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Diet

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

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Abstract

Background: Epidemiological evidence on the association between tea consumption and the risk of type 2 diabetes (T2D) is inconsistent. This study prospectively investigated whether green tea drinking affects the risk of T2D.

Methods: This study included participants from the Shanghai Women's Health Study ($N = 67\,058$) and the Shanghai Men's Health Study ($N = 52\,315$) without diabetes at study enrolment. Details of tea consumption, including types and amounts, were collected at the baseline and follow-up survey. Incident T2D was identified through follow-up surveys. Plasma level of caffeine metabolite was measured in a nested case-control study involving 592 diabetes case-control pairs. Cox regression analysis, with tea drinking as a time-dependent variable and covariates adjusted for by a propensity score, was applied to estimate the hazard ratio (HR) and 95% confidence interval (CI) for T2D risk. Logistic regression analysis was applied to evaluate the association between caffeine metabolites and T2D risk.

Results: Current green tea drinkers had an increased risk of T2D compared with non-current drinkers [HR = 1.20 (95% CI = 1.14–1.27)], and a dose-response relationship was observed for duration of drinking tea and the amount of tea consumed [P for trend <0.001]. The increased risk associated with green tea drinking was observed in both women and men, across the entire period of follow-up, with HR (95% CI) of 1.08 (0.97–1.19) within 5 years of follow-up, 1.22 (1.12–1.32) during the period of 5–10 years of follow-up and 1.16 (1.03–1.30) after 10 years of follow-up. This association did not vary

significantly by body mass index, waist-to-hip circumference ratio or smoking status. Plasma level of caffeine was also associated with increased diabetes risk ($P = 0.03$), confirming the results based on self-reported tea drinking.
Conclusions: Green tea drinking was associated with an increased risk of T2D in Chinese adults. The mechanisms underlying the association need to be elucidated.

Key words: Green tea, type 2 diabetes, cohort study, Chinese

Key Messages

- Previous studies have shown inconsistent associations between tea consumption and the risk of T2D.
- We conducted analyses in two large-scale population-based cohorts of Chinese men and women in order to examine the association between green tea drinking and the risk of T2D in Chinese adults, for whom tea is one of the most popular beverages.
- Our study provides evidence of a positive and dose-response association between green tea consumption and risk of T2D in a Chinese population.

Introduction

Tea, made from the *Camellia Sinensis* plant, has been one of the most popular beverages around the world for centuries. Tea can be broadly classified into green tea (unfermented), black tea (fully fermented), oolong tea (half-fermented) and pu-erh tea (post-fermented), based on production methods.[1] Green tea, one of the most popular types, accounts for 23% of all tea products[2] and is the type of tea most often consumed in Asian countries. Green tea contains various components with potential health benefits, such as polyphenols and catechins, which are believed to help protect against cancer, cardiovascular disease, obesity and T2D.[3,4]

A number of studies have investigated the association of tea consumption with the risk of T2D,[5–13] a chronic disease that has been increasing rapidly around the world. However, the results have not been entirely consistent. A cohort study in Europe reported that people who drank at least four cups of tea per day had a 16% lower risk of developing T2D than non-tea drinkers.[6] Yang *et al.*[14] found that daily tea consumption of more than three cups was associated with a decreased risk of T2D. A meta-analysis also reported that tea consumption was inversely associated with T2D risk.[15] On the other hand, Odegaard *et al.*[16] found that only black tea, but not green tea, was associated with a lower incidence of T2D in Chinese Singaporeans; and Hayashino *et al.*[13] observed a positive association between oolong tea intake and risk of diabetes among the Japanese. A community-based cohort study conducted in Japan did not find green tea consumption to be related to the risk of diabetes,[9] but another study conducted in Japan reported a positive association between green tea consumption and risk of T2D in women.[7] Speculated reasons for the inconsistency include variation in tea consumption assessment, study sample sizes, temperature of tea drinking, concurrent habits such as cigarette smoking and alcohol drinking, healthier lifestyle in tea drinkers and pesticide residue in tea leaves.[1,6,13–15] In this study, based on data from two large-scale prospective studies, we prospectively investigated the association between green tea consumption and incidence of T2D in Chinese adults.

Methods

Study population

The Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS) are two population-based prospective cohort studies conducted in urban Shanghai, China. Study design and details of the two cohort studies have been described previously.[17,18] Briefly, the SWHS recruited 74 941 women aged 40–70 years from 1996 to 2000, and the SMHS recruited 61 480 men aged 40–74 years from 2002 to 2006, from eight urban neighbourhood communities in Shanghai, China. Participants were followed up every 2–4 years through in-person surveys to update their health, lifestyle and other information (follow-up rates: $\geq$91.9% for both cohorts). All participants completed an in-person interview using structured questionnaires. Anthropometric measurements were also taken at the interview. The study protocols were approved

by the institutional review boards of all institutes involved in the studies, and written informed consent was obtained from all participants before interview.

Included in this analysis were 67 058 women of the SWHS and 52 315 men of the SMHS. Participants excluded from this study were those who were diagnosed with diabetes or had a positive result of urine glucose testing at baseline ($n = 5083$ and 4253, respectively) or who were possible diabetes cases ($n = 367$), who drank tea other than green tea ($n = 4408$), who reported extreme total energy intake (women: < 500 or > 3500 kcal/day, men: < 800 or > 4200 kcal/day) ($n = 290$) or who were lost to follow-up ($n = 457$). Incident diabetes patients during the first 2 years of follow-up ($n = 899$) or subjects who had less than 2 years of follow-up ($n = 1291$) were also excluded from analysis.

Assessment of tea consumption and other covariates

Tea consumption information was collected at the baseline survey. Participants were asked whether they drank tea regularly, which was defined as drinking tea at least three times per week for more than 6 consecutive months, and at what age they started this habit. They were also asked about the current status of their tea consumption and questioned on the types and amounts (dry weight) of tea (tea leaves) they consumed during the year preceding the interview. Tea drinking information was updated during the follow-up surveys. In this study, the period of green tea drinking and amount of green tea consumption per month were each classified into tertiles, and non-drinkers served as the reference group. Based on baseline drinking information, tertiles for period of green tea drinking were defined as short (<10.35 years for women and <21.25 years for men), medium (10.35 to 21.36 years for women and 21.25 to 30 years for men) and long (>21.36 years for women and >30 years for men); tertiles for amount of green tea consumption were defined as low (<100 g/month for women and <200 g/month for men), medium (100–150 g/month for women and 200–250 g/month for men) and high (>150 g/month for women and >250 g/month for men).

Sociodemographic characteristics such as birth date, educational level, income, occupation, smoking status and alcohol intake were collected using a structured questionnaire at baseline. Income (yuan/year per capita) was defined as low (<6000), middle (6000–10 000) and high ($>10\,000$) in men and low (<4000), middle (4000–8000) and high (>8000) in women. Dietary intake was assessed at the baseline survey through an in-person interview using a validated food frequency questionnaire, which covered 90% of food items commonly consumed in urban Shanghai during the study period.

Body weight, standing height, and circumferences of waist and hips were measured at recruitment according to a standard protocol by trained interviewers who were retired medical professionals. Based on these measurements, we created two variables: body mass index (BMI: weight in kilograms divided by the square of height in metres), and waist:hip ratio (WHR: waist circumference divided by hip circumference).

Identification of incident T2D

Incident T2D cases were identified through follow-up surveys. Participants who self-reported to be diagnosed with T2D by physicians and who met at least one of the following criteria recommended by the American Diabetes Association (ADA) during the follow-up survey were considered as incident cases: fasting glucose level ≥ 7 µl/l on at least one occasion, or a postprandial plasma glucose test with a value ≥ 11 µl/l on at least two separate occasions, and/or use of hypoglycaemic medication (i.e. insulin or oral hypoglycaemic drugs). Follow-up was censored at the date of diagnosis, date of last follow-up or the date of death, whichever occurred first.

Assessment of plasma level of caffeine metabolite

Plasma level of caffeine metabolite was measured for 592 diabetes cases (254 male and 338 female) and the same number of controls as part of a metabolomics study which was nested in the SWHS and SMHS. Only individuals who provided a fasting blood sample and were diabetes free at baseline were eligible for the study. Cases and controls were individually matched on sex, age (+/− 2 years), date of sample collection (+/− 30 days, relaxed to 70 days for 24 controls), and time interval between the last meal and blood draw (+/− 2 h). Metabolites were measured at the Broad Institute, USA, by mass spectrometry.[19]

Statistical analysis

Continuous variables were described as mean ± standard deviation (SD) and categorical variables as percentages. The differences across subgroups were compared using analysis of variance (ANOVA) tests for continuous variables and chi-square (χ^2) tests for categorical variables by adjusting for age.

Hazard ratios (HRs) and 95% confidence intervals (CIs) for T2D were estimated using Cox proportional hazards regression models, with age as the time scale and tea drinking, duration and amount of tea consumption, as time-dependent variables. Entry time was defined as age at baseline recruitment plus 2 years (as we excluded diabetes

patients within 2 years of follow-up from the study), and exit time was defined as age at T2D diagnosis, last follow-up or death, whichever came first. Logistic/multinomial logistic regression was used to calculate propensity score (PS) for tea drinking, duration and amount of consumption, at baseline using potential confounding variables (described below in detail) as independent variables in the model. The derived inverse of PS was used as a weight in the survival analysis with respect to duration and amount of tea consumption.[20] Among green tea drinkers, the duration and amount of green tea drinking were classified by tertile in men and women separately; non-current drinkers were used as the reference. Tests for trend were performed by entering categorical variables as continuous variables in the model. Potential confounding variables were chosen based on a priori considerations and literature references, including birth year, gender, educational level (four categories: elementary or below, junior high school, high school and college or above), income per capita (three categories; low, middle and high), cigarette smoking (ever smoked at least one cigarette per day for more than 6 consecutive months; yes or no), alcohol drinking (ever drank beer, wine or spirits at least three times per week for more than 6 consecutive months; yes or no), regular exercise in leisure time in metabolic equivalent of task (METs by tertile, no physical activity), presence of comorbidities at baseline (yes or no)[21] and total energy intake (tertiles).

Stratified analyses were conducted by the period of follow-up (from enrolment to diabetes diagnosis, death or end of interview, whichever came first; 2–5, >5–10 and >10 years), BMI (categorized for general obesity according to World Health Organization (WHO) recommendations; <25, 25–30 and >30) and WHR (categorized for central obesity according to German Society for Sports Medicine and Prevention (DGSP) recommendations; <0.80, 0.80–0.84 and ≥0.85 for women and <0.90, 0.90–0.99 and ≥1.00 for men).

Level of caffeine metabolites was analysed by conditional logistic regression analysis by nature log transferring and tertile categorization. Adjustment included age at diagnosis, BMI, WHR, total energy and fat intake, ever smoking, ever drinking and smoking pack-years. All statistical analyses were carried out using SAS version 9.4 (SAS Institute, Inc.). All statistical tests were based on two-sided probability.

Results

Baseline characteristics of study participants according to status of green tea drinking assessed at baseline are shown in Table 1. Overall, 27.5% of women and 65.8% of men in the two cohorts reported having ever drunk green tea, and the majority (95.6% of women and 95.8% of men) have maintained the habit since they started tea drinking. In both sexes, compared with non-current drinkers, current green tea drinkers were slightly younger, had a higher income per capita, were more likely to smoke cigarettes or to drink alcohol and were less likely to engage in leisure time exercise. They also consumed much more energy, fat, protein and fibre, but fewer carbohydrates, and appeared to have a poorer basic health status than non-drinkers. Compared with male tea drinkers, female tea drinkers drank a smaller amount of green tea, and had been doing so for a shorter duration, with a median of 100 (Interquartile Range (IQR): 50–150) g per month and for a median of 15.8 (IQR: 7.5–24.1) years in women versus 250 (IQR: 150–450) g per month and 25.1 (IQR: 19.0–32.3) years in men.

During an average of 10.2 years follow-up in women and 5.7 years in men, a total of 4199 female and 2000 male T2D cases were identified. The incidence rate of T2D was 7.44/1000 person-years (7.13 for women and 8.12 for men). Compared with non-current drinkers, current green tea drinkers had an excess risk of T2D of 20% (95% CI: 1.14-1.27) among all participants, 18% in women [HR = 1.18 (95% CI = 1.11-1.26)] and 23% in men [HR = 1.23 (95% CI = 1.11-1.36)]. The risk increased with increasing duration and amount of green tea drinking in both female and male tea drinkers (P for trend <0.001), (Table 2). Because no gender-specific association was observed, data from men and women were combined in the following analyses to improve statistical power.

To address the possibility that diabetes patients might drink more tea at an earlier stage of T2D, owing to the disease-related thirst symptom, we categorized the follow-up time into three periods: 2–5 years, >5–10 years and >10 years (Table 3). An elevated risk of T2D was observed in current tea drinkers versus non-current drinkers across the all periods of follow-up, with HR (95% CI) of 1.08 (0.97–1.19) within 5 years of follow-up, 1.22 (1.12–1.32) during the period of 5–10 years of follow-up and 1.16 (1.03–1.30) after 10 years of follow-up. Similarly, a dose-response relationship with amount of green tea consumption was also observed in all three time periods; participants having the highest green tea consumption had 29%, 18% and 28% excess risk of T2D, respectively, compared with non-current drinkers.

We further evaluated the associations between green tea consumption and T2D by BMI and WHR. As shown in Table 4, a tea consumption and T2D association was consistently seen across all BMI and WHR categories. No multiplicative interaction between BMI or WHR and green tea drinking was observed (data not shown).

We also evaluated the associations between green tea consumption and T2D by smoking status (Table 5). Tea drinking was positively associated with T2D risk

Table 1. Characteristics of the study participants by status of green tea drinking

	Women			Men		
	Non-current drinkers (N = 49 466)	Current drinkers (N = 17 592)	P-value	Non-current drinkers (N = 19 346)	Current drinkers (N = 32 969)	P-value
Age (years)	52.8±9.2	50.4±8.0	<0.001	56.5±10.1	53.9±9.2	<0.001
Educational level (%)			<0.001			0.001
Elementary or below	23.5	10.4		8.4	4.6	
Junior high school	38.3	36.2		32.5	34.4	
High school	26.6	33.5		34.9	37.9	
College or above	11.6	19.9		24.2	23.1	
Income (%)			<0.001			<0.001
Low	17.3	11.3		13.1	12.5	
Middle	74.5	74.9		78.2	77.4	
High	8.2	13.8		8.7	10.1	
Occupation (%)			<0.001			0.019
Professional	26.2	36.3		27.3	25.3	
Clerical	20.7	20.7		21.2	22.3	
Manual	52.7	42.8		51.5	52.4	
Housewife/retired	0.4	0.2		NA	NA	
Cigarette smoking (%)			<0.001			<0.001
Never	97.9	96.2		45.3	21.2	
Ever	2.1	3.8		54.7	78.8	
Alcohol drinking (%)			<0.001			<0.001
Never	98.4	96.0		76.6	60.3	
Ever	1.6	4.0		23.4	39.7	
Regular physical activity (%)			<0.001			<0.001
No	65.3	65.8		61.5	67.7	
Yes	34.7	34.2		38.5	32.3	
Exercise (MET-h/day/year) (%)			<0.001			<0.001
0	65.3	65.8		61.5	67.7	
≤0.91	12.6	13.1		12.1	11.8	
0.92-2.39	11.1	11.1		13.5	11.2	
>2.39	11.0	10.0		12.9	9.3	
BMI (kg/m^2) (%)			<0.001			<0.001
< 25	66.2	66.1		68.7	67.8	
25-29.9	29.2	29.4		29.2	29.8	
≥30	4.6	4.5		2.1	2.4	
WHR (%)			0.435			<0.001
Lower	41.3	43.6		53.9	50.4	
Medium	35.4	36.1		42.2	45.3	
Higher	23.3	20.3		3.9	4.3	
Energy intake (kcal/day)	1672.9±395.0	1688.1±385.6	0.0290	1915.6±471.9	1921.3±472.5	0.119
Fat intake (g/day)	28.7±12.9	31.0±12.8	<0.001	33.2±14.8	35.2±15.6	<0.001
Carbohydrate (g/day)	287.4±67.5	282.6±64.3	<0.001	327.4±84.5	321.5±84.1	<0.001
Protein (g/day)	66.1±20.4	69.5±20.5	<0.001	76.6±23.0	79.4±23.5	<0.001
Fibre intake (g/day)	10.8±4.1	11.5±4.2	<0.001	11.4±4.2	11.5±4.6	<0.001
Presence of comorbidities (%)			<0.001			<0.001
0	91.4	93.2		70.3	75.1	
1	8.6	6.8		29.7	24.9	

Values were described as mean ± SD or percentage, and all P-values were adjusted for age.

among non-smokers and smokers, following a dose-response for duration of drinking tea. A significant dose-response association for amount of tea drinking was observed among non-smokers but not in smokers. However, testing for multiplicative interaction was not significant (data not shown).

Plasma level of caffeine was positively associated with diabetes risk [odds ratio (OR) = 1.21 (95% CI = 1.02–1.43)

Table 2. Associations between tea consumption and the risk of type 2 diabetes in Chinese men and women

	Women		Men		Total	
	Cases/non-cases	HR (95% CI)[a]	Cases/non-cases	HR (95% CI)[a]	Cases/non-cases	HR (95% CI)[a]
Green tea drinking						
Non-current drinkers	3115/46 351	1.00	722/18 624	1.00	3837/64 975	1.00
Current drinkers	1084/16 508	1.18 (1.11-1.26)	1278/31 691	1.23 (1.11-1.36)	2362/48 199	1.20 (1.14-1.27)
P for heterogeneity				0.183		
Period of green tea drinking (years)						
Non-drinkers	3115/46 351	1.00	722/18 624	1.00	3837/64 975	1.00
Short	334/5508	1.19 (1.08-1.32)	437/10 737	1.13 (0.99-1.28)	771/16 245	1.14 (1.05-1.23)
Medium	350/5625	1.10 (1.00-1.21)	420/10 885	1.30 (1.15-1.46)	770/16 510	1.17 (1.09-1.26)
Long	400/5375	1.14 (1.03-1.26)	421/10 069	1.35 (1.20-1.53)	821/15 444	1.20 (1.12-1.29)
P for trend		0.001		<0.001		<0.001
P for heterogeneity				0.012		
Amount of green tea consumption (g/month)						
Non-drinkers	3115/46 351	1.00	722/18 624	1.00	3837/64 975	1.00
Low	598/10 205	1.12 (1.02-1.21)	400/11 052	1.26 (1.14-1.40)	998/21 257	1.16 (1.09-1.24)
Medium	199/2612	1.20 (1.06-1.36)	458/10 808	1.31 (1.14-1.52)	657/13 420	1.25 (1.14-1.37)
High	287/3691	1.21 (1.09-1.34)	420/9831	1.21 (0.99-1.47)	707/13 522	1.20 (1.10-1.31)
P for trend		<0.001		0.001		<0.001
P for heterogeneity				0.139		

[a]HR adjusted for propensity score in time-dependent model.

Table 3. Associations between tea consumption and risk of type 2 diabetes by the period of follow-up in Chinese men and women

	2-5 years		>5-10 years		>10 years	
	Cases/non-cases	HR (95% CI)[a]	Cases/non-cases	HR (95% CI)[a]	Cases/non-cases	HR (95% CI)[a]
Green tea drinking						
Non-current drinkers	1178/67 634	1.00	1655/60 659	1.00	1004/26 827	1.00
Current drinkers	754/49 807	1.08 (0.97-1.19)	1187/41 437	1.22 (1.12-1.32)	421/9905	1.16 (1.03-1.30)
Amount of green tea consumption (g/month)						
0	1178/67 634	1.00	1655/60 659	1.00	1004/26 827	1.00
Low	308/21 947	0.94 (0.84-1.05)	462/19 060	1.18 (1.08-1.30)	228/6181	1.13 (0.98-1.30)
Medium	221/13 856	1.35 (1.15-1.57)	345/11 010	1.25 (1.09-1.42)	91/1549	1.04 (0.84-1.30)
High	225/14 004	1.29 (1.10-1.52)	380/11 367	1.18 (1.02-1.35)	102/2175	1.28 (1.08-1.51)
P for trend		<0.001		<0.001		<0.001

[a]HR adjusted for propensity score in time-dependent model.

for one fold-increment ($p = 0.025$), and 2.32 (1.30-4.12) for the highest tertile compared with lowest tertile]. The association pattern was consistent for men and women [OR = 2.53 (95% CI = 0.94-6.84) for men versus 1.83 (0.89-3.76) for women, comparing the highest with the lowest tertile].

Discussion

In these two large-scale population-based cohorts of Chinese men and women, we observed a positive and dose-response association between green tea consumption and risk of T2D. This finding was confirmed in a subset of cases and controls for whom we measured plasma levels of caffeine. Our findings are inconsistent with several previous studies and meta-analyses in which an inverse association was observed,[14,15] but are in line with two studies reporting an increased risk of T2D in green tea and oolong tea drinkers.[12,13]

Tea is a beverage rich in antioxidants such as catechins that have postulated health benefits. For example, supplementation with tea extract high in catechins was found to reduce body fat, low-density lipoprotein and systolic blood pressure in a randomized clinical trial.[22] Green tea is derived from steamed fresh tea leaves and produced in an unfermented process, which results in the release of more

Table 4. Associations between tea consumption and the risk of type 2 diabetes by BMI and WHR in Chinese men and women

	BMI						WHR[a]					
	<25		25-29		≥30		Lower		Medium		Higher	
	Cases/ non-cases	HR (95% CI)[b]	Cases/ non-cases	HR (95% CI)[b]	Cases/ non-cases	HR (95% CI)[b]	Cases/ non-cases	HR (95% CI)[b]	Cases/ non-cases	HR (95% CI)[b]	Cases/ non-cases	HR (95% CI)[b]
Green tea drinking												
Non-current drinker	1382/44 627	1.00 (ref.)	1960/18 145	1.00 (ref.)	495/2203	1.00 (ref.)	733/29 367	1.00 (ref.)	1583/23 446	1.00 (ref.)	1468/10 744	1.00 (ref.)
Current drinker	935/33 052	1.21 (1.11-1.33)	1170/13 819	1.08 (1.00-1.17)	257/1328	1.09 (0.93-1.27)	540/22 396	1.23 (1.09-1.38)	1158/18 883	1.13 (1.04-1.23)	561/4309	1.19 (1.08-1.31)
Period of green tea drinking (years)												
0	1382/44 627	1.00 (ref.)	1960/18 145	1.00 (ref.)	495/2203	1.00 (ref.)	733/29 367	1.00 (ref.)	1583/23 446	1.00 (ref.)	1468/10 744	1.00 (ref.)
Short	306/11 384	1.17 (1.03-1.32)	393/4473	1.00 (0.90-1.12)	72/388	1.03 (0.83-1.29)	179/7751	1.16 (0.98-1.37)	382/6233	1.13 (1.01-1.26)	177/1354	1.12 (0.96-1.30)
Medium	304/11 636	1.17 (1.04-1.33)	386/4478	1.09 (0.98-1.21)	80/396	1.01 (0.82-1.25)	178/7896	1.14 (0.97-1.35)	380/6425	1.12 (1.01-1.25)	173/1305	1.16 (1.01-1.33)
Long	325/10 032	1.22 (1.08-1.38)	391/4868	1.12 (1.01-1.24)	105/544	1.12 (0.90-1.41)	183/6749	1.36 (1.16-1.59)	396/6225	1.10 (0.98-1.23)	211/1650	1.18 (1.04-1.35)
P for trend		<0.001		0.018		0.396		<0.001		0.042		0.002
Amount of green tea consumption (g/month)												
0	1382/44 627	1.00 (ref.)	1960/18 145	1.00 (ref.)	495/2203	1.00 (ref.)	733/29 367	1.00 (ref.)	1583/23 446	1.00 (ref.)	1468/10 744	1.00 (ref.)
Low	409/14 734	1.19 (1.07-1.32)	483/5995	1.08 (0.99-1.18)	106/528	1.06 (0.88-1.29)	246/9990	1.22 (1.06-1.40)	458/8151	1.07 (0.97-1.17)	265/2213	1.22 (1.09-1.38)
Medium	248/9148	1.28 (1.10-1.49)	338/3910	1.11 (0.98-1.27)	71/362	1.10 (0.85-1.43)	133/6086	1.50 (1.24-1.81)	351/5479	1.24 (1.08-1.41)	128/943	1.01 (0.84-1.22)
High	278/9170	1.19 (1.02-1.39)	349/3914	1.03 (0.91-1.17)	80/438	1.10 (0.88-1.39)	161/6320	1.04 (0.84-1.30)	349/5253	1.18 (1.03-1.36)	168/1153	1.19 (1.03-1.37)
P for trend		<0.001		0.206		0.294		0.009		<0.001		0.012

[a]Grouped as lower (<0.90 for men and <0.80 for women), medium (0.90–0.99 for men and 0.80–0.84 for women) and higher (>1.00 for men and >0.85 for women).

[b]HR adjusted for propensity score in time-dependent model.

Table 5. Associations between tea consumption and the risk of type 2 diabetes in Chinese men and women by smoking status

	Never Smokers		Ever Smokers	
	Cases/non-cases	HR (95% CI)[a]	Cases/non-cases	HR (95% CI)[a]
Green tea drinking				
Non-current drinkers	3352/53 827	1.00	458/11 148	1.00
Current drinkers	1300/22 607	1.21 (1.13-1.28)	1062/25 592	1.14 (1.01-1.29)
Period of green tea drinking (years)				
0	3352/53 827	1.00	485/11 148	1.00
Short	423/8076	1.25 (1.14-1.37)	348/8169	0.93 (0.79-1.08)
Medium	396/7096	1.10 (1.00-1.20)	374/9414	1.27 (1.11-1.46)
Long	481/7435	1.20 (1.09-1.31)	340/8009	1.22 (1.06-1.41)
P for trend		<0.001		<0.001
Amount of green tea consumption (g/month)				
0	3352/53 827	1.00	485/11 148	1.00
Low	691/13 666	1.13 (1.05-1.22)	307/7591	1.21 (1.07-1.37)
Medium	293/4511	1.28 (1.15-1.43)	346/8909	1.16 (0.98-1.37)
High	316/4430	1.26 (1.15-1.39)	391/9092	0.95 (0.76-1.20)
P for trend		<0.001		0.448

[a]HR adjusted for propensity score in time-dependent model.

catechins than other tea types, such as epigallocatechin gallate (EGCG), epigallocatechin (EGC), epicatechin gallate (ECG) and epicatechin (EC).[1] These compounds, mostly EGCG, have been shown to have antidiabetic effects.[23,24] Studies *in vivo* and *in vitro* have reported that green tea extract can decrease levels of fasting glucose, haemoglobin A1c (HbA1c) and insulin in diabetic rats.[25,26] In humans, clinical trials have shown beneficial effects of tea or tea extract on levels of fasting glucose and HbA1c and insulin sensitivity,[27] but null results have been reported from studies on green tea only.[28] In line with the beneficial effects of tea extracts, tea drinking was found to be associated with lower risk of T2D in Western populations.[5,6]

However, similar to the findings in our study, tea drinking has been associated with an increased risk of T2D in several studies of Asian populations who consume the most green tea.[12,13] Hayashino *et al.*[13] attributed the positive association of oolong tea with T2D, found in the Japanese study, to pesticide residue. Yang *et al.*[14] also suggested pesticide residue in tea as a possible mechanism. A number of studies have found a positive association between pesticides and T2D.[29–31] Evidence reviewed by Evangelou *et al.*[32] and Ngwa *et al.*[33] from epidemiological and experimental studies also supports the hypothesis that exposure to pesticides could increase the risk of T2D. Evidence from the Chinese population seems to support this possibility as well. In our previous report, we found that the median level of serum organochlorine pesticides (OCPs) was much higher in Chinese women living in urban Shanghai than levels reported in other populations.[34] The serum concentration of total OCPs was correlated with the amount of tea consumption ($r = 0.14$, $P < 0.05$) in that study.[34] It is possible that the high level of pesticide exposure in tea drinkers might have led to an increased risk of T2D. Direct measurement of pesticide level is needed to confirm this speculation. On the other hand, it is also possible that the less healthy lifestyle (e.g. cigarette smoking, alcohol drinking and lack of leisure time exercise) and poorer health status of tea drinkers compared with non-drinkers may partly explain the positive associations.[35–37] In addition, under-diagnosis of diabetes is more likely to occur among residents with lower income.[38] In our population, the average income of non-current tea drinkers was lower than that of tea drinkers. However, the tea and T2D association persisted after we carefully adjusted for the lifestyle factors and socioeconomic status, although a residual confounding effect cannot be completely ruled out. Our finding of a tea drinking and T2D association among individuals with longer than 10 years of follow-up also argues against the differential under-diagnosis as a sole explanation for the observed association.

One of the symptoms of diabetes is thirst, suggesting that diabetes and pre-diabetes patients might drink more tea, one of the most popular beverages among Chinese adults. Our finding of an association for individuals who started tea drinking more than 10 years before T2D diagnosis appears to argue against diabetes-related symptoms as the explanation. Obesity, central fat deposition and smoking are well-established risk factors for T2D and thus may modify the tea-T2D association.[39–41] However, we did not find that the positive tea-diabetes association varied significantly by BMI, WHR or smoking status.

Previous studies[5,7] have shown an inverse association between tea drinking and T2D risk only in women. In contrast, in the current study, green tea drinking was associated with an increased risk among both women and men, an association supported by self-reported data and measured blood level of caffeine.

To our knowledge, this is the first cohort study to investigate the association between green tea consumption and the risk of T2D in Chinese adults. With a large sample size and high participation rate, these prospective studies increase the validity of results. Furthermore, green tea consumption, albeit self-reported, was assessed comprehensively by including both amounts and duration of drinking. Limitations of our study should also be acknowledged. First, because the assessment of green tea consumption was self-reported rather than measured directly, misclassification bias in tea drinking assessment is unavoidable. However, data from our metabolomics study showed that plasma caffeine level was also associated with diabetes risk. Although plasma caffeine level may reflect other exposures, such as caffeine-containing beverage or food consumption or medication use, we found that the median level of plasma caffeine among tea drinkers was 10 times higher than that of non-tea drinkers, and the self-reported tea drinking amount was significantly associated with plasma caffeine level (correlation coefficient = 0.26, *P*-value <0.0001) in our study population. Because the measurement error for plasma caffeine is unrelated to that of the questionnaire data, when two different measurements reveal a similar association, validity of the observed tea-T2D association is strengthened. Second, the amount of tea consumption was estimated in grams, which may be more accurate but is not directly comparable with the 'cup' unit of measurement used in other studies. Moreover, diagnosis of T2D was also self-reported. Undiagnosed diabetes in the cohort members may have biased our results to null. In addition, we have no data on glycaemic traits in our study, which could be used to validate our findings. Finally, unknown confounding factors may exist, although multiple confounding factors have been adjusted.

In conclusion, results from our prospective cohort studies in Shanghai, China, suggest that green tea consumption is associated with an increased risk of T2D in Chinese adults following a dose-response pattern. Further studies are needed to elucidate the mechanisms underlying the associations, particularly regarding the possible role of pesticide contamination.

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Author Contributions

X.L., X.S. and H.C. performed the statistical analysis; X.L., W.X., H.C. and X.O.S. drafted the manuscript; H.C., Y.G., H.L., B.J., Z.W. and Y.B.X. assisted in interpreting the data and edited the manuscript; Z.W., X.O.S., Y.G. and Y.B.X. designed and managed the Shanghai Women's Health Study (SWHS) and the Shanghai Men's Health Study (SMHS). T.W., R.G. and X.O.S. designed and directed the nested case-control study. All authors have approved the manuscript and X.O.S. takes full responsibility for the work as a whole, including the study design, access to data and the decision to submit and publish the manuscript. All authors read and approved the final manuscript.

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