HHS Public Access

Author manuscript

J Am Acad Dermatol. Author manuscript; available in PMC 2022 July 01.

Published in final edited form as:

J Am Acad Dermatol. 2019 August ; 81(2): 395–402. doi:10.1016/j.jaad.2019.01.084.

Coffee, tea, caffeine, and risk of nonmelanoma skin cancer in a Chinese population: The Singapore Chinese Health Study

Choon Chiat Oh, MD, MRCP[a], **Aizhen Jin, MSc**[b], **Jian-Min Yuan, MD, PhD**[c,d], **Woon-Puay Koh, MD, PhD**[b,e]

[a]Department of Dermatology, Singapore General Hospital

[b]Health Services and Systems Research, Duke-NUS Medical School, Singapore

[c]Division of Cancer Control and Population Sciences, UPMC Hillman Cancer Center

[d]Department of Epidemiology, Graduate School of Public Health, University of Pittsburgh

[e]Saw Swee Hock School of Public Health, National University of Singapore.

Abstract

Background: Although epidemiologic studies in populations of European descent suggest a possible chemoprotective effect of caffeine against nonmelanoma skin cancer (NMSC), data in Asian populations are lacking.

Objectives: We examined the relationship of coffee, tea, and caffeine consumption with NMSC risk among Chinese in Singapore.

Methods: We used data from the Singapore Chinese Health Study, a prospective cohort of 63,257 men and women who were 45 to 74 years old at recruitment from 1993 to 1998. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated by using multivariable Cox proportional hazard models.

Results: Coffee drinking was associated with reduced NMSC risk in a dose-dependent manner (*P* trend < .0001). Compared with those who drank coffee less than weekly, those who drank 3 or more cups per day had a lower risk of basal cell carcinoma (HR, 0.54; 95% CI, 0.31–0.93) and a lower risk of squamous cell carcinoma (HR, 0.33; 95% CI, 0.13–0.84). Compared with nondrinkers of black tea, daily drinkers of black tea also had a reduced risk of NMSC (HR, 0.70; 95% CI, 0.52–0.94). Caffeine intake reduced NMSC risk in a stepwise manner (*P* trend = .0025); subjects with a caffeine intake of 400 mg/d or more had the lowest risk (HR, 0.59; 95% CI, 0.34–1.04).

Conclusion: Consumption of caffeinated drinks such as coffee and black tea may reduce the risk of NMSC among Chinese.

Correspondence to: Choon Chiat Oh, MD, MRCP, Department of Dermatology, Singapore General Hospital, 20 College Road, Academia, Singapore 169856, Singapore. oh.choon.chiat@singhealth.com.sg. Woon-Puay Koh, MD, PhD, Health Services and Systems Research, Duke-NUS Medical School, 8 College Road, Level 4, Singapore 169857, Singapore. woonpuay.koh@duke-nus.edu.sg.

Conflicts of interest: None disclosed.

Keywords

caffeine; Chinese; coffee; nonmelanoma skin cancer; tea

Nonmelanoma skin cancer (NMSC) is 1 of the most common cancers that inflict millions, and its incidence is on the rise worldwide.[1] Although the prognosis of NMSC is generally favorable compared with that of melanoma,[2] the public health burden of NMSC can be substantial owing to its high incidence, as well as to the cost of treatment.[3] In addition, up to 50% of patients with a primary basal cell carcinoma (BCC) or squamous cell carcinoma (SCC) may develop 1 or more additional carcinomas within the next 5 years.[1]

The incidence of NMSC increases with age, and it is the highest among people with Fitzpatrick skin types I and II.[4] Although the main environmental risk factor is ultraviolet (UV) radiation from the sun,[5] there has been great interest in identifying other modifiable risk factors for skin cancer and new approaches for skin cancer prevention.

Coffee and tea are 2 of the most widely consumed beverages in the world.[6,7] Because of high global consumption of both of these caffeinated drinks, there is much interest in their effects on human health[8] and diseases, including skin diseases with a generally poor prognosis such as melanoma.[9] Experimental evidence suggests that caffeine may have an antiproliferative effect on keratinocytes via induction of apoptosis in UV-damaged cells through multiple pathways.[10,11] A number of animal studies have consistently reported that caffeine intake or topical administration of caffeine on the skin inhibits UV-induced skin cancer and tumors.[12] Recent meta-analyses of studies involving populations of European descent have also provided evidence to support a possible protective role of caffeine against NMSC.[13,14]

Skin cancer is the sixth most common cancer among men and the seventh most common cancer among women in Singapore.[15] The most common skin cancer is BCC, followed by SCC, with the highest incidence rates among the Chinese,[16] who have Fitzpatrick skin types III and IV, compared with among their Malay and Indian counterparts, who have darker skin tones. To explore the association between caffeine consumption and the incidence of NMSC in the Chinese population, we conducted prospective analyses using data from the Singapore Chinese Health Study.

METHODS

Study population

The current study was conducted on the participants in the Singapore Chinese Health Study, who comprise a population-based prospective cohort of 63,257 men (n = 27,959) and women (n = 35,298) aged 45–74 years at recruitment between April 1993 and December 1998. This study was approved by the institutional review board at the National University of Singapore, and all enrolled participants gave written informed consent.

Baseline and dietary assessment

At baseline, an in-person interview was administered to all participants by using a structured questionnaire. We used a 165-item validated semiquantitative food frequency questionnaire (FFQ) to record participants' habitual dietary intake during the past year at enrollment. The details regarding the development and validation of the FFQ were reported previously.[17] For intake of coffee and tea, participants were asked in 4 separate questions how often on average they consumed (1) 1 cup of coffee (instant or freshly brewed); (2) 1 cup of 3-in-1 coffee; (3) 1 cup of Chinese red tea or Ceylon tea (ie, black tea); and (4) 1 cup of green tea, such as jasmine tea. Participants were asked to pick their response from 1 of the 9 predetermined categories: never or hardly ever, 1 to 3 cups a month, 1 cup a week, 2 or 3 cups a week, 4 to 6 cups a week, 1 cup a day, 2 or 3 cups a day, 4 or 5 cups a day, and 6 or more cups a day. The serving size of one cup of coffee or tea was assigned as 237 mL.

Dietary intake of caffeine and other nutrients was estimated from the Singapore Food Composition Database, which listed 96 nutritional and non-nutritional values per 100 g of the edible foods and beverages specific for this cohort. The foundation of this database relied heavily on the data published by the US Department of Agriculture; it was supplemented with information from multiple resources for other foods and components and referenced from published food composition tables from China, Malaysia, and Taiwan.[17] Coffee and tea accounted for 84% and 12% of total dietary caffeine intake in this cohort, respectively. The remaining minor contribution (4%) came from other caffeinated food sources such as soda (0.7%), cocoa drinks, and chocolate-related food items.

Identification of cancer cases

Cancer diagnoses and deaths in this cohort were identified via linkage with the Singapore Cancer Registry and the Singapore Registry of Births and Deaths. As of December 31, 2016, only 56 cohort participants (<0.1%) were known to be lost to follow-up on account of migration out of Singapore or for other reasons. The nationwide cancer registry has been in place since 1968 and has been shown to be comprehensive in its recording of cancer cases.[18] Because this was a study on the risk of cancer, we excluded 1936 participants with a history of invasive cancer at recruitment (these individuals were identified via self-report [n = 822] or linkage with the nationwide cancer registry in Singapore [n = 1114], including 3 individuals with melanoma and 15 with NMSC). As of December 31, 2016, among the 61,321 participants who did not have a history of cancer diagnosis at baseline, there were 632 incident cases of skin cancer diagnosed on the basis of histopathologic confirmation. These included 427 cases of BCC and 182 cases of SCC, as well as 23 cases of melanoma, 24 cases of lymphomas, 7 cases of sarcomas, 5 cases of sebaceous adenocarcinoma, 4 cases of extramammary Paget disease, and 13 cases of rare cancers involving other cell types.

Statistical analysis

Person-years of follow-up were computed from the recruitment date to the date of BCC or SCC diagnosis, death, migration, or December 31, 2016, whichever occurred first. A series of Cox proportional hazards regression analyses were performed to examine the associations of exposures of interest to us, namely, coffee, black tea, green tea, sodas, and caffeine with skin cancer incidence. As coffee was the main contributor of caffeine

intake in this population and a cup of coffee (237 mL) contained approximately 100 mg of caffeine, we created ordinal categories of caffeine intake to correspond to the categories of coffee consumption. We used hours sitting at work and watching television as surrogates of duration for indoor activities and also hours spent on moderate activities, strenuous sports, and vigorous work as surrogates of duration for outdoor activities in our analysis.

To control for confounding, the following were included as covariates in incremental models. Model 1 included sex, dialect group (Cantonese, Hokkien), age (years), interview year (1993–1995 or 1996–1998), and education level (no formal education/primary eduction, secondary education, or higher). Model 2 further included lifestyle factors such as cigarette smoking status (never, former, or current), alcohol consumption (none/monthly, weekly, or daily), body mass index (<20, 20 to <24, 24 to <28, or ≥28 kg/m^2), time sitting at work (h/d), time watching television (h/d), time engaging in moderate activity (h/wk), time engaging in strenuous activity (h/wk), time engaging in vigorous activity (h/wk), and history of physician-diagnosed diabetes (yes or no). Model 3 further included all caffeinated drinks (coffee, black tea, green tea, and soda) to examine the independent association of each caffeinated beverage with cancer risk.

RESULTS

After a mean follow-up of 18.3 years (standard deviation [SD], 5.7 years) among a total of 61,321 participants (27,293 men and 34,028 women), 427 incident cases of BCC and 182 incident cases of SCC were identified via linkage with the nationwide cancer registry. The mean age at skin cancer diagnosis was 74.3 years (SD, 8.9 years). Men accounted for 48.3% of all skin cancers.

The study participants had a mean age of 56.4 years (SD, 8.0 years) at baseline, and 55.5 % were women. About 70.4% of our cohort participants reported drinking coffee daily, whereas 11.2% reported drinking black tea daily and 12.4% reported drinking green tea daily. Comparatively, soda was less frequently consumed; only 4.3% reported drinking soda 3 or more times per week.

Table I shows the distribution of demographic characteristics of cohort members by the amount of daily caffeine consumption. Compared with those in the lowest quartile of intake, those in the highest quartile of caffeine intake (≥400 mg/d) were more likely to be men, be ever-smokers, engage in more hours of vigorous activities or strenuous sports per week, consume more alcohol, and have a lower prevalence of diabetes mellitus.

Table II shows the association between skin cancer incidence and the different types of caffeinated beverages in our study. Coffee drinking was associated with reduced NMSC risk in a dose-dependent manner (*P* trend = .0001); compared with the risk of NMSC faced by those who drank coffee less than once a week, the risk was significantly reduced in daily drinkers and with increasing number of cups per day. In the highest intake category of 3 or more cups/day, the hazard risk (HR) was 0.47 (95% confidence interval [CI], 0.29–0.75). Compared with nondrinkers (defined as drinking less than once a month), daily drinkers of black tea also had a statistically significantly reduced NMSC risk (HR, 0.70; 95% CI,

0.52–0.94). We noted that the risk estimates for drinkers of 1 or 2 cups of coffee daily (HR, 0.74; 95% CI, 0.61–0.89) and daily drinkers of black tea (HR, 0.70; 95% CI, 0.52–0.94) were comparable. However, because of the small number of daily black tea drinkers and because most of them drank only 1 cup per day, we were not able to perform an analysis by the number of cups among daily drinkers of black tea. Intake of green tea and intake of soda were not significantly associated with NMSC risk.

Table III shows that an inverse association between coffee and cancer risk was present for both BCC and SCC. For black tea, although the association was statistically significant for BCC, it was not statistically significant for SCC, possibly owing to the small number of cases (Table III). Caffeine intake reduced overall risk of NMSC in a stepwise manner (*P* trend = .0025); subjects in the highest caffeine intake category of 400 mg/d or more had a 41% reduced risk (HR. 0.59; 95% CI, 0.34–1.04) compared with those with an intake of less than 50 mg/d. This reduction in risk was observed for both BCC and SCC (Table IV). Finally, we did stratified a analysis by sex to look for an interaction between sex and coffee, black tea, and caffeine in association with risk of NMSC. There was no heterogeneity in the results between men and women; all *P* values for interactions were 0.10 or higher.

DISCUSSION

In this large prospective cohort of middle-aged and elderly Chinese, we found that those who consumed coffee or black tea daily had a reduced risk of developing NMSC. Specifically, coffee drinking was associated with reduced risk of both BCC and SCC, whereas daily tea drinking reduced the risk of BCC. Overall, caffeine intake reduced the risk of both types of NMSC in a dose-dependent manner.

Experimental studies have provided evidence of an in vitro proapoptotic effect of caffeine on keratinocytes.[10,11] Previous experimental studies have reported that caffeine has the ability to induce apoptosis in UV-damaged keratinocytes and prevent UV-induced carcinogenesis in animals.[19] This photo-protective effect of caffeine has also been seen in cultured human keratinocytes.[10] Caffeine inhibits the UV B—induced formation of thymidine dimers and may enhance apoptosis of precancerous cells through p53-dependent and p53-independent biologic pathways.[20] One of these proapoptotic pathways mediated by caffeine includes the inhibition of the protein ATR serine/threonine kinase (previously known as ataxia telangiectasia and Rad3 related),[21] which has preferential binding to UV-damaged DNA to obstruct premature chromatin condensation.[22] Our finding of a protective association of coffee and caffeine intake with BCC is consistent with all previous prospective studies in Australia,23 United States,[24] and Europe[25] that have examined the association between caffeinated coffee and risk of BCC. Conversely, decaffeinated coffee has not found to be associated with ris of BCC.[23,24]

To our best knowledge, this is the first prospective study to show an inverse association between coffee or caffeine and risk of SCC, which contradicts the largely null associations from previous studies. The earliest cohort study looking at coffee and NMSC was conducted in a Norwegian population, and it showed that coffee was associated with reduced risk of BCC but not with risk of SCC.[25] In another study from Australia, with 323 cases of

BCC and 196 cases of SCC, the authors reported that among those with previous skin cancer, those in the highest tertile intake of caffeine had reduced risk of BCC but not with risk of SCC.[23] The Nurses Health Study and the Health Professionals Follow-up Study in the United States also showed that with use of a reference group consisting of those who drank less than 1 cup a month, drinking 2 or more cups a day was associated with significantly reduced risk of BCC but not with risk of SCC, and correspondingly, caffeine was inversely associated with risk of BCC but not with risk of SCC in these 2 cohorts.[24] A hypothesis raised by these authors to explain the conflicting results with BCC and SCC is that SCC could have a lower tolerance of DNA damage and lower apoptotic threshold than BCC,[26] which thus could render SCC to be less susceptible to the apoptosis-inducing effect of caffeine. It has been observed that SCC in Asians has a greater tendency to occur in non–sun-exposed sites and a higher potential for metastasis than in whites; a possible explanation for this is that whereas SCC is related to sun exposure among the fairer whites, the development of SCC in darker-skinned Asians is more likely to be related to chronic scarring and areas of chronic inflammation.[27]

Population-based case-control studies in US populations have shown a protective effect of black tea drinking on the risk of SCC[28] or on the risk of both SCC and BCC.[29] However, a recent Australian cohort study of 1325 participants showed no association between intake of black tea and incidence of BCC or SCC.[23] Interestingly, a case-control study of SCC showed that the potential protective effect of black tea on risk of cancer was related to multiple definitions or markers of strong tea such as reported strength of tea and brewing time and temperature.[28] Consistent with our hypothesis that the inverse association between black tea and risk of NMSC could be mediated by caffeine, given that the concentration of caffeine in green tea is generally lower than in black tea,[30] the lack of association between green tea and NMSC risk in our study is not unexpected.

The strengths of this study include the design of a population-based prospective cohort with a long follow-up time and a large number of incident NMSC cases, particularly BCC and SCC cases. This is also one of the few populations that allowed us to examine the intake of black tea and green tea separately. Inevitably, our study has limitations. One limitation is a possible misclassification of intake of caffeine, coffee, or tea with use of the FFQ and measurement of this intake only at baseline. Another limitation is a lack of information on decaffeinated coffee or tea. Data on other potential confounders that are risk factors for NMSC, such as family history, history of radiation or chemical exposure, outdoor sun exposure, Fitzpatrick skin type, and use of sunscreen and/or protective outerwear were also not available. We have attempted to adjust for UV exposure by including durations of both indoor and outdoor activities as surrogate markers and covariates in the model. Although we did not ask about the use of sunscreen or other sunprotective practices during the recruitment, we do not suspect that such practices would be different between the participants.

In conclusion, our findings support experimental evidence that a high intake of caffeine could reduce the risk of NMSC. Specifically, the drinking of coffee was associated with reduced risk of SCC and BCC, and the drinking of black tea was associated with reduced risk of SCC. We hope that our study can provide the impetus for further research to

determine which component(s) of coffee and tea are responsible for the chemoprotective effect and whether caffeine is indeed the agent responsible for this effect.

Funding sources:

Supported by the National Institutes of Health (grants R01 CA144034 and UM1 CA182876). Dr Koh is supported by the National Medical Research Council, Singapore (grant NMRC/CSA/0055/2013).

We thank Siew-Hong Low of the National University of Singapore for supervising the fieldwork of the Singapore Chinese Health Study and Renwei Wang for the maintenance of the cohort study database. We also thank the Singapore Cancer Registry for identification of cancer cases via linkage.

REFERENCES

1. Donaldson MR, Coldiron BM. No end in sight: the skin cancer epidemic continues. In: Seminars in Cutaneous Medicine and Surgery. Vol 30. Frontline Medical Communications; 2011:3–5. [PubMed: 21540015]
2. Rees JR, Zens MS, Celaya MO, Riddle BL, Karagas MR, Peacock JL. Survival after squamous cell and basal cell carcinoma of the skin: a retrospective cohort analysis. Int J Cancer. 2015;137(4):878–884. [PubMed: 25598534]
3. Guy GP, Ekwueme DU. Years of potential life lost and indirect costs of melanoma and non-melanoma skin cancer. Pharmacoeconomics. 2011;29(10):863–874. [PubMed: 21846158]
4. Khalesi M, Whiteman DC, Tran B, Kimlin MG, Olsen CM, Neale RE. A meta-analysis of pigmentary characteristics, sun sensitivity, freckling and melanocytic nevi and risk of basal cell carcinoma of the skin. Cancer Epidemiol. 2013;37(5):534–543. [PubMed: 23849507]
5. Karagas MR, Weinstock MA, Nelson HH. Keratinocyte carcinomas (basal and squamous cell carcinomas of the skin). In: Cancer Epidemiology and Prevention. Oxford University Press; 2009.
6. Albert J World coffee consumption. 2013:4–5.
7. Graham HN. Green tea composition, consumption, and polyphenol chemistry. Prev Med. 1992;21(3):334–350. [PubMed: 1614995]
8. Higdon JV, Frei B. Coffee, and health: a review of recent human research. Crit Rev Food Sci Nutr. 2006;46(2):101–123. [PubMed: 16507475]
9. Wu S, Han J, Song F, et al. Caffeine intake, coffee consumption, and risk of cutaneous malignant melanoma. Epidemiology. 2015;26(6):898. [PubMed: 26172864]
10. Heffernan TP, Kawasumi M, Blasina A, Anderes K, Conney AH, Nghiem P. ATR–Chk1 pathway inhibition promotes apoptosis after UV treatment in primary human keratinocytes: potential basis for the UV protective effects of caffeine. J Invest Dermatol. 2009;129(7):1805–1815. [PubMed: 19242509]
11. Han W, Ming M, He Y-Y. Caffeine promotes ultraviolet B-induced apoptosis in human keratinocytes without complete DNA repair. J Biol Chem. 2011;286(26):22825–22832. [PubMed: 21561856]
12. Huang M-T, Xie J-G, Wang ZY, et al. Effects of tea, decaffeinated tea, and caffeine on UVB light-induced complete carcinogenesis in SKH-1 mice: demonstration of caffeine as a biologically important constituent of tea. Cancer Res. 1997; 57(13):2623–2629. [PubMed: 9205068]
13. Caini S, Cattaruzza S, Bendinelli B, et al. Coffee, tea and caffeine intake and the risk of non-melanoma skin cancer: a review of the literature and meta-analysis. Eur J Nutr. 2017; 56(1):1–12.
14. Vaseghi G, Haghjoo-Javanmard S, Naderi J, Eshraghi A, Mahdavi M, Mansourian M. Coffee consumption and risk of nonmelanoma skin cancer: a dose-response meta-analysis. Eur J Cancer Prev. 2018;27(2):164–170. [PubMed: 27902644]
15. Date R Singapore Cancer Registry interim annual registry report trends in cancer incidence in Singapore Cancer Registry interim annual registry report trends in cancer incidence in Singapore National Registry of Diseases Office (NRDO). Data Processing, Data Process. 2010;(May):1–15. doi:2.

16. Koh D, Wang H, Lee J, Chia KS, Lee HP, Goh CL. Basal cell carcinoma, squamous cell carcinoma and melanoma of the skin: analysis of the Singapore Cancer Registry data 1968–97. Br J Dermatol. 2003;148(6):1161–1166. [PubMed: 12828744]
17. Hankin JH, Stram DO, Arakawa K, et al. Singapore Chinese Health Study: development, validation, and calibration of the quantitative food frequency questionnaire. Nutr Cancer. 2001; 39(2):187–195. [PubMed: 11759279]
18. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB. Cancer Incidence in Five Continents. Vol VIII. Lyon, France: International Agency for Research on Cancer; 2002.
19. Lu Y-P, Lou Y-R, Peng Q-Y, Xie J-G, Nghiem P, Conney AH. Effect of caffeine on the ATR/Chk1 pathway in the epidermis of UVB-irradiated mice. Cancer Res. 2008;68(7):2523–2529. [PubMed: 18381462]
20. Lu Y-P, Lou Y-R, Peng Q-Y, Nghiem P, Conney AH. Caffeine decreases phospho—Chk1 (Ser317) and increases mitotic cells with cyclin B1 and caspase 3 in tumors from UVB-treated mice. Cancer Prev Res. 2011;4(7):1118–1125.
21. Nghiem P, Park PK, Kim Y, Vaziri C, Schreiber SL. ATR inhibition selectively sensitizes G1 checkpoint-deficient cells to lethal premature chromatin condensation. Proc Natl Acad Sci U S A. 2001;98(16):9092–9097. [PubMed: 11481475]
22. Ünsal-Kaçmaz K, Makhov AM, Griffith JD, Sancar A. Preferential binding of ATR protein to UV-damaged DNA. Proc Natl Acad Sci U S A. 2002;99(10):6673–6678. [PubMed: 12011431]
23. Miura K, Hughes MCB, Green AC, Van Der Pols JC. Caffeine intake and risk of basal cell and squamous cell carcinomas of the skin in an 11-year prospective study. Eur J Nutr. 2014;53(2): 511–520. [PubMed: 23824258]
24. Song F, Qureshi AA, Han J. Increased caffeine intake is associated with reduced risk of basal cell carcinoma of the skin. Cancer Res. 2012;72(13):3282–3289. [PubMed: 22752299]
25. Jacobsen BK, Bjelke E, Kvåle G, Heuch I. Coffee drinking, mortality, and cancer incidence: results from a Norwegian prospective study. J Natl Cancer Inst. 1986;76(5): 823–831. [PubMed: 3457969]
26. Gilchrest BA, Eller MS, Geller AC, Yaar M. The pathogenesis of melanoma induced by ultraviolet radiation. N Engl J Med. 1999;340(17):1341–1348. [PubMed: 10219070]
27. Kim GK, Del Rosso JQ. Skin cancer in Asians part 1: nonmelanoma skin cancer. J Clin Aesthet Dermatol. 2009; 2(8):39–42.
28. Hakim IA, Harris RB, Weisgerber UM. Tea intake and squamous cell carcinoma of the skin: influence of type of tea beverages. Cancer Epidemiol Prev Biomarkers. 2000;9(7):727–731.
29. Rees JR, Stukel TA, Perry AE, Zens MS, Spencer SK, Karagas MR. Tea consumption and basal cell and squamous cell skin cancer: results of a case-control study. J Am Acad Dermatol. 2007;56(5):781–785. [PubMed: 17261341]
30. Miura K, Hughes MCB, Arovah NI, Van Der Pols JC, Green AC. Black tea consumption and risk of skin cancer: an 11-year prospective study. Nutr Cancer. 2015;67(7):1049–1055. [PubMed: 26359536]

CAPSULE SUMMARY

- Although studies in whites suggest that caffeine may reduce the risk of nonmelanoma skin cancer, studies among darker-skinned populations are lacking.
- We showed that intake of coffee or caffeine may reduce the risk of squamous cell and basal cell carcinomas among Chinese in Singapore.

Table I.

Baseline characteristics of cohort participants by amount of caffeine consumed

	Amount of daily intake			
Characteristic	**<50 mg**	**50 to <250 mg**	**250 to <400 mg**	**≥400 mg**
Participants, n	10,330	42,361	6634	1996
Skin cancer cases, n	124	421	50	14
Mean age at recruitment ± SD, y	56.9 ± 8.4	56.4 ± 8.0	55.7 ± 7.6	55.5 ± 7.5
Men, n (%)	3378 (32.7)	18,518 (43.7)	4037 (60.8)	1360 (68.1)
Dialect, n (%)				
Cantonese	4749 (46.0)	19631 (46.3)	3142 (47.4)	803 (40.3)
Hokkein	5581 (54.0)	22,730 (53.7)	3492 (52.6)	1193 (59.7)
Secondary school or higher, n (%)	2977 (28.8)	11,818 (27.9)	2037 (30.7)	604 (30.3)
Ever-smoker, n (%)	1844 (17.9)	12,729 (30.0)	2969 (44.7)	1196 (60.0)
Mean BMI, kg/m^2	23.0 ± 3.3	23.2 ± 3.2	23.2 ± 3.4	23.1 ± 3.4
Mean time sitting at work ± SD, h/d	0.83 ± 1.3	0.92 ± 1.3	1.02 ± 1.4	1.03 ± 1.4
Mean time watching television ± SD, h/d	2.25 ± 0.9	2.26 ± 0.9	2.21 ± 0.9	2.18 ± 0.9
Mean time engaging in moderate activity ± SD, h/wk	0.99 ± 2.7	0.82 ± 2.5	0.99 ± 2.8	0.83 ± 2.7
Mean time engaging in vigorous activity ± SD, h/wk	0.31 ± 2.3	0.50 ± 3.1	0.98 ± 4.3	1.06 ± 4.4
Mean time engaging in strenuous sports ± SD, h/wk	0.18 ± 1.0	0.17 ± 1.0	0.24 ± 1.2	0.21 ± 1.1
Diabetes, n (%)	1158 (11.2)	3689 (8.7)	492 (7.4)	130 (6.5)
Alcohol intake, n (%)				
Nondrinker	9690 (93.8)	37,346 (88.2)	5464 (82.4)	1644 (82.4)
Weekly drinker	466 (4.5)	3451 (8.1)	851 (12.8)	250 (12.5)
Daily drinker	174 (1.7)	1564 (3.7)	319 (4.8)	102 (5.1)
Mean coffee intake ± SD, cups/wk	0.5 ± 0.9	9.5 ± 5.9	18.7 ± 7.5	31.5 ± 9.5
Mean green tea ± SD, cups/wk	0.4 ± 0.8	1.7 ± 4.2	6.6 ± 10.2	6.9 ± 12.5
Mean black tea intake ± SD, cups/wk	0.4 ± 1.0	1.5 ± 3.5	3.4 ± 5.9	2.8 ± 7.0
Mean soda intake ± SD, glasses/wk	0.3 ± 1.0	0.5 ± 1.9	1.2 ± 3.4	1.4 ± 3.8

P values are based on chi-square test for categoric variables and 1-way analysis of variance for continuous variables; all *P* values <.0001. *BMI*, Body mass index; *SD*, standard deviation.

Table II.

Association between the different types of caffeinated beverages and the risk of NMSC in the Singapore Chinese Health Study (N = 61,321)

Beverage	Cases	Person-years	Model 1* HR (95% CI)	Model 2† HR (95% CI)	Model 3‡ HR (95% CI)
Coffee					
None to <weekly	154	226,010	1.00	1.00	1.00
Weekly to <daily	59	102,896	0.85 (0.63–1.14)	0.85 (0.63–1.15)	0.86 (0.64–1.16)
1–2 cups/d	376	729,636	0.76 (0.63–0.91)	0.76 (0.63–0.92)	0.74 (0.61–0.89)
≥3 cups/d	20	64,043	0.48 (0.30–0.77)	0.49 (0.30–0.78)	0.47 (0.29–0.75)
P for trend			.0003	.0004	.0001
Black tea					
None to <monthly	419	713,857	1.00	1.00	1.00
Monthly to <weekly	47	87,532	1.00 (0.74–1.35)	0.99 (0.73–1.34)	1.00 (0.74–1.35)
Weekly to <daily	90	193,858	0.87 (0.69–1.09)	0.87 (0.69–1.10)	0.87 (0.69–1.09)
Daily	53	127,338	0.75 (0.56–1.01)	0.76 (0.57–1.01)	0.70 (0.52–0.94)
P for trend			.039	.04	.015
Green tea					
None to <monthly	364	660,272	1.00	1.00	1.00
Monthly to <weekly	72	130,987	1.01 (0.79–1.31)	1.01 (0.78–1.30)	1.02 (0.79–1.32)
Weekly to <daily	96	193,903	0.92 (0.74–1.16)	0.92 (0.73–1.15)	0.94 (0.75–1.18)
Daily	77	137,423	0.94 (0.74–1.21)	0.93 (0.73–1.20)	0.91 (0.71–1.17)
P for trend			.50	.45	.42
Soda, times per week					
<1	537	952,586	1.00	1.00	1.00
1	21	57,479	0.81 (0.52–1.25)	0.82 (0.53–1.27)	0.85 (0.55–1.32)
2–3	32	62,519	1.14 (0.80–1.64)	1.16 (0.81–1.67)	1.22 (0.85–1.75)
≥3	19	50,002	0.88 (0.55–1.39)	0.89 (0.56–1.41)	0.92 (0.58–1.46)
P for trend			.82	.91	.89

CI, Confidence interval; *HR*, hazard ratio; *NMSC*, nonmelanoma skin cancer.

*Model 1 is adjusted for age at recruitment, sex, dialect group, year of recruitment, education.

†Model 2 is adjusted for the variables in model 1 plus body mass index; smoking; alcohol consumption; history of diabetes; and time spent sitting at work, watching television, engaging in moderate activity, engaging in strenuous sports, and engaging in vigorous activity.

J Am Acad Dermatol. Author manuscript; available in PMC 2022 July 01.

[‡]Model 3 is adjusted for all variables in model 2, plus intake of black tea, green tea, coffee, and soda.

Table III.

Association between coffee and black tea intake and BCC or SCC in the Singapore Chinese Health Study (N = 61,321)

Carcinoma type	Cases	Person-years	HR (95% CI)
BCC			
Coffee			
None to <weekly	106	225,000	1.00
Weekly to <daily	34	102,516	0.73 (0.49–1.07)
1–2 cups/d	272	727,192	0.78 (0.62–0.98)
≥3 cups/d	15	63,939	0.54 (0.31–0.93)
P for trend			.017
Black tea			
None to < monthly	304	711,265	1.00
Monthly to <weekly	34	87,241	0.99 (0.70–1.42)
Weekly to <daily	51	193,172	0.69 (0.51–0.93)
Daily	38	126,969	0.74 (0.52–1.04)
P for trend			.01
SCC			
Coffee			
None to <weekly	48	224,351	1.00
Weekly to <daily	25	102,334	1.15 (0.71–1.87)
1–2 cups/d	104	725,077	0.64 (0.45–0.91)
≥3 cups/d	5	63,752	0.33 (0.13–0.85)
P for trend			.001
Black tea			
None to < monthly	115	708,806	1.00
Monthly to <weekly	13	86,954	1.01 (0.57–1.80)
Weekly to <daily	39	193,056	1.30 (0.90–1.89)
Daily	15	126,697	0.62 (0.36–1.08)
P for trend			.57

Adjusted for age at recruitment; sex; dialect group; year of recruitment; education; body mass index; smoking; alcohol consumption; history of diabetes; time spent sitting at work, watching television, engaging in moderate activity, engaging in strenuous sports, and engaging in vigorous activity; and intake of black tea, green tea, coffee. and soda.

BCC, Basal cell carcinoma; *CI*, confidence interval; *HR*, hazard ratio; *SCC*, squamous cell carcinoma.

Table IV.

Association between caffeine intake and the risk of NMSC in the Singapore Chinese Health Study (N = 61,321)

Cancer	Cases	Person-years	Model 1* HR (95% CI)	Model 2† HR (95% CI)
All skin cancers				
Caffeine intake, mg/d				
0 to <50	124	185,966	1.00	1.00
50 to <250	421	778,614	0.80 (0.66–0.98)	0.81 (0.66–0.99)
250 to <400	50	121,741	0.62 (0.45–0.87)	0.63 (0.45–0.88)
≥400	14	36,264	0.58 (0.33–1.01)	0.59 (0.34–1.04)
P for trend			.0017	.0025
Basal cell carcinoma				
Caffeine intake, mg/d				
0 to <50	87	185,224	1.00	1.00
50 to <250	299	775,848	0.84 (0.66–1.06)	0.85 (0.67–1.08)
250 to <400	30	121,359	0.57 (0.38–0.87)	0.59 (0.39–0.90)
≥400	11	36,217	0.70 (0.37–1.32)	0.76 (0.40–1.42)
P for trend			.01	.03
Squamous cell carcinoma				
Caffeine intake, mg/d				
0 to <50	37	184,620	1.00	1.00
50 to <250	122	773,586	0.73 (0.50–1.06)	0.71 (0.49–1.03)
250 to <400	20	121,234	0.71 (0.41–1.23)	0.67 (0.38–1.17)
≥400	3	36,072	0.35 (0.11–1.15)	0.33 (0.10–1.07)
P for trend			.0498	.03

CI, Confidence interval; *HR*, hazard ratio; *NMSC*, nonmelanoma skin cancer.

*Model 1 is adjusted for age at recruitment, sex, dialect group, year of recruitment, and education.

†Model 2 is adjusted for the variables in model 1 and body mass index; smoking; alcohol consumption; history of diabetes; and time spent sitting at work, watching television, engaging in moderate activity, engaging in strenuous sports, and engaging in vigorous activity.