai Men's Health Study. *Int J Epidemiol* **47**, 1887–1896.
- Hayashino Y, Fukuhara S, Okamura T, *et al.* (2011) High oolong tea consumption predicts future risk of diabetes among Japanese male workers: a prospective cohort study. *Diab Med* **28**, 805–810.
- Deng YT, Lin-Shiau SY, Shyur LF, *et al.* (2015) Pu-erh tea polysaccharides decrease blood sugar by inhibition of α -glucosidase activity *in vitro* and in mice. *Food Func* **6**, 1539–1546.
- Striegel L, Kang B, Pilkenton SJ, *et al.* (2015) Effect of black tea and black tea pomace polyphenols on α -glucosidase and α -amylase inhibition, relevant to type 2 diabetes prevention. *Front Nutr* **2**, 3.
- Yao Z, Gu Y, Zhang Q, *et al.* (2019) Estimated daily quercetin intake and association with the prevalence of type 2 diabetes mellitus in Chinese adults. *Eur J Nutr* **58**, 819–830.
- Yang W-S, Wang W-Y, Fan W-Y, *et al.* (2013) Tea consumption and risk of type 2 diabetes: a dose–response meta-analysis of cohort studies. *Br J Nutr* **111**, 1329–1339.
- Jing Y, Han G, Hu Y, *et al.* (2009) Tea consumption and risk of type 2 diabetes: a meta-analysis of cohort studies. *J General Internal Med* **24**, 557–562.
- Montgomery MP, Kamel F, Saldana TM, *et al.* (2008) Incident diabetes and pesticide exposure among licensed pesticide applicators: Agricultural Health Study, 1993–2003. *Am J Epidemiol* **167**, 1235–1246.
- Han K, Hwang E & Park J (2016) Excessive consumption of green tea as a risk factor for periodontal disease among Korean adults. *Nutrients* **8**, 408.
- Son HK, Kim SA & Kang JH, *et al.* (2010) Strong associations between low-dose organochlorine pesticides and type 2 diabetes in Korea. *Environ Int* **36**, 410–414.
- Kongpichitchoke T, Chiu MT, Huang TC, *et al.* (2016) Gallic acid content in Taiwanese teas at different degrees of fermentation and its antioxidant activity by inhibiting PKC δ activation: *in vitro* and *in silico* studies. *Molecules* **21**, 1346.
- Chen H, Qu Z, Fu L, *et al.* (2010) Physicochemical properties and antioxidant capacity of 3 polysaccharides from green tea, oolong tea, and black tea. *J Food Sci* **74**, C469–C474.
- Zheng XX, Xu YL, Li SH, *et al.* (2013) Effects of green tea catechins with or without caffeine on glycemic control in adults: a meta-analysis of randomized controlled trials. *Am J Clin Nutr* **97**, 750–762.
- Bhupathiraju SN, Pan A, Malik VS, *et al.* (2013) Caffeinated and caffeine-free beverages and risk of type 2 diabetes. *Am J Clin Nutr* **97**, 155–166.



32. Akter S, Goto A & Mizoue T (2017) Smoking and the risk of type 2 diabetes in Japan: a systematic review and meta-analysis. *J Epidemiol* **27**, 553–561.
33. Greenberg JA, Axen KV, Schnoll R, *et al.* (2005) Coffee, tea and diabetes: the role of weight loss and caffeine. *Int J Obes* **29**, 1121.
34. O'Connor L, Imamura F, Lentjes MAH, *et al.* (2015) Prospective associations and population impact of sweet beverage intake and type 2 diabetes, and effects of substitutions with alternative beverages. *Diabetologia* **58**, 1474–1483.
35. Wu LY, Juan CC, Ho LT, *et al.* (2004) Effect of green tea supplementation on insulin sensitivity in Sprague–Dawley rats. *J Agric Food Chem* **52**, 643–648.
36. Mahmoud F, Haines D, Al-Ozairi E, *et al.* (2016) Effect of black tea consumption on intracellular cytokines, regulatory T cells and metabolic biomarkers in type 2 diabetes patients. *Phytother Res* **30**, 454–462.
37. Āz H, Luna C & Estévez M (2016) Redox chemistry of the molecular interactions between tea catechins and human serum proteins under simulated hyperglycemic conditions. *Food Func* **7**, 1390–1400.
38. Neyestani TR, Shariatzade N, Kalayi A, *et al.* (2010) Regular daily intake of black tea improves oxidative stress biomarkers and decreases serum C-reactive protein levels in type 2 diabetic patients. *Ann Nutr Metabol* **57**, 40–49.