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ORIGINAL CONTRIBUTION

# Associations between tea and coffee beverage consumption and the risk of lung cancer in the Singaporean Chinese population

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## Abstract

**Background** Tea and coffee are widely consumed beverages. Tea flavonoids have been shown to inhibit lung tumorigenesis using in vitro and in vivo models. Conversely, coffee contains complex mixtures of biochemically active compounds, some of which may have genotoxic and mutagenic properties. However, previous epidemiologic studies have shown inconsistent results on tea and coffee in relation to lung cancer risk.

**Methods** The Singapore Chinese Health Study is a population-based prospective cohort of 63,257 Singaporean Chinese men and women, with an average of 17.7 years of follow-up. Information on tea and coffee consumption and other lifestyle factors was collected through in-person interviews at baseline. Multivariable Cox regression models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the associations with adjustment for potential confounders.

**Results** There were 1486 incident lung cancer cases. Compared to non-daily coffee drinkers, HRs (95% CIs) of lung cancer risk for those consuming one, two, and three or more cups of coffee per day were 1.18 (1.02–1.36), 1.21 (1.05–1.40), and 1.32 (1.08–1.62) respectively ($P$ for trend = 0.0034). The highest category of black tea consumption (at least 2 cups per day) was inversely associated with risk of lung cancer [HR (95% CI) = 0.73 (0.53–0.99)], particularly among men [HR (95% CI) = 0.67 (0.47–0.95)], compared to less-than-weekly black tea drinkers, although the interaction by sex was not statistically significant.

**Conclusions** Coffee beverage consumption was associated with higher risk of developing lung cancer. On the other hand, black tea intake was associated with lower risk of lung cancer among men in our cohort, and further studies are needed to confirm this association.

**Keywords** Coffee · Lung cancer · Tea

## Introduction

Second only to water, tea and coffee are two of the most widely consumed beverages in the world. As a result, it is critically important to understand their potentially beneficial or adverse health effects. Coffee contains a complex mixture of biologically active substances that may have both genotoxic and mutagenic effects, in addition to antimutagenic and antioxidant properties, partly depending on how the coffee beans are processed [1]. Moreover, coffee drinking is often highly correlated with unhealthy behaviors such as tobacco smoking in the general population [2, 3]. In contrast, tea drinking is increasingly perceived as a healthier alternative beverage due to its high levels of flavonoids, which possess antioxidant properties [4].

Lung cancer is the third most commonly diagnosed cancer and the leading cause of cancer mortality worldwide, accounting for over 1.8 million new cases and 1.6 million

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deaths in 2012 [5]. More than half of the world's lung cancer cases occur in Asia [6]. Tobacco smoking is a major established risk factor for lung cancer. Dietary factors that modify the risk of lung cancer include vegetables and fruits with high levels of carotenoids and isothiocyanates [7–10]. Several previous studies, including two meta-analyses, have suggested a possible positive association between coffee consumption and lung cancer risk [11–23]. However, in another recent meta-analysis that combined both prospective and retrospective studies, coffee drinking was not reported to be a risk factor for lung cancer when restricted to studies that adjusted for smoking, although it should be noted that coffee was still positively associated with lung cancer risk when looking at prospective studies [24]. The International Agency for Research on Cancer (IARC) recently re-evaluated the carcinogenicity of drinking coffee and found no conclusive evidence, reclassifying coffee drinking as *not classifiable as to its carcinogenicity to humans* (Group 3) [25].

Most studies conducted so far have been retrospective in design, had relatively small sample sizes, and therefore, have limited power to conduct stratified analysis by smoking status. Furthermore, very few prospective studies were conducted to examine the association between coffee consumption and lung cancer risk in Asian populations. Given the mixed findings and lack of well-powered prospective studies in the Asian population, further research powered by larger sample sizes and better methodological designs are needed to clarify the direction and nature of this relationship.

Tea consumption and lung cancer risk have been examined in numerous studies [20, 26, 27]. A recent meta-analysis of 59,041 cases and 396,664 controls found that both green and black tea consumption were associated with a reduced risk of lung cancer overall [28]. However, the association was different across different study populations. Among the 12 cohort studies included in this meta-analysis, four reported significant inverse associations between tea consumption and lung cancer risk for black tea (Finland) and green tea (Japan and China). Conversely, two cohort studies from Japan and the United Kingdom found positive associations between tea consumption and lung cancer risk. In addition, smoking, a strong risk factor for lung cancer, may not be well controlled in these studies, and therefore, there may be potential residual confounding [28]. A prospective study in populations with high consumption of green and black tea but lower prevalence of smoking may potentially rule out the confounding effect of smoking on the tea-lung cancer risk association, and clarify the association between tea consumption and lung cancer risk, especially in never smokers.

The Singapore Chinese Health Study (SCHS) is a population-based, prospective cohort consisting of over 63,000 Chinese men and women in Singapore. We sought to assess the association between tea and coffee consumption and lung cancer risk, with stratification by smoking status.

## Materials and methods

### Study population

The SCHS has been described in detail previously [29]. Briefly, a total of 63,257 Chinese participants 45–74 years of age were enrolled between April 1993 and December 1998. All participants were citizens or permanent residents of Singapore residing in government housing estates, which represented the majority (86%) of the Singapore population during the period of recruitment, and were restricted to the two major dialect groups of Chinese: Hokkien and Cantonese who originated from Fujian and Guangdong provinces in China, respectively. A structured questionnaire was administered in-person at recruitment to obtain detailed information on each participant's demographics, lifetime tobacco use, diet, and medical history. This study was approved by the Institutional Review Board at the National University of Singapore. Informed consent was obtained from all individual participants included in the study.

### Consumption of tea and coffee

Information on consumption of black tea, green tea, and coffee was assessed at baseline using a 165-item semi-quantitative food-frequency questionnaire that was specifically developed and subsequently validated for this study population [29]. The consumption frequency of a standard serving of coffee, black tea or green tea was determined using nine categories: never or hardly ever, 1–3 times a month, once a week, 2–3 times a week, 4–6 times a week, once a day, 2–3 times a day, 4–5 times a day, and 6 or more times a day. The standard serving size of one cup (equivalent to 237 mL) was used in the questionnaire. Consumption of different types of coffee, such as instant or freshly brewed, or 3-in-1 preparation, was asked in separate questions.

### Lung cancer incidence

Identification of incident lung cancer cases among cohort members was accomplished by annual record linkage of all surviving cohort participants with the database of the population-based Singapore Cancer Registry (C34 of the International Classification of Diseases, ICD-O-3). As of 31 December 2016, 1486 cohort participants who were free of cancer at baseline had developed lung cancer. The survival status was determined by a similar record linkage analysis with the Singapore Registry of Births and Deaths. As of 31 December 2016, only 56 (<0.1%) cohort participants were

known to be lost to follow-up due to migration out of Singapore or other reasons.

### Statistical analysis

The primary analysis included 61,321 subjects after 1937 subjects with a history of cancer at enrollment were excluded. All subjects were grouped into different categories of coffee consumption (none/less than daily, 1 cup/day, 2 cups/day, 3 + cups/day) and tea consumption (none/less than weekly, weekly to < 1 cup/day, 1 cup/day, 2 + cups/day). The Chi-squared test and the *t* test were used to compare the distributions of selected variables across different categories of coffee and tea consumption. Person-years of follow-up were calculated from the date of baseline interview to the date of diagnosis of lung cancer, death, migration, or 31 December 2016, whichever occurred first. Cox proportional hazards regression models were used to estimate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between tea and coffee consumption with lung cancer risk. *P* values for trend were obtained by treating the consumption categories as ordinal.

All models were adjusted for sex, age at baseline interview (years), interview year (1993–1995, 1996–1998), dialect group (Cantonese or Hokkien), level of education (none, primary school, ≥ secondary school), body mass index (BMI, < 20, 20 to < 24, 24 to < 28, ≥ 28), average number of cigarettes smoked per day (never smokers, 1–12, 13–22, or ≥ 23), number of years of smoking (never smokers, 1–19, 20–39, or ≥ 40), number of years since last smoked for quitters (< 1, 1–4, 5–19 or ≥ 20), dietary beta-cryptoxanthin (g/day) [8], fried meat, soy intake, fruits, vegetables, total calories (kcal) and second-hand smoke (ever or never). Second-hand smoke was measured as a semi-quantitative variable representing the number of smokers an individual lived with during both childhood and adulthood, and was defined as a binary variable: ever (ever lived with at least one smoker) or never (never lived with at least one smoker). Since coffee was the major source of caffeine intake (84%), the coffee categories were highly correlated with caffeine intake (Spearman correlation coefficient = 0.85, $P < 0.001$) in this population [30]. Therefore, we did not adjust for caffeine in our coffee analysis.

Analyses were further stratified by smoking status (never- and ever smokers) and sex (men and women). Tests for interaction were performed to assess potential effect modification by smoking status and sex using Chi squared tests. Additional sensitivity analyses were conducted by (1) further stratifying by smoking status (never-, former- and ever smokers), (2) mutually adjusting for coffee and tea, (3) restricting the analyses to participants who did not drink the other beverages. Non-linearity for all beverages was tested using spline analysis [31].

All statistical analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC, USA). All *P* values were reported based on two-sided tests and *P* values of $< 0.05$ were considered being statistically significant.

## Results

There were a total of 1486 incident lung cancer cases during the period of follow-up. Subjects who consumed three or more cups of coffee a day (heavy coffee drinkers) were more likely to be men, current smokers, and have a higher energy intake, as compared to non-daily coffee drinkers (Table 1). The highest category of consumers (2 + cups/day) of both black and green tea was more likely to be male, current smokers, and had a higher education level and a higher consumption of soy, fruits and vegetables, as compared with non-tea drinkers.

Compared to non-daily coffee drinkers, the HRs (95% CIs) of lung cancer risk for those consuming 1, 2, and 3 or more cups of coffee per day were 1.18 (1.02–1.36), 1.21 (1.05–1.40) and 1.32 (1.08–1.62), respectively (*P* for trend = 0.0034) (Table 2). A statistically significant positive association between coffee consumption and lung cancer risk was present in both never- (*P* for trend = 0.032) and ever smokers (*P* for trend = 0.0055), and the interaction between coffee consumption and smoking status was not statistically significant ($P = 0.70$). However, after further separating ever smokers into former or current smokers, the associations were not statistically significant for either group (Supplemental Table 1). Similarly, a significant coffee–lung cancer risk association was seen in both men (*P* for trend = 0.040) and in women (*P* for trend = 0.022) after adjustment for smoking intensity and duration and other potential confounders, and the interaction between coffee consumption and sex was not statistically significant (*P* for interaction = 0.97) (Table 2).

Overall, the highest category of black tea consumption (at least 2 cups per day) was significantly associated with lower lung cancer risk (HR = 0.73, 95% CI 0.53–0.99) (Table 3) compared to non- and less-than-weekly black tea drinkers. Among men, the highest category of black tea consumption (at least 2 cups per day) was associated with a statistically significant, 33% reduction in risk of lung cancer (95% CI 5–53%) compared with those who had less-than-weekly consumption of black tea. However, the interaction between black tea consumption and sex was not statistically significant (*P* for interaction = 0.24). Similar non-significant associations were observed among former smokers and current smokers (Supplemental Table 2).

No statistically significant associations were observed between green tea consumption and overall lung cancer risk (Table 4). Among women, moderate consumption of

**Table 1** Characteristics of the Singapore Chinese Health Study

| Variables | Coffee | | Black tea | | Green tea | |
|---|---|---|---|---|---|---|
| | None/less than daily | 3+ cups/day | None/less than weekly | 2+ cups/day | None/less than weekly | 2+ cups/day |
| Person-years of follow-up | 292,475 | 56,079 | 711,107 | 29,439 | 699,308 | 57,332 |
| Median age (IQR), years | 54 (13) | 54 (11) | 55 (13) | 54 (11) | 55 (12) | 56 (13) |
| Sex (%) | | | | | | |
| Male | 6182 (41) | 1725 (60) | 13,868 (38) | 1042 (69) | 14,158 (40) | 1724 (57) |
| Female | 8852 (59) | 1170 (40) | 22,628 (62) | 469 (31) | 21,532 (60) | 1302 (43) |
| Dialect group (Hokkien, %) | 7580 (50) | 1689 (58) | 18,679 (51) | 846 (56) | 19,439 (55) | 1137 (38) |
| Highest level of education (%) | | | | | | |
| No formal education | 3430 (23) | 661 (23) | 10,555 (29) | 243 (16) | 10,256 (29) | 517 (17) |
| Primary education | 6332 (42) | 1384 (48) | 16,445 (45) | 708 (47) | 15,782 (44) | 1470 (49) |
| Secondary education or higher | 5272 (35) | 850 (29) | 9496 (26) | 560 (37) | 9652 (27) | 1039 (34) |
| Body mass index, kg/m$^2$ (%) | | | | | | |
| $<20.0$ | 2229 (15) | 522 (18) | 5560 (15) | 234 (15) | 5818 (16) | 327 (11) |
| 20.0 to $<24.0$ | 7973 (53) | 1544 (53) | 19,856 (54) | 748 (50) | 19,542 (55) | 1484 (49) |
| 24.0 to $<28.0$ | 3654 (24) | 633 (22) | 8,462 (23) | 393 (26) | 7933 (22) | 906 (30) |
| $\geq 28.0$ | 1178 (8) | 196 (7) | 2618 (7) | 136 (9) | 2397 (7) | 309 (10) |
| Smoking history (%) | | | | | | |
| Never smoker | 11,900 (79) | 1423 (49) | 26,584 (73) | 853 (56) | 25,862 (72) | 1925 (64) |
| Former smokers | 1559 (10) | 319 (11) | 3592 (10) | 219 (15) | 3397 (10) | 455 (15) |
| Current smokers | 1575 (11) | 1153 (40) | 6320 (17) | 439 (29) | 6431 (18) | 646 (21) |
| Passive smoking (%) | | | | | | |
| Ever | 3087 (21) | 380 (13) | 6406 (18) | 281 (19) | 6280 (18) | 534 (18) |
| Never | 11,947 (79) | 2515 (87) | 30,090 (82) | 1230 (81) | 29,410 (82) | 2492 (82) |
| Mean daily intake | | | | | | |
| Total calories, kcal (SD) | 1521 (543) | 1821 (644) | 1506 (532) | 1828 (687) | 1520 (544) | 1672 (621) |
| Dietary beta-cryptoxanthin, g/kcal (SD) | 176 (221) | 132 (190) | 163 (214) | 161 (208) | 158 (208) | 186 (224) |
| Fried meat (%) | | | | | | |
| 1st tertile | 5378 (36) | 809 (28) | 11,995 (33) | 514 (34) | 11,741 (33) | 1065 (35) |
| 2nd tertile | 4876 (32) | 913 (32) | 12,139 (33) | 455 (30) | 11,818 (33) | 920 (30) |
| 3rd tertile | 4780 (32) | 1173 (41) | 12,362 (34) | 542 (36) | 12,131 (34) | 1041 (34) |
| Soy intake, g/kcal (SD) | 119 (87) | 98 (95) | 110 (80) | 105 (97) | 109 (80) | 112 (86) |
| Fruits, g/kcal (SD) | 221 (159) | 159 (153) | 200 (148) | 201 (182) | 195 (148) | 227 (178) |
| Vegetables, g/kcal (SD) | 117 (57) | 98 (56) | 112 (53) | 106 (62) | 109 (52) | 116 (59) |
| Caffeine, mg/kcal (SD) | 56 (61) | 390 (98) | 143 (109) | 248 (123) | 137 (105) | 278 (114) |

*SD* standard deviation, *IQR* interquartile range

green tea (weekly to $<1$ cup per day) was significantly associated with a statistically significant 30% lower risk of lung cancer (95% CI 7–47%) relative to non- and less-than-weekly green tea drinkers. Similarly, a statistically significant lower risk of lung cancer associated with moderate consumption of green tea (weekly to $<1$ cup per day) was present in never smokers (HR = 0.73, 95% CI 0.56–0.95), although no significant dose–response relationship was observed. However, no statistically significant interaction was observed for green tea consumption with sex ($P$ for interaction = 0.22) or smoking status ($P$ for interaction = 0.95) on risk of lung cancer. The $P$ value for non-linearity is statistically significant for green tea ($P = 0.0021$). Similar associations were observed after further stratifying by former- and current smokers (Supplemental Table 3).

Sensitivity analyses by mutually adjusting for other beverages and restricting the analyses to participants who did not drink the other beverages yielded similar results (Supplemental Tables 4–6).

**Table 2** Associations between coffee consumption and lung cancer risk

| Coffee consumption | None/less than daily | 1 cup/day | 2 cups/day | 3 + cups/day | *P* for trend | *P* for interaction[c] |
|---|---|---|---|---|---|---|
| All | | | | | | |
| Number of cases | 303 | 500 | 536 | 147 | | |
| HR (95% CI)[a] | 1.00 | **1.18 (1.02–1.36)** | **1.21 (1.05–1.40)** | **1.32 (1.08–1.62)** | **0.0034** | |
| Never smokers | | | | | | |
| Number of cases | 138 | 210 | 137 | 21 | | 0.70 |
| HR (95% CI)[b] | 1.00 | **1.27 (1.02–1.57)** | **1.27 (1.00–1.62)** | 1.40 (0.88–2.22) | **0.032** | |
| Ever smokers | | | | | | |
| Number of cases | 165 | 290 | 399 | 126 | | |
| HR (95% CI)[a] | 1.00 | 1.16 (0.96–1.41) | **1.25 (1.04–1.50)** | **1.35 (1.07–1.72)** | **0.0055** | |
| Men | | | | | | |
| Number of cases | 174 | 299 | 357 | 117 | | |
| HR (95% CI)[a] | 1.00 | **1.31 (1.08–1.58)** | 1.19 (0.99–1.43) | **1.38 (1.09–1.76)** | **0.040** | 0.97 |
| Women | | | | | | |
| Number of cases | 129 | 201 | 179 | 30 | | |
| HR (95% CI)[a] | 1.00 | 1.02 (0.82–1.28) | **1.31 (1.04–1.65)** | 1.23 (0.82–1.85) | **0.022** | |

*HR* hazard ratio, *CI* confidence interval

[a]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, cigarette smoking (number of years smoking, number of cigarettes per day, number of years since last smoked), dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[b]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[c]*P* for interaction was calculated using a Chi squared test

**Table 3** Associations between black tea consumption and lung cancer risk

| Black tea consumption | None/less than weekly | Weekly to < 1 cup/day | 1 cup/day | 2 + cups/day | *P* for trend | *P* for interaction[c] |
|---|---|---|---|---|---|---|
| All | | | | | | |
| Number of cases | 1094 | 226 | 125 | 41 | | |
| HR (95% CI)[a] | 1.00 | 0.97 (0.84–1.12) | 1.02 (0.85–1.23) | **0.73 (0.53–0.99)** | 0.20 | |
| Never smokers | | | | | | |
| Number of cases | 380 | 79 | 41 | 6 | | 0.73 |
| HR (95% CI)[b] | 1.00 | 0.97 (0.76–1.25) | 1.10 (0.79–1.52) | 0.53 (0.24–1.19) | 0.56 | |
| Ever smokers | | | | | | |
| Number of cases | 714 | 147 | 84 | 35 | | |
| HR (95% CI)[a] | 1.00 | 0.97 (0.81–1.16) | 0.98 (0.78–1.23) | 0.77 (0.55–1.08) | 0.22 | |
| Men | | | | | | 0.24 |
| Number of cases | 656 | 162 | 96 | 33 | | |
| HR (95% CI)[a] | 1.00 | 0.96 (0.81–1.14) | 1.00 (0.81–1.24) | **0.67 (0.47–0.95)** | 0.11 | |
| Women | | | | | | |
| Number of cases | 438 | 64 | 29 | 8 | | |
| HR (95% CI)[a] | 1.00 | 0.99 (0.76–1.29) | 1.08 (0.74–1.58) | 1.01 (0.50–2.04) | 0.81 | |

*HR* hazard ratio, *CI* confidence interval

[a]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, cigarette smoking (number of years smoking, number of cigarettes per day, number of years since last smoked), dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[b]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[c]*P* for interaction was calculated using a Chi squared test

**Table 4** Associations between green tea consumption and lung cancer risk

| Green tea consumption | None/less than weekly | Weekly to < 1 cup/day | 1 cup/day | 2 + cups/day | *P* for trend | *P* for interaction[c] |
|---|---|---|---|---|---|---|
| All | | | | | | |
| Number of cases | 1075 | 218 | 91 | 102 | | |
| HR (95% CI)[a] | 1.00 | 0.90 (0.78–1.05) | 0.93 (0.75–1.15) | 1.00 (0.82–1.23) | 0.55 | |
| Never smokers | | | | | | |
| Number of cases | 381 | 67 | 31 | 27 | | 0.95 |
| HR (95% CI)[b] | 1.00 | **0.73 (0.56–0.95)** | 0.90 (0.62–1.30) | 0.93 (0.63–1.38) | 0.23 | |
| Ever smokers | | | | | | |
| Number of cases | 694 | 151 | 60 | 75 | | |
| HR (95% CI)[a] | 1.00 | 1.00 (0.84–1.20) | 0.94 (0.72–1.23) | 1.03 (0.81–1.31) | 0.99 | |
| Men | | | | | | |
| Number of cases | 640 | 162 | 64 | 81 | | 0.22 |
| HR (95% CI)[a] | 1.00 | 1.01 (0.85–1.20) | 0.95 (0.73–1.23) | 1.06 (0.84–1.34) | 0.79 | |
| Women | | | | | | |
| Number of cases | 435 | 56 | 27 | 21 | | |
| HR (95% CI)[a] | 1.00 | **0.70 (0.53–0.93)** | 0.88 (0.60–1.31) | 0.86 (0.55–1.33) | 0.11 | |

*HR* hazard ratio, *CI* confidence interval

[a]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, cigarette smoking (number of years smoking, number of cigarettes per day, number of years since last smoked), dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[b]HRs and 95% CIs were adjusted for age at interview, dialect group, interview year, sex, education level, body mass index, dietary beta-cryptoxanthin, fried meat, soy intake, fruits, vegetables, total calories and second-hand smoke

[c]*P* for interaction was calculated using a Chi squared test

## Discussion

In this large prospective cohort of Chinese participants in Singapore, we observed a statistically significant, elevated risk of lung cancer for people who consumed one or more cups of coffee per day. We also found a suggestive association between black tea consumption and reduced lung cancer risk in men, although the interaction by sex was not statistically significant.

Consistent with our findings, three recent meta-analyses showed that higher levels of coffee consumption were associated with higher risk of lung cancer in prospective studies [12, 24, 32]. One of the three meta-analyses included 12 case–control studies and five prospective cohort studies and showed a statistically significant, higher risk of lung cancer associated with higher consumption of coffee in men or smokers across all race/ethnic groups, as well as in prospective cohort studies [12]. The five cohort studies had a follow-up time of 10–18 years with up to 161 incident cases of lung cancer and at least 7 cups of coffee consumption per day as the highest exposure category. Another meta-analysis of four prospective cohort studies of lung cancer in relation to coffee consumption (two of them were also included in the meta-analysis described above) reported a more than doubled risk of lung cancer for participants with highest relative to the lowest level of coffee consumption [32]. The higher risk estimate could be the result of confounding by smoking because heavy coffee drinkers are more likely to smoke cigarettes [33], and smoking is the strongest causal factor for lung cancer, which was not explicitly adjusted for in the meta-analysis [16]. The third meta-analysis of five prospective studies, including studies of non-smokers and studies that adjusted for smoking, also found a significant association between coffee consumption and lung cancer risk [24]. There is no prospective cohort study for coffee consumption and lung cancer risk in the Chinese population. Our study not only provided new data for coffee consumption and lung cancer risk in a Chinese population, but also conducted more detailed analysis by smoking status and sex. Larger prospective studies or consortia are warranted to confirm our findings.

To the best of our knowledge, this is the first population-based prospective cohort study in a Chinese population, and the largest Asian study to show a positive association between coffee consumption and lung cancer risk. Previous Asian prospective cohort studies from Korea and Japan identified similar positive associations in the highest coffee consumption group [15, 34]. However, most prior studies only adjusted for overall smoking status (i.e., never, former/current) without further accounting for smoking intensity and duration. Therefore, there could be potential residual confounding by smoking. Further, the coffee consumption

levels in most previous Asian studies were broadly categorized as non-drinkers and drinkers without detailed quantification in coffee consumption (e.g., the number of cups per day); hence, they were unable to assess the effect of low coffee consumption (e.g., 1 cup per day) or dose–response effect on lung cancer risk.

Coffee is a heterogeneous mixture that contains more than 1000 chemical compounds and includes caffeine, antioxidants, diterpenes and potential carcinogens such as furans, 3,4 benzopyrene, and acrylamide [35]. However, in vitro studies have shown that caffeine promotes apoptosis of cancer cells and as a result impedes carcinogenesis [36]. Therefore, the increased cancer risk from drinking coffee is possibly mediated by other intermediate components and biological mechanisms such as gallic acid and pyrogallol, which may cause DNA damage [37].

In our study, we observed a statistically significant overall 27% decrease in lung cancer risk in individuals who consume at least two cups of black tea daily, particularly among men. A previous meta-analysis of tea consumption and lung cancer risk reported an overall reduced lung cancer risk for black tea consumption; however, the study did not conduct a dose–response analysis of black tea consumption, and the associations were not statistically significant in prospective studies [28]. Black tea flavonoids such as polyphenols, epigallocatechin-3-gallate (EGCG), and theaflavins have been shown to inhibit lung tumorigenesis both in vitro and in vivo [38]. Some proposed key mechanisms for the observed protective effects of black tea include the anti-oxidative and anti-proliferative effects of tea polyphenols, hence promoting apoptosis of cancer cells [39]. A possible explanation for the protective effect observed only in men is that they have higher oxidative stress levels compared to women [40–42] and, as a result, the antioxidant effect of black tea to restore balance may be more prominent among men.

Contrary to previous studies, we did not find any significant associations between green tea and lung cancer. A meta-analysis with 26 case–control studies and 12 cohort studies found an overall lower risk of lung cancer in green tea drinkers than in non-drinkers, but did not further stratify by sex [28]. Another meta-analysis by Tang et al. also reported an overall negative green tea–lung cancer risk association [43]. Zhong et al. also found increased consumption of green tea to be associated with a reduced risk of lung cancer among non-smoking women in Shanghai, China [44]. However, we did observe a suggestive protective effect of green tea consumption against the development of lung cancer among women and never smokers who drink green tea on a weekly basis, although this could be a chance finding due to the lack of a dose-dependent response. Similar to our findings, a previous meta-analysis study found a significant non-linear association between green tea consumption and risk of lung cancer [45]. Further studies are needed to confirm these findings. Green tea consumption was previously reported to reduce oxidative stress, inflammation and tissue damage in rats that were exposed to cigarette smoke [46]. Green tea catechins have been shown both in vitro and in vivo to act as antitumorigenic agents and immune modulators, and protect against degenerative diseases [47–49]. For example, EGCG, which is a major catechin in green tea, promotes anticarcinogenic properties and has been demonstrated in vivo to suppress lung cancer cell growth through upregulating microRNA [50]. Combined treatments of EGCG with anticancer drugs such as leptomycin B have also been shown to enhance lung adenocarcinoma cell cytotoxicity, compared to administering the anti-cancer drug alone [51, 52].

Strengths of this study include high participation rates, a long follow-up period, and stratification by smoking status. However, there are several limitations to be considered. Firstly, since coffee drinking and smoking are positively correlated, there may be residual confounding due to smoking. To minimize this, we further adjusted for years of cigarette smoking and number of cigarettes smoked per day in the models. In addition, we do not have information to stratify by decaffeinated coffee and tea; however, this baseline survey was conducted in the 1990s, when decaffeinated beverages were rarely consumed in our study population and, therefore, only caffeinated coffee was assessed [29]. Although we collected information on different types of coffee (e.g., brewed versus instant) and different beverage additives (e.g., milk and sugar), the numbers were too small to perform any meaningful analysis. Further, information on beverage consumption was obtained from the baseline survey; therefore, we were unable to assess changes in coffee consumption patterns over time. This may lead to potential information bias, although this is most likely non-differential between the two groups.

## Conclusions

In summary, we found a statistically significant monotonic association between coffee consumption and increased risk of lung cancer. No overall associations between green or black tea consumption and lung cancer risk were observed. However, black tea appeared to be associated with reduced risk of lung cancer among men in our cohort, though further studies are needed to confirm this association. Further work is warranted in the study of underlying mechanisms, genetic susceptibility of habitual coffee drinking, as well as gene–environment interactions in this population.

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## Compliance with ethical standards

**Conflict of interest** On behalf of all authors, the corresponding author states that there is no conflict of interest.

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