ACTA ONCOLOGICA
2023, VOL. 62, NO. 6, 541–549
https://doi.org/10.1080/0284186X.2023.2224053

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ORIGINAL ARTICLE

Occupational variation in the incidence of lip cancer in the Nordic countries

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ABSTRACT

Introduction: While certain occupations, such as agriculture and fishery, have been associated with an increased risk of lip cancer, the occupational risk profile of lip cancer and its change over time remain poorly known. This study aims to evaluate the incidence of lip cancer across different occupations in the Nordic countries.

Methods: The Nordic Occupational Cancer Study (NOCCA) covers 14.9 million people and includes 45 years of cancer incidence data, from 1961 to 2005, linked to occupational categories for all the five Nordic populations. Standardized incidence ratios (SIRs) with 95% confidence intervals (CIs) were used to quantify the risk of lip cancer across occupational categories relative to the entire national populations.

Results: There were a total of 14,477 male and 3008 female lip cancer patients identified during follow up. The highest SIRs were observed among male fishermen (SIR 2.26, 95% CI: 2.04–2.50), gardeners (SIR 1.60, 95% CI: 1.48–1.72), and farmers (SIR 1.60, 95% CI: 1.55–1.66). A significantly reduced risk of lip cancer (SIR $<$ 0.50) was observed among male physicians, teachers, religious workers, artistic workers, journalists, administrators, printers, waiters, and hairdressers. Among women, no occupations were associated with an increased risk of lip cancer.

Conclusions: The incidence of lip cancer varies widely between outdoor and indoor occupations. Occupations involving outdoor activity and exposure to sunlight show the most elevated SIRs.

NOVELTY AND IMPACT

Certain outdoor occupations, such as agriculture and fishery, have been associated with an increased risk of lip cancer. However, the occupational risk profile of lip cancer and its change over time remain poorly known. This study highlights the excess risk of lip cancer among men with outdoor occupations and further corroborates previous studies. Efforts to counsel outdoor workers on the risk and prevention of lip cancer are needed to reduce the societal burden of the disease.

ARTICLE HISTORY
Received 6 April 2023
Accepted 5 June 2023

KEYWORDS
Head and neck cancer; oral cancer; incidence; lip cancer; occupational risk; risk

Introduction

Lip cancer is regarded as a type of oral cancer occurring at the outer boundary of the oral cavity, either on the inner lip, i.e., labial mucosa, or the external body of the lip, i.e., vermillion or 'lipstick zone', which, however, possesses distinct etiological features more akin to non-melanoma skin cancer [1,2]. The burden of lip cancer shows significant geographic variation, with incidence rates correlating inversely with latitude [3,4]. While rare in sub-Saharan Africa and southeast Asia, lip cancer is for instance more common than oral cavity cancer in Australia, which has one of the highest incidence rates worldwide, with an age-standardized rate (world standard) of 2.6 per 100,000 in 2012 [4,5]. Yet, the incidence of lip carcinoma is declining in several areas globally, owing, hypothetically, to heightened awareness, and use of sun protectants [5]. Indeed, cumulative ultraviolet radiation from exposure to sunlight prevails as the most cited risk factor [3,6–8]. A significantly increased risk of lip cancer has been previously described in individuals with occupations involving chronic solar exposure to the face, such as farming and commercial fishing [7,9].

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Squamous cell carcinoma entails 90–95% of all lip cancers and the vermillion border of the lower lip constitutes the most affected anatomical site, probably due to its position, rendering it more exposed to solar radiation and the effect of other potential carcinogens, such as tobacco [10–14]. The risk of developing lip cancer increases with age with the highest peak occurring after 60 years of age [11]. Furthermore, lower incidence rates of lip cancer have been described in females, perhaps because of the reduced frequency of outdoor occupations and the protective effects of lip cosmetics [4–6,11]. Dark-skinned populations also display significantly lower incidences of lip cancer than fair-skinned individuals [4,11], which is presumably due to the photoprotective role of natural skin pigmentation [15].

The occupational risk profile of lip cancer and its change over time remain poorly known. The goal of this study was to assess the variation in lip cancer incidence across occupations and over time in the Nordic countries (Denmark, Finland, Iceland, Norway, and Sweden) to potentially uncover additional occupational settings at risk of lip cancer.

Materials and methods

Population

The Nordic Occupational Cancer Study (NOCCA) includes 45 years of cancer incidence data, from 1961 to 2005, linked to occupational categories for the populations of Denmark, Finland, Iceland, Norway, and Sweden. The study obtained needed permissions, as required in each of the Nordic countries. The data comprised 14.9 million men and women aged 30–64 years in the 1960, 1970, 1980/1981, and 1990 censuses. Subjects alive on January 1st of the year after the first available census, were linked to their occupational data and cancer data with the help of the unique personal identity codes given to all residents of the Nordic countries.

Occupational data

Information on occupation for each person was retrieved *via* census questionnaires which were subsequently centrally coded and computerized in the national statistical offices. The censuses were carried out in Denmark in 1970, in Finland in 1970, 1980, and 1990, in Iceland in 1981, in Norway in 1960, 1970, and 1980, and Sweden in 1960, 1970, 1980, and 1990. For each given person, the occupation recorded in the first census the person participated in, was recorded. For the NOCCA project, the original occupational codes were reclassified into 53 occupational categories and one group of economically inactive persons, i.e., not fully employed in the year of the first census the person participated in). Information on vital status and emigration was retrieved from the national population information systems. Person years were calculated from January 1st of the year following the first available census of the person until date of death, censoring due to emigration, or December 31st of the following years: 2003 in Norway and Denmark, 2004 in Iceland, and 2005 in Finland and Sweden (whichever came first). A detailed description of the NOCCA cohort and occupational data are presented in a previous publication [16].

Cancer data

Data on lip cancer cases (International Classification of Diseases, 7th Revision, 140 ICD-9) were obtained from the cancer registry of each country. A nationwide registration of primary cancer cases was initiated in 1943 in Denmark, in 1953 in Finland and Norway, in 1955 in Iceland, and in 1958 in Sweden [17]. During the follow-up period of our study, all cancer registries received clinical notifications from hospitals and all, except Denmark, also from pathological departments in the public and private sectors. All Nordic countries, except Sweden, also trace missing cases identified *via* death certificates.

Statistical analyses

Standardized incidence ratios (SIRs) were used to quantify the risk of lip cancer across occupational categories relative to the entire national populations. The SIR is the ratio of the observed and expected numbers of cases of lip cancer. The expected number of cases in each country, gender, 5-year calendar period, and 5-year age category was calculated by multiplying the number of person-years in the stratum by the respective national incidence rate of lip cancer. Exact 95% confidence intervals (CIs) were determined by Poisson distribution, and the SIR was considered statistically significant if its 95% CI did not include 1.0. For data privacy reasons, observed numbers and risk estimates are not shown, when less than five cases were reported. Analyses were conducted using Stata 17 software (StataCorp. 2021. *Stata Statistical Software: Release 17*. College Station, TX: StataCorp LLC).

Results

Among the 14.9 million study participants, 17,479 cases of lip cancer, 14,471 in men (83%) and 3008 in women (17%), were diagnosed during the study period between 1961 and 2005 (Table 1). The numbers of observed and expected cases and SIRs for each occupational category are summarized in Table 2.

Men

Among men, the highest relative risk (RR) of lip cancer was observed in fishermen (SIR 2.26, 95% CI: 2.04–2.50), gardeners (SIR 1.60, 95% CI: 1.48–1.72), farmers (SIR 1.60, 95% CI: 1.55–1.66), construction workers (SIR 1.52, 95% CI: 1.41–1.64), forestry workers (SIR 1.40, 95% CI: 1.27–1.54), and miners and quarry workers (SIR 1.39, 95% CI: 1.12–1.69).

The risk of lip cancer was also slightly, but significantly elevated in seamen (especially Sweden), drivers (especially Denmark and Sweden), glass makers (especially Sweden), engine operators (especially Denmark), other workers (especially Norway and Sweden), and economically inactive

Table 1. Study population by country, and number of lip cancer cases by country, age, and follow-up period.

			Lip cancers			
			Men		Women	
Characteristics			*N*	%	*N*	%
Country, study population (Million), and follow-up period						
Total	14.9		14,471	100	3008	100
Denmark	2.0	1971–2003	2639	18	394	13
Finland	3.4	1971–2005	3231	22	868	29
Iceland	0.1	1982–2004	45	0.3	7	0.2
Norway	2.6	1961–2003	2996	21	454	15
Sweden	6.8	1961–2005	5560	38	1285	43
Age at diagnosis						
30–49			1087	8	161	5
50–69			7583	52	1010	34
≥70			5801	40	1837	61
Period at diagnosis						
1961–1975			3423	24	228	8
1976–1990			6617	46	1037	34
1991–2005			4431	31	1743	58

individuals (especially Denmark and Finland). SIRs for men stratified by country are presented in Table 3.

The SIR of lip cancer for fishermen, gardeners, farmers, construction workers, and forestry workers was significantly elevated throughout each 15-year period between 1961 and 2005 (Table 4). The SIRs for fishermen, gardeners, farmers, and construction workers were also significantly elevated in each age stratum (Table 5).

Significantly reduced SIRs of lip cancer – less than half of the population average or less than one-third of the incidence in high-risk occupations – were found for male physicians, teachers, religious workers, artistic workers, journalists, administrators, printers, waiters, and hairdressers. The SIRs did not show significant variations across the follow-up periods nor between the different age strata.

Women

Among women, we found no occupations with systematically increased or decreased SIRs across all countries. A statistically significant excess risk of lip cancer was observed among Danish assistant nurses (SIR 2.42, 95% CI: 1.25–4.22) and domestic assistants (SIR 1.96, 95% CI: 1.16–3.09). Female farmers had a significantly decreased risk of lip cancer in Denmark (SIR 0.42, 95% CI: 0.17–0.86) and Sweden (no cases observed, 5.37 cases expected).

Discussion

The results from our study closely echo previously published occupation-specific risk estimates of lip cancer. Among men, a higher incidence was observed, throughout each follow-up period and in virtually all age groups in individuals working as fishermen, gardeners, farmers, construction workers, and forestry workers.

In our study, the highest RR of lip cancer was observed in fishermen (SIR 2.26, 95% CI: 2.04–2.50). Spitzer et al. [9] described almost 50 years ago a significant age-adjusted RR of 1.65 for lip cancer in Newfoundlander fishermen as compared to the general population. Actinic cheilitis, also known as 'sailor's lip', is a well-known premalignant lesion of the lip, associated with chronic sunlight exposure, and is frequently diagnosed in fishermen [18]. Indeed, a Brazilian study [19] reported a prevalence of 11%, and a Chilean study [20] a prevalence of 43% of actinic cheilitis among fishermen. Concerning the general population, a Brazilian multicenter study [21] reported a 1% rate of actinic cheilitis in lip biopsy specimens submitted for examination.

Among men, a high excess risk (SIR > 1.4) was also observed in gardeners, farmers, construction workers, and forestry workers, which corroborates previous reports, linking agricultural, commercial fishing, and other outdoor professions to an increased incidence of the disease. In a meta-analysis pooling 37 studies published in 1998, Acquavella et al. [22] concluded that lip cancer among farmers was the sole cancer with an elevated risk (pooled RR 1.95, 95% CI 1.82–2.09). In a article, not included in the meta-analysis, Spinelli et al. [23] evaluated 6,389 male cancer patients in British Columbia and reported an excess risk of lip cancer in farmers (OR 2.5, 95% CI: 2.0–3.2) and forestry workers (OR 1.8, 95% CI: 1.2–2.6). Kenborg et al. [24] also reported an increased risk of lip cancer in Danish outdoor workers (OR after 10 years of outdoor working 1.67, 95% CI: 1.35–2.03). The study comprised 2341 cases and 9361 controls.

Kawachi et al. [25] conducted a registry-based case-control study in New Zealand comprising 19,904 male cancer patients diagnosed during 1980–84. For lip cancer evaluation, the control group consisted of all other cancer patients, except lung cancer. The authors uncovered an increased risk of lip cancer in woodworkers (17 cases, OR 1.77, 95% CI: 1.07–2.90) which was mainly due to the excess risk among carpenters. In our markedly larger study, the SIR of lip cancer in male woodworkers was 1.06 (887 cases, 95% CI: 0.99–1.13).

The most obvious risk factor for the increased risk associated with these outdoor occupations is the carcinogenic effect of the UVA and UVB components of ultraviolet radiation, as seen in non-melanoma skin cancer [26]. This rationale is also supported by the observation that lip cancer occurs rarely on the upper lip, and most frequently on the

Table 2. Observed (Obs) and expected (Exp) numbers of lip cancer cases, standardized incidence ratios (SIRs), and 95% confidence intervals (CIs) among men and women in Denmark, Finland, Iceland, Norway, and Sweden during 1961–2005, by occupational category.

	Men				Women			
Occupational category	Obs	Exp	SIR	95% CI	Obs	Exp	SIR	95% CI
Administrators	279	629.0	0.44	0.39–0.50	15	15.3	0.98	0.55–1.61
Artistic workers	20	61.7	0.32	0.20–0.50				
Assistant nurses	10	13.3	0.75	0.36–1.38	64	51.8	1.24	0.95–1.58
Beverage workers	16	15.5	1.03	0.59–1.67				
Bricklayers	117	120.4	0.97	0.80–1.17				
Building caretakers	154	159.7	0.96	0.82–1.13	155	141.0	1.10	0.93–1.29
Chemical process workers	202	178.2	1.13	0.98–1.30	7	6.3	1.12	0.45–2.31
Chimney sweeps	11	9.9	1.11	0.55–1.98				
Clerical workers	239	462.4	0.52	0.45–0.59	212	224.5	0.94	0.82–1.08
Cooks and stewards	26	31.0	0.84	0.55–1.23	28	34.1	0.82	0.55–1.19
Dentists	13	22.2	0.59	0.31–1.00				
Domestic assistants					91	74.1	1.23	0.99–1.53
Drivers	**746**	**666.5**	**1.12**	**1.04–1.20**				
Electrical workers	272	313.5	0.87	0.77–0.98	7	8.5	0.82	0.33–1.69
Engine operators	**316**	**276.0**	**1.14**	**1.02–1.28**	6	2.5	2.45	0.90–5.33
Farmers	**3138**	**1958.9**	**1.60**	**1.55–1.66**	68	76.2	0.89	0.69–1.13
Fishermen	**384**	**170.1**	**2.26**	**2.04–2.50**				
Food workers	190	222.5	0.85	0.74–0.98	32	29.1	1.10	0.75–1.55
Forestry workers	**445**	**318.1**	**1.40**	**1.27–1.54**				
Gardeners	**677**	**423.5**	**1.60**	**1.48–1.72**	136	116.2	1.17	0.99–1.38
Glass makers, etc.	**207**	**178.0**	**1.16**	**1.01–1.33**	21	16.1	1.31	0.81–2.00
Hairdressers	13	31.6	0.41	0.22–0.70	9	13.1	0.69	0.31–1.30
Journalists	12	28.9	0.42	0.21–0.73				
Laboratory assistants	9	13.3	0.68	0.31–1.28				
Launderers	10	19.7	0.51	0.24–0.93	13	17.2	0.75	0.40–1.29
Mechanics	701	902.4	0.78	0.72–0.84	8	12.6	0.64	0.27–1.25
Military personnel	66	91.4	0.72	0.56–0.92				
Miners and quarry workers	**98**	**70.7**	**1.39**	**1.12–1.69**				
Nurses					44	39.4	1.12	0.81–1.50
'Other construction workers'[a]	**725**	**476.6**	**1.52**	**1.41–1.64**	6	3.4	1.74	0.64–3.79
'Other health workers'[b]	24	44.5	0.54	0.35–0.80	35	28.3	1.24	0.86–1.72
Packers	355	345.2	1.03	0.92–1.14	28	26.1	1.07	0.71–1.55
Painters	117	199.8	0.59	0.48–0.70				
Physicians	16	55.4	0.29	0.17–0.47				
Plumbers	80	108.5	0.74	0.58–0.92				
Postal workers	82	130.6	0.63	0.50–0.78	36	36.8	0.98	0.68–1.35
Printers	36	103.4	0.35	0.24–0.48	10	8.0	1.25	0.60–2.29
Public safety workers	123	182.2	0.67	0.56–0.81				
Religious workers, etc.	82	187.5	0.44	0.35–0.54	17	23.0	0.74	0.43–1.18
Sales agents	301	562.2	0.54	0.48–0.60	29	30.2	0.96	0.64–1.38
Seamen	**185**	**154.8**	**1.19**	**1.03–1.38**				
Shoe and leather workers	32	55.6	0.58	0.39–0.81				
Shop workers	198	365.5	0.54	0.47–0.62	146	151.9	0.96	0.81–1.13
Smelting workers	195	221.8	0.88	0.76–1.01				
Teachers	136	316.7	0.43	0.36–0.51	72	77.9	0.92	0.72–1.16
Technical workers, etc.	485	853.3	0.57	0.52–0.62	11	10.4	1.06	0.53–1.90
Textile workers	97	137.9	0.70	0.57–0.86	79	82.9	0.95	0.75–1.19
Transport workers	204	243.0	0.84	0.73–0.96				
Waiters	7	21.0	0.33	0.13–0.69	26	32.9	0.79	0.52–1.16
Welders	85	93.9	0.91	0.72–1.12				
Wood workers	887	835.2	1.06	0.99–1.13	10	9.7	1.03	0.49–1.89
Other economically active[c]	676	**530.4**	**1.27**	**1.18–1.37**	57	53.2	1.07	0.81–1.39
Economically inactive	**966**	**852.3**	**1.13**	**1.06–1.21**	1500	1511.5	0.99	0.94–1.04

Significantly elevated risks highlighted in bold.

[a]Includes workers in the building and construction industry who do not constitute separate occupational categories in this study, i.e., reinforced concreters, cement finishers, terrazzo workers, insulators, glaziers, underwater workers, and other unspecified building and construction workers.

[b]Includes workers in the health sector who do not constitute separate occupational categories in this study, i.e., veterinarians, pharmacists, physiotherapists. Some of them perform technical tasks related to research and practical application and operational methods in the field of medicine, veterinary medicine, dentistry, pharmacy, and sanitation.

[c]Consists of all occupational titles not included in previous occupational categories, i.e., precision mechanic workers, athletes and sportsmen, photographers, bath attendants, and several subcategories of service workers.

lower lip which receives considerably more direct sunlight than the upper lip [8,12,27]. An excess incidence of lip cancer has been observed in rural areas, where the proportion of outdoor workers is higher [27–30]. In Finland, a three-fold risk of lip cancer was described for people living in municipalities where agricultural livelihood contributed to more than 70% of livelihood when compared to areas where less than 2% of livelihood stemmed from agriculture [30]. Still, the disease risk could emanate from an interplay of chronic solar radiation along with cumulative carcinogenic exposure to other potential risk factors, such as tobacco. Corroborative of this theory is the study by Lindqvist et al. [14] who evaluated 290 lip cancer patients employing a questionnaire survey. While the RRs of lip cancer for outdoor workers and

Table 3. Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for male lip cancer patients in Denmark, Finland, Iceland, Norway, and Sweden during 1961–2005, by occupational category and stratified by country.

	Denmark		Finland		Iceland		Norway		Sweden	
Occupational category	SIR	95% CI	SIR	95% CI	SIR	95% CI	SIR	95% CI	SIR	95% CI
Administrators	0.40	0.31–0.50	0.36	0.25–0.49			0.50	0.39–0.63	0.49	0.40–0.60
Artistic workers									0.37	0.18–0.68
Beverage workers	1.10	0.53–2.02							1.33	0.49–2.90
Bricklayers	1.16	0.84–1.57	0.84	0.50–1.33			1.19	0.78–1.75	0.75	0.51–1.07
Building caretakers	0.89	0.61–1.24	0.75	0.52–1.05			0.82	0.46–1.36	1.21	0.95–1.53
Chemical process workers	1.10	0.70–1.63	1.00	0.67–1.44			1.22	0.94–1.57	1.12	0.90–1.39
Chimney sweeps			1.78	0.65–3.86						
Clerical workers	0.40	0.28–0.56	0.60	0.44–0.80			0.43	0.32–0.58	0.57	0.47–0.69
Cooks and stewards							1.05	0.59–1.74	0.82	0.38–1.56
Dentists							0.98	0.36–2.13	0.59	0.22–1.29
Drivers	**1.45**	**1.26–1.67**	0.91	0.77–1.07			1.00	0.83–1.19	**1.14**	**1.01–1.29**
Economically inactive	**1.27**	**1.08–1.47**	**1.28**	**1.16–1.40**	2.24	0.82–4.88	0.95	0.76–1.17	0.94	0.83–1.06
Electrical workers	0.56	0.34–0.88	0.75	0.55–0.98			0.93	0.72–1.17	0.97	0.81–1.15
Engine operators	**1.52**	**1.14–1.97**	1.08	0.87–1.33			0.99	0.71–1.34	1.14	0.96–1.36
Farmers	**1.76**	**1.62–1.90**	**1.53**	**1.44–1.63**	2.18	1.04–4.01	**1.45**	**1.33–1.57**	**1.68**	**1.58–1.79**
Fishermen	**3.19**	**2.42–4.14**	1.79	0.98–3.0			**1.92**	**1.68–2.19**	**3.65**	**2.90–4.55**
Food workers	0.92	0.71–1.18	0.94	0.57–1.45			0.82	0.60–1.10	0.77	0.58–1.00
Forestry workers	**2.35**	**1.40–3.72**	**1.35**	**1.12–1.61**			**1.58**	**1.31–1.90**	**1.29**	**1.11–1.49**
Gardeners	**1.34**	**1.05–1.70**	**1.53**	**1.27–1.83**			**1.44**	**1.20–1.70**	**1.76**	**1.58–1.96**
Glass makers, etc.	1.26	0.94–1.65	0.92	0.61–1.33			0.82	0.51–1.25	**1.32**	**1.08–1.60**
Hairdressers									0.47	0.19–0.97
Journalists									0.39	0.13–0.92
Mechanics	0.78	0.64–0.94	0.57	0.46–0.69			0.68	0.56–0.82	0.90	0.81–1.00
Military personnel			0.61	0.26–1.20			0.76	0.46–1.18	0.95	0.66–1.32
Miners and quarry workers			1.44	0.89–2.2			**1.56**	**1.04–2.24**	1.28	0.94–1.72
'Other construction workers'[a]	**1.97**	**1.74–2.23**	**1.21**	**1.03–1.42**			**1.39**	**1.05–1.79**	**1.46**	**1.28–1.65**
'Other health workers'[b]			0.62	0.23–1.35					0.86	0.48–1.42
Packers	1.12	0.80–1.51	1.20	0.95–1.49			0.83	0.65–1.05	1.05	0.89–1.23
Painters	0.55	0.33–0.87	0.73	0.50–1.05			0.65	0.41–0.96	0.51	0.37–0.68
Physicians							0.37	0.12–0.86	0.52	0.25–0.96
Plumbers	0.70	0.32–1.32	0.73	0.45–1.13			0.67	0.35–1.14	0.79	0.56–1.08
Postal workers	0.88	0.55–1.33	0.34	0.15–0.64			0.73	0.44–1.14	0.61	0.42–0.86
Printers	0.22	0.07–0.51	0.44	0.18–0.92			0.29	0.11–0.63	0.41	0.24–0.65
Public safety workers	0.61	0.37–0.94	0.61	0.41–0.87			0.72	0.46–1.06	0.72	0.52–0.96
Religious workers, etc.	0.46	0.25–0.78	0.26	0.12–0.5			0.39	0.22–0.64	0.53	0.38–0.71
Sales agents	0.60	0.39–0.88	0.48	0.36–0.64			0.51	0.39–0.65	0.55	0.47–0.65
Seamen	1.44	0.96–2.09	1.25	0.79–1.87			1.06	0.85–1.30	**1.42**	**1.03–1.92**
Shoe and leather workers							0.76	0.36–1.39	0.62	0.36–0.99
Shop workers	0.47	0.38–0.58	0.62	0.40–0.91			0.69	0.47–0.98	0.58	0.43–0.76
Smelting workers	0.81	0.59–1.09	1.02	0.68–1.47			1.03	0.74–1.41	0.81	0.65–1.01
Teachers	0.48	0.33–0.67	0.38	0.25–0.56			0.44	0.30–0.62	0.42	0.31–0.56
Technical workers, etc.	0.45	0.35–0.57	0.49	0.39–0.62			0.47	0.34–0.64	0.66	0.58–0.74
Textile workers	0.49	0.26–0.86	0.78	0.44–1.29			0.75	0.47–1.14	0.74	0.55–0.98
Transport workers	0.84	0.58–1.17	0.76	0.56–1.03			0.74	0.52–1.03	0.95	0.76–1.16
Welders			0.53	0.27–0.92			1.27	0.83–1.87	0.93	0.68–1.24
Wood workers	1.02	0.83–1.24	1.06	0.92–1.21			**1.15**	**1.01–1.30**	1.02	0.91–1.14
Other economically active[c]	1.12	0.94–1.33	0.98	0.73–1.28			**1.42**	**1.24–1.61**	**1.34**	**1.18–1.52**
Economically inactive	**1.27**	**1.08–1.47**	**1.28**	**1.16–1.40**	2.24	0.82–4.88	0.95	0.76–1.17	0.94	0.83–1.06

Significantly elevated risks highlighted in bold.
[a]See footnote in Table 2, [b]see footnote in Table 2, and [c]see footnote in Table 2.

smokers were 1.4 and 2.0, respectively, when compared to other patients with skin squamous cell carcinoma of the head and neck, together these two risk factors induced a significant 15.4-fold increased risk of lip cancer.

In contrast to the increased association with the aforementioned outdoor occupations, a significantly decreased incidence of lip cancer (SIR $<$ 0.50) was observed in male physicians, teachers, religious workers, artistic workers, journalists, administrators, printers, waiters, and hairdressers. The finding is conceivable if we accept the contention that solar radiation increases the risk of lip cancer, as individuals in these indoor professions are less prone to sunlight exposure, as opposed to, among others, fishermen, gardeners, and farmers.

The independent association between solar radiation and other potential risk factors such as smoking and alcohol, and lip cancer remains intricate to evaluate. According to the newest TNM classification (2017), while a malignant tumor in the external part of the lip, i.e., vermillion, is nowadays considered a skin cancer, it is considered an oral cavity cancer if located in the internal part, i.e., labial mucosa. However, in the period covered by the NOCCA study, the whole lip was classified as one site. The internal and external lip share distinct etiological and histopathological profiles [31], and studies may have consequently encompassed these two subtypes. Other oral cavity cancers may exert an undue influence on lip cancer statistics and *vice-versa,* which complicates contextualizing the observations and comparing study

Table 4. Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for male lip cancer patients in Denmark, Finland, Iceland, Norway, and Sweden during 1961–2005, by occupational category and stratified by 15-year periods.

	1961–1975		1976–1990		1991–2005	
Occupational category	SIR	95% CI	SIR	95% CI	SIR	95% CI
Administrators	0.35	0.26–0.47	0.41	0.34–0.49	0.55	0.45–0.66
Artistic workers	0.40	0.13–0.93	0.26	0.11–0.54	0.36	0.15–0.71
Assistant nurses			0.87	0.28–2.03		
Beverage workers	1.45	0.47–3.38	0.89	0.36–1.83		
Bricklayers	1.00	0.67–1.45	0.92	0.69–1.21	1.03	0.72–1.43
Building caretakers	0.91	0.64–1.27	1.02	0.81–1.28	0.91	0.66–1.23
Chemical process workers	1.01	0.75–1.33	**1.31**	**1.07–1.59**	0.95	0.70–1.28
Chimney sweeps	2.29	0.74–5.33	0.65	0.13–1.90		
Clerical workers	0.45	0.33–0.60	0.45	0.36–0.55	0.66	0.53–0.80
Cooks and stewards	0.94	0.38–1.93	0.53	0.21–1.08	1.18	0.61–2.06
Dentists			0.53	0.17–1.23		
Drivers	0.93	0.77–1.11	**1.20**	**1.08–1.33**	1.12	0.99–1.27
Electrical workers	0.91	0.69–1.17	0.72	0.58–0.88	1.02	0.84–1.22
Engine operators	1.08	0.83–1.39	1.12	0.94–1.32	**1.21**	**1.01–1.45**
Farmers	**1.67**	**1.56–1.79**	**1.56**	**1.49–1.65**	**1.60**	**1.50–1.72**
Fishermen	**2.32**	**1.93–2.77**	**2.27**	**1.95–2.63**	**2.15**	**1.71–2.67**
Food workers	0.78	0.56–1.06	0.83	0.66–1.02	0.96	0.74–1.23
Forestry workers	**1.33**	**1.10–1.60**	**1.48**	**1.29–1.70**	**1.33**	**1.10–1.59**
Gardeners	**1.68**	**1.45–1.94**	**1.47**	**1.31–1.65**	**1.73**	**1.50–1.98**
Glass makers, etc.	**1.36**	**1.03–1.76**	1.18	0.96–1.44	0.98	0.74–1.29
Hairdressers			0.47	0.19–0.96	0.59	0.19–1.37
Journalists					0.48	0.16–1.13
Laboratory assistants					0.91	0.30–2.14
Launderers			0.76	0.31–1.57		
Mechanics	0.80	0.68–0.94	0.80	0.72–0.90	0.73	0.63–0.83
Military personnel	0.64	0.31–1.18	0.73	0.49–1.06	0.74	0.49–1.08
Miners and quarry workers	1.25	0.80–1.86	1.38	1.00–1.85	**1.53**	**1.03–2.18**
'Other construction workers'[a]	**1.70**	**1.46–1.97**	**1.46**	**1.31–1.62**	**1.49**	**1.30–1.71**
'Other health workers'[b]			0.45	0.20–0.85	0.77	0.40–1.34
Packers	0.80	0.63–1.00	1.04	0.89–1.21	**1.25**	**1.03–1.51**
Painters	0.47	0.30–0.70	0.61	0.46–0.80	0.64	0.45–0.88
Physicians			0.42	0.20–0.77	0.24	0.08–0.56
Plumbers	0.75	0.43–1.19	0.72	0.50–1.01	0.75	0.51–1.08
Postal workers	0.55	0.32–0.89	0.59	0.41–0.83	0.73	0.49–1.03
Printers	0.21	0.07–0.50	0.37	0.22–0.60	0.41	0.22–0.68
Public safety workers	0.63	0.40–0.94	0.71	0.54–0.92	0.66	0.47–0.89
Religious workers etc.	0.46	0.27–0.73	0.40	0.27–0.57	0.47	0.32–0.66
Sales agents	0.47	0.36–0.60	0.51	0.42–0.61	0.62	0.51–0.75
Seamen	1.28	0.94–1.69	1.04	0.82–1.31	**1.36**	**1.04–1.73**
Shoe and leather workers	0.40	0.16–0.82	0.55	0.30–0.92	0.88	0.44–1.57
Shop workers	0.38	0.24–0.56	0.50	0.40–0.61	0.69	0.55–0.86
Smelting workers	0.84	0.62–1.12	0.91	0.73–1.11	0.87	0.65–1.13
Teachers	0.30	0.18–0.49	0.37	0.27–0.49	0.55	0.43–0.69
Technical workers, etc.	0.60	0.48–0.73	0.53	0.45–0.61	0.60	0.52–0.69
Textile workers	0.65	0.42–0.97	0.52	0.36–0.73	1.07	0.76–1.46
Transport workers	0.89	0.64–1.20	0.85	0.69–1.04	0.80	0.62–1.01
Waiters					0.78	0.25–1.83
Welders	0.70	0.36–1.23	0.81	0.55–1.15	1.09	0.78–1.47
Wood workers	0.99	0.86–1.14	1.09	0.98–1.20	1.08	0.96–1.22
Other economically active[c]	**1.35**	**1.17–1.55**	**1.19**	**1.06–1.34**	**1.35**	**1.15–1.56**
Economically inactive	0.92	0.81–1.04	**1.25**	**1.14–1.36**	**1.20**	**1.04–1.38**

Significantly elevated risks highlighted in bold.
[a]See footnote in Table 2, [b]see footnote in Table 2, and [c]see footnote in Table 2.

results. For instance, the influence of smoking and alcohol on specifically the risk of external lip cancer remains unclear, and so far, limited evidence is available [32]. Our study is also affected by this caveat, as lip cancer here does not differentiate between internal and external lip cancers.

In our study, lip cancer occurred more often in men (83%) than in women (17%), consistent with tabulations from cancer registries all-around the world. The preponderance of lip cancer among men might be partly attributed to a gendered distribution of the labor force and behavioral differences: a higher proportion of men in outdoor occupations or leisure activities, and resultantly a more prolonged exposure to solar radiation, and also a higher smoking prevalence in the past in men [33–35]. Supportive of this theory is the decreasing number of European farmers and the concurrent declining incidence of lip cancer in men in Europe [5,36]. In addition, some authors have postulated that the more frequent application of sunscreen products and lip cosmetics renders women less susceptible to UV radiation and may also explain the lower rate of lip cancer in women [6].

Among women, there were no occupations with systematically increased or decreased SIRs across all countries.

Table 5. Standardized incidence ratios (SIRs) and 95% confidence intervals (CIs) for male lip cancer patients in Denmark, Finland, Iceland, Norway, and Sweden during 1961–2005, by occupational category and age at follow-up.

	Age at follow-up					
	30–49		50–69		>70	
Occupational category	SIR	95% CI	SIR	95% CI	SIR	95% CI
Administrators	0.32	0.18–0.52	0.41	0.35–0.49	0.51	0.42–0.60
Artistic workers			0.27	0.12–0.52	0.40	0.18–0.75
Beverage workers			1.16	0.56–2.13		
Bricklayers	1.30	0.65–2.32	1.04	0.81–1.33	0.82	0.58–1.12
Building caretakers	0.77	0.33–1.53	0.92	0.72–1.15	1.05	0.82–1.33
Chemical process workers	1.55	0.92–2.46	**1.25**	**1.04–1.51**	0.92	0.71–1.16
Chimney sweeps			0.9	0.29–2.10		
Clerical workers	0.41	0.24–0.67	0.49	0.41–0.59	0.57	0.47–0.70
Cooks and stewards	1.41	0.46–3.30	0.81	0.44–1.36	0.69	0.28–1.42
Dentists			0.44	0.14–1.02	0.81	0.33–1.67
Drivers	1.16	0.91–1.45	**1.17**	**1.06–1.28**	1.03	0.90–1.17
Electrical workers	0.76	0.49–1.13	0.91	0.77–1.06	0.84	0.67–1.03
Engine operators	1.27	0.87–1.78	1.16	1.00–1.34	1.09	0.89–1.32
Farmers	**1.90**	**1.61–2.22**	**1.65**	**1.57–1.73**	**1.53**	**1.45–1.61**
Fishermen	**3.90**	**2.80–5.28**	**2.31**	**2.01–2.65**	**1.95**	**1.64–2.30**
Food workers	1.07	0.63–1.69	0.85	0.70–1.04	0.81	0.63–1.03
Forestry workers	1.09	0.68–1.67	**1.45**	**1.27–1.65**	**1.38**	**1.19–1.59**
Gardeners	**1.98**	**1.47–2.61**	**1.65**	**1.49–1.84**	**1.48**	**1.32–1.67**
Glass makers, etc.	1.26	0.73–2.01	1.15	0.94–1.39	1.16	0.92–1.44
Hairdressers			0.48	0.21–0.95	0.38	0.12–0.89
Journalists			0.51	0.22–1.01		
Laboratory assistants					1.36	0.44–3.18
Launderers			0.49	0.16–1.14	0.61	0.20–1.43
Mechanics	0.97	0.77–1.20	0.77	0.69–0.85	0.74	0.65–0.84
Military personnel	0.82	0.37–1.56	0.78	0.56–1.06	0.59	0.34–0.94
Miners and quarry workers	1.37	0.55–2.82	**1.46**	**1.10–1.90**	1.29	0.90–1.79
'Other construction workers'[a]	**1.86**	**1.42–2.41**	**1.59**	**1.44–1.76**	**1.37**	**1.20–1.54**
'Other health workers'[b]			0.34	0.15–0.66	0.90	0.50–1.49
Packers	0.82	0.48–1.29	0.95	0.81–1.11	1.16	0.99–1.35
Painters	0.90	0.48–1.54	0.57	0.43–0.73	0.55	0.40–0.74
Physicians			0.21	0.08–0.45	0.49	0.23–0.89
Plumbers			0.86	0.64–1.13	0.67	0.43–0.99
Postal workers			0.62	0.45–0.84	0.72	0.50–0.99
Printers			0.35	0.22–0.55	0.32	0.17–0.57
Public safety workers	0.54	0.23–1.07	0.73	0.57–0.92	0.62	0.45–0.84
Religious workers etc.	0.37	0.15–0.75	0.44	0.32–0.59	0.46	0.31–0.64
Sales agents	0.67	0.46–0.95	0.52	0.44–0.61	0.53	0.43–0.63
Seamen	1.38	0.85–2.11	**1.26**	**1.03–1.51**	1.04	0.78–1.35
Shoe and leather workers			0.48	0.25–0.82	0.70	0.41–1.10
Shop workers	0.71	0.46–1.06	0.51	0.41–0.61	0.55	0.43–0.70
Smelting workers	0.94	0.54–1.53	0.89	0.73–1.08	0.85	0.67–1.07
Teachers	0.46	0.26–0.75	0.36	0.28–0.46	0.53	0.40–0.68
Technical workers, etc.	0.40	0.28–0.55	0.55	0.49–0.63	0.64	0.55–0.73
Textile workers	0.88	0.35–1.81	0.80	0.61–1.04	0.56	0.39–0.79
Transport workers	1.00	0.60–1.55	0.81	0.66–0.98	0.85	0.67–1.06
Welders	1.07	0.55–1.87	0.88	0.65–1.17	0.89	0.58–1.30
Wood workers	**1.39**	**1.09–1.74**	1.01	0.92–1.11	1.08	0.97–1.19
Other economically active[c]	0.90	0.61–1.28	**1.35**	**1.21–1.49**	**1.24**	**1.10–1.40**
Economically inactive	**1.41**	**1.08–1.81**	**1.15**	**1.05–1.25**	1.08	0.98–1.19

Significantly elevated risks highlighted in bold.
[a]See footnote in Table 2, [b]see footnote in Table 2, and [c]see footnote in Table 2.

However, with a higher participation rate among women in the Nordic labor market [37], the findings may not be applicable nowadays. The statistically significant excess risks among Danish assistant nurses and domestic assistants may well be chance findings that always exist in this type of extensive tabulation.

The main strength of this study is the large-scale population-based dataset and long follow-up of cancer incidence, which permit capturing epidemiology with great statistical power and negligible sampling bias. Quality assessment studies have demonstrated high inclusion and precision of cancer diagnoses, and validity studies indicate a reasonable accuracy in the classification of occupational information in the Nordic censuses [16,17].

Studies based on administrative databases include some inherent shortcomings related to the study design worth further discussing. First, the lack of information on non-occupational confounding factors, such as tobacco smoking and alcohol consumption, hinders us from estimating causal relationships between direct occupational exposure and lip cancer. Second, our analyses did not consider data on occupational duration. While labor mobility might affect the risk estimates, occupational stability is deemed high, especially in men, in the early decades of follow-up [38]. It would

also be unusual for individuals with outdoor occupations at the first available census years not to remain in similar occupations during their later earlier work careers.

Most of the data included in this study were collected decades ago and the results may not be generalized to modern-day occupational conditions. Since the SIRs remained similar throughout the 45 years from 1961 to 2005, there is little reason to suppose that they would markedly change.

Conclusion

Our study showed that the incidence of lip cancer across different occupations displayed typical epidemiological profiles, supportive of previous studies: an excess risk of lip cancer was observed in men with outdoor occupations and a decreased incidence was associated with indoor occupations. Outdoor workers – especially smokers – should be informed about the increased risk of lip cancer and encouraged to apply appropriate sunscreen to any skin, including the lips, when exposed to the sun for extended periods.

Author contributions

The study was designed by Rayan Mroueh, Timo Carpén, Antti Mäkitie, and Eero Pukkala. Elsebeth Lynge, Jenny Selander, Ingrid Sivesind Mehlum, Jóhanna Eyrún Torfadóttir, and Eero Pukkala are responsible for the accuracy of the NOCCA data from Denmark, Sweden, Norway, Iceland, and Finland, respectively. Jan Ivar Martinsen performed all statistical analyses. The manuscript was devised by Rayan Mroueh, Timo Carpén, Antti Mäkitie, Sanna Heikkinen, Elsebeth Lynge, Ingrid Sivesind Mehlum, Tuula Salo, and Eero Pukkala. All authors contributed to the revision of the manuscript and have approved the final version.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Funding

This work was supported by Finska Läkaresällskapet, the Helsinki University Hospital Research Funding, and Nordic Cancer Union (NCU).

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Data availability statement

Most of the tabulated data available on https://astra.cancer.fi/NOCCA/

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