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Tea, coffee, and caffeine and early-onset basal cell carcinoma in a case-control study

Leah M. Ferrucci, PhD[1,2], **Brenda Cartmel, PhD**[1,2], **Annette M. Molinaro, PhD**[1,2,3], **David J. Leffell, MD**[2,4], **Allen E. Bale, MD**[2,4], and **Susan T. Mayne, PhD**[1,2]

[1]Yale School of Public Health, New Haven, CT 06520

[2]Yale Cancer Center, New Haven, CT 06520

[3]UCSF Departments of Neurological Surgery and Epidemiology and Biostatistics, San Francisco, CA 94143

[4]Yale University School of Medicine, New Haven, CT 06520

Abstract

Objectives—Tea and coffee are hypothesized to play a protective role in skin carcinogenesis via bioactive components, such as caffeine, yet the epidemiologic evidence is mixed. Existing data supports an inverse association with basal cell carcinoma (BCC) more so than for melanoma or squamous cell carcinoma. To understand if tea, coffee, and caffeine are related to early-onset BCC, we evaluated data from 767 non-Hispanic Whites under age 40 in a case-control study in Connecticut.

Methods—BCC cases (n=377) were identified through Yale's Dermatopathology database. Controls (n=390) were randomly sampled from individuals in the same database with benign skin diagnoses and frequency matched to cases on age, gender, and biopsy site. Subjects completed an in-person interview including assessment of caffeinated coffee and hot tea. We calculated multivariate odds ratios (OR) and 95% confidence intervals (CIs) with unconditional logistic regression for regular consumption and frequency and duration measures.

Results—Combined regular consumption of caffeinated coffee plus hot tea was inversely associated with early-onset BCC (OR=0.60, 95% CI=0.38–0.96). Those in the highest category of caffeine from these sources had a 43% reduced risk of BCC compared to non-consumers (OR=0.57, 95% CI=0.34–0.95, p-trend=0.037).

Conclusions—Our findings suggest a modest protective effect for caffeinated coffee plus tea in relation to early-onset BCC that may, in part, be due to caffeine. This study adds to the growing body of literature suggesting potential health benefits from these beverages.

Keywords

non-melanoma skin cancer; tea; coffee; caffeine; epidemiology

Corresponding Author and Request for Reprints: Leah M. Ferrucci, PhD, MPH; Yale School of Public Health; 55 Church Street, Suite 801; New Haven, CT 06510; Phone: 203-764-9088; Fax: 203-764-5824; leah.ferrucci@yale.edu.

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Introduction

Ultraviolet (UV) radiation is the primary environmental etiologic agent in non-melanoma and melanoma skin cancer [1, 2]. Lifestyle and other environmental exposures inversely associated with skin cancer may function through inhibiting UV induced proliferation and inducing apoptosis in UV damaged cells. Tea and coffee, two of the most commonly consumed beverages in the world, have been hypothesized to play a protective role in skin carcinogenesis, as both contain numerous bioactive compounds, such as polyphenols and phytochemicals, with anti-carcinogenic potential [3–5].

There is considerable experimental evidence for a role of bioactive compounds from tea and coffee in skin cancer prevention. Several studies have observed a reduction in skin tumor incidence in mice treated with black tea polyphenols potentially via induction of apoptosis [6, 7]. Research in mice, human keratinocytes, and humans also indicates a protective role forepigallocatechin-3-gallate, a catechin in green tea, in skin cancer through several possible pathways, including antioxidant activity, anti-inflammatory effects, and cutaneous photoprotection [8–13]. Other compounds, such as myricetin, a flavanol and polyphenol found in tea, inhibited skin tumors in mouse models [14]. In addition, caffeic acid, a phenolic phytochemical and antioxidant that is a metabolite of chlorogenic acid found in coffee, suppressed ultraviolet B (UVB) induced skin carcinogenesis in mouse epidermal cells [15]. Caffeine, which occurs naturally in the seeds of the coffee plant and in the leaves of tea plants, has also been posited as playing a protective role in skin carcinogenesis. There are considerable data from mouse models indicating topical application or oral administration of caffeine to UVB-treated mice increases apoptosis in skin tumors [16–22]. Additional research on caffeine and UVB-irradiated human keratinocytes has found similar pro-apoptotic effects [23, 24].

Epidemiologic studies of non-melanoma skin cancer have observed inverse associations with these malignancies in relation to tea [25, 26] and caffeinated coffee [27–29]. In the most recent study of caffeinated coffee consumption and caffeine from coffee, the protective effect was only for basal cell carcinoma (BCC), which constitutes approximately 80% of non-melanoma skin cancers [30, 31], and not squamous cell carcinoma (SCC) [28]. There was also an inverse association with melanoma for coffee consumption among women, but not men observed in one population in Norway [32, 33] as well as a protective effect of coffee in a mixed gender case-control study in Italy [34]. In addition, while studies of tea and melanoma are sparse, in one case-control study to date there was a borderline statistically significant inverse association [35].

Not only has the overall incidence of BCC, the most common human cancer, increased in the last several decades [36–44], but the rise has been noted in young people under the age of 40 [36, 42, 45], especially women [42, 45]. Given the ubiquity of BCC across ages, identifying even modest protective effects from lifestyle factors could be particularly relevant at the population level. Therefore, to better understand the association between tea, coffee, and caffeine from these beverages and BCC under age 40, we evaluated these relationships in a case-control study.

Material and Methods

Yale Study of Skin Health in Young People

The Yale Study of Skin Health in Young People is a case-control study of early-onset BCC conducted in Connecticut [46]. BCC cases and controls with minor benign skin conditions diagnosed between July 1, 2006 and September 30, 2010 were identified through Yale University's Dermatopathology database. Eligible participants had to: be less than 40 years of age at the time of skin biopsy, reside in Connecticut, speak English, and themselves (or appropriate guardian for decisionally impaired individuals and those under age 18) be mentally and physically capable of completing all study components. Participants completed an in-person interview, self-administered questionnaires, and provided a saliva sample. Yale University's Institutional Review Board approved the study and participants (or guardians) provided written informed consent.

A total of 389 cases enrolled (participation rate=72.8%) in the study. Cases were classified into single (only one BCC, n=242) or multiple (two or more BCCs, n=147) BCC under the age of 40 based on the Yale Dermatopathology database (data from 1990 on) and participant self-report. Randomly sampled controls were frequency matched to BCC cases on age at biopsy, gender, and biopsy site. The study enrolled 458 controls (participation rate=60.7%). The three most common skin conditions in our controls were cyst (16.4%), seborrheic keratosis (16.2%), and wart (11.4%). All other conditions were present in less than 10% of controls.

The structured in-person interview assessed a wide range of characteristics, including sociodemographics, outdoor UV exposure, indoor tanning, history of sunburns, sunscreen use, melanoma and non-melanoma skin cancer among first degree relatives, height, weight, alcohol intake, smoking status, and self-reported phenotype characteristics (eye, skin, and hair color; skin reaction to strong sunlight for the first time in the summer for one hour without sunscreen; skin reaction after repeated and prolonged exposure to sunlight). Interviewers were blinded to case-control status until the end of the interview, when personal history of cancer was assessed.

Assessment of Caffeinated Coffee and Hot Tea

Participants were asked about their consumption of caffeinated coffee and hot tea (all kinds). For coffee, participants were first asked if they ever drank at least one cup of caffeinated coffee per week for six months or longer. Those who responded affirmatively to this question were then asked at what age they began drinking caffeinated coffee with this frequency. Participants were also asked if they were currently drinking one or more cups of caffeinated coffee per week and if not currently drinking coffee, the age at which they had stopped this practice. Participants reported the average number of cups of coffee they drank per day and the number of years of consumption.

We assessed similar frequency and duration information for hot tea of all kinds. Regular consumption was first queried as at least one cup of hot tea per month for six months. Those who answered this affirmatively were then asked about the total number of years they consumed hot tea, as well as the frequency and duration of consumption for each of the

following types of hot tea individually: regular black tea, decaffeinated black tea, green tea, herbal tea, and other (specified by participant).

Based on food composition data from the U.S. Department of Agriculture, and other epidemiologic studies of tea and coffee [28], we estimated caffeine content for caffeinated coffee and hot tea as: 137 mg/cup for caffeinated coffee, 47 mg/cup for hot black tea, 6 mg/cup for hot decaffeinated black tea, and 32 mg/cup for hot green tea.

Statistical Analysis

For this analysis we restricted our sample to non-Hispanic Whites; 380 (97.7%) cases and 390 (85.2%) controls. An additional three BCC cases with Gorlin Syndrome, which predisposes individuals to multiple BCCs early in life [47], were further excluded, leaving an analytic population of 767 individuals; 377 cases and 390 controls.

Using multivariate unconditional logistic regression, we calculated odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between regular consumption of coffee, tea, and caffeine and early-onset BCC. For those individuals who provided detailed frequency and duration information, we evaluated average cups per day during the time they were consuming each beverage and calculated cup-years for each beverage by multiplying the average cups per day of each beverage by the total number of years consumed for that beverage. We also calculated lifetime caffeine from caffeinated coffee and hot tea by multiplying the respective caffeine contents by the total lifetime cups per day (average cups per day multiplied by total years of beverage consumption) for each beverage and summing across the beverages. For the average number of cups per day, cup-years, and lifetime caffeine variables, we created low and high categories based on the median consumption for each beverage in controls; the exception to this was for coffee cups/per day which was split at 1 versus 2 or more cups per day for comparability to other analyses. Individuals who did not consume the specific beverage served as the referent.

We adjusted for the following potential confounders and known skin cancer risk factors, though only smoking status altered risk estimates by more than 10%: skin color, skin reaction after repeated and prolonged exposure to sunlight, education, body mass index, smoking status, outdoor UV exposure during warm months, and ever indoor tanning. Multivariate models were adjusted for the study frequency matching variables of age at biopsy, body site of skin biopsy, and gender. Trend tests were based on ordinal categorical variables. We also evaluated interactions by smoking and gender by including cross-product terms in the multivariate models and assessed the exposure variables in relation to all BCC cases as well as multiple BCC and single BCC case status. Reported p-values, except for tests of trend, are two-sided. All descriptive and multivariate analyses were conducted using SAS Version 9.3 (SAS, Cary, NC).

Results

In our sample of 767 participants, 69.2% were female and the median age at skin biopsy was approximately 36 years. Individuals with BCC were more likely to have fairer pigment-related characteristics for hair, skin, and eyes, sunburned or freckled with sun exposure,

spent more time outdoors during warm months, and had more sunburns than controls (Table 1). Cases were also more likely to have never smoked, have normal BMIs, and have attained higher education levels compared to controls.

Regular consumption of caffeinated coffee was reported by 553 (72.1%) individuals; with a statistically significant higher percentage of regular consumption in controls (75.4%) as compared to cases (68.7%) (Table 1). Just over 50% of participants (n=394) reported regular consumption of hot tea and this was also more common in controls (52.6%) than cases (50.1%), though the difference was not statistically significant. Among all participants, black tea was the most regularly consumed hot tea (n=264, 34.4%), followed by herbal tea (n=140, 18.3%) and green tea (n=130, 17.0%); individuals could report multiple tea types.

With multivariate adjustment, regular consumption of caffeinated coffee was inversely associated with risk of early-onset BCC, but the relationship was not statistically significant (OR=0.76, 95% CI=0.53–1.10) (Table 2). There was a borderline statistically significant inverse linear trend for average daily number of cups of caffeinated coffee (p-trend=0.085), with a suggestive association for 2 or more cups of caffeinated coffee per day (OR=0.70, 95% CI=0.47–1.06). A similar pattern was present for cup-years of caffeinated coffee, though these associations were not statistically significant.

There was no evidence of an association with regular consumption of hot tea, average daily cups of tea or cup-years of consumption. Similarly, the individual types of hot tea were not statistically significantly associated with BCC (data not shown).

Combined regular consumption of caffeinated coffee and hot tea was statistically significantly inversely associated with early-onset BCC (OR=0.60, 95% CI=0.38–0.96) (Table 3). With detailed frequency and duration information, there was a suggestive inverse linear trend with cup-years of tea plus caffeinated coffee (p-trend=0.096). Estimated lifetime caffeine intake from these beverages exhibited a similar pattern with a statistically significant inverse trend with BCC (p-trend=0.037), with the highest level of caffeine from these sources associated with a 43% reduced risk of BCC compared to non-consumers (OR=0.57, 95% CI=0.34–0.95).

All of the inverse associations we observed for caffeinated coffee, combined caffeinated coffee and tea, and caffeine, were more strongly associated with single BCC (OR=0.71, 95% CI=0.47–1.07; OR=0.55, 95%CI=0.33–0.92; OR=0.55, 95% CI= 0.31–0.97, respectively) than multiple BCC (OR=0.79, 95% CI=0.47–1.31; OR=0.71, 95%CI=0.37–1.36; OR=0.63, 95% CI=0.31–1.30, respectively). Finally, there was no evidence of effect modification by smoking or gender for the regular consumption, frequency, or duration variables for the beverages separately or combined in relation to BCC (data not shown).

Discussion

As common beverages, both coffee and tea have been of interest with regard to their effect on the risk of numerous cancers. A meta-analysis of cohort studies found that coffee consumption was inversely associated with total cancer incidence [48]. Early ecologic studies indicated a lower incidence of some cancers in areas with higher tea consumption

[49], but an increased risk of other cancers [49, 50] and more recent epidemiologic studies of tea and cancer have continued to be mixed [51]. In this case-control study of early-onset BCC, we observed an inverse association for BCC with regular consumption of hot tea and caffeinated coffee combined. The protective role for these beverages may, in part, be due to their associated caffeine content, as lifetime estimated caffeine consumption from hot tea and caffeinated coffee was associated with a reduced risk of early-onset BCC.

Our borderline statistically significant results for caffeinated coffee and combined caffeinated coffee and hot tea, as well as the statistically significant finding for lifetime caffeine from these beverages indicates a potential protective role for these exposures in early-onset BCC. This is in line with a recent prospective analysis, in which caffeine from coffee and caffeinated coffee, but not decaffeinated coffee, were associated with a decreased risk of BCC in the Nurses' Health Study and the Health Professionals Follow-up Study [28]. Additional evidence comes from the Women's Health Initiative Observational Study with an inverse association for nonmelanoma skin cancer with caffeinated coffee, but no association for decaffeinated coffee [27]. Even though the latter study did not differentiate between BCC and SCC, it appears in line with a protective role for caffeinated coffee and caffeine in BCC, as the majority of non-melanoma skin cancers are BCCs [27]. A recent study in Australia of caffeine intake, found that only among people with prior skin cancer was there an inverse association for subsequent BCC [52]. Though there was no association with BCC risk in the whole sample, this population had low levels of coffee intake. A weak inverse association was also observed in a Norwegian study of coffee and non-melanoma skin cancer, but they did not assess if the coffee was caffeinated or decaffeinated [29]. As we lacked data on decaffeinated coffee consumption, we could not evaluate potential effects of coffee independent of caffeine. Interestingly, across studies, the inverse associations for coffee and caffeine intake appear to hold most strongly for BCC and are not as apparent for SCC [28, 52, 53] or melanoma [28, 35, 54].

Animal studies indicate that topical application or oral administration of caffeine in UVB-treated mice increases apoptosis in skin tumors [16–22]. Additional research on caffeine and UVB-irradiated human keratinocytes has found similar pro-apoptotic effects [23, 24]. In mice, caffeine has been found to induce apoptosis selectively in skin tumors by inhibiting the ataxia-telangiectasia and Rad3-related (ATR) kinase/checkpoint kinase 1 (Chk1) pathway; UVB-induced skin tumors have elevated activation and dependence on this pathway [19]. In a mouse model with partially inhibited ATR function in skin exposed to chronic UV, the primary keratinocytes had lower Chk1 phosphorylation and a two-fold increase in apoptosis [55]; mimicking the effects of caffeine on this pathway. There is also some evidence in UV-damaged human keratinocytes for caffeine acting through the ATR-Chk1 pathway to induce apoptosis [24]. Despite viable biological mechanisms for caffeine in skin cancer, both coffee and tea contain many other compounds, and it is possible that other bioactive components common to caffeinated coffee and hot tea could be strongly correlated with caffeine content and be driving the observed association.

We observed stronger effects for caffeinated coffee plus hot tea and lifetime caffeine from these beverages in relation to single BCC than in relation to multiple BCC. This could be due to a lack of power for assessing this exposure for the multiple BCC cases, as they made

up only one-third of total BCC cases. Alternatively, through sequencing of the melanocortin 1 receptor gene we saw that our multiple BCC cases have a stronger underlying genetic susceptibility to BCC as compared to single BCC cases [46]. Thus, it is plausible that lifestyle factors, such as caffeine intake, are unable to compensate adequately for the increased genetic risk in this group.

Two epidemiologic studies of non-melanoma skin cancer have observed inverse associations with tea and SCC [26], as well as both SCC and BCC [25]. This finding was not supported by our null results for tea alone, as well as studies of SCC [53, 56] and BCC [56]. This could in part be due to the wide variety of types of tea and their differing bioactive components, and the potential for high levels of some phenolics in tea to induce oxidative DNA damage [57]. We found that black tea, green tea, and herbal tea were all commonly consumed by participants and some reported drinking multiple types of tea. Overall, epidemiologic data on tea and other cancers do not clearly indicate a protective association [51]. If the association between coffee and BCC is due to caffeine in this beverage, then associations with tea alone, which contains lower levels of caffeine, may be difficult to detect. In the recent US prospective analysis of skin cancer, caffeine from tea, cola, and chocolate combined only accounted for 21% of the population's caffeine intake, as compared to 78.5% from coffee, and while there was an inverse relationship with caffeine from these other sources and BCC, the association was not statistically significant [28].

Temperature of tea, which could be a part of preparation methods as well as concentration of caffeine or other compounds, may also play a role in risk. One study of SCC found that hot black tea, but not iced tea, was inversely associated with disease [26]. Although we also queried iced tea consumption in our population, we did not include this exposure in our analysis, as we had concerns about the measurement error associated with this exposure. More specifically, we lacked detailed questions on exact serving sizes, how diluted the beverages were by ice, brewed versus mixes versus bottled/canned.

This study has several strengths including data on a wide range of potential confounders, a relatively large sample of pathologically confirmed early-onset BCC cases and controls who had seen a dermatologist, more recent recall of consumption history as compared to skin cancer case-control studies of predominantly older individuals, and information on individual types of tea. However, there are certain limitations that should be noted, including a lack of information on exact serving sizes, quantification of other potential chemopreventive compounds in these beverages, and brewing time for hot tea and roasting and preparation methods for coffee, which could influence the amount of caffeine and other compounds in these beverages. In addition to our inability to quantify iced tea, our questionnaire did not query decaffeinated or iced coffee consumption, or other foods and medications containing caffeine, making our lifetime assessment of caffeine an underestimate. It is also possible that the observed findings could be due to other unmeasured or inadequately assessed factors. While recall bias is a potential concern given the nature of the case-control design, it is unlikely that the general public would link these beverages with skin cancer risk thereby reducing differential reporting by case status.

In conclusion, regular consumption of hot tea and caffeinated coffee combined, as well as lifetime caffeine intake from these beverages was associated with a reduced risk of early-onset BCC. These findings agree with results from another recent prospective epidemiologic study of BCC among individuals of all ages and support a potential inverse association between these popular beverages and a common malignancy.

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Abbreviations

ATR	ataxia-telangiectasia and Rad3-related kinase
BCC	basal cell carcinoma
BMI	body mass index
Chk1	checkpoint kinase 1
CI	confidence interval
OR	odds ratio
SCC	squamous cell carcinoma
UV	ultraviolet
UVB	ultraviolet B

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Table 1

Selected characteristics of participants in the Yale Study of Skin Health early-onset BCC case-control study

Characteristic	Cases, N=377 N[1] (%)	Controls, N=390 N[1] (%)	p-value[2]
Age (y), median (IQR)	36.3 (33.2–38.5)	36.8 (32.8–38.5)	0.955
Female	257 (68.2)	274 (70.3)	0.531
Body site of skin biopsy			<0.001
Head	204 (54.1)	164 (42.1)	
Extremity	72 (19.1)	126 (32.3)	
Trunk	101 (26.8)	100 (25.6)	
Education			0.014
≤ Some college	105 (27.9)	143 (36.9)	
College graduate	113 (30.1)	116 (29.9)	
≥ Some graduate school	158 (42.1)	129 (33.2)	
Hair color			<0.001
Black/Dark brown	101 (26.9)	161 (41.3)	
Light brown	136 (36.2)	155 (39.7)	
Blonde/Fair	100 (26.6)	63 (16.2)	
Red	39 (10.4)	11 (2.8)	
Skin color (inner upper arm)			<0.001
Olive	15 (4.0)	77 (19.7)	
Fair	213 (56.5)	236 (60.5)	
Very fair	149 (39.5)	77 (19.7)	
Skin reaction with first summer sun exposure			<0.001
Turn brown, no sunburn	6 (1.6)	31 (8.0)	
Mild sunburn followed by tan	142 (37.7)	200 (51.4)	
Painful sunburn peeling	199 (52.8)	144 (37.0)	
Severe sunburn blistering	30 (8.0)	14 (3.6)	
Skin reaction with prolonged sun exposure			<0.001
Very brown, deeply tanned	39 (10.3)	71 (18.2)	
Moderately tanned	169 (44.8)	223 (57.2)	
Mildly tanned peeling tendency	123 (32.6)	78 (20.0)	
Freckled, no suntan	46 (12.2)	18 (4.6)	
Body mass index (kg/m^2)			<0.001
<25.0	246 (65.3)	209 (53.6)	
25–29.9	91 (24.1)	106 (27.2)	
≥30.0	40 (10.6)	75 (19.2)	
Smoking status			<0.001
Never	233 (62.3)	199 (51.4)	
Former	111 (29.7)	122 (31.5)	
Current	30 (8.0)	66 (17.1)	
Outdoor sun in warm months (h), mean ± SD	8942 ± 3422	8310 ±3265	0.009[3]
Sunburns (n), median (IQR)	6 (1–16)	3 (1–9)	<0.001

Characteristic	Cases, N=377 N[1] (%)	Controls, N=390 N[1] (%)	p-value[2]
Sunbathing sessions (n), median (IQR)	318 (58–714)	279 (84–689)	0.582
Regular caffeinated coffee consumption	259 (68.70)	294 (75.4)	0.039
Regular hot tea consumption	189 (50.1)	205 (52.6)	0.501

[1] May not sum to total due to missing data. May sum to greater than 100% due to rounding

[2] χ^2 for categorical variables, Wilcoxon Rank Sum for continuous variables.

[3] T-test

Table 2

Association between caffeinated coffee and hot tea consumption and early-onset BCC

Characteristic	Cases/Controls	Multivariate OR[a] (95% CI)
Regular caffeinated coffee consumption		
No	115/93	1.00
Yes	258/293	0.76 (0.53–1.10)
Average daily caffeinated coffee consumption while drinking caffeinated coffee regularly (cups/day)		
None	115/93	1.00
1	124/116	0.92 (0.60–1.40)
≥2	129/163	0.70 (0.47–1.06) p-trend=0.085
Caffeinated coffee cup-years		
None	115/93	1.00
Low (≤ 22 cup-years)	144/141	0.86 (0.58–1.30)
High (> 22 cup-years)	108/136	0.74 (0.48–1.14) p-trend=0.167
Regular hot tea consumption		
No	185/184	1.00
Yes	188/202	0.89 (0.64–1.23)
Average daily hot tea consumption (cups/day) while drinking tea regularly		
None	185/184	1.00
Low (≤ 0.43 cups/day)	89/91	0.90 (0.60–1.35)
High (≥0.43 cups/day)	99/110	0.88 (0.60–1.29) p-trend=0.486
Hot tea cup-years		
None	185/184	1.00
Low (≤ 3 cup-years)	101/105	0.83 (0.57–1.22)
High (> 3 cup-years)	87/96	0.96 (0.64–1.44) p-trend=0.722

[a] Adjusted for age, gender, body site (trunk, extremity, head/neck), skin color (olive, fair, very fair), skin reaction after repeated and prolonged exposure to sunlight (very brown/deeply tanned, moderately tanned, mildly tanned some peeling, only freckled, no tan), education (some college or less, college graduate, at least some post-graduate school), BMI (normal, overweight, obese), smoking status (never, former, current), outdoor UV exposure during warm months (continuous, hours), and ever indoor tanning.

Table 3

Association between caffeinated coffee plus hot tea and caffeine consumption and early-onset BCC

Characteristic	Cases/Controls	Multivariate OR[a] (95% CI)
Regular hot tea and/or caffeinated coffee consumption		
No	67/45	1.00
Yes	306/341	0.60 (0.38–0.96)
Hot tea cup-years plus caffeinated coffee cup-years		
None	67/45	1.00
Low (≤ 32 cup-years)	167/167	0.65 (0.40–1.06)
High (> 32 cup-years)	133/158	0.61 (0.36–1.02) p-trend=0.096
Lifetime caffeine from caffeinated coffee and hot tea[b]		
None	67/45	1.00
Low (≤1,000,785 mg)	174/161	0.68 (0.42–1.17)
High (>1,000,785 mg)	121/159	0.57 (0.34–0.95) p-trend=0.037

[a] Adjusted for age, gender, body site (trunk, extremity, head/neck), skin color (olive, fair, very fair), skin reaction after repeated and prolonged exposure to sunlight (very brown/deeply tanned, moderately tanned, mildly tanned some peeling, only freckled, no tan), education (some college or less, college graduate, at least some post-graduate school), BMI (normal, overweight, obese), smoking status (never, former, current), outdoor UV exposure during warm months (continuous, hours), and ever indoor tanning.

[b] Based on estimated caffeine content in caffeinated coffee (137 mg/cup), caffeinated hot black tea (47 mg/cup), decaffeinated hot black tea (6 mg/cup), and hot green tea (32 mg/cup) and lifetime cups of each beverage.