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# Coffee and tea consumption and endometrial cancer risk in a population-based study in New Jersey

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## Abstract

We evaluated the role of tea and coffee and substances added (sugar/honey, creamers, and milk) on endometrial cancer risk in a population-based case–control study in six counties in New Jersey, including 417 cases and 395 controls. Multivariate odds ratios (OR) and 95% confidence intervals (CI) were computed using unconditional logistic regression. There was a moderate inverse association with coffee consumption, with an adjusted OR of 0.65 (95% CI: 0.36–1.17) for women who reported more than two cups/day of coffee compared to none. Tea consumption appeared to increase risk (OR: 1.93; 95% CI: 1.08–3.45), but after including the variables sugar/honey and cream/milk added to tea in the model, the risk estimate was attenuated and no longer statistically significant (OR: 1.77; 95% CI: 0.96–3.28 for those consuming more than one cup/day of tea compared to


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nonusers). There was a suggestion of a decreased risk associated with green tea, but the confidence interval included one (adjusted OR for one or more cups/week vs. none: 0.75; 95% CI: 0.48–1.18). We found an association with adding sugar/honey to tea, with those adding two or more teaspoons/cup having an OR of 2.66 (95% CI: 1.42–4.98; *p* for trend <0.01) after adjusting for relevant confounders. For sugar/honey added to coffee the corresponding OR was 1.43 (95% CI: 0.81–2.55). Our results indicate that sugars and milk/cream added to coffee and tea should be considered in future studies evaluating coffee and tea and endometrial cancer risk.

### Keywords

Endometrial cancer; Diet; Nutrition; Coffee; Tea; Sugar

## Introduction

Endometrial cancer is mainly caused by prolonged and excessive exposure to unopposed estrogens [1]. Obesity, which is associated with higher levels of estrogens and insulin, is a well-established risk factor for endometrial cancer [2]. Hyperinsulinemia and diabetes have been also implicated as independent risk factors [1].

Coffee and tea are widely consumed beverages worldwide, and their role as anticarcinogenic agents in experimental studies, mostly attributed to their content in polyphenols, is well documented [3,4]. Both coffee and tea have been shown to reduce risk of type 2 diabetes mellitus, decrease insulin secretion, and assist in weight loss [5,6]. However, relatively few studies have evaluated their role on endometrial cancer, with the limited available data pointing to a weak inverse association particularly for coffee consumption [2,7].

Both coffee and tea vary widely in processing (e.g., roasting) and preparation, which have major impact on their composition [7,8]. Both coffee and tea are usually consumed with other substances such as sweeteners and milk and/or creamers. To our knowledge, these added substances, particularly the use of sugar in coffee and tea, have not been previously taken into account when evaluating tea and coffee.

The main objective of our study was to evaluate the association of coffee and tea consumption, including added sweeteners and milk, cream/half and half, or nondairy creamers, and the risk of developing endometrial cancer in a population-based case–control study in New Jersey.

## Methods

The methods used in the EDGE Study (Estrogen, Diet, Genetics, and Endometrial Cancer) have been described elsewhere [9,10]. In brief, women older than 21 years (y) and able to understand English or Spanish, and living in one of six NJ counties (Bergen, Essex, Hudson, Middlesex, Morris, and Union) were eligible to participate in the study. The cases were women with a newly diagnosed, histologically confirmed epithelial endometrial cancer, identified through the New Jersey State Cancer Registry between July 1, 2001 and June 30, 2005. A total of 1,559 eligible cases were identified, of whom 1,104 could be contacted within 1 year of diagnosis and 469 of them (42%) completed the interview.

Women who had a hysterectomy were excluded from the control group. Controls were identified from various sources. Women aged <65 were initially located through random digit dialing conducted by a commercial research service. One hundred and seventy-five of the 355 eligible women (49%) completed the interview. For women aged ≥65, we initially identified potential controls by random selection from lists purchased from the Centers for Medicare and

Medicaid Services (CMS). We identified 316 women, of whom 68 (22%) completed the interview, while the remainder declined; for 40% of those who declined, eligibility was unknown. Beginning in August 2003, we undertook area sampling for controls, initially seeking women aged ≥65 and later including women aged ≥55. We contacted by mail and home visits 30 consecutive households in each randomly chosen neighborhood. We identified 524 eligible women, of whom 224 (43%) completed the interview. In total, 467 controls completed the interview. Informed consent was obtained from all participants, and the study was approved by the Institutional Review Boards at Robert Wood Johnson Medical School, Memorial Sloan-Kettering Cancer Center, and the New Jersey Department of Health and Senior Services.

Interviews, conducted by telephone for most respondents, covered established and possible risk factors for endometrial cancer. In addition to the interview, participants were mailed a package with instructions for providing buccal specimens and waist and hip circumference measurements and the Block 98.2 food frequency questionnaire (FFQ). Participants were instructed to report their usual intake of the food items in the questionnaire during the 6 months before diagnosis (for cases) or the date of the interview (for controls). Four hundred and twenty-four cases (90.4%) and 398 controls (85.2%) returned the FFQ. The participants who returned the FFQ tended to be older, but there were no significant differences in education, body mass index (BMI), unopposed estrogen replacement therapy (ERT) use, or hormone replacement therapy (HRT) use (data not shown).

The Block 98.2 FFQ includes 110 foods and beverages and was developed using the NHANES (National Health and Nutrition Examination Survey) III dietary recall data. The item addressing coffee consumption asked about “coffee, regular or decaf,” and the item addressing tea consumption asked about “tea or iced tea (not herb teas).” As one of the main aims of the study was to evaluate the association between phytoestrogen consumption and endometrial cancer risk, we added one page to the Block FFQ with 21 additional food items [10], based on the LACE questionnaire [11] and including other food items that have been identified as important sources of phytoestrogens, including green tea [12]. Use of sugar or honey (teaspoons of sugar or honey added to coffee and tea: 1, 2, 3–4 or 5+) and use of cream/half and half, nondairy creamer, or milk added to coffee and tea was also ascertained (“what do you usually add to coffee/tea?” with the options: cream or half and half, nondairy creamer, milk, and none of these). Berkeley Nutrition Services provided nutrient calculations using the USDA Nutrient Database for Standard Reference.

We evaluated the association between intake of tea and coffee, as well as sugar/honey and creamers and milk added to coffee and tea and endometrial cancer risk. We excluded seven cases and three controls with missing values for major covariates, such as menopausal status or BMI, resulting in a final analytical sample of 417 cases and 395 controls. We evaluated the number of teaspoons usually added to each cup of coffee (or tea), and also evaluated the total sugar added to coffee (or tea) in teaspoons per day, by multiplying the number of teaspoons of sugar per cup by the number of cups of coffee (or tea) per day. Odds ratios (OR) and 95% confidence intervals (CI) were estimated by unconditional multiple logistic regression. Tests for trend were derived by assigning the median value to each quantile in controls. Potential confounding variables considered were age; race; BMI, calculated as weight (in kg) divided by height (in $m^2$); education (high school or less, college, graduate school); parity (0–1, 2, ≥3); age at menarche (≤11, 12–13, >13 years); menopausal status/age at menopause (premenopausal, age at menopause <40, age at menopause 40–54, age at menopause ≥55 and post-menopausal with age at menopause unknown); oral contraceptive (OC) use (ever, never used); use of hormone replacement therapy (HRT) (never used any HRT, used unopposed estrogen only, used combined therapy, i.e., estrogen and progesterone); total energy intake (as a continuous variable); smoking (status and pack-years for current and former smokers);

alcohol use (drinks/month); physical activity (METs); diabetes; hypertension; and sugar (or honey) and milk, cream, or nondairy creamer added to coffee and tea.

We evaluated possible effect modification by examining the association between tea/green tea and coffee intakes and endometrial cancer by categories of BMI, waist to hip ratio (WHR), and self-reported hypertension. We were unable to conduct stratified analyses by menopausal status or diabetes status because the number of premenopausal (60 cases and 48 controls) or diabetic women (64 cases and 34 controls) in our study was small. However, results were similar when analyses were restricted to postmenopausal women or women without a known diagnosis of diabetes (data not shown). We evaluated interactions by including cross-product terms in logistic regression models. SAS version 9.1 (SAS Institute, Cary NC) was used for analysis.

## Results

The characteristics of the study population have been shown in detail elsewhere [10]. In summary, the study population was mostly white (85% of the cases and 89% of the controls) and the mean age was 61.6 years for cases and 64.3 years for controls. As expected, cases were heavier and had fewer children. They were also less likely to use oral contraceptives and to smoke. A diagnosis of diabetes or hypertension was more commonly reported among cases than controls. Cases were less likely to have ever used any combined hormone replacement therapy, but similar to controls in the proportion that ever used estrogen replacement therapy (8.2% vs. 7.9%).

Risk estimates for endometrial cancer associated with consumption of coffee and tea are shown in Table 1. For coffee, there was an inverse association after adjustment for all major risk factors, with an OR of 0.57 (95% CI: 0.32–1.01; *p* for trend: 0.03) for women consuming more than two cups per day compared to nondrinkers (data not shown). Further adjustment for smoking attenuated the estimate (OR: 0.65; 95% CI: 0.36–1.17), whereas adding sugar/honey and cream/milk in coffee to the model did not substantially change risk estimates. Adjusting for all these factors, the OR was 0.69 (95% CI: 0.36–1.33) for those drinking more than two cups/day of coffee vs. none. Further adjustment for alcohol intake, physical activity, hypertension, diabetes, and tea intake essentially did not change estimates.

Consuming more than one cup of tea per day was associated with an increased risk (OR: 1.93; 95% CI: 1.08–3.45), after adjusting for major factors known to affect risk, including smoking (Table 1). However, with additional adjustment for sugar/honey added to tea risk estimates were attenuated and no longer statistically significant (OR: 1.58; 95% CI: 0.87–2.86). Adding cream/milk to the model also seemed to have some confounding effect, with an OR of 1.77 (95% CI: 0.96–3.28). For green tea, the OR was below one, but the confidence interval included the null (OR: 0.75; 95% CI: 0.48–1.18) for drinking one or more cups per week compared to none. Adding sugar/honey and cream/milk added to tea to the model essentially did not change risk estimates (Table 1).

We also evaluated the risk associated with cream/milk and sugar/honey added to coffee and tea. As shown in Table 2, there was not a clear association with sugar/honey, cream/creamers, or milk added to coffee and endometrial cancer risk. However, there was some indication that risk was lower for women reporting adding milk to tea (OR: 0.63; 95% CI: 0.43–0.93) compared to those not using milk or any creamers. Furthermore, women who usually added more than two teaspoons of sugar/honey per cup of tea were at increased risk (OR: 2.66; 95% CI: 1.42–4.98). However, there was not a clear dose–response association with total sugar added to coffee and tea per day at these levels of intake.

Stratified analyses by body mass index, waist to hip ratio, and hypertension did not reveal a major pattern of effect modification for tea, coffee, or green tea (data not shown). As previously mentioned, the small number of premenopausal and diabetic women did not allow stratified analyses by menopausal or diabetes status. However, repeating analyses excluding premenopausal women or women with a diagnosis of diabetes essentially did not change results.

## Discussion

In this population-based case–control study, there was little evidence that coffee and tea consumption play a major role in modulating endometrial cancer risk after adjusting for major confounders. However, our results suggest that sugar/honey and cream/milk added to tea and coffee should be considered as potential covariates in future studies. Consumption of green tea was not very common in this population. However, we found that women who consumed one or more cups of green tea per week had a 25% reduction in risk compared to nondrinkers, but the confidence interval included the null.

We also evaluated the role of substances added to coffee and tea, such as creamers, milk, and sugar. Controlling for sugar/honey added to coffee did not have a major impact in risk estimates. We found that adding two or more teaspoons of sugar or honey per cup of tea was associated with an increased risk of developing endometrial cancer, compared to not using sugar/honey. While the OR was above one for adding the same amount of sugar/honey to coffee, the confidence interval included one. We found no major impact on endometrial cancer risk for creamers and milk added to coffee, whereas there was some indication of a risk reduction for women adding milk to tea.

Our findings of a weak inverse association of coffee with endometrial cancer are in general agreement with previous studies. Two cohort studies [13,14], three population-based case–control studies [15–17], and four hospital-based case–control studies [18–21] have suggested an inverse association between coffee consumption and endometrial cancer risk. In contrast, a small cohort study [22], one population-based case–control study [23] and two hospital-based studies [24,25] did not find an association. A recent meta-analysis reported a summary risk estimate of 0.93 (95% CI: 0.89–0.97) per cup of coffee per day [7].

Several mechanisms have been proposed to explain a possible beneficial effect of coffee consumption, including effects in glucose metabolism and diabetes prevention, favoring weight loss [6], as well as anticarcinogenic effects due to its content in antioxidants [7].

While the antioxidant and anticarcinogenic properties of tea, mainly attributed to tea polyphenols, are well documented in experimental studies, epidemiologic studies of tea and cancer have not offered conclusive results [26]. For endometrial cancer, the few cohort and case–control studies that have previously evaluated the role of tea offered inconsistent results [2]. In the Iowa Women's Health Study [27], the relative risk (RR) for those consuming more than two cups per day versus never or rarely was 0.76 (95% CI: 0.45–1.27). Out of the four population-based case–control studies evaluating tea [15,23,28,29], two suggested an inverse association [28,29], but in one of them the confidence interval included one [29]. The other two studies, one conducted in the United States [23] and the other in Canada [15], did not find an association. Out of the four hospital-based case–control studies evaluating tea [19,21,24, 30], only one found an inverse association [21]. An additional small hospital-based case–control study evaluated soda, coffee, and tea combined and found no association [31].

While all tea, oolong, green, and black tea, comes from the same plant (*Camellia sinensis*), its composition varies substantially according to processing [32]. Green tea, which is processed to prevent oxidation and fermentation, has much higher levels of some antioxidant polyphenols

than black tea [26]. It represents approximately 20% of the world tea consumption [32]. Only a few studies have examined the association of endometrial cancer specifically with green tea. A cohort study in Japan found a RR of 0.75 (95% CI: 0.44–1.30) for women consuming more than five cups/day of green tea versus consuming it four or less days/week [13]. While two population-based case–control studies conducted in China [28] and Japan [33] found an inverse association, there was no association in a third study conducted in the United States [23]. Different levels of consumption and preparation methods may explain these discrepant findings.

An important caveat of this study is the lack of detailed assessment of coffee and tea consumption. We used the Block FFQ, which includes only one question for coffee (therefore, not separating regular from decaffeinated coffee) and one for tea (which included hot and iced tea, but not herbal teas). For this study, we added one more page to the questionnaire, as described elsewhere [10], which included frequency and portion size of green tea consumption. Although the inability of this study to separate regular from decaffeinated coffee is a limitation, both types have been shown to reduce diabetes risk and to be associated with weight loss [6]. Furthermore, an inverse association was found with plasma C-peptide levels, a marker of insulin secretion, for both types of coffee among participants in the Nurses' Health Study [34]. To our knowledge, only two studies [21,24], both hospital-based studies, have evaluated the risk of endometrial cancer associated with regular and decaffeinated coffee separately. One of them suggested an inverse association only for regular coffee, while there was no association for decaffeinated coffee [21]. The other study did not find an association for either type [24]. With respect to tea, our inability to separate the different types of tea (e.g., hot tea vs. iced tea; green, black, oolong tea) is also a drawback. However, the majority of tea consumption in the United States is in the form of iced tea (approximately 85%) [35], and most commercial iced teas contain a variety of additives, such as sweeteners. This may explain the suggestion of an increased risk associated with tea consumption in our study.

To our knowledge, this is the first study that evaluated the role of sugar or honey added to coffee and tea on endometrial cancer risk. Long-term high sugar intake leads to hyperglycemia and chronic hyperinsulinemia, which in turn has been associated with increased endometrial cancer risk [36]. Interestingly, in our study we found a stronger association with sugar/honey added to tea than to coffee. The reason for this is uncertain. However, as most of the tea consumed was probably in the form of iced tea, it is possible that the added sugar/honey was to already sweetened tea. It is also possible that the increased association observed for adding sugar to tea is a spurious finding. For instance, sugar may be acting as a marker for other behaviors that are related to an increased endometrial cancer risk and that were not taken into account in this study. Future studies need to explore this issue further by obtaining a more detailed history of tea consumption, including type of tea and form of preparation and addition of milk or milk substitutes and sweeteners.

In addition to these limitations in exposure assessment, as in all case–control studies, potential recall bias and selection bias should be considered. Recall bias may have occurred if cases systematically over reported or underreported coffee and tea consumption. While this cannot be ruled out, it is unlikely that the general public would think that tea or coffee may impact endometrial cancer risk. Not unlike other population-based case–control studies [37], response rates in our study were low. However, nonresponse bias would only affect study validity if willingness to participate is related to the factors under evaluation [37,38]. It is unlikely that coffee and tea intakes were related to the likelihood of subjects agreeing to participate in the study.

Our study represents an addition to the scientific literature of coffee/tea and endometrial cancer risk, as it stresses the need for future studies to separate types of tea and coffee, as well as to

assess substances added, such as sugar and other additives, and milk and creamers. Ideally, the association of these beverages and endometrial cancer should be evaluated in countries with a wide range of intake, particularly of tea subtypes, such as green tea, which is relatively uncommon in some countries.

In summary, our study did not offer support for a major role of tea or coffee consumption on endometrial cancer prevention. Our findings of increased risk associated with sugar/honey added to tea and decreased risk with milk added to tea are intriguing, but require replication in other population-based studies.

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**Table 1**

Endometrial cancer risk associated with coffee and tea consumption

| | Cases (n) | Controls (n) | OR1 | 95% CI | OR2 | 95% CI | OR3 | 95% CI |
|---|---|---|---|---|---|---|---|---|
| Coffee (cups/day) | | | | | | | | |
| 0 | 70 | 54 | 1.00 | | 1.00 | | 1.00 | |
| ≤1 | 181 | 162 | 0.99 | (0.62–1.57) | 0.93 | (0.57–1.51) | 1.05 | (0.58–1.89) |
| >1–2 | 110 | 101 | 0.99 | (0.59–1.64) | 0.93 | (0.55–1.56) | 1.02 | (0.56–1.88) |
| >2 | 52 | 73 | 0.65 | (0.36–1.17) | 0.63 | (0.35–1.13) | 0.69 | (0.36–1.33) |
| *p* for trend | | | | 0.10 | | 0.10 | | 0.11 |
| Tea (cups/day) | | | | | | | | |
| 0 | 34 | 57 | 1.00 | | 1.00 | | 1.00 | |
| ≤1 | 289 | 239 | 2.41 | (1.43–4.07) | 1.95 | (1.14–3.34) | 2.24 | (1.29–3.88) |
| >1 | 91 | 89 | 1.93 | (1.08–3.45) | 1.58 | (0.87–2.86) | 1.77 | (0.96–3.28) |
| *p* for trend | | | | 0.81 | | 0.95 | | 0.98 |
| Green tea (cups/week) | | | | | | | | |
| 0 | 172 | 141 | 1.00 | | 1.00 | | 1.00 | |
| <1 | 160 | 158 | 0.95 | (0.67–1.35) | 1.00 | (0.70–1.43) | 1.04 | (0.72–1.50) |
| ≥1 | 65 | 74 | 0.75 | (0.48–1.18) | 0.77 | (0.49–1.21) | 0.76 | (0.48–1.21) |
| *p* for trend | | | | 0.20 | | 0.22 | | 0.20 |

*OR* odds ratio, *CI* confidence interval

*OR1* adjusted for age (continuous), education, race, age at menarche (continuous), menopausal status and age at menopause for postmenopausal women, parity, OC use, HRT use, BMI (continuous), smoking (pack-years), smoking status

*OR2* further adjusted for sugar/honey added in coffee/tea (in teaspoons per cup)

*OR3* further adjusted for milk, cream, or nondairy creamer added in coffee/tea (yes vs. no)

Further adjustment for physical activity (METs), alcohol (drinks/month), diabetes and hypertension, and coffee (when evaluating tea) and tea (when evaluating coffee) essentially did not change risk estimates

Tea includes iced tea (not herbal teas)

## Table 2

Risk associated with use of sugar/honey and cream/milk among coffee and/or tea drinkers

| | Cases *n* (%) | Controls *n* (%) | OR1 (95% CI) | OR2 (95% CI) |
|---|---|---|---|---|
| **Added to coffee**[1] | | | | |
| Cream/milk[a] | | | | |
| None | 70 (20.6) | 71 (21.3) | 1.00 (Ref) | 1.00 (Ref) |
| Cream, half and half/nondairy creamer | 99 (29.1) | 86 (25.8) | 0.88 (0.53–1.45) | 0.83 (0.50–1.37) |
| Milk | 171 (50.3) | 177 (53.0) | 0.90 (0.58–1.40) | 0.86 (0.55–1.33) |
| Sugar/honey (teaspoons/cup)[b] | | | | |
| 0 | 228 (66.7) | 233 (69.6) | 1.00 (Ref) | 1.00 (Ref) |
| 1 | 58 (17.0) | 67 (20.0) | 0.84 (0.53–1.33) | 0.88 (0.56–1.41) |
| ≥2 | 56 (16.4) | 35 (10.5) | 1.33 (0.76–2.35) | 1.43 (0.81–2.55) |
| *p* for trend | | | 0.35 | 0.24 |
| Total sugar/honey (teaspoons/day)[b] | | | | |
| 0 | 228 (66.7) | 233 (69.6) | 1.00 (Ref) | 1.00 (Ref) |
| <1–2 | 67 (19.6) | 54 (16.1) | 1.04 (0.63–1.72) | 1.10 (0.66–1.83) |
| ≥2 | 47 (13.7) | 48 (14.3) | 0.95 (0.57–1.61) | 1.01 (0.60–1.72) |
| *p* for trend | | | 0.91 | 0.88 |
| **Added to tea**[2] | | | | |
| Cream/milk[a] | | | | |
| None | 253 (67.8) | 203 (63.8) | 1.00 (Ref) | 1.00 (Ref) |
| Cream, half and half/nondairy creamer | 22 (5.9) | 9 (2.8) | 1.62 (0.67–3.89) | 1.50 (0.61–3.65) |
| Milk | 98 (26.3) | 106 (33.3) | 0.65 (0.44–0.95) | 0.63 (0.43–0.93) |
| Sugar/honey (teaspoons/cup)[b] | | | | |
| 0 | 210 (55.6) | 204 (62.6) | 1.00 (Ref) | 1.00 (Ref) |
| 1 | 98 (25.9) | 94 (28.8) | 1.04 (0.71–1.54) | 1.09 (0.73–1.62) |
| ≥2 | 70 (18.5) | 28 (8.6) | 2.76 (1.50–5.07) | 2.66 (1.42–4.98) |
| *p* for trend | | | <0.01 | <0.01 |
| Total sugar/honey (teaspoons/day)[b] | | | | |
| 0 | 210 (55.7) | 204 (62.6) | 1.00 (Ref) | 1.00 (Ref) |
| <1–2 | 122 (32.4) | 84 (25.8) | 1.31 (0.87–1.96) | 1.34 (0.89–2.03) |
| ≥2 | 45 (11.9) | 38 (11.7) | 1.38 (0.75–2.52) | 1.40 (0.75–2.60) |
| *p* for trend | | | 0.18 | 0.17 |
| **Total sugar/honey added to coffee or tea (teaspoons/day)**[3,b] | | | | |
| 0 | 215 (53.2) | 222 (58.9) | 1.00 (Ref) | 1.00 (Ref) |
| <1 | 63 (15.6) | 47 (12.5) | 1.17 (0.72–1.91) | 1.26 (0.76–2.08) |
| ≥1–<3 | 68 (16.8) | 63 (16.7) | 1.02 (0.65–1.60) | 1.04 (0.65–1.64) |
| ≥3 | 58 (14.4) | 45 (11.9) | 1.47 (0.88–2.48) | 1.58 (0.92–2.71) |
| *p* for trend | | | 0.21 | 0.17 |

*OR1* odds ratio, *CI* confidence interval adjusted for age, education, race, age at menarche (continuous), menopausal status and age at menopause for postmenopausal women, parity, OC use, HRT use, BMI (continuous), smoking (pack-years), smoking status, coffee and/or tea consumption, and total energy intake

*OR2:* [a]Further adjusted for sugar/honey added in coffee/tea (in teaspoons per cup); [b]Further adjusted for milk, cream, or nondairy creamer added in coffee/tea (yes vs. no)

Further adjustment for physical activity (METs), alcohol (drinks/month), and diabetes essentially did not change risk estimates

[1]Includes only coffee drinkers

[2]Includes only tea drinkers

[3]Includes drinkers of either coffee or tea