

Occupation and relative risk of cutaneous squamous cell carcinoma (cSCC): A 45-year follow-up study in 4 Nordic countries



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Background: The age-adjusted incidence of cutaneous squamous cell carcinoma (cSCC) in the Nordic countries has increased during the last 60 years, and the identification of occupational variation in the relative risk of cSCC may have preventive implications.

Objective: We sought to describe variation in the relative risk of cSCC between occupational categories in Finland, Iceland, Norway, and Sweden.

Methods: This is a historical prospective cohort study based on record linkages between census data for 12.9 million people and cancer registry data from 1961 to 2005. Standardized incidence ratios for cSCC were estimated for 53 occupational categories with the cSCC incidence rates for the national population of each country used as reference.

Results: During follow-up, 87,619 incident cases of cSCC were reported to the national cancer registries. In all countries combined, significant increased standardized incidence ratios were observed among seamen, military personnel, public safety workers, technical workers, teachers, transport workers, physicians, dentists, nurses, other health workers, religious workers, clerical workers, administrators, and sale agents (standardized incidence ratios between 1.08 and 1.77).

Limitations: Information on occupation was based on 1 point in time only.

Conclusion: The occupational variation of the relative risk of cSCC might be associated with socioeconomic factors, and to some extent to occupational exposures. (J Am Acad Dermatol 2016;75:548-55.)

Key words: cohort; cutaneous squamous cell carcinoma; epidemiology; general population; occupation; relative risk; socioeconomic position.

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In the Nordic countries, the age-adjusted incidence of cutaneous squamous cell carcinoma (cSCC), the second most frequent keratinocyte carcinoma,¹ has increased about 3-fold during the last 60 years.² High recurrence rates and occurrence of multiple cSCC impose a significant burden worldwide.^{3,4}

Cumulative exposure to solar ultraviolet (UV) radiation is the major risk factor for cSCC.⁵ For instance, strong evidence of an association between occupational exposure to solar UV radiation and excess risk of cSCC in outdoor workers has been reported in a meta-analysis by Schmitt et al.⁶

In addition, the excess risk of cSCC previously reported for tar refinery workers,⁷ transport workers,⁸ and firefighters⁹ has been attributed to occupational skin exposure to polycyclic aromatic hydrocarbons, which is carcinogenic after skin absorption and metabolism.^{10,11} The excess risk of cSCC found among health workers¹² has been discussed in relation to occupational exposure to artificial UV radiation, ionizing radiation, or both, but no consistent evidence about increased skin cancer risk as a result of these occupational exposures has been found.^{13,14}

Although cSCC is one of the few preventable cancers through exposure reduction, few prospective population-based studies with long follow-up have examined occupational variation in the relative risk of cSCC. Therefore, this historical prospective study with 45-year follow-up aimed to describe occupational variation of the relative risk of cSCC in the adult population of 4 Nordic countries, and to discuss findings in light of potential exposure to occupational carcinogens and socioeconomic position.

METHODS

Population

The Nordic Occupational Cancer Study project (<http://astra.cancer.fi/NOCCA>) linked occupational information from censuses in the 5 Nordic countries to information on cancer diagnoses from the respective cancer registries, by using the unique personal identity codes.¹⁵ Denmark was excluded from the current analysis because it was not possible

to separate basal cell carcinoma from cSCC cases before 1978. The details of study materials, coding systems, and analysis were described earlier.¹⁵ Briefly, the study base consisted of approximately 12.9 million persons, born between 1896 and 1960, participating in any computerized population census in 4 Nordic countries: Sweden (1960, 1970, 1980, and 1990); Finland (1970, 1980, and 1990); Norway (1960, 1970, and 1980); and Iceland (1981).

Fig 1 shows an overview of the population sample and the linkage details.

Men and women aged 30 to 64 years who were alive and living in the country on January 1 in the year after the census were included. The choice of this age group aimed to include working-age individuals. The lower age limit was set to 30 years to avoid potential occupational misclassification related to more occupational

mobility in the beginning of the work career.¹⁵

Census questionnaires, centrally coded and computerized in the national statistical offices, included questions related to economic activity and occupation of the whole population. The population registration system on electronic media is daily updated on births, deaths, immigration, and emigration. The linkage among the census data, mortality, and emigration data was based on the unique personal identity codes.

Person-years were then counted until the date of emigration, death, or to December 31 of 2003 in Norway, 2004 in Iceland, and 2005 in Finland and Sweden. Follow-up was done for as long a time as possible in each country, thus the end dates were determined by the timeliness of each cancer registry at the time of linkage.

Study approval was obtained from the national review board of each participating country.

Occupation

Occupational classification was based on the occupation recorded in the first available census in which the person participated in the age range of 30 to 64 years. In Finland, Norway, and Sweden occupation was coded according to national adaptations of the Nordic Occupational Classification,¹⁶ which is a Nordic adaptation of the International Standard Classification of Occupations-58,¹⁷ and in

CAPSULE SUMMARY

- Few population-based studies described relative risk of cutaneous squamous cell carcinoma among occupational categories.
- Occupational categories with high socioeconomic position, some with outdoor work, and some with potential exposure to chemical substances showed increased standardized incidence ratios of cutaneous squamous cell carcinoma.
- The occupational categories identified in this report should be targeted in prevention strategies.

Abbreviations used:

| | |
|-------|-----------------------------------|
| CI: | confidence interval |
| cSCC: | cutaneous squamous cell carcinoma |
| SIR: | standardized incidence ratio |
| UV: | ultraviolet |

Iceland occupation was coded according to a national adaptation of International Standard Classification of Occupations-68.¹⁸ The original national occupational codes were converted to a common classification with 53 occupational categories, and an additional category of economically inactive persons. Detailed descriptions of each occupational category were previously given (Appendices 1 and 2 of Ref. [15] available at: <http://astra.cancer.fi/NOCCA/Incidence/Appendix/appendix-tables.pdf>).

Classification of occupational categories

Occupational categories were further classified as regards to outdoor/indoor work according to previously published studies (Table I)^{19,20}; and merged into socioeconomic groups as previously done by Lynge et al²¹ (Table II).

Cancer data

National cancer registration started in 1953 in Finland and Norway, in 1955 in Iceland, and in 1958 in Sweden. The cancer registries receive information on cancer cases from general and specialist practitioners, hospital departments, pathology departments, and pathology autopsy notifications. Unlike the other Nordic countries, Sweden does not register cancer cases from death certificates.

For this study, cSCC topography, morphology, and date of diagnosis were registered. The cases were classified according to *International Classification of Diseases, Revision 7*. For all countries, only the first incident case of cSCC (primary cSCC) was included. Multiple cSCC at the time of diagnosis were counted as 1 incident case, and patients were censored after the initial diagnosis.

Statistical analysis

The relative risk of the cancer incidence of each occupational category is described by the standardized incidence ratio (SIR), which is calculated as the ratio of the observed to the expected number of cancer cases, using the cSCC incidence rates for the entire national study population of each country as reference. For a given sex (g), the SIR for a given occupational category (o) in a given country (c) was calculated as:

$$SIR_{goc} = \frac{\sum_a \sum_p Obs_{gocap}}{\left\{ \sum_a \sum_p PY_{gocap} \frac{\sum_o Obs_{gocap}}{\sum_o PY_{gocap}} \right\}}$$

Where Obs = observed number of cases; PY = person years; a = age; and p = period. The denominator in the equation is the expected number of cancer cases for the given sex category, occupational category, age, period, and country.

The observed number of cancer cases and person-years were stratified into 2 sex categories, eight 5-year attained age categories (30-34; 35-39; ...; ≥85 years), and 5 calendar periods (1961-1975; 1976-1980; ...; 2001-2005). The expected number of cancer cases was based on number of person-years in each stratum (country, sex, age, and calendar period), and the respective reference rates of each country.

The 95% confidence intervals (CI) were determined by assuming a Poisson distribution of the observed number of cases. The SIR was regarded as statistically significant if the 95% CI did not include 1.0.

After this initial calculation, the combined sex-specific occupational SIRs across different countries, age, and period were calculated by the ratio between the sum of all the observed cases and the sum of all the expected cases for each specific strata.

We assume that increased SIRs after 50 years of age may better reflect a plausible occupational association attributable to cumulative exposure to carcinogens.⁸ Therefore, we present results stratified by 2 age categories (30-49 and ≥50 years). To evaluate consistency and trends across periods, we present results in 3 calendar periods (1961-1975; 1976-1990; 1991-2005). Analysis were performed with software (STATA, Version 12 and 13; StataCorp LP, College Station, TX).

RESULTS

In total 87,619 incident cases of first primary cSCC were reported to the cancer registries from 1961 to 2005. The number of person-years of follow-up accumulated was 333.5 million.

Table III shows the SIR estimates for cSCC for occupational categories with significant increased SIRs according to age. Among men, at the national level, excess risk after 50 years of age was observed in Swedish fishermen (SIR 1.47; 95% CI 1.25-1.71) and postal workers (SIR 1.13; 95% CI 1.00-1.25); and Norwegian building caretakers (SIR 1.25; 95% CI 1.00-1.54). Among women, at the national level, excess risk after 50 years of age was observed only

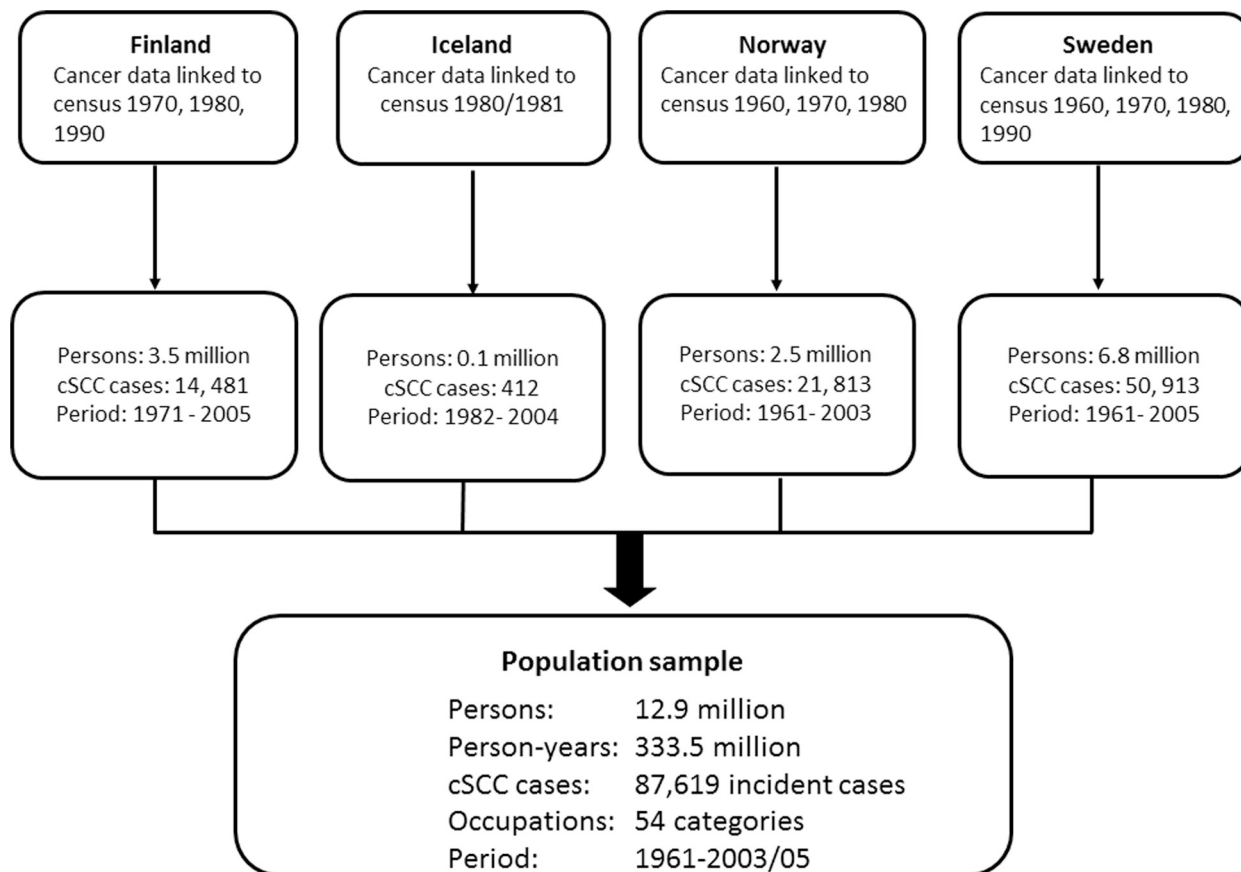


Fig 1. Occupation and relative risk of cutaneous squamous cell carcinoma (cSCC) in 4 Nordic countries. Population sample included in the study.

Table I. Classification of occupational categories according to occupational solar exposure

| | |
|-------------------------------|---|
| Outdoor work | Seamen, farmers, fishermen, forestry workers, gardeners, bricklayers, other construction workers |
| Mixed outdoor/ indoor work | Mechanics, woodworkers, waiters, food workers, chimney sweeps, technical workers, electrical workers, painters, teachers, plumbers, public safety workers, postal workers, building caretakers, military personnel, drivers, transport workers, welders |
| Indoor work | All remaining occupational categories |

among Finnish woodworkers (SIR 1.31; 95% CI 1.04-1.64).

Among men, occupational categories with outdoor work had a consistent tendency of decreasing SIRs across periods (Fig 2). Occupational categories with mixed indoor/outdoor work and with indoor work did not show any consistent trend across periods (results not shown).

Among women, no consistent trend across periods was observed for the occupational categories stratified according to outdoor/indoor work (results not shown).

A trend of increasing SIRs across periods for the top of the socioeconomic hierarchy (“managers” and “lower administrative”) was observed. Conversely, the group of farmers, forestry workers, and fishers showed a consistent trend of decreasing SIRs (Fig 3). A similar pattern was found for men and women.

DISCUSSION

In general, there was a modest variation of the SIR estimates. Occupational categories with high socioeconomic status, some categories with outdoor work, and some with potential exposure to chemical

Table II. Coding of socioeconomic groups

| Socioeconomic group | Occupational categories |
|---------------------------------|--|
| Managers | Technical workers, physicians, dentists, teachers, administrators |
| Lower administrative | Laboratory assistants, nurses, religious workers, artistic workers, journalists, clerical workers, sales agents, shop workers, transport workers, drivers, postal workers, public safety workers |
| Skilled and specialized workers | Assistant nurses, other health workers, miners and quarry workers, seamen, textile workers, shoe and leather workers, smelting workers, mechanics, plumbers, welders, electrical workers, woodworkers, painters, bricklayers, printers, chemical process workers, food workers, beverage workers, tobacco workers, glass makers, engine operators, cooks and stewards, waiters, chimney sweeps, hairdressers, launderers |
| Unskilled workers | Other construction workers, packers, domestic assistants, building caretakers |
| Farmers/forestry/fishing | Farmers, gardeners, fishermen, forestry workers |
| Inactive | Economically inactive |
| Not classified | Military personnel, "other workers" |

Table III. Increased standardized incidence ratios and 95% confidence intervals for cutaneous squamous cell carcinoma among men and women, according to age groups in Finland, Iceland, Norway, and Sweden

| Men | Age 30-49 y | Age >50 y |
|-------------------------|------------------|------------------|
| Occupational categories | SIR (95% CI) | SIR (95% CI) |
| Seamen | 1.19 (0.74-1.83) | 1.23 (1.14-1.32) |
| Military personnel | 1.47 (0.91-2.25) | 1.29 (1.17-1.41) |
| Public safety workers | 1.20 (0.82-1.71) | 1.25 (1.16-1.34) |
| Teachers | 1.15 (0.89-1.46) | 1.20 (1.13-1.26) |
| Technical workers, etc | 0.97 (0.82-1.14) | 1.13 (1.09-1.16) |
| Transport workers | 1.02 (0.65-1.53) | 1.10 (1.03-1.16) |
| Physicians | 2.15 (1.36-3.22) | 1.75 (1.57-1.95) |
| Dentists | 0.85 (0.18-2.50) | 1.30 (1.08-1.56) |
| Nurses | 3.44 (1.48-6.77) | 1.06 (0.34-2.49) |
| Assistant nurses | 1.89 (0.82-3.72) | 1.36 (1.04-1.75) |
| "Other health workers" | 0.40 (0.08-1.15) | 1.16 (1.00-1.35) |
| Clerical workers | 1.36 (1.07-1.70) | 1.18 (1.13-1.23) |
| Religious workers, etc | 1.41 (1.10-1.78) | 1.27 (1.19-1.36) |
| Administrators | 1.31 (1.03-1.63) | 1.32 (1.27-1.37) |
| Sales agents | 0.81 (0.63-1.03) | 1.16 (1.11-1.20) |
| Printers | 1.26 (0.76-1.97) | 1.13 (1.02-1.24) |
| Artistic workers | 1.95 (1.20-2.98) | 1.01 (0.88-1.15) |
| All categories | 1.00 Ref | 1.00 Ref |
| Women | Age 30-49 y | Age >50 y |
| Occupational categories | SIR (95% CI) | SIR (95% CI) |
| Gardeners | 1.16 (0.73-1.73) | 1.04 (1.00-1.10) |
| Teachers | 1.02 (0.80-1.28) | 1.18 (1.10-1.25) |
| Physicians | 1.80 (0.72-3.71) | 1.76 (1.28-2.37) |
| Dentists | 0.51 (0.01-2.83) | 1.41 (1.00-1.91) |
| Nurses | 1.13 (0.81-1.53) | 1.11 (1.01-1.22) |
| "Other health workers" | 0.94 (0.61-1.37) | 1.13 (1.01-1.26) |
| Clerical workers | 1.06 (0.91-1.22) | 1.11 (1.07-1.15) |
| Administrators | 2.01 (1.32-2.92) | 1.16 (1.00-1.34) |
| Journalists | 0.74 (0.09-2.66) | 1.41 (1.00-1.95) |
| All categories | 1.00 Ref | 1.00 Ref |

CI, Confidence interval; SIR, standardized incidence ratio.

substances showed increased SIRs, compared with the general population.

Increased SIRs after 50 years of age, which suggest a plausible occupational association attributable to cumulative exposure to carcinogens,⁶ were found among some occupational categories with outdoor work (seamen, female gardeners, Swedish fishermen, and Finnish female woodworkers); some with mixed outdoor/indoor work (military personnel, transport workers, Swedish postal workers, Norwegian male building caretakers); and in occupational categories with potential exposure to polycyclic aromatic hydrocarbon (technical workers, seamen, transport workers, and public safety workers). These findings are in line with previous studies.^{6,7,22-24}

Approximately half of public safety workers were firefighters,¹⁵ with potential exposure to human carcinogens such as polycyclic aromatic hydrocarbons and arsenic.⁹ In addition, scars are known risk factors for cSCC,²⁵ and together with long-term chronic heat exposure,²⁶ may contribute to excess risk of cSCC. The increased SIR in male printers older than 50 years may be explained by exposure to photosensitizing chemicals used in the printing industry, which enhance the association between UV exposure and skin cancer.¹² To our knowledge, excess risk of skin cancer for printers has only been reported for melanoma skin cancer.²⁷

It is noteworthy that not all occupational categories with outdoor work showed consistently increased SIRs as compared with the general working-age population. This unexpected finding, which should not be interpreted as a contradiction to the existing evidence,⁶ can be explained by several factors. First is the about 2-fold increase in the reference incidence rate from 1960 to 2005.² For instance, we observed elevated SIRs in male farmers

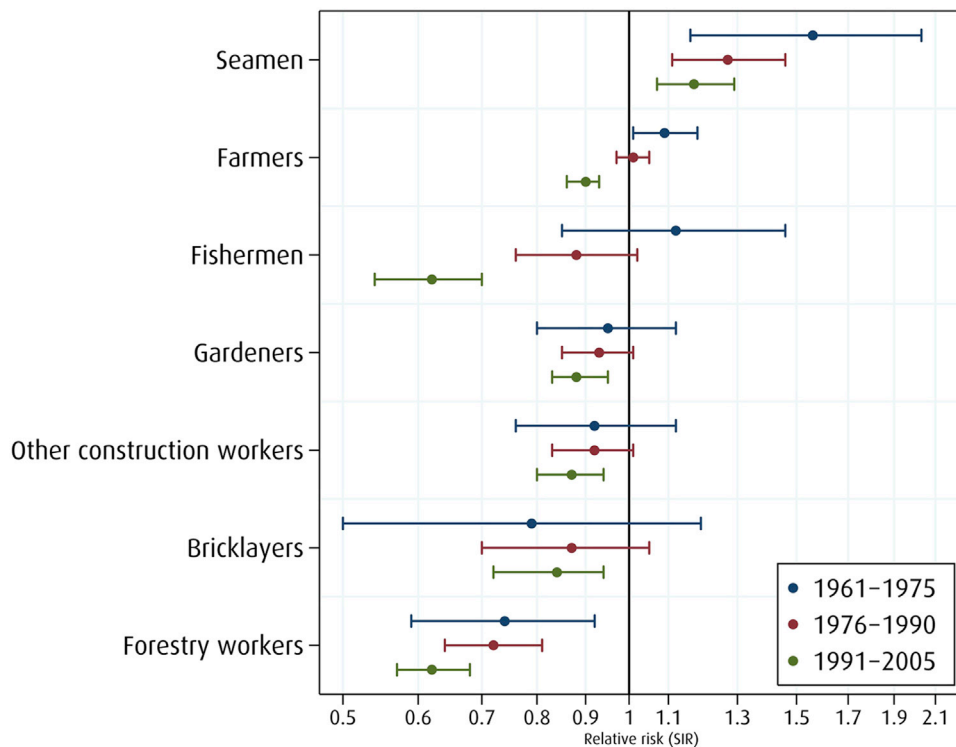


Fig 2. Cutaneous squamous cell carcinoma. Standardized incidence ratios (SIR), by period, in occupational categories with outdoor work among men in 4 Nordic countries. 1961 through 2005. X axis is in logarithmic scale.

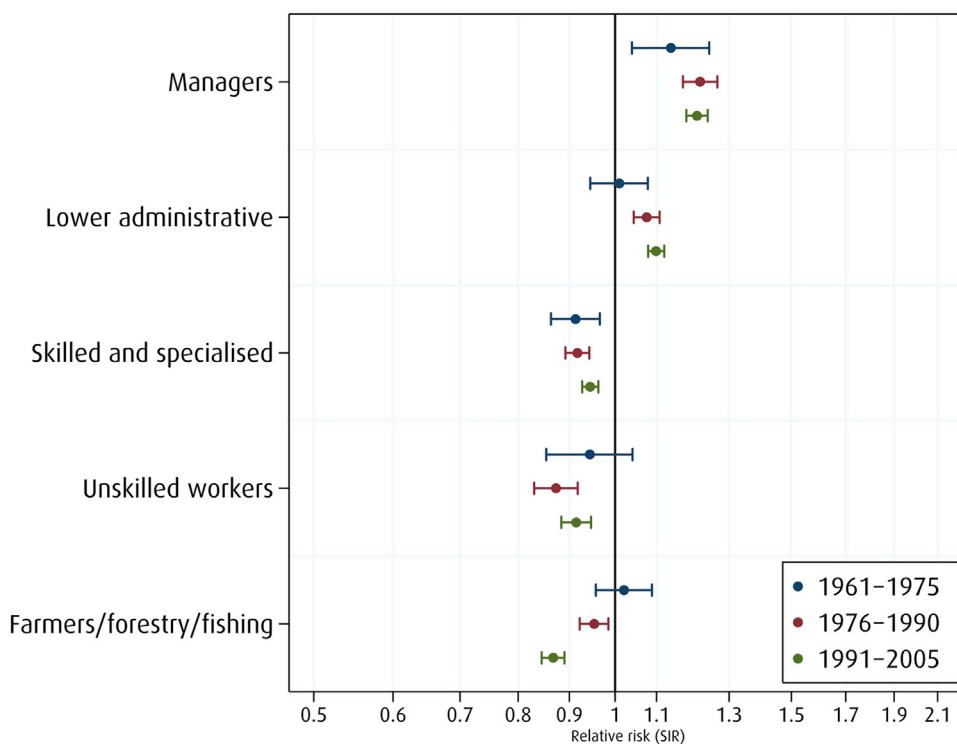


Fig 3. Cutaneous squamous cell carcinoma. Standardized incidence ratios (SIR), by socio-economic group and period, among men and women in 4 Nordic countries. 1961 through 2005. X axis is in logarithmic scale.

only for the period 1961 through 1975 (Fig 2); and a trend of decreasing SIRs for occupational categories of the primary sector (Figs 2 and 3). Secondly, the skin of outdoor workers in the Nordic countries is often quite covered as a result of weather conditions. In fact, outdoor workers have elevated relative risk of lip cancer, which is mainly attributed to UV sun exposure.¹⁵ It is not so easy to cover mouth/lips while working, even when wearing a hat. Moreover, a higher occupational mobility among outdoor workers may contribute to the relative risks observed. For instance, the proportion of the population working in the primary sector (agriculture, fishing, forestry, and hunting) has decreased dramatically since 1960. Thus, only 2% to 6% of the working population in each Nordic country were occupied in this sector by 2005.²⁸

Our findings suggest that socioeconomic factors are of relevance when analyzing variation of SIRs across occupational categories. We analyzed socioeconomic position as a proxy for recreational sun exposure, under the assumption that more money for recreational activities, including outdoor activities, and sunny vacations in lower latitudes may contribute to the overall lifetime UV dose.²⁹ Thus, those employed in occupational categories from the top of the socioeconomic hierarchy may be more prone to excessive sun habits. Another plausible explanation is a greater chance of being given a diagnosis of cSCC, as a result of more awareness, and information leading to more periodic health examinations.³⁰ Nevertheless, the role of occupational factors cannot be excluded. First, some occupational categories could have included seasonal outdoor work in tropical and subtropical areas. Biological modeling suggested that outdoor seasonal work contributes greatly to the overall lifetime UV dose.³¹ Furthermore, growing evidence regarding stressful experiences as potential risk factors for all types of skin cancer is available.²⁹

The strengths of this population-based study are its prospective design, the large study population, the long follow-up, and the high quality of the outcome data.^{32,33}

Loss to follow-up is common in cohort-based studies.³⁴ However, the Nordic population register systems offer very accurate data on the vital status of all residents, and the censuses covered the whole population. Thus, no loss to follow-up and precise person-years calculations are additional strengths of this study.

Because it was based on incident cSCC cases and exact person-years, there was no bias attributable to occupational variation in cancer survival and in mortality from competing causes of death.

Few studies have investigated relative risk of cSCC associated to a variety of occupational categories. Validity studies indicate that the occupational classification in the Nordic censuses is reasonably accurate,¹⁵ but the lack of the complete occupational history is a limitation of this study. The proportion of individuals who had the same occupational category in the first and second census available (ie, 1960 and 1970 censuses in Norway and Sweden, and 1970 and 1980 censuses in Finland) was previously described¹⁵; stability was highest among men, and in occupational categories where a long education is required such as physicians, dentists, and teachers. Occupational stability was lower for occupational categories with outdoor work (from 21.5% for male gardeners in Norway to 77.8% for male farmers in Finland).¹⁵ Accordingly, outdoor workers who switched to a job with less outdoor UV exposure could have contributed to less cumulative UV exposure, and thus to a lower relative risk for cSCC.

Some of the occupational categories used are heterogeneous and potential nondifferential misclassification may underestimate the true associations between specific exposures and cSCC relative risk.³⁵ For instance, a stronger association between occupational UV sun exposure and cSCC risk was reported for studies that directly assessed individual outdoor UV exposure compared with studies that used the occupation title as a proxy for exposure.⁶ Future studies with the inclusion of specific exposure data are warranted.

We were unable to take into account the role of other individual risk factors, such as recreational sun exposure, skin sensitivity,²⁹ long-term use of immunosuppressive drugs,³⁰ and smoking, and this is a limitation of the study. However, we analyzed socioeconomic position as a proxy for recreational sun exposure. For factors such as skin phototype or use of immunosuppressants, we do not expect an important variation between occupational categories.

Overall, a high specificity and sensitivity for cSCC is guaranteed by the multiple sources of information, which combine clinical and pathological reports, and validity studies performed in the Nordic countries.³⁶ Nevertheless, we cannot exclude the possibility that some cases were missed, as cSCC has a low lethal potential and not all cases are necessarily diagnosed or treated, in particular in elderly people with comorbidities.³⁷ This would, however, introduce a serious bias only if case ascertainment differed between the occupational categories, which is a minor problem in the Nordic countries with generally free and available health care.¹⁵

As the prevention potential for cSCC is large, our findings are relevant for public health planning, emphasizing the need of targeting occupational categories with increased SIRs in prevention strategies, and not only occupational categories with outdoor work.

Pär Sparen participated in generating and gathering the data from Sweden for the Nordic Occupational Cancer Study.

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