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# Epidemiology of nonmelanoma skin cancer in Japan: Occupational type, lifestyle, and family history of cancer

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## Abstract

Skin cancer is the most frequently diagnosed cancer in the fair-skinned population. In recent years, the incidence of nonmelanoma skin cancer (NMSC) has been increasing worldwide. However, there is no epidemiological study on skin cancer in the Asian population. A prospective cohort study including 140 420 participants was initiated in 1990 for cohort I and 1993 for cohort II at baseline survey from 11 public health center (PHC) areas. Of these participants, 284 NMSC cases were diagnosed during the follow-up period (through 2012 in the Osaka PHC area and 2013 in the other PHC areas). The Cox proportional hazards model was used to estimate hazard ratios and 95% confidence intervals (CI) for NMSC incidence according to occupational type, lifestyle factors (alcohol consumption, coffee consumption, smoking status, physical activity, and body mass index), and family history of cancer. Among men, compared with indoor workers, outdoor workers were associated with 2.18 (95% CI, 1.17-4.04) higher risk of squamous cell carcinoma (SCC) but not of basal cell carcinoma (BCC). Furthermore, men who have a family history of cancer had 1.99 (95% CI, 1.10-3.62) higher SCC risk. In women, we did not observe any association between occupational type and the risk of SCC (1.26; 95% CI, 0.68-2.32) or BCC (0.74; 95% CI, 0.42-1.28). In conclusion, men who are outdoor workers or have a family history of cancer had an increased risk of SCC.

**KEYWORDS**

Asian population, epidemiology, nonmelanoma skin cancer, occupational UV radiation exposure, prospective cohort study

## 1 | INTRODUCTION

Skin cancer, including melanoma and NMSC, ranks as the most frequently diagnosed cancer in the white population.[1-3] The two most common subtypes of NMSC are cutaneous SCC and BCC. In recent years, incidence rates of both SCC and BCC have been increasing worldwide.[4] Exposure to solar UV radiation was considered to be the main factor for NMSC occurrence. Findings in previous studies supported this, stating that occupational UV exposure was linked to both SCC and BCC.[5-7]

**Abbreviations:** BCC, basal cell carcinoma; BMI, body mass index; CI, confidence interval; HR, hazard ratio; IL, interleukin; JPHC, Japan Public Health Center-based Prospective Study; NHS-HPFS, Nurses' Health Study and Health Professionals' Follow-up Study; NMSC, nonmelanoma skin cancer; PHC, public health center; SCC, squamous cell carcinoma.

In addition to UV exposure, other potential exposures have been investigated in previous studies for their effects on developing NMSC. Among lifestyle factors, alcohol and coffee consumption might be associated with the incidence of NMSC. However, the results of epidemiological studies relating alcohol consumption and NMSC risk were largely inconsistent.[8-11] Coffee consumption could protect against NMSC development through the biological effect of caffeine.[12,13] The findings from several metaanalysis studies concluded that caffeinated coffee might have protective effects against NMSC and BCC development but there is a lack of evidence for SSC risk reduction.[14,15]

With regard to smoking and physical activity, previous studies found that smoking increased the risk of SCC but did not increase the risk of BCC.[11,16,17] There was no clear support for the relation of physical activity with skin cancer.[18,19] Prospective studies that investigated the relationship between BMI and NMSC yielded inconsistent findings.[20-23] However, a metaanalysis study, containing 18 cohort studies from Europe, America, and Australia, revealed that there was no association between BMI and NMSC, SCC, or BCC.[24] In terms of family history, several previous studies provided evidence on the observed increased risk of SCC in a person with first-degree relatives with SCC[25-27]; however, no study has analyzed SCC risk and family history of cancer.

More importantly, all the previous studies in relation to skin cancer were based on fair-skinned people. The cumulative incidence risk of NMSC in Asians is lower than Caucasians.[28] To the best of our knowledge, there is no epidemiological study that has investigated the incidence of skin cancer in an Asian population. It is still unclear what potential factors mainly influence the occurrence of skin cancer in the Asian population. Therefore, we evaluated the epidemiology of NMSC according to occupational type, lifestyle, and family history of cancer in a large population-based prospective study in Japan to provide some guidelines for the prevention of skin cancer.

## 2 | MATERIALS AND METHODS

### 2.1 | Study population

The JPHC was initiated in 1990 for cohort I and 1993 for cohort II, including 140 420 participants aged 40-69 years at the time of the baseline survey from 11 PHC areas. Details of the JPHC study design have been described.[29] Participants enrolled in Tokyo were not eligible because of unavailable information on cancer incidence ($n$ = 7097). Participants who were of non-Japanese nationality ($n$ = 18), late reported moving out of the PHC area ($n$ = 21), had incorrect date of birth ($n$ = 3), had duplicate registration ($n$ = 2), and were lost to follow-up at the end date ($n$ = 148) were excluded. We established a cohort of 133 131 participants. Of these, 105 699 participants (79.4%) responded to the baseline questionnaire.

We further excluded participants with incomplete information on study factors ($n$ = 7472) and those who had a history of cancer before the baseline survey ($n$ = 2237). Finally, we included a total of 95 990 participants (45 329 men and 50 661 women) into our present analysis. The study protocol was approved by the Institutional Review Board of the National Cancer Center (Tokyo, Japan) and the Ethical Review Board of Osaka University (Osaka, Japan).

### 2.2 | Exposure assessment and classification

#### 2.2.1 | Occupational type

In cohort I, occupational types of obtained participants were agriculture, forestry, fishery, manager, clerk, sales, profession, service, protective service, transport and communications, labor, and unemployed. In cohort II, the baseline questionnaire contained items regarding the current jobs of the participants, namely, agriculture, forestry, fishery, employee (administrator and manager, clerk, manual labor [construction and factory worker], sales work, etc), self-employed (shop owner, restaurant owner, construction company owner, clerical worker, etc), profession, homemaker, and unemployed. Participants were asked to choose all matched options if they have more than one job at the same time or change jobs according to season. We defined individuals who worked for agriculture, forestry, or fishery as outdoor workers, and the others as indoor workers.

#### 2.2.2 | Lifestyle factors

Alcohol and coffee consumption were retrieved from a baseline self-administered questionnaire survey and measured through a validated food frequency questionnaire.[30,31] We evaluated alcohol consumption by multiplying weekly consumption frequency and the grams of ethanol contained in each specific alcoholic beverage.[32] Because of the small number of events, nondrinkers and occasional drinkers (1-3 days/mo) were merged into one group. The participants were finally classified into non/occasional drinkers, and two groups of regular drinkers (<150, ≥150 g/wk). Information on coffee consumption was obtained using three categories based on the frequency and amount of consumption as follows: never, 1-4 times/wk, 1 or more cups/d. Smoking status was categorized as never, former, and current smoker. The frequency of physical activity was assessed as never, 1-3 d/mo, 1 or more d/wk in men, and as yes or no in women (because the limited number of cases in the 1-3 d/mo group, we merged the 1-3 d/mo and ≥1 d/wk groups). As a BMI of 23 kg/m$^2$ or higher and 25 kg/m$^2$ or higher have been identified by the WHO as cut-off points for increased risk and overweight, respectively, in the Asian population,[33] BMI (calculated as body weight [kg] divided by squared height [m$^2$]) was classified into less than 23, 23-25, 25 kg/m$^2$ or higher, with 23-25 kg/m$^2$ as the reference (a category which contains the mean BMI, 23.4 kg/m$^2$) in the study.

### 2.2.3 | Family history of cancer

Participants who reported having first-degree relatives that had been diagnosed with any type of cancer were denoted as having a family history of cancer.

## 2.3 | Follow-up and case identification

The follow-up period was from the date the participants enrolled in the baseline questionnaire survey until the date of moving out from the study area, date of death, date of diagnosis with NMSC, or the end of follow-up (31 December 2012 in the Osaka area; 31 December 2013 in other areas), whichever happened first.

Incidence data on NMSC cases were identified from major local hospitals in the study area and from data linkage with population-based cancer registries, with permission from the local authorities responsible for the registries. Death certificate information was used as a supplementary information source. According to the Third Edition of the *International Classification of Diseases for Oncology*,[34] topography codes from C44.0 to C44.9 represent incident skin cancer on specific body sites. We defined newly diagnosing NMSC during the study period as study outcome using topography codes C44.0-C44.9 and excluding histology codes 8720, 8721, 8742, 8743, 8744, 8745, 8780, and 8761. Nonmelanoma skin cancer with histology codes 8051, 8070, 8074, and 8075 were defined as SCC, and codes 8090, 8091, 8092, 8093, and 8097 as BCC in accordance with WHO histological classifications for skin cancer.

## 2.4 | Statistical analysis

The Cox proportional hazards model was used to calculate the sex-specific HR and 95% CI for the incidence of NMSC according to occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, BMI, and family history of cancer. The HR estimates are presented as basic models and multivariable-adjusted models. Basic models were adjusted for age and PHC areas; multivariable-adjusted models were further adjusted for the consumption of Japanese tea, Chinese tea, and black tea (never, 1-4 times/wk, ≥1 cup/d), and the study factors mutually (occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, BMI, and family history of cancer). Due to the limited number of cases, with regard to histological subtypes analyses, the classifications of some study factors were merged into more simplified groups (alcohol intake: non/occasional drinkers and regular drinkers; coffee consumption: no, yes; physical activity: no, yes) and not all study factors were included in the analyses. The assessment of *P* for trend was carried out by entering the ordinal values of each group as a continuous term into the models. All statistical testing was two-sided and considered statistically significant when the value was less than 0.05. The statistical analyses were undertaken using SAS software (version 9.4; SAS Institute).

**TABLE 1** Baseline characteristics of Japanese study participants with and without a diagnosis of nonmelanoma skin cancer

| | Cases | Noncases |
|---|---|---|
| No. of participants | 284 | 95 706 |
| Age (y), mean ± SD | 57.8 ± 7.8 | 52.2 ± 8.0 |
| Outdoor workers (%) | 31.2 | 42.3 |
| Alcohol consumption, yes (%) | 38.7 | 30.3 |
| Coffee consumption, yes (%) | 69.4 | 60.0 |
| Smoking status (%) | | |
| Former smokers | 20.1 | 12.1 |
| Current smokers | 16.6 | 28.3 |
| Physical activity, yes (%) | 30.0 | 28.9 |
| BMI (kg/m$^2$), mean ± SD | 23.7 ± 3.1 | 23.4 ± 3.0 |
| Family history of cancer, yes (%) | 22.0 | 20.8 |

BMI, body mass index.

## 3 | RESULTS

During 1 829 813 person-years of follow-up (median, 21.0 years) of 95 990 participants, a total of 284 (133 men and 151 women) cases of NMSC were newly diagnosed. The distribution of histological subtypes of NMSC was as follows: SCC ($n$ = 98), BCC ($n$ = 117), and unknown ($n$ = 69).

The baseline characteristics of the participants with and without a diagnosis of NMSC are summarized in Table 1. On comparing baseline characteristics between participants with and without NMSC, participants with NMSC tended to be indoor workers and were more likely to consume alcohol and coffee.

Table 2 shows the sex-specific adjusted HR and 95% CI for NMSC in relation to the study factors. Overall, there was no association of any study factor with the risk of NMSC in either men or women.

Sex-specific HR with 95% CI for SCC and BCC in relation to all study factors are presented in Tables 3 and 4. In multivariable models, we found that outdoor working men were associated with higher risk of SCC (2.18; 95% CI, 1.17-4.04) but not of BCC (1.13; 95% CI, 0.58-2.21). Men who had a family history of cancer had 1.99 (95% CI, 1.10-3.62) higher risk of SCC as well. However, we did not observe an association between occupational type and the risk of SCC (1.26; 95% CI, 0.68-2.32) or BCC (0.74; 95% CI, 0.42-1.28) in women. With regard to lifestyle factors, none of the estimates were statistically significant in men or women.

Table S1 shows the distribution of skin lesions on different body sites. The percentage of skin cancer that occurred on sun-exposed body sites was relatively high: NMSC, 63.92% for men and 68.87%

**TABLE 2** Hazard ratios (HR) (95% confidence intervals [CI]) of study factors for nonmelanoma skin cancer

| | Cases | Person-years | Age, PHC-adjusted HR (95% CI) | *P* trend[a] | Multivariable-adjusted HR (95% CI)[b] | *P* trend[a] |
|---|---|---|---|---|---|---|
| Men | | | | | | |
| Occupation type | | | | | | |
| Indoor workers | 73 | 615 269 | 1.00 | | 1.00 | |
| Outdoor workers | 60 | 219 052 | 1.30 (0.89-1.91) | .177 | 1.37 (0.93-2.03) | .109 |
| Alcohol consumption | | | | | | |
| Non/occasional drinkers | 54 | 263 745 | 1.00 | | 1.00 | |
| Regular drinkers <150g/d | 26 | 183 064 | 0.87 (0.55-1.40) | | 0.87 (0.54-1.40) | |
| Regular drinkers ≥150g/d | 53 | 387 513 | 0.80 (0.54-1.19) | .274 | 0.81 (0.54-1.20) | .288 |
| Coffee consumption | | | | | | |
| Never | 50 | 247 600 | 1.00 | | 1.00 | |
| 1-4 times/wk | 36 | 249 155 | 0.78 (0.51-1.21) | | 0.78 (0.51-1.21) | |
| ≥1 cup/d | 47 | 337 566 | 0.95 (0.63-1.43) | .765 | 0.99 (0.65-1.51) | .938 |
| Smoking status | | | | | | |
| Never smokers | 35 | 203 259 | 1.00 | | 1.00 | |
| Former smokers | 53 | 199 934 | 1.40 (0.91-2.15) | | 1.42 (0.92-2.20) | |
| Current smokers | 45 | 431 129 | 0.74 (0.48-1.16) | .114 | 0.79 (0.50-1.25) | .216 |
| Physical activity | | | | | | |
| Never | 84 | 540 179 | 1.00 | | 1.00 | |
| 1-3 d/mo | 21 | 135 727 | 1.48 (0.91-2.41) | | 1.53 (0.93-2.50) | |
| ≥1 d/wk | 28 | 158 415 | 1.13 (0.73-1.74) | .401 | 1.14 (0.74-1.77) | .376 |
| BMI | | | | | | |
| <23 kg/m$^2$ | 50 | 367 167 | 0.79 (0.52-1.20) | | 0.82 (0.54-1.24) | |
| 23-25 kg/m$^2$ | 40 | 234 851 | 1.00 | | 1.00 | |
| ≥25 kg/m$^2$ | 43 | 232 303 | 1.10 (0.72-1.70) | .104 | 1.09 (0.71-1.68) | .169 |
| Family history of cancer | | | | | | |
| No | 99 | 654 805 | 1.00 | | 1.00 | |
| Yes | 34 | 179 516 | 1.36 (0.92-2.03) | .127 | 1.38 (0.92-2.05) | .116 |
| Women | | | | | | |
| Occupation type | | | | | | |
| Indoor workers | 103 | 755 112 | 1.00 | | 1.00 | |
| Outdoor workers | 48 | 240 380 | 0.88 (0.61-1.26) | .478 | 0.81 (0.56-1.17) | .252 |
| Coffee consumption | | | | | | |
| Never | 64 | 314 830 | 1.00 | | 1.00 | |
| 1-4 times/wk | 47 | 293 084 | 0.95 (0.65-1.39) | | 0.97 (0.66-1.43) | |
| ≥1 cup/d | 40 | 387 578 | 0.76 (0.50-1.17) | .225 | 0.77 (0.50-1.17) | .236 |
| Physical activity | | | | | | |
| No | 118 | 748 108 | 1.00 | | 1.00 | |
| Yes | 33 | 247 384 | 0.76 (0.51-1.12) | .164 | 0.76 (0.51-1.13) | .175 |
| BMI | | | | | | |
| <23 kg/m$^2$ | 68 | 476 847 | 0.98 (0.66-1.46) | | 0.97 (0.66-1.44) | |
| 23-25 kg/m$^2$ | 40 | 241 361 | 1.00 | | 1.00 | |
| ≥25 kg/m$^2$ | 43 | 277 283 | 0.82 (0.53-1.26) | .369 | 0.83 (0.54-1.28) | .448 |

(Continues)

**TABLE 2** (Continued)

| | Cases | Person-years | Age, PHC-adjusted HR (95% CI) | *P* trend[a] | Multivariable-adjusted HR (95% CI)[b] | *P* trend[a] |
|---|---|---|---|---|---|---|
| Family history of cancer | | | | | | |
| No | 126 | 779 710 | 1.00 | | 1.00 | |
| Yes | 25 | 215 782 | 0.88 (0.57-1.36) | .554 | 0.87 (0.56-1.36) | .549 |

PHC, public health center.

[a]*P* for trend was calculated by entering the ordinal values of each group as a continuous term into the models.

[b]Adjusted for age, area, occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, body mass index (BMI), family history of cancer mutually, and green tea, Chinese tea, black tea consumption.

for women; SCC, 66.66% for men and 68.10% for women; and BCC, 77.09% for men and 84.07% for women.

## 4 | DISCUSSION

We undertook a prospective cohort study on the association between NMSC and occupational type, lifestyle, and family history of cancer in the Japanese population. In men, there was no association between NMSC and occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, BMI, or family history of cancer. We found an increased risk of SCC in outdoor workers compared to indoor workers; however, a similar increased risk was not shown for BCC. Men with a family history of cancer had a high risk of SCC but not of BCC. In women, none of the study factors was associated with NMSC, SCC, or BCC.

The findings of incidence of SCC with regard to the different occupational types in men were consistent with a cohort study from Germany that found an increased risk of both SCC and BCC in outdoor working men and women.[35] Similarly, several previous studies of fair-skinned people have indicated that outdoor workers are at significantly increased risk for both SCC and BCC.[36-39] Our present study did not reveal evidence for an increased risk of BCC in outdoor workers. However, due to a relatively high percentage of skin cancer occurring on sun-exposed body sites (SCC, 66.66% for men and 68.10% for women; BCC, 77.09% for men and 84.07% for women), protection against the sun is an important strategy to avoid skin cancer in a Japanese population. Evidently, after skin is damaged by UV radiation, the cells secrete many inflammatory cytokines, including IL-1,[40] IL-6,[41] tumor necrosis factor-α,[42] and macrophage migration inhibitory factor,[43] which are related to the progression of erythema, photoaging, immunosuppression, and ultimately, carcinogenesis of the skin. However, a similar increased risk of SCC was not observed in women in our study; this might be due to aesthetic values and awareness of using sun protection products. A widespread Japanese aesthetic view is that fair skin symbolizes beauty. Many women tend to use sunblock and cosmetics in their daily life and thus protect the exposed skin from UV radiation.

Although SCC and BCC are usually considered together as histological subtypes of NMSC, they present unique differences in etiology. Chronic UV radiation exposure appears to be related to the risk of SCC,[5] and the risk of BCC increases with either intensive or chronic UV radiation exposure. A study at the molecular level[44] showed that the mechanism of incidence of BCC is not only the same as that of SCC, which results from the mutated *TP53* gene by UV radiation, but is also affected by the *PTCH* gene that has an unclear relationship with UV. This evidence from epidemiological and molecular level studies indicated that the mechanism of BCC development is more complicated than SCC. The factors that could affect the occurrence of BCC in the Asian population need to be investigated further.

In the present study, no association was found between alcohol and coffee consumption and NMSC and its histological subtypes. A prospective study in Australia found no association between total alcohol consumption and SCC and BCC risk.[8] However, another large cohort study from the US, the NHS-HPFS, found that alcohol consumption was related to an elevated SCC risk.[10] A metaanalysis published recently suggested that high alcohol consumption is linked to increasing SCC and BCC risk, although the conclusion should be interpreted with caution because of potential residual confounding.[45] Previous studies about coffee consumption and NMSC revealed that high coffee intake was associated with reduced NMSC and BCC risk.[14,46] The inconsistency of the association between coffee consumption and NMSC in previous studies and our present study might be attributable to the lower coffee intake in Japan compared with that in Finland and United States.[47]

Epidemiological studies reported no positive correlation between smoking and NMSC. Several studies have identified smoking as an independent adverse factor for SCC development.[16,17] No convincing evidence so far has supported an inverse association between physical activity and NMSC.[19,48] A few studies addressed the relationship between BMI and NMSC risk, and the findings were conflicting. Some studies showed no association between BMI and risk of NMSC.[20,24,49] In contrast, the NHS-HPFS study concluded that obesity reduced NMSC risk,[23] and a cohort study from Denmark found a decreased risk of BCC in women in the highest quartile of BMI than in those in the lowest quartile of BMI.[22] Our null findings for smoking and physical activity might be because the sample sizes were insufficient to detect modest effects. As for the BMI, because of the small sample size and few overweight individuals in our study, it is still difficult to conclude its association with NMSC.

**TABLE 3** Hazard ratios (HR) (95% confidence intervals [CI]) of study factors for squamous cell carcinoma

| | Cases | Person years | Age, PHC-adjusted HR (95% CI) | *P* trend[a] | Multivariable-adjusted HR (95% CI)[b] | *P* trend[a] |
|---|---|---|---|---|---|---|
| Men | | | | | | |
| Occupation type | | | | | | |
| Indoor workers | 22 | 615 269 | 1.00 | | 1.00 | |
| Outdoor workers | 29 | 219 052 | **2.00 (1.09-3.68)** | .026 | **2.18 (1.17-4.04)** | .014 |
| Alcohol consumption | | | | | | |
| Non/occasional drinkers | 18 | 263 745 | 1.00 | | 1.00 | |
| Regular drinkers | 33 | 570 577 | 0.96 (0.53-1.74) | .900 | 0.96 (0.53-1.74) | .898 |
| Coffee consumption | | | | | | |
| No | 23 | 247 600 | 1.00 | | 1.00 | |
| Yes | 28 | 586 721 | 0.70 (0.40-1.22) | .205 | 0.74 (0.42-1.31) | .302 |
| Smoking status | | | | | | |
| Never smokers | 14 | 203 259 | 1.00 | | 1.00 | |
| Former smokers | 21 | 199 934 | 1.34 (0.68-2.66) | | 1.38 (0.69-2.75) | |
| Current smokers | 16 | 431 129 | 0.64 (0.31-1.32) | .163 | 0.69 (0.33-1.44) | .261 |
| Physical activity | | | | | | |
| No | 34 | 540 179 | 1.00 | | 1.00 | |
| Yes | 17 | 294 142 | 1.12 (0.62-2.03) | .700 | 1.21 (0.67-2.21) | .529 |
| BMI (kg/m$^2$) | | | | | | |
| <23 | 23 | 367 167 | 0.98 (0.50-1.91) | | 1.02 (0.52-2.00) | |
| 23-25 | 14 | 234 851 | 1.00 | | 1.00 | |
| ≥25 | 14 | 232 303 | 1.12 (0.53-2.35) | .717 | 1.05 (0.50-2.21) | .945 |
| Family history of cancer | | | | | | |
| No | 34 | 6 564 805 | 1.00 | | 1.00 | |
| Yes | 17 | 179 516 | **1.90 (1.05-3.45)** | .034 | **1.99 (1.10-3.62)** | .024 |
| Women | | | | | | |
| Occupation | | | | | | |
| Indoor workers | 26 | 755 112 | 1.00 | | 1.00 | |
| Outdoor workers | 21 | 240 380 | 1.37 (0.75-2.52) | .310 | 1.26 (0.68-2.32) | .465 |
| Coffee consumption | | | | | | |
| No | 25 | 314 830 | 1.00 | | 1.00 | |
| Yes | 22 | 680 662 | 0.69 (0.38-1.24) | .213 | 0.72 (0.39-1.31) | .284 |
| Physical activity | | | | | | |
| No | 37 | 748 108 | 1.00 | | 1.00 | |
| Yes | 10 | 247 384 | 0.72 (0.36-1.47) | .371 | 0.76 (0.37-1.55) | .452 |
| BMI (kg/m$^2$) | | | | | | |
| <23 | 20 | 476 847 | 1.00 (0.49-2.05) | | 0.96 (0.47-1.96) | |
| 23-25 | 12 | 241 361 | 1.00 | | 1.00 | |
| ≥25 | 15 | 277 283 | 0.92 (0.43-1.97) | .814 | 0.95 (0.45-2.04) | .919 |

PHC, public health center.

The men who are outdoor workers or have a family history of cancer had an increased risk of SCC (In bold).

[a]*P* for trend was calculated by entering the ordinal values of each group as a continuous term into the models.

[b]Adjusted for age, area, occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, body mass index (BMI), family history of cancer mutually, and green tea, Chinese tea, black tea consumption.

Due to the relatively low prevalence of skin cancer in Asia and the limitation of our cohort study design, we could only evaluate the effect of family history of any type of cancer, but not for the effect of family history of skin cancer. In our study, we found that

**TABLE 4** Hazard ratio (HR) (95% confident interval [CI]) of study factors for basal cell carcinoma

| | Cases | Person years | Age, PHC-adjusted HR (95% CI) | *P* trend[a] | Multivariable-adjusted HR (95% CI)[b] | *P* trend[a] |
|---|---|---|---|---|---|---|
| Men | | | | | | |
| Occupation type | | | | | | |
| Indoor workers | 30 | 615 269 | 1.00 | | 1.00 | |
| Outdoor workers | 18 | 219 052 | 1.11 (0.57-2.14) | .759 | 1.13 (0.58-2.21) | .715 |
| Alcohol consumption | | | | | | |
| Non/occasional drinkers | 20 | 263 745 | 1.00 | | 1.00 | |
| Regular drinkers | 28 | 570 577 | 0.81 (0.45-1.45) | .476 | 0.80 (0.44-1.44) | .450 |
| Coffee consumption | | | | | | |
| No | 16 | 247 600 | 1.00 | | 1.00 | |
| Yes | 32 | 586 721 | 0.91 (0.50-1.68) | .773 | 0.88 (0.48-1.64) | .692 |
| Smoking status | | | | | | |
| Never smokers | 13 | 203 259 | 1.00 | | 1.00 | |
| Former smokers | 16 | 199 934 | 1.24 (0.59-2.61) | | 1.27 (0.60-2.68) | |
| Current smokers | 19 | 431 129 | 0.89 (0.44-1.83) | .684 | 1.02 (0.49-2.10) | .988 |
| Physical activity | | | | | | |
| No | 30 | 540 179 | 1.00 | | 1.00 | |
| Yes | 18 | 294 142 | 1.22 (0.67-2.19) | .518 | 1.19 (0.65-2.17) | .570 |
| BMI (kg/m$^2$) | | | | | | |
| <23 | 13 | 367 167 | 0.55 (0.26-1.15) | | 0.56 (0.27-1.17) | |
| 23-25 | 16 | 234 851 | 1.00 | | 1.00 | |
| ≥25 | 19 | 232 303 | 1.12 (0.58-2.19) | .052 | 1.16 (0.59-2.27) | .050 |
| Women | | | | | | |
| Occupation type | | | | | | |
| Indoor workers | 49 | 755 112 | 1.00 | | 1.00 | |
| Outdoor workers | 20 | 240 380 | 0.79 (0.45-1.37) | .392 | 0.74 (0.42-1.28) | .279 |
| Coffee consumption | | | | | | |
| No | 27 | 314 830 | 1.00 | | 1.00 | |
| Yes | 42 | 680 662 | 0.88 (0.53-1.46) | .619 | 0.90 (0.54-1.48) | .653 |
| Physical activity | | | | | | |
| No | 53 | 748 108 | 1.00 | | 1.00 | |
| Yes | 16 | 247 384 | 0.79 (0.45-1.40) | .425 | 0.78 (0.44-1.39) | .405 |
| BMI (kg/m$^2$) | | | | | | |
| <23 | 28 | 476 847 | 0.91 (0.50-1.64) | | 0.90 (0.50-1.64) | |
| 23-25 | 18 | 241 361 | 1.00 | | 1.00 | |
| ≥25 | 23 | 277 283 | 0.97 (0.52-1.79) | .810 | 0.97 (0.52-1.81) | .777 |
| Family history of cancer | | | | | | |
| No | 54 | 779 710 | 1.00 | | 1.00 | |
| Yes | 15 | 215 782 | 1.32 (0.73-2.37) | .360 | 1.29 (0.72-2.33) | .392 |

PHC, public health center.

[a]*P* for trend was calculated by entering the ordinal values of each group as a continuous term into the models.

[b]Adjusted for age, area, occupational type, alcohol consumption, coffee consumption, smoking status, physical activity, body mass index (BMI), family history of cancer mutually, and green tea, Chinese tea, black tea consumption.

a person with first-degree relatives with cancer had a higher risk of developing SCC. In contrast with the Asian population, skin cancer is one of the most common cancers in the Caucasian population; thus, existing studies are specifically about the family history of skin cancer and not the family history of cancer. A positive association between SCC and family history of skin cancer emerged from

Caucasian population studies.[26,27] A case-control study from the US found that a family history of skin cancer is an independent risk factor for developing SCC.[25] Therefore, the findings on the association between family history of cancer and SCC risk in our study should be interpreted with caution.

To the best of our knowledge, this is the first study to investigate factors that affect the incidence of skin cancer among the Asian population. As a prospective cohort study with a long follow-up period, data were collected before the onset of NMSC to avoid potential recall bias, which is another strength of this study.

The present study is limited in the questionnaire design in terms of the imprecise definition of the occupational type. For example, protective service and labor occupations might be exposed to UV radiation to some degree. Thus, the reference group, indoor workers, might not be truly unexposed to UV radiation at the workplace. This potential imprecise classification by inference based on job titles might lead to an underestimation of the true effect. Additionally, we focused on sunlight exposure from the job description as a proxy for occupational UV radiation exposure, which might reduce or obscure the true associations. Moreover, we only used the occupation data from the baseline survey for the analysis and did not consider subsequent individual job changes during the long follow-up period, which might impact the estimation. Furthermore, we did not take individual UV sensitivity and usage of sunblock products into consideration because of the lack of this information. Because of the substantially small number of cases, the statistical power of our study was small. Caution should be taken when referring our findings to other research on skin cancer. Nonetheless, because UV exposure in outdoor workers is prevalent and could be avoided to some extent, reducing exposure to sunlight could serve as a prevention strategy to reduce the prevalence of NMSC in the Japanese population.

In conclusion, our study found an increased risk of SCC among men who are outdoor workers or have a family history of cancer. Other factors, such as alcohol consumption, coffee consumption, smoking status, physical activity, and BMI, were not related to NMSC, SCC, or BCC incidence in men or women.

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## CONFLICT OF INTEREST

The authors declare no potential conflicts of interest.

## ETHICAL CONSIDERATION

The JPHC study was approved by the Institutional Review Board of the National Cancer Center, Tokyo, Japan. The present study protocol was approved by the Ethical Review Board of Osaka University, Osaka, Japan.

## DATA AVAILABILITY STATEMENT

For information on how to apply to gain access to JPHC data, please follow the instructions at https://epi.ncc.go.jp/en/jphc/805/8155.html.

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## SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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