

Tea consumption and the risk of atherosclerotic cardiovascular disease and all-cause mortality: The China-PAR project

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Abstract

Aims: The role of tea consumption in the primary prevention of atherosclerotic cardiovascular disease remains unclear in cohort studies. This prospective cohort study aimed to investigate the associations of tea consumption with the risk of atherosclerotic cardiovascular disease and all-cause mortality.

Methods: We included 100,902 general Chinese adults from the project of Prediction for ASCVD Risk in China (China-PAR) in 15 provinces across China since 1998. Information on tea consumption was collected through standardized questionnaires. Outcomes were identified by interviewing study participants or their proxies, and checking hospital records and/or death certificates. Cox proportional hazard regression models were used to calculate hazard ratios and their corresponding 95% confidence intervals related to tea consumption.

Results: During a median follow-up of 7.3 years, 3683 atherosclerotic cardiovascular disease events, 1477 atherosclerotic cardiovascular disease deaths, and 5479 all-cause deaths were recorded. Compared with never or non-habitual tea drinkers, the hazard ratio and 95% confidence interval among habitual tea drinkers was 0.80 (0.75–0.87), 0.78 (0.69–0.88), and 0.85 (0.79–0.90) for atherosclerotic cardiovascular disease incidence, atherosclerotic cardiovascular disease mortality, and all-cause mortality, respectively. Habitual tea drinkers had 1.41 years longer of atherosclerotic cardiovascular disease-free years and 1.26 years longer of life expectancy at the index age of 50 years. The observed inverse associations were strengthened among participants who kept the habit during the follow-up period.

Conclusion: Tea consumption was associated with reduced risks of atherosclerotic cardiovascular disease and all-cause mortality, especially among those consistent habitual tea drinkers.

Keywords

Tea consumption, atherosclerotic cardiovascular disease, all-cause mortality, prospective cohort study, Chinese population

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Introduction

Cardiovascular disease (CVD) is the leading cause of premature death worldwide, responsible for more than 330 m years of life lost (YLLs) annually.¹ In 2017, approximate 4.38 m deaths were attributable to CVD, which accounted for over 40.0% of total deaths, and coronary heart disease (CHD) and stroke have become the top two causes in China.²

Tea is one of the most popular beverages globally, especially in Asia. It has attracted great attention from both the public and researchers because of its potential benefits, especially for atherosclerotic cardiovascular disease (ASCVD). Epidemiology studies from other countries have related tea consumption to lower risks of CVD and all-cause mortality. However, study conclusions remain inconsistent and may not be applicable to the Chinese population due to different tea cultures and lifestyles, as well as disease spectrums.^{3–11} Evidence from China is still limited to male gender, local areas, or a certain disease outcome.^{12–17} Therefore, the inverse association of tea consumption with ASCVD and all-cause mortality warrants further investigations based on nationwide cohorts.

This study was aimed to systematically examine the associations between tea consumption and ASCVD morbidity and mortality, as well as all-cause mortality among 100,902 Chinese adults, using data from the project of Prediction for ASCVD Risk in China (China-PAR).

Subjects and methods

Study population

The study population consisted of three cohorts from the China-PAR project, including the China Multi-Center Collaborative Study of Cardiovascular Epidemiology (China MUCA (1998)), the International Collaborative Study of CVD in Asia (InterASIA), and the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study (CIMIC), with detailed description in the Supplemental Material.¹⁸ A total of 113,448 Chinese adults were initially enrolled in 1998, 2000–2001, and 2007–2008 altogether, of which 105,263 participants were followed up for at least once by the end of 2015. We excluded 1896 participants who reported a history of ASCVD or cancer at baseline and 2465 participants with missing data on tea consumption. Finally, 100,902 participants were available for this analysis. This process is showed in detail in the flow chart (Supplemental Material Figure 1).

These preceding studies were approved by the Institutional Review Board at Fuwai Hospital. Informed consent was obtained from each participant prior to data collection.

Assessment of tea consumption and covariates

Tea consumption habit during the past year was assessed face to face through questionnaires (see the Supplemental Material for details) at baseline and during follow-up visits by trained and certificated staff. Participants were classified as habitual tea drinkers (≥ 3 times/week) and never or non-habitual tea drinkers (< 3 times/week). Habitual tea drinkers were required to choose the most frequently consumed types of tea, including green tea, black tea, and other types, while non-*Camellia sinensis* teas were not included.

Information on demographic characteristics, lifestyle risk factors, and family and personal medical history was also collected via standardized questionnaires. Body weight and height were measured twice only wearing light clothes without shoes. Blood pressure was measured three times in a seated position after at least five minutes of rest, and the average of three measurements was used for analysis. In addition, blood specimens were drawn from participants after fasting for at least 10 h to test blood glucose and blood lipid levels.

Outcome measures

ASCVD was defined as the first occurrence of nonfatal acute myocardial infarction (AMI), or CHD death or fatal or non-fatal stroke and the detailed definitions are elaborated in the Supplemental Material.¹⁸ Information on ASCVD, CHD, and stroke incidence or mortality, as well as all-cause mortality during follow-up surveys, was collected by interviewing study participants or their proxies, and checking hospital records and/or death certificates.

Statistical analysis

Age- and sex-adjusted incidence rates per 100,000 person-years of study outcomes were calculated using Poisson regression.¹⁹ We used Cox regression to calculate hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs) in relation to baseline tea consumption, as well as behavior changes of tea consumption during follow-up visits. Moreover, gained event-free years and life expectancy were estimated as the differences of areas under the survival curves based on Cox models with age as the timescale (details in the Supplemental Material).

The influence of tea drinking behavior changes was assessed among participants with two follow-up surveys (2007–2008, and 2012–2015) in the InterASIA and the China MUCA (1998) cohorts. After further excluding participants with missing information on tea consumption during follow-up surveys or having incident ASCVD or those who passed away by the end of 2008, a total of 14,081 participants were included.

These participants were divided into three categories: those who never drank tea (reference group), those who began or stopped drinking tea after the baseline survey, and those who maintained their tea consumption habits all along.

Additional analyses were conducted to compare the effect of different tea types. Subgroup analyses were based on baseline characteristics and their interactions with tea consumption were tested through addition of cross-product terms to the multivariate models. Sensitivity analyses were carried out after excluding the first two years of follow-up.

Multivariate models adjusted for baseline covariates, including age, sex, region (north/south), area (rural/urban), cohort, education level (≥ 12 years or not), family history of ASCVD (yes or no), smoking (yes or no), alcohol drinking (yes or no), physical activity level (ideal or not), dietary factors (ideal or not in consumption of fresh fruits and vegetables, red meat, soybean products, and fish), body mass index (BMI), systolic blood pressure, fasting blood glucose, total cholesterol, and high density lipoprotein-cholesterol. Detailed definitions for ideal physical activity level²⁰ and each dietary factor^{21,22} are described in the Supplemental Material.

Data were analyzed using SAS statistical package (version 9.4. SAS Institute, Inc., Cary, North

Carolina, USA) and graphs were plotted in R (version 3.5.1). All tests were two-sided, and $p < 0.05$ was considered statistically significant.

Results

During the 777,163 person-years (a median of 7.3 years) of follow-up, we recorded 3683 ASCVD events, 1477 ASCVD deaths, and 5479 all-cause deaths. Overall, 31.6% of all participants (48.2% men and 20.4% women) drank tea ≥ 3 times/week at baseline. Of these habitual tea drinkers 49.0% consumed green tea most frequently, 8.0% preferred black tea, and the remaining 43.0% preferred scented tea or other types. Habitual tea drinkers were more likely to be men, smokers, and alcohol drinkers (Table 1).

Association of tea consumption frequency with ASCVD and cause-specific mortality

Habitual tea drinkers had lower incidence and mortality rates of ASCVD, and lower all-cause mortality rate. Compared with never or non-habitual tea drinkers, habitual tea drinkers had lower risks, with the multivariate-adjusted HR of 0.80 (95% CI, 0.75–0.87), 0.82 (95% CI, 0.70–0.96) and 0.80 (95% CI, 0.73–0.87) for ASCVD, CHD, and stroke, respectively (Table 2). And

Table 1. Baseline characteristics of the study participants according to sex and tea drinking habits.

	All participants		Men		Women	
	Never or <3 times/week	≥ 3 times/week	Never or <3 times/week	≥ 3 times/week	Never or <3 times/week	≥ 3 times/week
No. of participants	51.97 \pm 12.42	50.46 \pm 11.64	21,080	19,590	47,937	12,295
Age, years	30.54	61.44	52.78 \pm 12.83	51.05 \pm 11.66	51.61 \pm 12.22	49.52 \pm 11.54
Northern, N (%)	45.41	54.41	10625 (50.40)	9206 (46.99)	20713 (43.21)	8144 (66.24)
Urban, N (%)	6.76	14.37	1668 (7.91)	2794 (14.26)	2996 (6.25)	1788 (14.54)
Education ≥ 12 years, N (%)	11.54	18.20	3573 (16.99)	4041 (20.69)	4373 (9.15)	1741 (14.22)
Smokers, N (%)	17.74	43.53	11242 (53.36)	13434 (68.69)	980 (2.05)	412 (3.36)
Habitual alcohol drinkers, N (%)	13.10	30.60	7327 (34.77)	9201 (46.98)	1708 (3.56)	552 (4.49)
Family history of ASCVD, N (%)	9.87	10.70	2206 (10.46)	2032 (10.37)	4606 (9.61)	1380 (11.22)
BMI, kg/m ²	23.60 \pm 3.62	24.02 \pm 3.59	23.13 \pm 3.39	23.67 \pm 3.46	23.81 \pm 3.70	24.57 \pm 3.72
SBP, mmHg	127.48 \pm 21.36	130.20 \pm 21.32	128.14 \pm 19.81	130.55 \pm 20.16	127.19 \pm 22.01	129.65 \pm 23.03
DBP, mmHg	77.95 \pm 11.64	80.81 \pm 11.75	78.90 \pm 11.73	81.42 \pm 11.66	77.54 \pm 11.58	79.85 \pm 11.83
Fasting blood glucose, mg/dl	91.71 \pm 26.10	92.17 \pm 27.25	90.70 \pm 24.43	92.30 \pm 26.34	92.15 \pm 26.79	91.96 \pm 28.63
Total serum cholesterol, mg/dl	174.57 \pm 35.13	176.44 \pm 35.51	170.87 \pm 34.28	174.59 \pm 35.05	176.20 \pm 35.38	179.39 \pm 36.02
HDL-C, mg/dl	51.52 \pm 12.88	51.05 \pm 12.94	50.33 \pm 13.51	50.16 \pm 13.30	52.05 \pm 12.56	52.45 \pm 12.22
LDL-C, mg/dl	96.29 \pm 29.65	98.31 \pm 30.47	94.36 \pm 29.14	96.55 \pm 30.22	97.11 \pm 29.77	101.05 \pm 30.63

ASCVD, atherosclerotic cardiovascular disease; BMI, body mass index; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein-cholesterol; SBP, systolic blood pressure.

Continuous variables are presented as means (SD) and categorical variables as percentages.

Table 2. Hazard ratios of atherosclerotic cardiovascular disease (ASCVD) incidence associated with habitual tea drinking.

	Never or <3 times/week (n = 69,017)	≥3 times/week (n = 31,885)
ASCVD incidence		
Number of events	2570	1,113
Age, sex-adjusted incidence rate (no./100,000 person-years)	521 (494–549)	462 (431–495)
Age, sex-adjusted HR (95% CI)	1.00	0.89 (0.83–0.96)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.80 (0.75–0.87)
CHD incidence		
Number of events	556	274
Age, sex-adjusted incidence rate (no./100,000 person-years)	114 (102–127)	108 (94–124)
Age, sex-adjusted HR (95% CI)	1.00	0.95 (0.82–1.11)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.82 (0.70–0.96)
Stroke incidence		
Number of events	2049	854
Age, sex-adjusted incidence rate (no./100,000 person-years)	412 (388–438)	359 (332–388)
Age, sex-adjusted HR (95% CI)	1.00	0.87 (0.80–0.95)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.80 (0.73–0.87)

CHD: coronary heart disease; CI: confidence interval; HR: hazard ratio.

^aAdjusted for age, sex, region (north/south), area (rural/urban), cohort, education level (≥12 years or not), family history of ASCVD (yes or no), smoking (yes or no), drinking (yes or no), physical activity level (ideal or not), dietary factors (ideal or not for consumption of fresh vegetables and fruits, red meat, soy products, fish), body mass index, systolic blood pressure, fasting blood glucose, total cholesterol, high-density lipoprotein-cholesterol.

the inverse associations were also observed for ASCVD (HR, 0.78 (95% CI, 0.69–0.88)), stroke (HR, 0.73 (95% CI, 0.63–0.86)) and all-cause mortality (0.85 (95% CI, 0.79–0.90)), while the result for CHD mortality did not reach statistical significance (Table 3). Gender-specific analyses showed that habitual tea drinking could reduce the risk of ASCVD for both men and women. The inverse associations remained robust for incidence and mortality of ASCVD and stroke, and all-cause mortality for men, while for women, only results for ASCVD and CHD incidence reached the statistical significant level (Supplemental Material Tables 1 and 2).

Habitual tea consumption was associated with greater disease-free years and greater life expectancy. For example, habitual tea drinkers could have 1.41, 0.32, and 1.23 years of delay in developing ASCVD, CHD, and stroke compared with never or non-habitual tea drinkers, and their life expectancy was 1.26 years longer at the index age of 50 years (Figure 1).

Association of tea drinking behavior changes with ASCVD and cause-specific mortality

Consistent habitual tea drinkers maintained their habits from baseline to the first follow-up survey for at least 8.2 years on average. The inverse associations of tea consumption from the primary analyses were strengthened. Participants who maintained their habit of tea consumption had much lower risks of ASCVD

(HR, 0.61 (95% CI, 0.46–0.80)), ASCVD mortality (HR, 0.44 (95% CI, 0.26–0.76)), and all-cause mortality (HR, 0.71 (95% CI, 0.56–0.90)), as compared with consistent never or non-habitual tea drinkers (Table 4). Similar enhancement was observed for stroke and CHD among consistent habitual tea drinkers (Supplementary Material Table 3). No significant association of tea consumption with any outcome was observed among those who began or stopped drinking tea during the follow-up period.

Subgroup and sensitivity analysis

Habitual green tea consumption was inversely associated with the risks of all study outcomes except CHD mortality, as compared with those never or non-habitual tea drinkers. No significant association was observed for black tea while other types of tea were inversely and significantly associated with the risk of ASCVD, stroke, and all-cause mortality (Supplemental Material Figure 2). In addition, the inverse associations between habitual tea consumption and ASCVD incidence and mortality as well as all-cause mortality were similar across most subgroups stratified by demographic characteristics and other potential risk factors (Supplemental Material Figures 3–5). The significant inverse associations of tea consumption with ASCVD incidence and mortality as well as all-cause mortality did not substantially

Table 3. Hazard ratios of atherosclerotic cardiovascular disease (ASCVD) and all-cause mortality associated with habitual tea drinking.

	Never or <3 times/week (n = 69,017)	≥3 times/week (n = 31,885)
ASCVD mortality		
Number of deaths	1046	431
Age, sex-adjusted mortality rate (no./100,000 person-years)	210 (191–231)	178 (158–200)
Age, sex-adjusted HR (95% CI)	1.00	0.84 (0.74–0.94)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.78 (0.69–0.88)
CHD mortality		
Number of deaths	345	159
Age, sex-adjusted mortality rate (no./100,000 person-years)	71 (60–83)	62 (52–76)
Age, sex-adjusted HR (95% CI)	1.00	0.93 (0.76–1.13)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.87 (0.71–1.07)
Stroke mortality		
Number of deaths	701	272
Age, sex-adjusted mortality rate (no./100,000 person-years)	139 (123–157)	115 (100–134)
Age, sex-adjusted HR (95% CI)	1.00	0.79 (0.68–0.92)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.73 (0.63–0.86)
All-cause mortality		
Number of deaths	3,787	1,692
Age, sex-adjusted mortality rate (no./100,000 person-years)	779 (745–814)	659 (623–698)
Age, sex-adjusted HR (95% CI)	1.00	0.85 (0.80–0.90)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.85 (0.79–0.90)

CHD: coronary heart disease; CI: confidence interval; HR: hazard ratio.

^aAdjusted for age, sex, region (north/south), area (rural/urban), cohort, education level (≥12 years or not), family history of ASCVD (yes or no), smoking (yes or no), drinking (yes or no), physical activity level (ideal or not), dietary factors (ideal or not for consumption of fresh vegetables and fruits, red meat, soy products, fish), body mass index, systolic blood pressure, fasting blood glucose, total cholesterol, high-density lipoprotein-cholesterol.

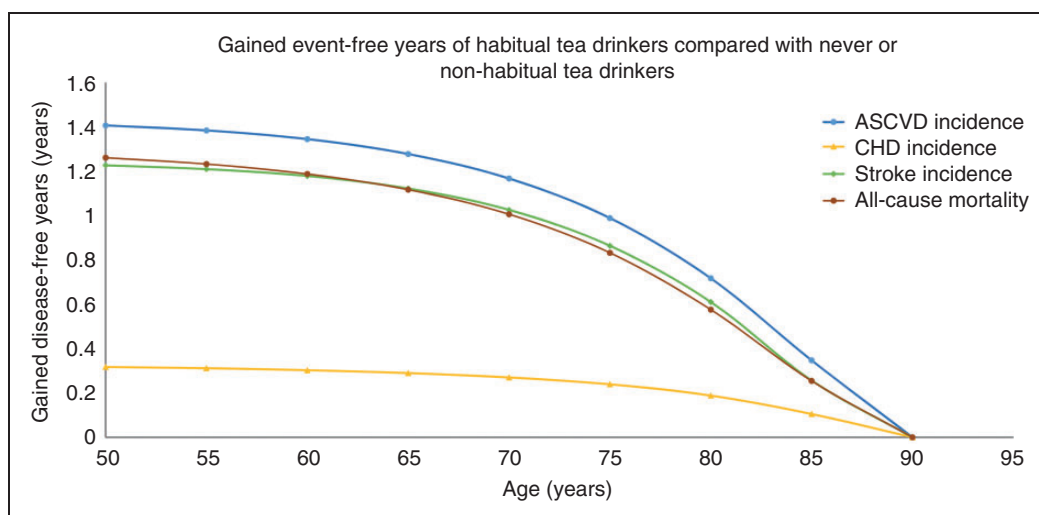


Figure 1. Gained event-free years and gained life expectancy of habitual tea drinkers compared with never or non-habitual tea drinkers. Gained event-free years and gained life expectancy of habitual tea drinkers were estimated as the differences of areas under the survival curves based on Cox models with age as the timescale. ASCVD: atherosclerotic cardiovascular disease; CHD: coronary heart disease.

Table 4. Hazard ratios of atherosclerotic cardiovascular disease (ASCVD) incidence and mortality, and all-cause mortality according to tea drinking behavior changes.

	Participants who never drank tea (n = 6620)	Participants who changed the habit (n = 3194)	Participants who kept the habit (n = 4267)
ASCVD incidence			
Number of events	178	92	94
Age, sex-adjusted incidence rate (no./100,000 person-years)	208 (179–241)	185 (150–228)	170 (137–211)
Age, sex-adjusted HR (95% CI)	1.00	1.00 (0.78–1.29)	0.69 (0.53–0.90)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.89 (0.68–1.15)	0.61 (0.46–0.80)
ASCVD mortality			
Number of deaths	67	37	21
Age, sex-adjusted incidence rate (no./100,000 person-years)	76 (58–100)	68 (48–97)	47 (30–74)
Age, sex-adjusted HR (95% CI)	1.00	1.08 (0.71–1.62)	0.41 (0.25–0.68)
Multivariate-adjusted HR (95% CI) ^a	1.00	1.04 (0.67–1.61)	0.44 (0.26–0.76)
All-cause mortality			
Number of deaths	252	134	136
Age, sex-adjusted incidence rate (no./100,000 person-years)	298 (262–339)	272 (227–326)	236 (196–284)
Age, sex-adjusted HR (95% CI)	1.00	0.99 (0.80–1.22)	0.67 (0.54–0.83)
Multivariate-adjusted HR (95% CI) ^a	1.00	0.96 (0.76–1.21)	0.71 (0.56–0.90)

CHD: coronary heart disease; CI: confidence interval; HR: hazard ratio.

^aAdjusted for age, sex, region (north/south), area (rural/urban), cohort, education level (≥ 12 years or not), family history of ASCVD (yes or no), smoking (yes or no), drinking (yes or no), physical activity level (ideal or not), dietary factors (ideal or not for consumption of fresh vegetables and fruits, red meat, soy products, fish), body mass index, systolic blood pressure, fasting blood glucose, total cholesterol, high-density lipoprotein cholesterol.

change after we excluded the first two years of follow-up (Supplemental Material Table 4).

Discussion

Using large prospective cohorts among general Chinese adults, we have provided novel evidence on the protective role of tea consumption on ASCVD events and all-cause mortality, especially among those who kept the habit all along. The current study indicates that tea might be a healthy beverage for primary prevention against ASCVD and premature death.

Several previous studies assessed the association between tea consumption and CVD and all-cause mortality, but the results remained inconsistent.^{3–17} Studies among Welsh men⁶ and US adults⁷ did not observe significant inverse associations of tea consumption (mainly as black tea) with CHD or CVD risks. In the Japanese population, green tea consumption could reduce the risk of CVD while there was no unanimous conclusion on all-cause mortality.^{8–10} Previous Chinese studies found inverse association between tea consumption and CHD incidence,^{12,13} but the reports for stroke and cause-specific mortality were only based on men.^{14–16} According to our study, habitual tea consumption is associated with a lower risk of ASCVD incidence (including CHD and stroke), ASCVD

mortality (especially for stroke), and all-cause mortality and these inverse associations were persistent across subgroups. More colloquially, habitual tea drinkers might develop ASCVD 1.41 years later or die 1.26 years later than those who never or seldom drank tea. The observed inverse associations were strengthened among participants who stuck to their habit all along. Similarly, previous studies in the USA and in China also reported more evident health effects with longer years of tea consumption.^{7,12}

There was no study in China that assessed the effects of habitual tea consumption on different CVD outcomes in the same population before. According to our results, habitual tea consumption is more protective against stroke than against CHD, especially for men. Consistently, green tea consumption has been reported to be significantly associated with reduced risk of mortality for stroke but not for CHD among the Japanese population.⁸ This might result from the different epidemiological profiles of stroke and CHD. Firstly, consistent with the overall condition in East Asian populations, we had much higher incidence and mortality rates of stroke.^{2,23} Thus, we were more likely to observe significant results for stroke, while the number of CHD cases was less adequate. Secondly, the cardiovascular protective effects of tea could be mediated by ameliorating high blood pressure,²⁴ the high prevalence

of which is a major contributor to the heavy burden of stroke in China.^{23,25}

There were also sex differences in that the inverse associations were more robust across different outcomes for men. One reason might be that the proportion of habitual tea consumers among men was approximately two and a half times as high as that among women. In addition, women had much lower incidence and mortality of ASCVD, though this advantage would be lost after menopause. These differences made it more likely to find robust results among men. Thus, further studies among women with a higher proportion of tea consumption and detailed information on menstruation and hormonal changes might help to clarify these questions.

Tea, especially green tea, is a rich source of flavonoids including mainly epicatechin, catechin, and epigallocatechin-3-gallate (EGCG), etc. Mechanism studies have revealed that these bioactive compounds could attenuate oxidative stress, relieve inflammation, enhance endothelial and cardiomyocyte function.^{26–28} Studies in rat models showed that tea extracts could reduce the formation of vascular reactive oxygen species and improve endothelium-dependent relaxation in the aorta; and could reduce the solubility of cholesterol in micelles and inhibit cholesterol absorption from the intestine.^{29,30} Observational studies and randomized controlled trials (RCTs) have also suggested that these bioactive compounds could ameliorate CVD risk factors including hypertension and dyslipidemia.^{24,28,31,32} Tea polyphenols might be oxidized into pigments and inactivated during fermentation, which might be partly the reason why black tea was prone to be less associated with health benefits in many studies.^{6,7} However, despite these possible mechanisms or interventional studies on the health effects of tea consumption on CVD risk factors, RCTs with clinical CVD events as outcomes are still warranted to confirm our findings and to provide robust evidence in order to develop dietary guidelines and make lifestyle recommendations.

Rigorous field work, reliable information collection process, adjustment of important covariates, and high rate of follow-up (only 7.2% of all participants were out of touch afterward) guaranteed the data quality and the credibility of our results. However, several limitations should be noted. First, the numbers of CHD incidence and death cases were only modest at best, which weakened the statistical power for detecting significant results. Second, the findings for different tea types should be interpreted with cautions, as results might have been contaminated by participants habitually consuming more than one type of tea and the proportion of black tea consumers was limited. Third, some of the recognized targets of tea bioactive compounds including inflammatory and oxidative stress

biomarkers were not measured. In addition, tea consumption is part of a cultural heritage, and its health effects might be confounded by other eating and drinking patterns, for example, consumption of other flavonoid-rich foods or beverages like coffee. Thus, our results from the current study population might be generalizable to the general Chinese adults or other East Asia populations with similar dietary pattern and tea drinking habits but not for the West.

In conclusion, habitual tea consumption could reduce the risk for both ASCVD morbidity and mortality, as well as all-cause mortality in China, and long-term adherence to the habit could provide with stronger protections. Our findings give a further insight into the beneficial role of tea consumption, and have great public health implications for guiding primary prevention among general Chinese adults.

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Author contribution

The authors' responsibilities were as follows, WXY: performed the statistical analysis, interpreted the data and drafted the initial manuscript; LF: performed the statistical analysis, interpreted the data, and critically reviewed the manuscript; LJ, YX: interpreted the data, and critically reviewed the manuscript; CJc, CJ, WXg, LXf, HJ, LY, ZL, SC, HD, YL, LXq, WXp, and WS: performed data acquisition and critically reviewing the manuscript; GD: conceived and designed the study, performed data acquisition and critically reviewing the manuscript; and all authors: read and approved the final manuscript.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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