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Tea consumption and risk of ischaemic heart disease

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ABSTRACT

Objective To prospectively examine the association between tea consumption and the risk of ischaemic heart disease (IHD).

Methods Prospective study using the China Kadoorie Biobank; participants from 10 areas across China were enrolled during 2004–2008 and followed up until 31 December 2013. After excluding participants with cancer, heart disease and stroke at baseline, the present study included 199 293 men and 288 082 women aged 30–79 years at baseline. Information on IHD incidence was collected through disease registries and the new national health insurance databases.

Results During a median follow-up of 7.2 years, we documented 24 665 (7.19 cases/1000 person-years) incident IHD cases and 3959 (1.13 cases/1000 person-years) major coronary events (MCEs). Tea consumption was associated with reduced risk of IHD and MCE. In the whole cohort, compared with participants who never consumed tea during the past 12 months, the multivariable-adjusted HRs and 95% CIs for less than daily and daily tea consumers were 0.97 (0.94 to 1.00) and 0.92 (0.88 to 0.95) for IHD, 0.92 (0.85 to 1.00) and 0.90 (0.82 to 0.99) for MCE. No linear trends in the HRs across the amount of tea were observed in daily consumers for IHD and MCE ($P_{\text{Linear}} > 0.05$). The inverse association between tea consumption and IHD was stronger in rural ($P_{\text{Interaction}} = 0.006$ for IHD, < 0.001 for MCE), non-obese ($P_{\text{Interaction}} = 0.012$ for MCE) and non-diabetes participants ($P_{\text{Interaction}} = 0.004$ for IHD).

Conclusions In this large prospective study, daily tea consumption was associated with a reduced risk of IHD.

INTRODUCTION

Tea is one of the most widely consumed beverages in the world, especially in China. Polyphenols, particularly flavonoids, which are of great abundance in tea, have been experimentally demonstrated to inhibit oxidation reactions caused by free radicals and prevent or delay atherosclerosis.^{1–2} Flavonoids have also been shown to have antithrombotic³ and anti-inflammatory properties,⁴ and may reverse endothelial dysfunction.⁵ Experimental evidence may collectively support a protective effect of tea consumption on ischaemic heart disease (IHD). Several previous prospective studies have related tea consumption with reduced risk of IHD,^{6–10} but several have not.^{11–16} These studies mostly had small sample sizes and were too low-powered to obtain precise effect estimates.

We therefore used data from the China Kadoorie Biobank (CKB) study,^{17–18} an ongoing cohort of

0.5 million adults, to prospectively examine the association of regular consumption of tea with the risk of IHD.

SUBJECTS AND METHODS

Study population

Details of the CKB study design and characteristics of the study participants have been described elsewhere.^{17–18} In brief, 512 891 participants aged 30–79 years were recruited between 2004 and 2008 from five urban and five rural regions of China.

A total of 10 964 men and 14 549 women was excluded from the present study because of a history of cancer ($n=2577$), heart disease ($n=15 472$) or stroke ($n=8884$) at baseline. Additionally, three participants who were recorded with an implausible censoring date for loss to follow-up were excluded. The final analyses included 199 293 men and 288 082 women.

Assessment of tea consumption

In the baseline questionnaire, all CKB participants were asked to report their frequency of tea consumption during the past 12 months. Five frequency categories were provided (never, only occasionally, only at certain seasons, monthly but less than weekly and at least once a week). Participants who consumed at least once a week were further asked about days consuming in a typical week (1–2 days/week, 3–5 days/week or almost every day), amount of tea (in 300 mL-sized cup) consumed in one consuming day, tea leaves (in gram) added each time, times of changing tea leaves in one consuming day, type of tea consumed most commonly (green tea, oolong tea, black tea or others) and age when they started tea consumption in most weeks. Participants were provided a pictorial guide to gauge the amount of tea in cup and tea leaves. The tea leaves added in one consuming day was calculated by multiplying amount added each time by times of changing tea leaves. To test the reproducibility of tea consumption frequency, 15 728 participants who completed the same question on frequency of tea consumption twice at a mean interval of 17 days were analysed. The weighted kappa coefficient for tea consumption was 0.77.

For the present analyses, all participants were grouped into three categories regarding their consumption frequency: never, less than daily and daily. Daily tea consumers were further categorised, according to rounded quartiles, as adding tea leaves 0.1–2.0, 2.1–3.0, 3.1–5.0 and > 5.0 g/day; or consuming 1–2, 3–4, 5–6 and ≥ 7 cups of tea/day.

Assessment of covariates

Covariate information was obtained from baseline questionnaire, including sociodemographic characteristics (age, sex, education, occupation, household income and marital status), lifestyle behaviours (alcohol consumption, tobacco smoking, physical activity and intakes of red meat, fresh fruits and vegetables), personal medical history (hypertension, diabetes, chronic hepatitis or cirrhosis, peptic ulcer and gallstones or cholecystitis), women's menopausal status and family history of heart attack. The daily level of physical activity was calculated by multiplying the metabolic equivalent tasks (METs) value for a particular type of physical activity by hours spent on that activity per day and summing the MET-hours for all activities. Habitual dietary intake in the past year was assessed by a qualitative food frequency questionnaire. Prevalent hypertension was defined as measured systolic blood pressure ≥ 140 mm Hg, measured diastolic blood pressure ≥ 90 mm Hg, self-reported diagnosis of hypertension or self-reported use of antihypertensive medication at baseline. Prevalent diabetes was defined as measured fasting blood glucose ≥ 7.0 mmol/L, measured random blood glucose ≥ 11.1 mmol/L or self-reported diagnosis of diabetes. Trained staff undertook baseline measurements of bodyweight, height, waist circumference and blood pressure.

Assessment of outcome

The vital status of all CKB participants was obtained through linkage with local disease surveillance points system death registries¹⁹ and residential records. Information on IHD incidence was collected through linkage with established disease registries, electronic linkage with the new national health insurance (HI) claim databases.¹⁸ Participants who failed to be linked to local HI database were actively followed annually by staff to ascertain their status including hospital admission, death and moving out of the study area.

Trained staff blinded to baseline information coded all diagnoses and deaths using the International Classification of Diseases, Tenth Revision. The primary outcomes were (1) incident major coronary events (MCEs) including fatal IHD (I20–I25) and non-fatal myocardial infarction (I21–I23); and (2) a broader IHD outcome including incident fatal and non-fatal IHD (I20–I25), of which 80% coded as chronic IHD (I25). The outcome adjudication process of incident IHD cases has been started since 2014. The medical records of cases were retrieved, and the diagnosis was adjudicated centrally by qualified cardiovascular specialists blinded to study assay. By August 2015, of 12 923 incident IHD cases reported since baseline and whose medical records have been retrieved, the diagnosis was confirmed in 82.4% cases.

Statistical analysis

Person-years at risk were calculated for each participant from baseline (2004–2008) to the diagnosis of the outcome, death, loss to follow-up or 31 December 2013, whichever occurred first. By 31 December 2013, 2411 (0.5%) participants were lost to follow-up. Cox proportional hazards model was used to estimate the HR and 95% CI for the associations between tea consumption and outcomes with age as the underlying time scale, and stratified jointly by survey region and age at baseline in 5-year interval. The proportional hazards assumption for the Cox model was checked using Schoenfeld residuals and no violation was found.

Multivariate models were adjusted for established and potential risk factors for IHD: age, sex, level of education, marital

status, alcohol consumption, smoking status, physical activity, body mass index (BMI), intake frequencies of red meat, fresh fruits and vegetables, prevalent hypertension and diabetes at baseline, menopausal status (for women only) and family history of heart attack. Tests for linear trend were only conducted in daily consumers by modelling the amount of tea consumption (in g/day or cup/day) as a continuous variable in separate models.

We examined the associations between tea consumption and outcomes according to the types of tea and years of tea consumption, all as compared with those who did not consume tea during the past 12 months. We also examined whether the associations of tea consumption with outcomes differed according to age, region, smoking status, alcohol consumption, the level of physical activity, BMI, hypertension at baseline and diabetes at baseline. In the subgroup analyses aforementioned, we combined four categories of daily tea consumption into one to ensure sufficient statistical power under the circumstance that no linear trend was observed across the amount of tea leaves added in the present analyses. The test for interaction was performed using likelihood ratio test, which involved comparing models with and without cross-product term between the baseline stratifying variable and tea consumption as an ordinal variable.

The statistical analyses were performed with Stata (V13.1, Stata). All *p* values were two-sided, and statistical significance was defined as *p* < 0.05.

RESULTS

Of 487 375 study participants, 128 280 (26.3%) reported consuming tea almost every day. Table 1 presents age-adjusted and region-adjusted baseline characteristics of the study participants according to tea consumption. Compared with participants who never consumed tea during the past 12 months, daily tea consumers who usually used more tea leaves were more likely to be younger, and urban residents, and more likely to smoke tobacco and drink alcohol. Green tea was the most common type of tea consumed in daily tea consumers.

During a median follow-up of 7.2 years, we documented 24 665 (7.19 cases/1000 person-years) incident IHD cases and 3959 (1.13 cases/1000 person-years) MCEs (including 2601 fatal IHD and 1358 non-fatal myocardial infarction). In the whole cohort, compared with participants who never consumed tea during the past 12 months, the multivariable-adjusted HRs (95% CIs) for IHD were 0.97 (0.94 to 1.00) for those who consumed tea less than daily, and 0.92 (0.87 to 0.97), 0.91 (0.85 to 0.98), 0.92 (0.87 to 0.98) and 0.91 (0.86 to 0.97) for those who consumed 0.1–2.0, 2.1–3.0, 3.1–5.0 and >5.0 g of tea leaves per day, respectively (table 2). The corresponding HRs (95% CIs) for MCE were 0.92 (0.85 to 1.00), 0.83 (0.74 to 0.95), 0.99 (0.85 to 1.15), 0.87 (0.75 to 1.00) and 0.97 (0.84 to 1.11). The HRs across four groups in daily consumers were statistically similar (*p* values for linear trend: 0.465 for IHD and 0.218 for MCE). After merging categories, the HRs (95% CIs) for daily consumers were 0.92 (0.88 to 0.95) for IHD and 0.90 (0.82 to 0.99) for MCE compared with participants who never consumed tea during the past 12 months. Tea consumption was consistently associated with reduced risks of IHD and MCE among both men and women (*p* values for interaction with sex: 0.158 for IHD and 0.659 for MCE). Sex-specific associations between tea consumption and both outcomes are presented in online supplementary table S1.

We also examined the associations of tea consumption measured in cups per day with the risk of IHD and MCE. The

Table 1 Baseline characteristics of the study participants according to tea consumption

	Men (n=199 293)						Women (n=288 082)					
	Never	Less than daily	Daily (g/day)				Never	Less than daily	Daily (g/day)			
			0.1–2.0	2.1–3.0	3.1–5.0	>5.0			0.1–2.0	2.1–3.0	3.1–5.0	>5.0
Participants (n)	38 360	78 466	26 654	12 661	19 602	23 550	131 974	110 295	22 548	9510	7743	6012
Age (year)	53.9	50.1	53.4	53.0	52.4	51.2	51.7	48.9	51.0	51.2	50.6	49.9
Rural area (%)	60.3	56.2	63.9	67.2	52.2	48.4	57.0	52.8	66.7	84.0	45.0	49.4
Married (%)	91.6	93.2	92.7	93.3	93.9	94.1	88.9	89.7	90.7	90.3	90.3	90.8
Middle school and higher (%)	52.1	58.1	58.8	60.5	60.7	60.5	38.9	46.0	47.9	48.8	48.9	47.5
Current smoker (%)	49.8	58.1	67.5	69.9	72.2	76.9	1.9	2.2	3.5	4.7	4.1	6.3
Weekly alcohol drinking (%)	22.8	32.0	39.3	40.3	42.7	42.6	1.2	2.3	4.5	5.7	5.1	7.4
Physical activity (MET hour/day)	22.9	23.1	22.0	22.5	21.8	21.8	21.0	21.0	20.0	19.9	20.2	19.8
Body mass index (kg/m ²)*	23.1	23.4	23.4	23.4	23.6	23.6	23.5	23.9	24.1	24.1	24.3	24.6
Average weekly consumption†												
Red meat (day)	3.7	3.9	4.1	3.9	4.2	4.3	3.4	3.6	3.8	3.4	3.8	3.8
Fresh vegetables (day)	6.8	6.8	6.9	6.8	6.9	6.9	6.8	6.8	6.9	6.9	6.9	6.9
Fresh fruits (day)	2.1	2.2	2.4	2.2	2.4	2.4	2.5	2.9	3.2	3.0	3.3	3.2
Diabetes (%)	4.9	5.0	5.0	5.0	5.4	5.5	5.4	5.6	6.2	5.6	5.7	5.9
Hypertension (%)	34.7	35.3	36.2	37.3	37.9	37.1	31.7	31.8	34.2	33.6	35.3	35.5
Family history of heart attack (%)	6.4	6.5	6.5	6.6	6.7	7.1	5.5	5.9	6.0	6.0	6.2	6.8
Postmenopausal (%)	–	–	–	–	–	–	51.2	50.5	50.3	50.0	49.7	49.6
Characteristics of daily tea consumer												
Age of starting tea consumption (year)	–	–	28.6	28.1	27.4	26.0	–	–	27.0	26.9	25.8	24.6
Years of tea consumption (year)	–	–	23.9	24.3	25.1	26.5	–	–	23.8	23.9	25.1	26.3
Green tea consumer (%)	–	–	82.7	82.4	82.4	82.3	–	–	91.6	91.2	92.0	91.5

All variables were adjusted for age and survey regions, as appropriate. All exposures were associated with tea consumption, with $p < 0.001$ for trend across categories, except for diabetes (men: $p = 0.004$; women: $p = 0.003$), and green tea consumer in women ($p = 0.309$). Tests for linear trend were only conducted in daily consumers by modelling the amount of tea consumption (in g/day) as a variable in regression models.

*Body mass index was defined as the bodyweight divided by the square of the height.

†Average weekly consumptions of red meat, fresh vegetables and fruits were calculated by assigning participants to the midpoint of their consumption category. MET, metabolic equivalent task.

results were approximately similar (see online supplementary table S2). The associations of tea consumption with IHD and MCE did not change appreciably with additional adjustment for occupation and household income; or additional adjustment for histories of chronic hepatitis or cirrhosis, peptic ulcer and gallstone or cholecystitis; or adjustment for waist circumference instead of BMI; or exclusion of participants whose outcomes occurred during the first two years of follow-up; or exclusion of participants with prevalent diabetes at baseline; or exclusion of former tea consumers from never group (see online supplementary table S4).

We further performed subgroup analyses according to types of tea consumed most commonly and years of tea consumption in participants who consumed tea at least once a week. Similar associations of tea consumption with IHD and MCE were observed for both green tea consumers and non-green tea consumers. The inverse associations of daily tea consumption with both outcomes appeared to be stronger among participants who reported longer years of tea consumption (table 3).

We also analysed the associations of tea consumption with IHD and MCE according to potential baseline risk factors. The associations were similar across subgroups stratified according to age, smoking status, alcohol consumption, physical activity and prevalent hypertension (all p values for interaction > 0.05). Significant differences in association with IHD and MCE across strata were observed for the region (p values for interaction: 0.006 for IHD and < 0.001 for MCE), with stronger inverse associations among participants who resided in rural regions. Stronger inverse associations were also observed among

participants with BMI < 24 kg/m² for MCE (p value for interaction: 0.012) and those without diabetes at baseline for IHD (p value for interaction: 0.004) (figure 1 and online supplementary table S3).

DISCUSSION

In this large prospective Chinese cohort, tea consumption was associated with a reduced risk of IHD. Compared with participants who never consumed tea during the past 12 months, those who consumed tea daily showed an 8% relative risk reduction in IHD and a 10% lower risk of MCE. The protective effect of tea consumption on IHD was stronger among participants who drank tea for more than three decades, who resided in a rural region, who had normal or lower BMI or who did not have diabetes at baseline.

Previous prospective studies have provided inconsistent results on the relationship between tea consumption and IHD.^{6–16} Two studies^{7, 8} conducted in the Dutch population have shown that statistically significant protective effect of tea consumption, mainly black tea, on coronary heart disease (CHD) incidence were only observed for participants who drank tea > 6 cups/day (HR 0.64, 95% CI 0.46 to 0.90)⁷ or for those who drank > 375 mL/day (0.57, 0.33 to 0.98).⁸ The Netherlands Cohort Study also observed an inverse association between an increment of 253 mL/day tea consumption and IHD mortality in men (HR 0.91, 95% CI 0.83 to 1.00).¹⁰ Findings from a Japanese population⁹ showed that the multivariable-adjusted HR (95% CI) for women drinking 1–6 cups/week, 1–2 cups/day, 3–5 cups/day and > 6 cups/day were 0.34 (0.06 to 1.75), 0.28 (0.07 to 1.11), 0.39

Table 2 Association of tea consumption (in g/day) with the risk of ischaemic heart disease (IHD) among 487 375 participants*

Endpoints	Daily (g/day)					p for trend*		
	Never	Less than daily	0.1–2.0	2.1–3.0	3.1–5.0		>5.0	All
IHD (n)								
Person years	1 197 163	1 330 065	343 163	155 009	192 500	211 506	902 178	
Cases	10 013	8266	2407	1112	1398	1469	6386	
Cases/person-years (1/1000)	8.36	6.21	7.01	7.17	7.26	6.95	7.08	
Model 1	1.00	0.97 (0.94–1.00)	0.94 (0.90–0.99)	0.93 (0.87–1.00)	0.96 (0.90–1.02)	0.97 (0.91–1.03)	0.95 (0.92–0.99)	0.698
Model 2	1.00	0.98 (0.95–1.02)	0.94 (0.90–0.99)	0.94 (0.87–1.01)	0.95 (0.90–1.01)	0.95 (0.89–1.01)	0.95 (0.91–0.98)	0.793
Model 3	1.00	0.97 (0.94–1.00)	0.92 (0.87–0.97)	0.91 (0.85–0.98)	0.92 (0.87–0.98)	0.91 (0.86–0.97)	0.92 (0.88–0.95)	0.465
MCE								
Person years	1 224 560	1 351 949	349 206	157 565	196 065	215 249	918 085	
Cases (n)	1518	1192	433	264	256	296	1249	
Cases/person-years (1/1000)	1.24	0.88	1.24	1.68	1.31	1.38	1.36	
Model 1	1.00	0.88 (0.81–0.96)	0.84 (0.74–0.95)	0.97 (0.84–1.13)	0.87 (0.75–1.00)	1.02 (0.89–1.17)	0.90 (0.83–1.00)	0.028
Model 2	1.00	0.94 (0.87–1.02)	0.86 (0.76–0.98)	1.02 (0.88–1.19)	0.90 (0.78–1.04)	1.02 (0.88–1.17)	0.93 (0.85–1.03)	0.138
Model 3	1.00	0.92 (0.85–1.00)	0.83 (0.74–0.95)	0.99 (0.85–1.15)	0.87 (0.75–1.00)	0.97 (0.84–1.11)	0.90 (0.82–0.99)	0.218

Values are HRs (95% CIs) unless stated otherwise. Multivariate models were adjusted for: model 1: age (years) and sex (male or female); model 2: additionally included level of education (no formal school, primary school, middle school, high school, college, or university or higher); marital status (married, widowed, divorced or separated, or never married); alcohol consumption (never, occasional; former and having quit ≤ 2 , 3–4, 5–9, 10–19 or ≥ 20 years; current smoking 1–4, 5–9, 10–14, 15–19, 20–24 or ≥ 25 cigarettes/day); physical activity (MET hour/day); intake frequencies of red meat, fruits and vegetables (daily, 4–6 days/week, 1–3 days/week, monthly, or rarely or never); family history heart attack (presence, absence or unknown); model 3: additionally included body mass index; prevalent hypertension and diabetes at baseline (presence or absence).

*Tests for linear trend were only conducted in daily consumers by modelling the amount of tea consumption (in g/day) as a variable in regression models.

MCE, major coronary events; MET, metabolic equivalent task.

Table 3 Subgroup analyses of associations between tea consumption and risk of ischaemic heart disease (IHD) according to types of tea and years of tea consumption

Subgroups	Never			Less than daily*			Daily		
	No. of cases	Cases/person-years (1/1000)	HR	No. of cases	Cases/person-years (1/1000)	HR (95% CI)	No. of cases	Cases/person-years (1/1000)	HR (95% CI)
IHD	10 013	8.36	1.00						
Type of tea									
Green tea				1363	6.58	0.99 (0.93–1.05)	5690	7.38	0.91 (0.87–0.95)
Non-green tea				203	4.46	0.92 (0.79–1.06)	696	5.32	0.89 (0.81–0.98)
Years of tea consumption									
≤10				507	5.38	0.95 (0.86–1.04)	1079	6.52	0.96 (0.90–1.03)
11–30				613	5.19	1.01 (0.93–1.10)	2242	5.01	0.91 (0.86–0.97)
≥31				446	11.02	0.94 (0.85–1.04)	3065	10.62	0.84 (0.79–0.90)
MCE	1518	1.24	1.00						
Type of tea									
Green tea				224	1.06	0.99 (0.85–1.16)	1123	1.43	0.91 (0.81–1.01)
Non-green tea				38	0.82	1.07 (0.75–1.53)	126	0.95	1.03 (0.81–1.32)
Years of tea consumption									
≤10				74	0.78	0.97 (0.76–1.24)	194	1.15	1.01 (0.86–1.19)
11–30				98	0.82	1.07 (0.85–1.33)	372	0.82	0.88 (0.76–1.01)
≥31				90	2.16	0.93 (0.73–1.18)	683	2.31	0.87 (0.75–1.00)

Multivariate HRs are calculated using Cox proportional hazard model with adjustment for age (years), sex (male or female), level of education (no formal school, primary school, middle school, high school, college, or university or higher), marital status (married, widowed, divorced or separated, or never married), alcohol consumption (never; occasional; former and having quit ≤2, 3–4 or ≥5 years; weekly consuming 1–286, 287–426 or ≥427 g of alcohol for men or 1–146, 147–286 or ≥287 g of alcohol for women), smoking status (never; occasional; former and having quit ≤2, 3–4, 5–9, 10–19 or ≥20 years; current smoking 1–4, 5–9, 10–14, 15–19, 20–24 or ≥25 cigarettes/day), physical activity (MET hour/day), intake frequencies of red meat, fruits and vegetables (daily, 4–6 days/week, 1–3 days/week, monthly, or rarely or never), family history heart attack (presence, absence or unknown), body mass index, prevalent hypertension and diabetes at baseline (presence or absence).

*Excluded 153 120 participants who reported their tea consumption as 'only occasionally, only at certain seasons or monthly but less than weekly' and whose information on commonly consumed tea type or years of tea consumption was not collected.
MCE, major coronary events; MET, metabolic equivalent task.

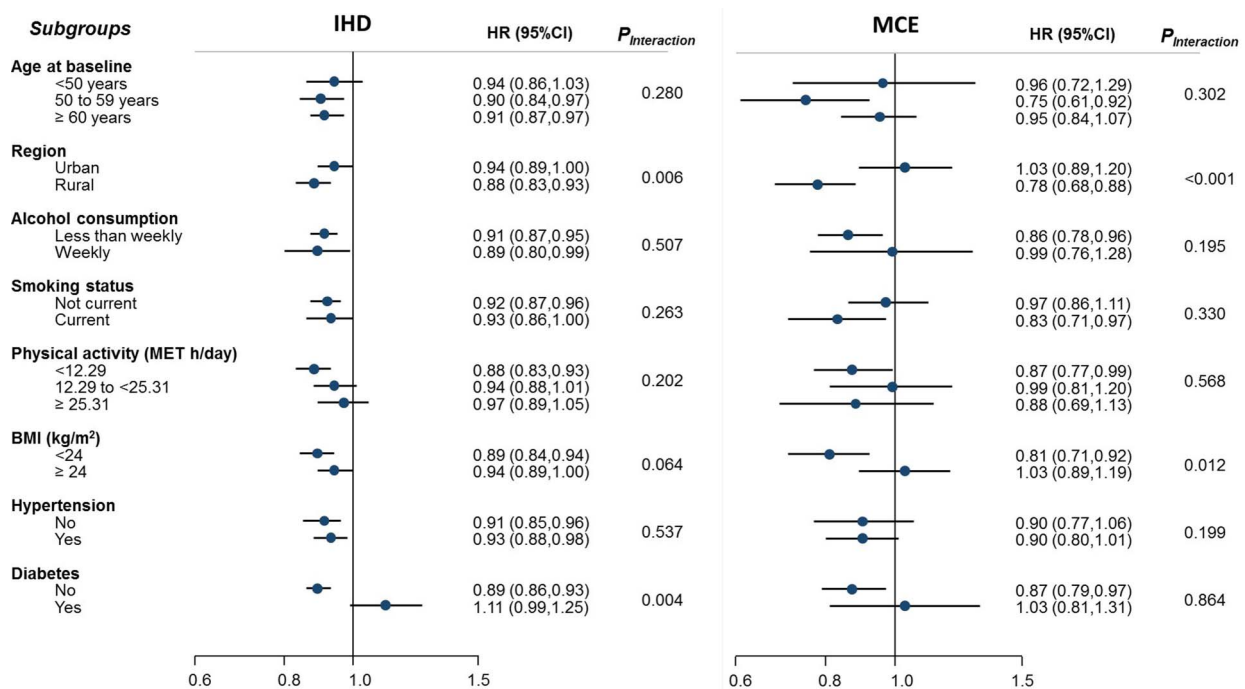


Figure 1 Subgroup analysis of associations between daily tea consumption and risk of ischaemic heart disease (IHD) according to potential baseline risk factors. HRs for IHD or major coronary events (MCEs) are for comparison of daily tea consumer with participants who never consumed tea during the past 12 months. Risk estimates for other categories of tea consumption are shown in online supplementary table S3. Solid dots represent point estimates, and horizontal lines represent 95% CIs. An HR of <1 means daily tea consumption was associated with a reduction in the risk of the outcome of interest. The tests for interaction were performed using likelihood ratio tests, which involved comparing models with and without cross-product terms between the baseline stratifying variable and tea consumption as an ordinal variable. BMI, body mass index; MET, metabolic equivalent task.

(0.18 to 0.85) and 0.42 (0.15 to 0.92) for CHD mortality compared with non-drinkers of green tea. The inverse association was not observed among men. Another prospective study of Chinese⁶ reported that green tea consumption was associated with lower risk of CHD incidence (0.89, 0.81 to 0.98) compared with non-green tea consumers. No statistically significant association was found between tea consumption and IHD in other prospective studies conducted in the Japanese^{11 16} and Western population.^{12–15} In the present study, we observed that daily tea consumers were at a lower risk of IHD incidence than those who drank less than daily. However, the increasing amount of tea did not further reduce the risk of IHD, suggesting a possible threshold effect. Possible mechanisms might involve the bioaccessibility and bioavailability of polyphenols of tea,²⁰ which needed to be verified by further studies.

Different types of tea differ in active ingredients, such as flavonoids, due to the difference in the degree of fermentation during the manufacturing process,²⁰ suggesting potentially different cardiovascular protective effects. However, we found similar effects of green tea and non-green tea on reduced risk of IHD. Fewer participants in our population consumed other tea than green tea, which precluded further comparison of effects of black tea, oolong tea or other types of tea on IHD. Previous studies, either in the population mainly drinking black tea^{7–8 10} or in the population mainly drinking green tea,^{6 9} have observed the protective effect of tea consumption on IHD.

In the subgroup analysis by years of tea consumption, we found that the protective effect of tea consumption on the risk of IHD appeared to be stronger in participants who reported a longer history of consumption. Sesso *et al*¹² have also indicated that long-term tea consumption may be necessary to confer health benefits. It has been suggested that there is no long-term storage of polyphenols in the body.²¹ Frequent exposure to physiological concentration of active ingredients over a long period of time may be necessary for beneficial effect.

Previous studies^{6–8 10 16} found that the association between tea consumption and the risk of IHD was consistent across subgroups defined by age, smoking status, BMI and the prevalence of hypertension and diabetes. However, in the present analyses, the protective effect of tea consumption on IHD was only observed in non-obese or non-diabetic participants. Polyphenols from tea, especially flavonoids, are the predominant contributor to the protective health effect.²² The mutual relationship between polyphenols and gut microbiota has received increasing attention in recent years.²³ The gut microbiota transform polyphenols into their potentially more bioactive metabolites. The abundance and composition of gut microbiota have also been recently related to the obesity,²⁴ diabetes²⁵ and cardiovascular disease.²⁶ Whether the altered gut microbiota among patients who are obese or diabetic may influence the assimilation and metabolism of polyphenols has yet to be further investigated. In addition, we observed that the protective effect of tea consumption on IHD was more pronounced in rural participants. It is possible that the flavonoids are easily available from other various food sources such as vegetables and fruits²⁷ in the urban diet, and tea consumption added only modestly beneficial effect on IHD.

To our knowledge, this is by far the largest prospective study assessing the association between tea consumption and incident IHD. We have carefully controlled for established and potential risk factors for IHD. We measured tea consumption in gram of tea leaves added, which may be a better measure of tea

consumption and at least partly reflect the intake amount of active ingredient.

A few limitations need to be considered. Tea consumption was self-reported, raising the possibility of misclassification. The questions on tea consumption have not yet validated directly. However, measurement errors in the prospective study design may be non-differential, and the association is more likely to be attenuated towards the null. Tea consumption may be correlated with other dietary habits and lifestyle behaviours. Residual confounding by other unmeasured or unknown factors was still possible. For example, coffee consumption may be a confounder but was not collected in this population at baseline. However, coffee is rarely consumed in the present population. Therefore, it is less likely that coffee consumption confounds the observed association substantially. Further, information was not available on tea brewing methods, which may influence the release of active ingredients of tea.²⁸ Lack of detailed dietary information in this study limited our ability to examine whether population-specific dietary patterns modify the association between tea consumption and IHD and generalise the results to other population. Reverse causality could happen. Participants with diagnosed or subclinical chronic diseases may change consumption habits. However, we excluded participants with major diseases in our analyses. Moreover, the results did not change appreciably when we additionally adjusted for digestive system

Key messages

What is already known on this subject?

- ▶ Previous prospective cohort studies observed inconsistent results on the role of tea in the prevention of ischaemic heart disease (IHD). In addition, evidence from the Netherlands and Japan suggested that the association might be dose–response relationship in daily tea consumers. However, these studies mostly had small sample sizes and were too low-powered to obtain precise effect estimates, leaving the relation between the tea consumption and IHD still less well established.

What might this study add?

- ▶ Daily tea consumption was associated with a reduced risk of IHD in Chinese tea consumers. Intriguingly, daily tea consumers were at a lower risk of IHD incidence than those who drank less than daily, but the increasing amount of tea did not further reduce the risk.
- ▶ The protective effect of tea consumption on IHD appeared to be stronger among participants who reported longer years of tea consumption, resided in rural regions, participants with body mass index <24 kg/m², and those without diabetes at baseline.
- ▶ In addition to measuring tea consumption by cups, which conducted by previous studies, we measured tea consumption in gram of tea leaves added, which may be a better measure of tea consumption and at least partly reflect the intake amount of active ingredient.

How might this impact on clinical practice?

- ▶ The present study yields compelling evidence on understanding the role of tea in cardiovascular health and referring tea as a healthy beverage.

disorders or excluded participants who had IHD event during the first two years of follow-up.

In conclusion, data from this largest prospective cohort of Chinese adults showed that daily tea consumption was associated with a decreased risk of IHD incidence. Given the observational nature, this study alone could not establish a causal relationship. Further randomised studies may be needed to confirm the protective effect of tea consumption on IHD.

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REFERENCES

- Higdon JV, Frei B. Tea catechins and polyphenols: health effects, metabolism, and antioxidant functions. *Crit Rev Food Sci Nutr* 2003;43:89–143.
- Cheng TO. All teas are not created equal: the Chinese Green tea and cardiovascular health. *Int J Cardiol* 2006;108:301–8.
- Kang WS, Lim IH, Yuk DY, et al. Antithrombotic activities of Green tea catechins and (-)-epigallocatechin gallate. *Thromb Res* 1999;96:229–37.
- Li R, Huang YG, Fang D, et al. (-)-Epigallocatechin gallate inhibits lipopolysaccharide-induced microglial activation and protects against inflammation-mediated dopaminergic neuronal injury. *J Neurosci Res* 2004;78:723–31.
- Vita JA. Tea consumption and cardiovascular disease: effects on endothelial function. *J Nutr* 2003;133:3293S–7S.
- Tian C, Huang Q, Yang L, et al. Green tea consumption is associated with reduced incident CHD and improved CHD-related biomarkers in the Dongfeng-Tongji cohort. *Sci Rep* 2016;6:24353.
- de Koning Gans JM, Uiterwaal CS, van der Schouw YT, et al. Tea and coffee consumption and cardiovascular morbidity and mortality. *Arterioscler Thromb Vasc Biol* 2010;30:1665–71.
- Geleijnse JM, Launer LJ, Van der Kuip DA, et al. Inverse association of tea and flavonoid intakes with incident myocardial infarction: the Rotterdam Study. *Am J Clin Nutr* 2002;75:880–6.
- Mineharu Y, Koizumi A, Wada Y, et al. Coffee, Green tea, black tea and oolong tea consumption and risk of mortality from cardiovascular disease in Japanese men and women. *J Epidemiol Community Health* 2011;65:230–40.
- Leurs LJ, Schouten LJ, Goldbohm RA, et al. Total fluid and specific beverage intake and mortality due to IHD and stroke in the Netherlands Cohort Study. *Br J Nutr* 2010;104:1212–21.
- Kokubo Y, Iso H, Saito I, et al. The impact of Green tea and coffee consumption on the reduced risk of stroke incidence in Japanese population: the Japan public health center-based study cohort. *Stroke* 2013;44:1369–74.
- Sesso HD, Paffenbarger RS Jr, Oguma Y, et al. Lack of association between tea and cardiovascular disease in college alumni. *Int J Epidemiol* 2003;32:527–33.
- Hirvonen T, Pietinen P, Virtanen M, et al. Intake of flavonols and flavones and risk of coronary heart disease in Male smokers. *Epidemiology* 2001;12:62–7.
- Woodward M, Tunstall-Pedoe H. Coffee and tea consumption in the Scottish Heart Health Study follow up: conflicting relations with coronary risk factors, coronary disease, and all cause mortality. *J Epidemiol Community Health* 1999;53:481–7.
- Rimm EB, Katan MB, Ascherio A, et al. Relation between intake of flavonoids and risk for coronary heart disease in male health professionals. *Ann Intern Med* 1996;125:384–9.
- Kuriyama S, Shimazu T, Ohmori K, et al. Green tea consumption and mortality due to cardiovascular disease, cancer, and all causes in Japan: the Ohsaki study. *JAMA* 2006;296:1255–65.
- Chen Z, Lee L, Chen J, et al. Cohort profile: the Kadoorie Study of Chronic Disease in China (KSCDC). *Int J Epidemiol* 2005;34:1243–9.
- Chen Z, Chen J, Collins R, et al. China Kadoorie Biobank of 0.5 million people: survey methods, baseline characteristics and long-term follow-up. *Int J Epidemiol* 2011;40:1652–66.
- Yang G, Hu J, Rao KQ, et al. Mortality registration and surveillance in China: history, current situation and challenges. *Popul Health Metr* 2005;3:3.
- Harbowy ME, Balentine DA, Davies AP, et al. Tea chemistry. *Crit Rev Plant Sci* 1997;16:415–80.
- Pandey KB, Rizvi SI. Plant polyphenols as dietary antioxidants in human health and disease. *Oxid Med Cell Longev* 2009;2:270–8.
- Hollman PC, Katan MB. Dietary flavonoids: intake, health effects and bioavailability. *Food Chem Toxicol* 1999;37:937–42.
- Ozdal T, Sela DA, Xiao J, et al. The Reciprocal Interactions between Polyphenols and Gut Microbiota and Effects on Bioaccessibility. *Nutrients* 2016;8:78.
- DiBaise JK, Zhang H, Crowell MD, et al. Gut microbiota and its possible relationship with obesity. *Mayo Clin Proc* 2008;83:460–9.
- Larsen N, Vogensen FK, van den Berg FW, et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. *PLoS ONE* 2010;5:e9085.
- Wang Z, Klipfell E, Bennett BJ, et al. Gut flora metabolism of phosphatidylcholine promotes cardiovascular disease. *Nature* 2011;472:57–63.
- Cook N, Samman S. Flavonoids—chemistry, metabolism, cardioprotective effects, and dietary sources. *J Nutr Biochem* 1996;7:66–76.
- Hu J, Zhou D, Chen Y. Preparation and antioxidant activity of Green tea extract enriched in epigallocatechin (EGC) and epigallocatechin gallate (EGCG). *J Agric Food Chem* 2009;57:1349–53.