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Lung Cancer Mortality in the Swiss Working Population

The Effect of Occupational and Non-Occupational Factors

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Objective: To assess the effect of occupational exposures on lung cancer mortality in Switzerland after adjustment for non-occupational lung carcinogens. **Methods:** Using data on 4,351,383 Swiss residents, we used negative binomial regression to assess the effect occupation on lung cancer mortality between 1990 and 2014, accounting for socio-demographic factors, predicted probabilities of smoking and measured environmental radon exposure. **Results:** After adjustment, male machine operators and workers in mining, stone working and building materials manufacturing showed the highest risk. Women working in electrical engineering, electronics, watch-making, vehicle construction and toolmaking, and transport occupations also remained at high risk. Radon exposure had no effect on lung cancer mortality, while smoking demonstrated a significant effect in both sexes. **Conclusions:** The results suggest the presence of occupational exposures to lung carcinogens in addition to non-occupational factors.

Keywords: gender differences, longitudinal study, lung cancer, occupational exposures, Switzerland, workers

Lung cancer usually has a poor prognosis and results in the highest mortality among all cancers, with 1.8 million deaths worldwide in 2020.[1,2] While tobacco consumption and exposure to radon are considered as the two main risk factors, occupational exposures are also another important risk factor of lung cancer. A recent study showed that the PAF for occupational lung cancer in France, Canada, and Great Britain was estimated to be between 18% and 25% for men and between 2% and 6% for women.[3] Accounting for 86% of all occupational cancers,[4] lung cancer is considered the most common occupational cancer, with many IARC Group 1 human carcinogens identified in occupational settings (arsenic, asbestos, beryllium, cadmium, chromium VI, diesel exhaust, SHS, nickel, polycyclic aromatic hydrocarbons [PAHs], and silica).

In Switzerland, 12,946 men and 8314 women were diagnosed with lung cancer between 2011 and 2015, representing, respectively, 11.9% and 8.9% of the overall cancer cases. In the same period, lung cancer death accounted for 21.6% of all cancer deaths among men ($n = 10,017$) and 15.7% among women ($n = 5872$).[5] Applying the French PAF estimated at 19.3% for males and 2.6 for females,[6] the lung cancer burden would have diminished by 2500 and 740 cases of lung cancer in men and women over this period, respectively, in absence of occupational exposures to lung carcinogens. The Swiss National Accident Insurance Fund (Suva) recognizes less than 200 cases (mainly mesotheliomas) yearly as occupational cancers,[7,8] which contrasts with expected numbers. To investigate this discrepancy, an epidemiological study based on individual occupational exposure data is necessary. Nonetheless, the occupational exposure to lung carcinogens is poorly documented in Switzerland.[9] Conversely, environmental exposure data are available nationwide. Previous findings showed that residential exposures to radon, with relatively high levels in some Swiss regions, increased the risk of lung cancer.[10] For smoking, data showed that 29% of Swiss adult males and 21% of females were smokers in 2015.[11] A large discrepancy, though, has been noted between smoking consumption from surveys and actual consumption derived from aggregate data on sales. An underestimation of the true prevalence is therefore likely.[12]

A previous study describing age-standardized lung cancer mortality rates across occupations in Switzerland found that men working in construction and in mining and quarrying, and women working in industries of trade, repair of motor vehicles and domestic articles, and in manufacture of goods had a significantly higher risk of lung cancer mortality, compared to the Swiss general population.[13] Working in hotels and restaurants was also associated with an excess of lung cancer mortality in both sexes. Nevertheless, this first study was purely descriptive. Consequently, the present study aims at assessing the effect of occupational exposures on lung cancer mortality in Switzerland after adjustment for non-occupational lung carcinogens.

METHODS

Data Sources

The data of the Swiss National Cohort (SNC) were used to examine lung cancer in the working Swiss population. The SNC is a national longitudinal research platform for the entire resident population of Switzerland. The records of the 1990 and 2000 Swiss censuses were linked to mortality, life birth, and emigration records until 2015, using a combination of deterministic and probabilistic methods.[14] Censuses were mandatory, with population coverage estimated at 98.6%.[15] No data on smoking or radon exposure were

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The Swiss National Cohort and the present study were approved by the Cantonal Ethics Committees of Bern and Zurich, and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

The authors report no conflicts of interest.

Clinical significance: This article identified occupations at high risk for lung cancer, after adjustment for non-occupational factors. Our results will allow the application of further research on at-risk groups to better understand the occupational carcinogens associated with these occupations. This will enable the design of appropriate preventive interventions.

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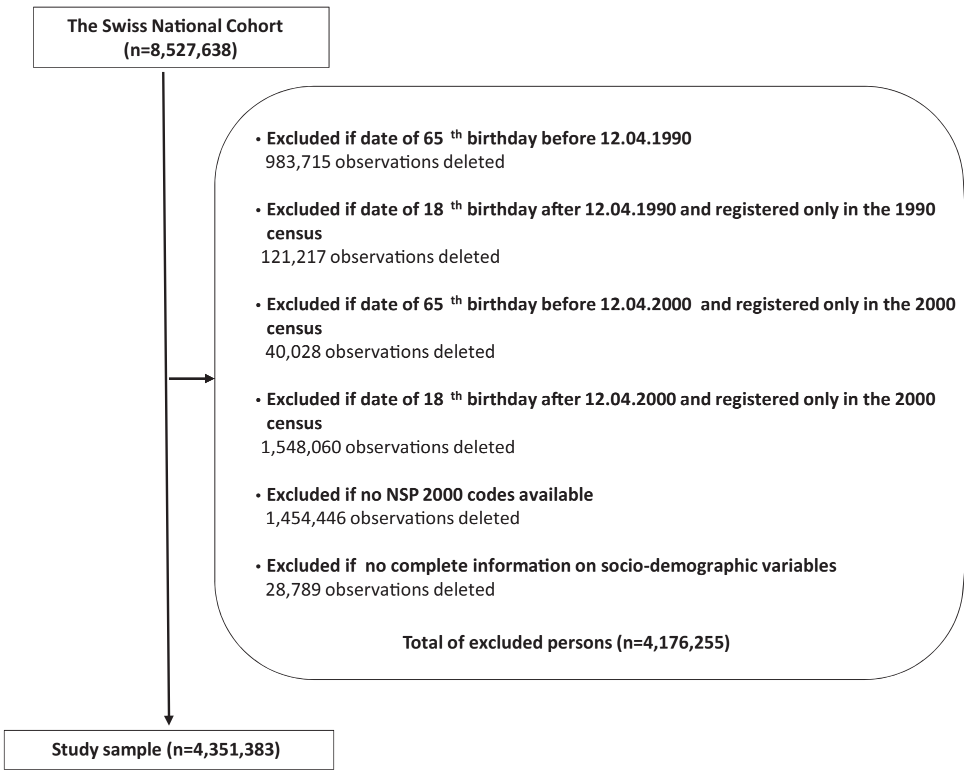

FIGURE 1. Flowchart of study population selection.

available within the SNC. Therefore, we used data from the 1992 Swiss Health Survey (SHS) provided by the Swiss Federal Statistical Office (SFSO) for the former,[16] and the household radon concentration measured in 2013 by the FOPH for the latter.

Study Population

The study sample comprised adults aged 18 to 65 years included in the SNC in either the 1990 or 2000 census, with known occupation (Fig. 1). Participants with no information on socio-demographic variables (geographical regions, civil status, educational level, nationality, and municipality) were excluded.

Mortality Follow-up and Outcome Definition

The follow-up started either on December 4th 1990 (the date of the 1990 census) or on December 5th 2000 (date of the census) and lasted until the earliest of their 85th birthday, the date of emigration, death, or end of the study (December 31st 2014). Since the start and end dates of employment were unavailable, participants with a single occupation contributed to this occupation for the entire period of their follow-up, while participants who changed occupation between 1990 and 2000 census, contributed to the first occupation between 1990 and 2000, and to the second one afterward until the earliest between their 85th birthday or the end of follow-up. Causes of death from the death certificate were coded by the SFSO using the International Classification of Disease (ICD) 8th and 10th edition. Lung cancer deaths were identified using ICD8 initial cause code 162 and ICD10 primary cause code C33-C34.

Occupational Exposure

The occupation was used as a proxy of all potential occupational exposures, given the unavailability of public occupational exposure data in Switzerland. They were coded using the Swiss Standard Classification of Occupations of the SFSO, version 1990 (NSP 1990) for the 1990 census and version 2000 (NSP 2000) for the 2000 census. To harmonize the coding, we recoded NSP 1990 codes to NSP 2000 and aggregated all codes at two digits, corresponding to 39 occupational groups.

Smoking and Radon Exposure

To calculate smoking predictions, we used the data from the SHS. This is a weighted sample representative of the Swiss population including 15,278 participants, 55% of whom were women. Among them, we selected 6010 (88%) men and 6548 (78%) women who had available information on occupation (coded on NSP 2000). We then recoded the available smoking information for these participants and assigned them to either smoking or non-smoking category. Smoking probability was predicted using sex-specific logistic regressions, with smoking status as dependent variable and age, geographical region, civil status, educational level, nationality, and occupation as predictors.[17] We then matched the predicted smoking probability to each SNC participant using as key variables the same variables as those applied in the logistic regression. The occupations with fewer than 10 observations were aggregated at the correspondent 1-digit NSP code.

Concerning radon, we used the risk of exposure based on the household radon concentration in Bq/m^3 measured in 2013 by the FOPH. We assigned to each participant a risk of radon exposure (low, medium, high) based on the municipality in which they lived at the time of either of the censuses. For most municipalities, low risk was defined with an average household radon exposure lower than 100 Bq/m^3, medium risk between 100 and 200 Bq/m^3, and high risk with higher than 200 Bq/m^3.

Statistical Analysis

For each participant, we computed person-years at risk that we stratified by calendar period (1990 to 1995, 1995 to 2000, 2000 to 2005, 2005 to 2010, and 2010 to 2014) and age group (18 to 35, 35 to 45, 45 to 55, 55 to 65, and 65+). The lung cancer mortality rate per 100,000 person-years was assessed using negative binomial regression in order to account for overdispersion.[18] We started with a model with age groups, calendar periods, and occupation to assess the effect of occupation on lung cancer mortality rate (model 1). We then created two other models with the addition of non-occupational factors and potential confounders. The model 2 contained the model 1 plus socio-demographic variables (geographical regions, marital status, education level, and nationality) to assess whether these variables, previously identified as being associated with smoking,[19,20] had an impact on lung cancer mortality. The model 3 encompassed the model 1 adjusted for radon exposure and predicted smoking probability. All results were expressed as relative risk (RR) with respect to a reference category for each variable and the associated confidence interval at 95% (95%-CI).[21] In all models, we used health occupations as a reference, as it has recently been identified as one of the occupational groups with the lowest risk of lung cancer.[22] The statistical analyses were run on STATA version 16 (StataCorp LP; TX).

RESULTS

Cohort Description

In total, 4,351,383 Swiss residents were included in this study (67,922,468 person-years), 45% of whom were women (Table 1). Figure 1 illustrates their selection. The mean age at study entry was 38.1 ± 12.4 years in men and 37.2 ± 12.3 years in women, while the mean age at study end-point was 54.2 ± 12.7 years and 52.3 ± 12.7 years, respectively. A total of 208,308 participants died during the follow-up (4.8%), of whom 16,075 and 4818 were male and female lung cancer deaths, respectively. The proportions of smokers predicted on the basis of 1992 SHS data ranged between 19% and 93% in the different NSP 2 digit job categories among men, and between 1% and 89% among women. In men, the median predicted proportion was 54%, with nationality and civil status being the main independent predictors. In women, the median predicted proportion was 34%, with language region and civil status being the main independent predictors. In both sexes, occupation as coded according to NSP 2 digit was also a statistically significant predictor. Regarding exposure, the household address of about two-thirds of the participants corresponded to a low level of exposure and only 4% had a high level. Most of participants in construction, mining, technical, and computer occupations were men, while women were more than twice as likely as men to work in health, education, cultural, and scientific occupations, and three times as likely to work in hotel, restaurant, and personal service occupations.

Lung Cancer Risk Among the Swiss Working Population

Overall, the differences observed across age groups and calendar periods were statistically significant (Tables S1, http://links.lww.com/JOM/A951 and S2, http://links.lww.com/JOM/A952). While the risk decreased over time in men, we found an opposite trend in women with the highest risk in the last calendar period (2010 to 2014). In both sexes, all socio-demographic

TABLE 1. Characteristics of the Study Sample with an Available Occupation: the Swiss National Cohort (1990–2014)

Characteristics	Male				Female			
	n	(%)	*n* of Lung Cancer Death	(%)	*n*	(%)	*n* of Lung Cancer Death	(%)
Total	2,403,226	(100)	16,075	(100)	1,948,157	(100)	4818	(100)
Person-years (in 100,000)	386.04				293.19			
Nationality (binary)								
Swiss	1,865,423	(78)	13,360	(83)	1,636,679	(84)	4415	(92)
Non-Swiss	537,803	(22)	2715	(17)	311,478	(16)	403	(8)
Language region								
German and Rhaeto-Romansch	1,756,963	(73)	11,446	(71)	1,416,669	(73)	3401	(71)
French	546,069	(23)	3849	(24)	454,766	(23)	1215	(25)
Italian	100,194	(4)	780	(5)	76,722	(4)	202	(4)
Civil status								
Single	707,098	(29)	1649	(10)	599,919	(31)	678	(14)
Married	1,532,055	(64)	12,270	(76)	1,103,268	(57)	2636	(55)
Widowed	18,413	(1)	1804	(11)	61,036	(3)	404	(8)
Divorced	145,660	(6)	352	(2)	183,934	(9)	1100	(23)
Highest education achieved								
Compulsory education or less	421,356	(18)	3838	(24)	434,894	(22)	1372	(28)
Upper secondary level education	1,304,783	(54)	9246	(58)	1,227,791	(63)	2927	(61)
Tertiary level education	677,087	(28)	2991	(19)	285,472	(15)	519	(11)
Vital status at study end-point								
Alive	1,847,092	(77)			1,611,687	(83)		
Lost to follow-up	403,581	(17)			280,715	(14)		
Deceased	136,478	(6)			50,937	(3)		
Deceased from lung cancer	16,075	(1)			4818	(0)		
Age (years): mean ± standard deviation								
At study entry	38.1 ± 12.4				37.2 ± 12.3			
At study end	54.2 ± 12.7				52.3 ± 12.7			
At death from lung cancer	61.7 ± 7.9				59.6 ± 8.4			
Duration (years): mean ± standard deviation								
Follow-up	16.1 ± 6.9				15.1 ± 6.4			
Between the last occupational information and death by lung cancer	6.9 ± 3.8				7.6 ± 3.8			

TABLE 2. Relative Risk (RR) and Confidence Interval (CI-95%) for Lung Cancer Mortality by Occupation Among Males Aged 18–85 in the Swiss National Cohort (1990–2014)

2-Digit NSP 2000[§]	n Subjects	Observed Lung Cancer Deaths	Person-years (in 100,000)	Model 1*		Model 2[†]		Model 3[‡]	
11. Occupations in agriculture, forestry, animal husbandry, and care of animals	123,314	1009	20.55	1.77	[1.53,2.05]	1.31	[1.13,1.53]	1.81	[1.56,2.09]
21. Occupations in the production of food, beverages, and tobacco	38,214	256	6.21	1.95	[1.63,2.34]	1.59	[1.33,1.91]	1.82	[1.52,2.18]
22. Occupations in the textile and leather industry	12,220	99	1.68	1.85	[1.46,2.34]	1.46	[1.15,1.86]	1.67	[1.32,2.12]
24. Occupations in metalworking and mechanical engineering	162,233	1399	25.87	2.51	[2.17,2.89]	1.94	[1.67,2.24]	2.31	[2.00,2.67]
25. Occupations in electrical engineering, electronics, watchmaking, vehicle and tool construction	88,094	463	15.02	1.98	[1.68,2.32]	1.55	[1.32,1.82]	2.00	[1.70,2.34]
26. Occupations in the wood and paper industry	50,724	305	8.50	1.84	[1.55,2.19]	1.46	[1.22,1.74]	1.76	[1.48,2.10]
27. Graphic arts occupations	22,734	177	3.79	1.95	[1.60,2.38]	1.52	[1.24,1.86]	1.99	[1.63,2.42]
28. Occupations in the chemical and plastics industry	18,697	164	2.96	2.55	[2.08,3.13]	2.03	[1.65,2.49]	2.14	[1.74,2.62]
29. Other processing and manufacturing occupations	66,719	722	9.58	2.78	[2.39,3.23]	2.01	[1.72,2.35]	2.23	[1.91,2.60]
31. Engineers	71,669	295	12.34	0.97	[0.82,1.16]	1.04	[0.87,1.24]	1.00	[0.84,1.19]
32. Technicians	46,279	248	7.71	1.61	[1.34,1.93]	1.45	[1.21,1.74]	1.62	[1.35,1.94]
33. Occupations in technical drawing	22,733	88	4.34	2.03	[1.58,2.60]	1.59	[1.24,2.04]	2.13	[1.66,2.72]
34. Technical staff	68,643	530	11.18	1.64	[1.40,1.92]	1.42	[1.21,1.66]	1.68	[1.43,1.97]
35. Machine operators	37,600	382	5.43	3.35	[2.83,3.95]	2.42	[2.05,2.87]	2.79	[2.35,3.30]
36. Computer occupations	76,532	221	12.44	1.43	[1.18,1.72]	1.28	[1.06,1.54]	1.44	[1.19,1.73]
41. Construction occupations	256,288	1847	40.00	2.79	[2.42,3.21]	2.17	[1.88,2.50]	2.53	[2.20,2.91]
42. Occupations in mining, stone working, and building materials manufacturing	4383	43	0.58	2.99	[2.15,4.14]	2.08	[1.50,2.89]	2.63	[1.90,3.65]
51. Commercial and sales occupations	140,670	993	22.81	1.73	[1.49,2.00]	1.43	[1.23,1.66]	1.63	[1.40,1.88]
52. Occupations in advertising and marketing, tourism, and trust administration	50,279	230	7.87	1.30	[1.08,1.56]	1.22	[1.01,1.47]	1.20	[1.00,1.45]
53. Transport and traffic occupations	149,100	1460	23.27	2.53	[2.20,2.92]	1.82	[1.57,2.11]	2.35	[2.03,2.71]
54. Postal and telecommunications occupations	32,257	215	5.37	1.70	[1.41,2.05]	1.28	[1.05,1.55]	1.59	[1.32,1.92]
61. Occupations in the hotel and restaurant business and home economics	90,935	583	13.37	2.82	[2.41,3.29]	2.16	[1.84,2.53]	2.54	[2.17,2.97]
62. Cleaning, hygiene and personal care professionals	42,006	523	6.19	2.65	[2.26,3.10]	2.03	[1.73,2.39]	2.46	[2.10,2.88]
71. Contractors, directors, and senior officials	231,017	1281	36.80	1.21	[1.05,1.40]	1.13	[0.98,1.30]	1.21	[1.05,1.40]
72. Commercial and administrative occupations	150,625	941	24.28	1.68	[1.45,1.95]	1.38	[1.19,1.60]	1.66	[1.43,1.93]
73. Banking professionals and insurance employees	55,569	258	9.25	1.41	[1.18,1.69]	1.17	[0.98,1.41]	1.48	[1.24,1.78]
74. Occupations related to law enforcement and security	42,182	267	6.83	1.71	[1.43,2.04]	1.37	[1.14,1.64]	1.61	[1.34,1.92]
75. Judicial occupations	14,098	58	2.42	1.03	[0.77,1.37]	1.11	[0.83,1.49]	1.10	[0.82,1.47]
81. Media occupations and related occupations	24,712	142	3.97	1.49	[1.20,1.83]	1.29	[1.04,1.60]	1.50	[1.21,1.85]
82. Artistic occupations	30,856	215	5.01	1.85	[1.53,2.23]	1.53	[1.26,1.84]	1.57	[1.30,1.90]
83. Occupations of social and spiritual assistance and education	23,026	93	3.69	1.06	[0.83,1.35]	1.02	[0.80,1.30]	1.10	[0.86,1.40]
84. Teaching and education occupations	79,678	286	13.71	0.84	[0.70,1.00]	0.82	[0.69,0.98]	0.87	[0.73,1.04]
85. Occupations in the social, human, natural, physical, and exact sciences	18,432	53	3.01	0.76	[0.57,1.03]	0.82	[0.60,1.10]	0.79	[0.59,1.07]
86. Health occupations	57,225	220	9.53	1.00	Ref.	1.00	Ref.	1.00	Ref.

*Model 1 is adjusted for age and calendar period.
†Model 2 is adjusted for age, calendar period, and socio-demographic variables.
‡Model 3 is adjusted for age, calendar period, radon annual average exposure and smoking probability (only occupational groups with more than 10 observed lung cancer deaths are presented).
§Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits.

variables in model 2 yielded significant results with respect to lung cancer mortality. However, we observed that the addition of radon exposure level in model 3 had no statistically significant effect whatever the sex. In contrast, dichotomizing the predictive probability of smoking to the median demonstrated a significant effect. This effect was stronger in women than in men, with a 37% versus 33% increase in lung cancer mortality, in those with a smoking probability greater than the median versus those smoking less than the median. In the three models, the differences identified across occupations were statistically significant with a *P*-value lower than 0.001.

Adding socio-demographic variables in model 2, we observed that most of the RR across occupational groups decreased in both sexes compared to the reference category of health occupations (Table 2). On average, we found a 16% decrease in relative risks among occupational groups between model 1 and model 2. In

TABLE 3. Relative Risk (RR) and Confidence Interval (CI-95%) for Lung Cancer Mortality by Occupation Among Females Aged 18–85 in the Swiss National Cohort (1990–2014)

2-Digit NSP 2000§	n Subjects	Observed Lung Cancer Deaths	Person-years (in 100,000)	Model 1*		Model 2†		Model 3‡	
11. Occupations in agriculture, forestry, animal husbandry, and care of animals	54,054	57	7.57	0.65	[0.49,0.86]	0.66	[0.50,0.87]	0.66	[0.50,0.87]
21. Occupations in the production of food, beverages and tobacco	11,417	21	1.61	1.65	[1.06,2.57]	1.57	[1.01,2.44]	1.63	[1.05,2.53]
22. Occupations in the textile and leather industry	38,115	76	4.82	1.11	[0.86,1.42]	1.15	[0.89,1.47]	1.10	[0.85,1.40]
24. Occupations in metalworking and mechanical engineering	12,934	28	1.69	1.58	[1.07,2.32]	1.47	[1.00,2.16]	1.51	[1.03,2.22]
25. Occupations in electrical engineering, electronics, watchmaking, vehicle, and tool construction	12,662	55	1.66	2.69	[2.02,3.57]	2.33	[1.75,3.10]	2.13	[1.59,2.85]
27. Graphic arts occupations	9902	27	1.51	2.24	[1.52,3.32]	2.03	[1.37,3.00]	2.07	[1.40,3.06]
28. Occupations in the chemical and plastics industry	18,353	41	2.82	1.57	[1.13,2.16]	1.49	[1.08,2.06]	1.28	[0.92,1.77]
29. Other processing and manufacturing occupations	22,657	74	3.03	1.99	[1.55,2.56]	1.84	[1.43,2.37]	1.80	[1.40,2.32]
34. Technical staff	5716	20	0.83	2.19	[1.40,3.44]	2.05	[1.31,3.22]	2.24	[1.42,3.51]
36. Computer occupations	13,458	36	2.04	2.48	[1.76,3.49]	2.38	[1.69,3.35]	2.18	[1.54,3.07]
41. Construction occupations	6554	13	0.88	1.93	[1.11,3.36]	1.82	[1.05,3.17]	1.64	[0.94,2.86]
51. Commercial and sales occupations	246,896	755	36.16	1.77	[1.56,2.01]	1.66	[1.46,1.89]	1.68	[1.48,1.91]
52. Occupations in advertising and marketing, tourism and trust administration	27,534	42	4.03	1.31	[0.95,1.80]	1.29	[0.94,1.78]	1.23	[0.89,1.69]
53. Transport and traffic occupations	24,748	83	3.69	2.43	[1.91,3.09]	2.23	[1.75,2.83]	2.38	[1.87,3.02]
54. Postal and Telecommunications occupations	41,879	99	6.53	1.47	[1.18,1.84]	1.37	[1.09,1.71]	1.38	[1.10,1.73]
61. Occupations in the hotel and restaurant business and home economics	181,476	585	25.25	2.15	[1.88,2.45]	1.97	[1.72,2.25]	1.96	[1.71,2.24]
62. Cleaning, hygiene and personal care professionals	123,150	363	17.34	1.74	[1.50,2.02]	1.72	[1.48,2.00]	1.70	[1.47,1.97]
71. Contractors, directors and senior officials	78,435	243	11.79	1.74	[1.48,2.05]	1.71	[1.45,2.01]	1.56	[1.32,1.84]
72. Commercial and administrative occupations	454,431	1288	71.23	1.76	[1.56,1.98]	1.67	[1.48,1.88]	1.67	[1.48,1.88]
73. Banking professionals and insurance employees	40,452	91	6.13	1.80	[1.43,2.26]	1.63	[1.29,2.05]	1.55	[1.23,1.95]
74. Occupations related to law enforcement and security	7024	19	1.02	1.69	[1.06,2.68]	1.52	[0.96,2.41]	1.47	[0.93,2.34]
75. Judicial occupations	6734	11	1.05	1.31	[0.72,2.38]	1.43	[0.78,2.62]	1.21	[0.66,2.21]
81. Media occupations and related occupations	21,536	48	3.33	1.16	[0.86,1.57]	1.22	[0.90,1.65]	1.12	[0.83,1.51]
82. Artistic occupations	25,295	50	3.86	1.32	[0.98,1.77]	1.32	[0.98,1.77]	1.24	[0.92,1.66]
83. Occupations of social and spiritual assistance and education	51,075	98	7.68	1.08	[0.87,1.36]	1.08	[0.86,1.35]	1.08	[0.86,1.35]
84. Teaching and education occupations	135,579	201	22.31	0.82	[0.69,0.98]	0.86	[0.73,1.03]	0.84	[0.70,1.00]
85. Occupations in the social, human, natural, physical, and exact sciences	9449	13	1.46	0.85	[0.49,1.48]	0.97	[0.56,1.69]	0.87	[0.50,1.51]
86. Health occupations	242,690	355	38.21	1.00	Ref.	1.00	Ref.	1.00	Ref.

*Model 1 is adjusted for age and calendar period.
†Model 2 is adjusted for age, calendar period, and socio-demographic variables.
‡Model 3 is adjusted for age, calendar period, radon annual average exposure, and smoking probability (only occupational groups with more than 10 observed lung cancer deaths are presented).
§Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits.

men, machine operators and workers in mining, stone working and building materials manufacturing identified with the highest RRs (model 1) showed the largest decrease from 3.35 (95%-CI: 2.83 to 3.95) to 2.42 (95%-CI: 2.05 to 2.87) and 2.99 (95%-CI: 2.15 to 4.14) to 2.08 (95%-CI: 1.50 to 2.89), respectively (Table 2). Men working in hotel and restaurant business and home economics, and in construction were also observed with two-fold higher RRs. In women, occupation was also a statistically significant predictor for lung cancer mortality in all models, although adjusting for socio-demographic variables had less impact on RRs than in men. We observed an average decrease of 3% in RRs between model 1 and model 2 (Table 3). Two of the largest decreases were identified in women working in electronics, watchmaking, vehicle construction, toolmaking (from 2.69 [95%-CI: 2.02 to 3.57] to 2.33 [95%-CI: 1.75 to 3.10]), and transport and traffic occupations (from 2.43 [95%-CI: 1.91 to 3.09] to 2.23 [95%-CI: 1.75 to 2.83]). Female workers in computer science, technical staff, and graphic arts were also found at high risk, with RRs more than twice that of health workers.

In model 3, the occupational groups identified with the highest risks of lung cancer mortality were the same as those observed in model 2 in both sexes. Nevertheless, the average risk reduction compared to model 1 was lower for men (4%) but higher for women (6%).

DISCUSSION

Three models were compared to estimate the effect of occupation after accounting for socio-demographic variables and non-occupational risk factors on lung cancer mortality in Switzerland. Although the variation of RRs for occupation between models was small in most female occupational groups, in men the effect of occupation was lower when accounting for non-occupational factors. Even after adjustment for non-occupational risk factors and potential confounders, occupation as a machine operator, construction worker, and worker in hotels and restaurants was evidenced as a risk factor for lung cancer mortality, as suggested in our first descriptive study.[23] In women working in transport and traffic occupation and electrical engineering, electronics, watchmaking occupations, vehicle, and toolmaking was also confirmed as a risk factor of lung cancer mortality after accounting for potential confounders. All of these occupational groups are known to involve occupational exposure to Group 1 human carcinogens by IARC,[24] adding consistency to our findings.

Contribution of Non-Occupational Factors

We observed that lung cancer risk decreased in men and increased in women over time, which appears to parallel the respective smoking trends in both sexes.[25] Although Swiss men have historically smoked more than women, smoking prevalence among men has declined over time, while it has increased among women. Noteworthy, though, that a decrease in smoking prevalence has been observed among women born since 1970.[26] In our study, no adjustment was made for these temporal effects, since we used SHS cross-sectional data to compute the smoking probability. Additionally, the decrease in RRs observed for all occupational groups after the addition of the socio-demographic variables in model 2 suggests that the risk for lung cancer in some occupations may be partially explained by non-occupational factors. Part of this risk can be also explained by differences in smoking behavior between categories.[19,20,27,28]

Contrary to previous reports suggesting an 8% increase in lung cancer mortality per 100 Bq/m^3[10,29] radon exposure, we did not observe this trend when the model was adjusted for occupational exposure and other confounding factors. Since we used aggregated data on radon exposure, we cannot rule out a potential ecological bias. However, another explanation could be that the use of residential radon exposures did not accurately reflect the true exposure to radon as most participants spent a significant portion of their time outside their household. For smoking, although the matching of socio-demographic variables in the SNC was performed at the individual level, the probability to be smoker was calculated based on aggregated data. The results suggest a limited, though statistically significant, effect of smoking on lung cancer mortality in men and women with a smoking probability greater than the median. Nonetheless, when considering the RRs reported in the literature per histological type of lung cancer, our results seem consistent with smokers' risk estimates for adenocarcinoma. Compared with never smokers, the RR in smokers was estimated at 2.34 in men and 1.31 in women, although only significant in the former.[30] This histologic type is less sensitive to smoking than squamous cell carcinoma, small cell carcinoma, and large cell lung cancer[30,31] and occurs at a young age.[30,32] As SNC participants were 53 years old on average at the end of follow-up, we may suppose that most of the observed lung cancer deaths were likely due to adenocarcinoma, although this information is not available in the SNC.

Contribution of Occupational Factors

Recent findings estimated that the burden of occupational exposures was likely to outrank many prominent risk factors for lung cancer such as indoor and outdoor air pollution and second-hand tobacco smoke outside the workplace.[33] However, it is difficult to disentangle the effect of occupational exposures from other risk factors. Our strategy consisted of accounting for the effect of non-occupational exposures and confounders to improve the estimation of lung cancer risk due to occupational exposures. Although we used external aggregated data in model 3 to adjust for the two most important non-occupational lung carcinogens (ie, smoking and radon exposure), we think that our analysis allowed us to correctly identify occupational groups at risk. While individual data would have been more accurate, previous studies showed that confounding from tobacco use in occupational studies of lung cancer was unlikely to cause more than 20% to 60% change in the relative risk in large studies.[34–36] With some occupations identified with a RR greater than two in all of our models, we believe it is very likely that the observed excess risk is related to occupational carcinogens. In men, the largest decrease between crude and adjusted RR was observed in machine operators, compared to the reference category of health care workers. Concerning SHS data, this occupational group was more likely to smoke than most of other groups. However, the RR in both models 2 and 3 remained high, which is consistent with a previous study that found an OR of 1.61 among plant and machine operators and assemblers, after adjusting for sex, age, ethnicity, smoking, and socio-economic status.[37] Nevertheless, this result should be interpreted with caution as authors showed that the risk might greatly vary between subcategories, with ORs greater than four for rubber and plastics or wood panel machine operators. Further analysis by the type of industry in which these operators worked is therefore suitable to better identify carcinogens to which they may have been exposed. Construction workers were also identified as at risk of lung cancer mortality. They were found at higher risk of lung cancer than other blue-collar workers, even after adjusting for smoking and socio-demographic variables [38] and we also observed this. Therefore, we think it is likely that Swiss construction workers may have been exposed to IARC group 1 carcinogens such as asbestos, silica dust, and diesel engine exhaust,[22] highly prevalent in this occupational group. Mining, stone working and building materials manufacturing workers were also observed with a RR greater than two compared to health occupations. Consistent with SHS data showing that smoking prevalence was high in this group, we found that the risk of lung cancer mortality significantly decreased between model 1 and model 2. This is in line with prior findings where crude ORs for lung cancer among miners and quarrymen decreased from 1.59 to 2.74 to 1.18 to 2.34, when smoking-adjusted.[39] We can assume that the remaining part of the lung cancer risk could be partially explained by exposure to occupational lung cancer carcinogens, including arsenic, asbestos, chromium (VI), nickel, PAH, silica, and diesel engine exhaust.[22,40,41] Lastly, cleaning, hygiene and personal care, as well as transport and traffic occupations, for which there is also a high potential for exposure to lung carcinogens, would also deserve further attention.[42–44]

In women, the recent Swiss descriptive study on lung cancer mortality demonstrated that motor vehicle drivers were more than twice as likely as the general population to die from lung cancer.[13] After adjustment for non-occupational factors, we found that the RR in transport and traffic occupations remained higher than two compared with health occupations. Although previous findings have shown that these workers were exposed to diesel exhausts,[42,43] they were limited to men. Moreover, authors showed that in trucking industry, smoking behavior did not explain variations in lung cancer risk. To our knowledge, this result is original and should be confirmed by further investigations. Moreover, the extent to which female workers in electrical engineering, electronics, watchmaking occupations, vehicle, and toolmaking were exposed to lung cancer carcinogens would also deserve more in-depth analyses. This occupational group includes different types of occupations, which makes it difficult to accurately assess the potential for occupational exposures, although exposure to welding fumes, engine exhaust, PAH, and beryllium might be present in these occupational settings.[24] Lastly, we found no studies explaining the high RR in both computer science and graphic art in women. Assessing second-hand smoke in these occupational groups might potentially help to better understand whether the risk of lung cancer mortality is due to occupational settings or/and other risk factors.

In both sexes, workers in hotel, restaurant, and domestic economics occupations presented a significantly higher risk of lung cancer mortality than the reference group (health occupations). Almost one-quarter of hospitality workers reported being occupationally exposed to second-hand smoke between 2.1 and 4.4 hours per day.[45] Bar workers were the most exposed group with a mean exposure to second-hand smoke of 4.4 hours a day. We can thus assume that second-hand smoke would explain the excess risk of lung cancer mortality found in this study. The ban on smoking in public places was only recently signed in Switzerland and implemented between 2008 and 2010.[26] With a longer follow-up of this cohort and additional individual data, it should be possible to assess the effect of this measure on lung cancer mortality in these occupations.

Limitations and Strengths

One of the main strengths of this study lies in the availability of information at a population level with a 24-year long follow-up. Using one of the largest cohorts worldwide, we were able to define the occupational settings to approximate the occupational carcinogens before the occurrence of the outcome of interest, and thus to limit any potential information bias. The accuracy of death certificate in Switzerland was found to be satisfactory with most of malignant neoplasm,[14] limiting outcome misclassification bias. As information was derived from national data sources, we believe that our results correctly identified occupational groups exposed to occupational lung carcinogens. Since the study sample included 45% of women, this study fulfilled the recommendation to improve the knowledge of occupational exposures and their effect on women.[46]

In terms of limitations, the occupational information was unavailable for 39% of men and 56% of women, which corresponded to 51% and 66% of all lung cancer, respectively. However, a comparison of socio-demographic information showed that excluded participants without information on occupation were similar to included participants, except that the former were more likely to be non-Swiss and to have compulsory education. Assigning occupations as a time-dependent variable based on two-time points and assuming that participants kept the last assigned occupation until the end of follow-up could result in some misclassification of occupational exposures. Nevertheless, the information on occupation was found to be correct [47] and we believe that we assigned it in a sufficiently accurate way, since the majority of participants held the same between the two censuses. Having information on the longest-held occupation would be more accurate and better reflect long-term exposure to carcinogens, but such information is not available in the SNC, while other Swiss cohorts of general population are still too small and too young for analyzing occupation-related lung cancer mortality.[48] As latency of solid cancers is generally 10 to 12 years[49] and even longer for some occupational carcinogens (up to 40 years for asbestos), a 24-year follow-up can be insufficient to capture all pictures of occupation-related mortality from lung cancer in Switzerland. Moreover, given that more than 80% of lung cancers are diagnosed after 55 years,[50] further follow-up of the SNC seems important to assess the role of occupational and other factors, such as smoking patterns in lung cancer. For this, better data on smoking and histological type of lung cancer are essential. An ongoing review of existing or new methods of adjustment on smoking when individual smoking data are missing, conducted by the European network OMEGA-NET,[51] will allow considering a more accurate adjustment on smoking in this and other occupational cohorts. Moreover, a forthcoming study of the five cancer registries data in French-speaking Switzerland of will allow us to investigate the here-hypothesized predominance of adenocarcinoma among the Swiss working population and to analyze its relationship based on individual smoking data.

CONCLUSIONS

This study reports sex-specific risk of lung cancer mortality at a national level across occupational groups, after accounting for socio-demographic variables, and radon exposure and smoking probability. Our results demonstrated that non-occupational factors, such as civil status, linguistic region, nationality, education, and smoking, were significant predictors of lung cancer. After adjusting for these factors, we observed that the risk of lung cancer mortality remained significant among some occupational groups. Men working as machine operators and in mining and construction and women working in electrical engineering, electronics, watchmaking, vehicle construction and toolmaking, computer, transport and traffic, and graphic arts presented the highest risks. In both sexes, workers in hotels and restaurants were also at risk of lung cancer mortality. Some results in women are original, as occupational exposures and their effects were rarely studied in women.

As most of the occupational groups at risk have been potentially exposed to lung cancer carcinogens, additional research should be conducted to identify occupational carcinogens related to these occupations and quantify the exposure to them. This would make it possible to target the most hazardous exposures in high-risk occupations and tailor appropriate preventive interventions. Further analyses on the histological type of lung cancer are also needed to improve both occupational risk estimates and the number of occupational lung cancers in Switzerland.

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