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Occupational lung cancer in Switzerland

Bovio Nicolas

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Centre universitaire de médecine générale et santé publique, Lausanne (Unisanté)

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Expert·e·s	Madame	Dre	Ann	**Olsson**
	Monsieur	Prof.	Ben	**Spycher**

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Nicolas Bovio

Master of Arts in socio-economics, Université de Genève, Suisse

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A mes parents.

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Abstract

Lung cancer generally has a poor prognosis with a five-year survival rate ranging from 10% to 20%, depending on the country. It has the highest mortality of all cancers, with 1.8 million deaths worldwide estimated in 2020. While tobacco use and radon exposure are considered the two main risk factors, occupational exposures are another important risk factor for lung cancer. The population attributable fraction for occupational lung cancer was estimated to be between 18% and 25% for men and between 2% and 6% for women. Moreover, lung cancer accounted for 86% of all occupational cancers. Before this thesis work, Switzerland had no exhaustive publically available report on occupational cancers. The last epidemiological study on cancer risk by occupation and socioeconomic group was conducted 20 years ago and was limited to men aged 25 to 65 years.

The objective of this thesis was therefore to produce estimates of mortality risk and survival of lung cancer by sex for occupation and other work-related variables in Switzerland. For mortality, we first evaluated whether the distribution of mortality rates was homogeneous according to both occupation and economic activity by comparing three risk estimates of lung cancer mortality: the Standardized Mortality Ratio (SMR), the Causal Mortality Ratio (CMR) and the relative SMR. We then assessed the effect of occupational exposures on lung cancer mortality in Switzerland after adjustment for non-occupational lung carcinogens, using the occupation as a proxy for occupational exposures. For survival, our objective was to determine whether three different occupational-based measures (occupation, skill level required for the occupation and socio-professional category) were associated with lung cancer survival. We used the relative survival, which allowed estimating the survival that would be observed if the only possible underlying cause of death was lung cancer.

Our results demonstrated the existence of significant differences in both mortality and survival across different occupational groups. Overall, we were able to identify that 18 out of 95 occupations in men, 10 out of 55 occupations in women and 3 economic activities/industries in each sex had a significantly higher risk of lung cancer mortality than the general Swiss population. 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, watchmaking, vehicle construction and toolmaking, and transport occupations also remained at high risk. Predicted radon exposure showed no effect on lung cancer mortality, while smoking demonstrated a significant effect in both sexes. Regarding survival, we observed that male workers in paid employment but without specific occupational information had lower net survival than those in top management positions and independent professions. Women working as technicians and associate professionals had higher survival than senior officials and managers. The skill level required for occupation had no statistically significant effect.

In conclusion, this thesis work allowed us to calculate the first Swiss estimates of mortality and survival according to work-related variables and to demonstrate the existence of significant differences between occupational groups. We believe that future studies should focus on identified high-risk groups to better define the impact of occupational factors on lung cancer. For mortality and survival, individual data on smoking status are needed for a more accurate adjustment of this confounding factor. For survival, the treatment received by the patient after diagnosis should also be considered. The inclusion of potential occupational carcinogens, their dose and potency should also be taken into account for mortality. For survival, this pre- and post-diagnosis information are also essential, along with changes in working conditions after diagnosis.

Résumé

Le cancer du poumon a généralement un mauvais pronostic, avec un taux de survie à cinq ans allant de 10% à 20%, selon les pays. Il présente la mortalité la plus élevée de tous les cancers, avec 1,8 million de décès dans le monde en 2020. Si le tabagisme et l'exposition au radon sont considérés comme les deux principaux facteurs de risque, les expositions professionnelles constituent un autre facteur de risque important pour le cancer du poumon. En effet, la fraction de la population attribuable au cancer professionnel du poumon a été estimée entre 18% et 25% pour les hommes et entre 2% et 6% pour les femmes. De plus, le cancer du poumon représentait 86% de tous les cancers professionnels. Avant ce travail de thèse, la Suisse ne disposait d'aucun rapport public exhaustif récent sur les cancers professionnels. La dernière étude épidémiologique disponible, réalisée il y a 20 ans, fournissait des résultats par profession et groupe socio-économique et était limitée aux hommes âgés de 25 à 65 ans.

L'objectif de cette thèse était donc de produire des estimations du risque de mortalité et de survie par sexe en fonction de la profession et d'autres variables liées au travail en Suisse. Pour la mortalité, nous avons d'abord évalué si la distribution des taux de mortalité était homogène en fonction de la profession et de l'activité économique en comparant trois estimations du risque de mortalité par cancer du poumon : le ratio standardisé de mortalité (SMR), le ratio de mortalité causale (CMR) et le SMR relatif. Nous avons ensuite évalué l'effet des expositions professionnelles sur la mortalité par cancer du poumon en Suisse après ajustement pour les carcinogènes pulmonaires non professionnels, en utilisant la profession comme proxy pour les expositions professionnelles. Pour la survie, notre objectif était de déterminer si les différentes variables liées à la profession (profession, niveau de compétence requis pour la profession et catégorie socioprofessionnelle) étaient associées à la survie après le diagnostic d'un cancer du poumon. Pour ce faire, nous avons utilisé la survie relative, qui permet d'estimer la survie qui serait observée si la seule cause sous-jacente possible de décès était le cancer du poumon.

Nos résultats ont démontré l'existence de différences significatives tant au niveau de la mortalité que de la survie entre les différents groupes professionnels. Globalement, nous avons pu identifier que 18 professions sur 95 chez les hommes, 10 professions sur 55 chez les femmes et 3 activités économiques/industries dans chaque sexe présentaient un risque significativement plus élevé de mortalité par cancer du poumon que la population générale suisse. Après ajustement, les opérateurs de machines et les travailleurs des mines, du travail de la pierre et de la fabrication de matériaux de construction présentaient le risque le plus élevé. Les femmes travaillant dans les secteurs de l'électrotechnique, de l'électronique, de l'horlogerie, de la construction de véhicules et de la fabrication d'outils, ainsi que dans les transports, présentaient également un risque élevé. L'exposition prédite au radon n'a eu aucun effet sur la mortalité par cancer du poumon, alors que le tabagisme a eu un effet significatif chez les deux sexes. En ce qui concerne la survie, nous avons observé que les hommes exerçant un emploi rémunéré mais ne disposant pas d'informations professionnelles spécifiques avaient une survie nette plus faible que ceux occupant des postes de direction et des professions indépendantes. Les femmes travaillant comme techniciennes et professionnelles associées avaient un taux de survie plus élevé que les hauts fonctionnaires et les cadres. Le niveau de compétence n'avait pas d'effet statistiquement significatif sur la survie nette.

En conclusion, ce travail de thèse nous a permis de calculer les premières estimations suisses de mortalité et de survie selon les variables liées au travail et démontrer l'existence de différences significatives entre les groupes professionnels. Les études suivantes devraient se concentrer sur les groupes à haut risque identifiés, afin de mieux définir l'impact des facteurs professionnels sur le cancer du poumon. Pour la mortalité et la survie, des données individuelles sur le statut tabagique sont nécessaires pour un ajustement plus précis de ce facteur de confusion. Pour la survie, le traitement reçu par le patient après le diagnostic est aussi à considérer. L'inclusion de cancérogènes professionnels potentiels, de leur dose et de leur puissance sont aussi à prendre en compte pour la mortalité. Pour la survie, ces informations avant et après le diagnostic sont également essentielles, de même que les changements dans les conditions de travail après le diagnostic.

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I. Concept definition and State of knowledge

I.I. General introduction to cancer epidemiology and carcinogenesis

Cancer epidemiology

Cancer is considered as a leading cause of death worldwide and accounts for about 10 million deaths in 2020 (IARC 2021b). While cardiovascular disease remains the leading cause of death in high socio-demographic index (SDI) regions, the most recent Global Burden of Disease (GBD) estimates demonstrated that neoplasms accounted for 28.9% (95%-IC: 26.4-30.2) of all deaths (GBD 2022a). Both cancer incidence and mortality rates per 100’000 people were higher in men than in women, with 348.7 versus 246.1 cases and 156.1 versus 99.9 deaths, respectively (GBD 2022b). Moreover, between 2010 and 2019, cancer incidence in both sexes combined decreased by 1.1% and mortality by 5.9% (Table 1).

Table 1 Global prevalence, incidence and deaths in counts and age-standardized rates in 2019, with percentage change between 2010 and 2019 (Global Burden of Disease, 2022b)

	Prevalence		Incidence		Deaths	
	Cases (millions)	Rate (per 100 000)	Cases (millions)	Rate (per 100 000)	Deaths (millions)	Rate (per 100 000)
2019						
Both Sexes	85·8 (80·3 to 92·1)	1046·7 (977·6 to 1122·0)	23·6 (22·2 to 24·9)	290·5 (274·0 to 307·1)	10·0 (9·36 to 10·6)	124·7 (116·4 to 132·0)
Females	45·2 (41·8 to 48·6)	1056·0 (975·2 to 1134·1)	10·6 (9·92 to 11·4)	246·1 (229·8 to 263·1)	4·34 (3·97 to 4·66)	99·9 (91·5 to 107·3)
Males	40·6 (37·3 to 44·5)	1058·5 (975·5 to 1159·2)	12·9 (12·1 to 13·8)	348·7 (327·3 to 370·8)	5·69 (5·25 to 6·10)	156·1 (143·9 to 167·2)
Percentage change 2010-19						
Both Sexes	28·7% (21·2 to 36·3)	2·7% (–3·2 to 8·7)	26·3% (20·3 to 32·3)	–1·1% (–5·8 to 3·5)	20·9% (14·2 to 27·6)	–5·9% (–11·0 to –0·9)
Females	26·0% (17·6 to 34·8)	1·7% (–5·1 to 8·7)	24·7% (18·0 to 31·5)	–1·2% (–6·5 to 4·2)	22·2% (14·2 to 30·1)	–4·4% (–10·7 to 1·7)
Males	31·9% (22·1 to 42·1)	3·8% (–3·6 to 11·5)	27·6% (19·9 to 35·7)	–1·5% (–7·1 to 4·4)	19·9% (11·0 to 29·3)	–7·3% (–13·7 to –0·5)

Numbers in parentheses are 95% uncertainty intervals.

Among men, lung and colorectal cancers were the two most common causes of cancer death. In women, breast and lung cancer were the most frequent. Both sexes combined, lung cancer remained the most deadly cancer, with 1.8 million deaths worldwide and accounted for 18% of all cancer deaths (Fig. 1) (IARC 2022c). This was the cancer with the highest incidence in men. In women, it was breast cancer. In both sexes combined, breast and lung cancers accounted for 2.26 million and 2.21 million cases in 2020, respectively.

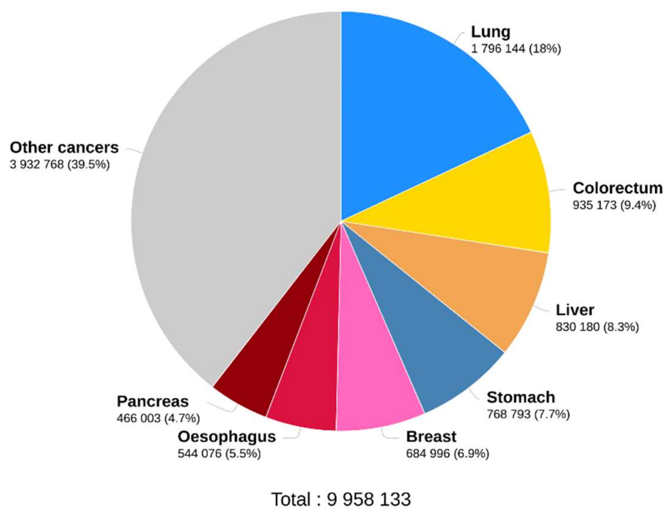


Figure 1 : estimated number of deaths in 2020, worldwide in both sexes, all ages (IARC 2022c)

Overall, the burden of cancer is increasing rapidly worldwide, reflecting both aging and population growth, but also changes in the prevalence and distribution of major cancer risk factors, many of which are associated with socioeconomic development (Sung et al. 2021). The distribution of incidence and mortality varies, however, by geographic region. Although breast cancer was the cancer with the highest mortality in 108 countries, dying from cervix uteri cancer was the leading cause of cancer death in many countries in Africa, Central and South America, Kyrgyzstan and Nepal in women. Lung cancer was also the first cause of cancer death in 28 countries, including USA, Canada, China and Australia (IARC 2022b). Among men, lung cancer was the leading cause of cancer death in 93 countries, while prostate cancer demonstrated the highest cancer mortality in 57 countries, mostly in Africa.

Exposome and carcinogens

Cancer results from complex interactions between exogenous and endogenous factors. Toxic effects are mediated by chemicals that affect critical molecules, cells and physiological processes in the body, but exposures are not limited to chemicals that enter the body (Rappaport and Smith 2010). It also includes chemicals produced by inflammation, oxidative stress, infections and other natural processes. To represent all the environmental exposures, i.e., nongenetic, drivers of health and disease, that an individual can be exposed to, Christopher Wild (Wild 2005) developed the concept of exposome (Fig. 2).

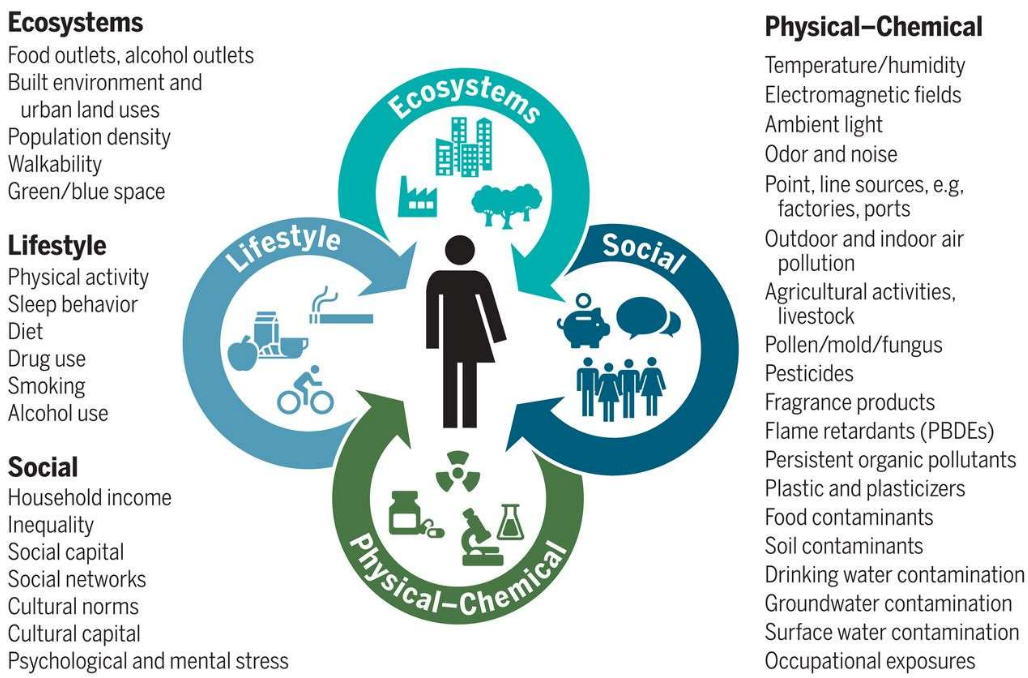


Figure 2: the exposome concept (Vermeulen et al. 2020)

The exposome comprises all environmental exposures over the course of a lifetime, from the prenatal period onward, and is divided into three broad categories of exposures (internal, specific external and general external). The internal exposures encompass all the endogenous processes such as metabolism, endogenous circulating hormones, body morphology, physical activity, gut microbiota, inflammation, and aging. The specific external exposome contains different environmental and lifestyle factors, including radiation, infection, chemical contaminants and pollutants, diet, smoking, alcohol, occupation, and medical interventions. Lastly, the broader social, economic, and psychological influences on the individual constitute the third part of the exposome and include, for example, social capital, education, financial status, urban and rural environment, and climate. These three exposome domains overlap, so it can be difficult sometimes to place a particular exposure in one particular domain, but this description helps to illustrate the full scope of the exposome and the variety of exposures to which the individual is subject to (Wild et al. 2013).

Some factors or their combination may act as carcinogens. To be classified as a human carcinogen, a specific chemical, biological, or physical agent must have the capacity to cause cancer in people exposed to it (NIH 2022a). It can be natural or manmade, and works by interacting with a cell's DNA and/or inducing genetic mutations. The International Agency for Research on Cancer (IARC) is responsible for classifying substances considered carcinogenic for humans. In its monographs, IARC has classified nearly 200 exposures as carcinogenic (Group 1) or probably carcinogenic to humans (Group 2A) (IARC 2022a). In 2010, an IARC working group recorded all cancer sites associated with each agent and listed the known and suspected causes for each cancer site (Cogliano et al. 2011). Authors classified carcinogenic agents with sufficient evidence in humans in seven main categories: chemicals and mixtures, occupations, dusts and fibers, radiation, biological agents, personal habits and pharmaceuticals. This approach was essential to determine which exposures were associated with which cancers and to improve primary prevention. The latter is a particularly relevant mean in the fight against cancer, since between 30% and 50% of cancers can be prevented (Vineis and Wild 2014).

Carcinogenesis

With advances in molecular biology and analytical technologies, carcinogenesis, the formation of cancer, is demonstrated to be much more complex than the simple clonal evolution of a cell that has been subjected to one or two genetic "hits" by a carcinogen or an inherited genetic susceptibility. The multi-step model of carcinogenesis comprises numerous mutations or functional alterations in genes, with at least 80 cancer gene mutations or alterations according to some reports (Malarkey et al. 2018). Some of these are considered to be drivers of cancer growth pathways, the results of which are manifested in the form of the well-accepted characteristics of carcinogenesis. Initially, six biological characteristics were described (Fig 3): sustaining proliferative signaling, evading growth suppressors, resisting cell death, enabling replicative immortality, inducing angiogenesis, and activating invasion and metastasis (Hanahan and Weinberg 2000).

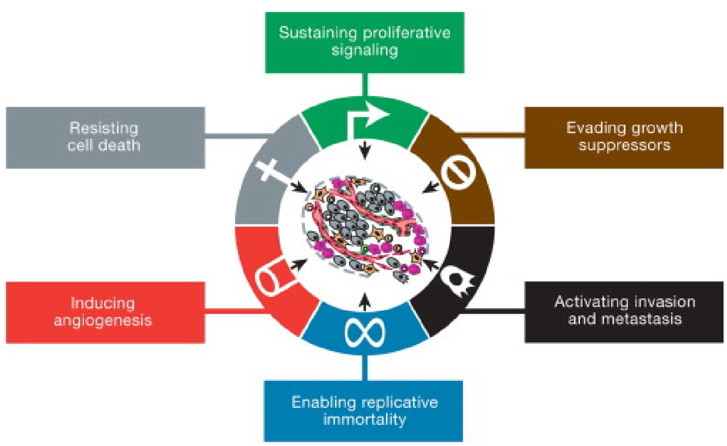


Figure 3 : hallmarks of cancer (Hanahan and Weinberg 2011)

In addition to the dysregulated control of cell proliferation, corresponding adjustments in energy metabolism to fuel cell growth and division have been observed. Because these alterations in energy metabolism are as prevalent in cancer cells as many other cancer-associated features, deregulation of cellular energy metabolism was proposed as another key characteristic in 2011. Evading the immune system was also added as such. Under normal conditions, the immune system constantly monitors the tissues and is responsible for recognizing and eliminating the vast majority of incipient cancer cells and thus nascent tumors. However, emerging solid tumors somehow manage to avoid detection by the various branches of the immune system or to limit the extent of immunological destruction, thus escaping eradication. It should also be noted that all the characteristics defined above are underpinned by genome instability, which generates the genetic diversity that accelerates their acquisition, and by inflammation, which promotes the appearance of multiple characteristic functions (Hanahan and Weinberg 2011) (Fig. 4).

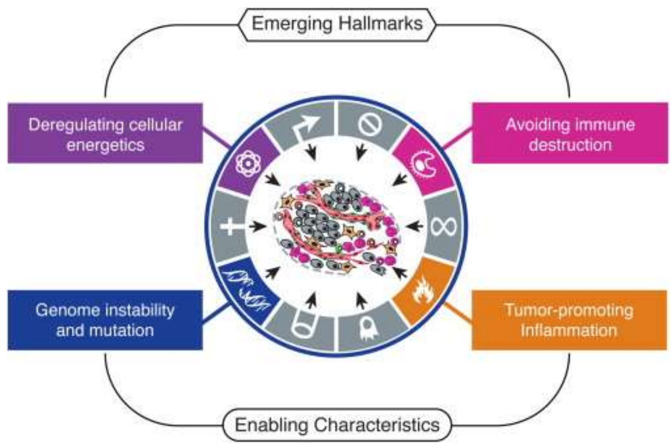


Figure 4: emerging hallmarks of cancer (Hanahan and Weinberg 2011)

In a simpler description of the carcinogenesis, the three main steps are: initiation, promotion and progression (Oliveira et al. 2007). During the initiation phase, irreversible genetic changes happen, which predispose susceptible normal cells to malign evolution and immortality. DNA damage has been established as the initiation event of carcinogenesis. The initiated cells are not neoplastic yet and can remain latent for a long period. The promotion is defined by the selective clonal expansion of initiated cells. Since the accumulation rate of mutations is proportional to the one of cell division, or at least to the one of stem cell replacement, clonal expansion of initiated cells therefore produces a larger population of cells that are likely to undergo further genetic changes and become malignant cells. Tumor progression, the final stage, is characterized by the expression of the malignant phenotype and the tendency of the malignant cells to develop more aggressive characteristics over time (Weston and C. Harris

2003). This stage marks the transition from precancerous to malignant lesions, involving independent cell proliferation, invasive spread of the tumor and its ability to metastasize. The cancer cells will progressively develop a number of properties that differentiate them from normal cells (Oliveira et al. 2007).

I.II. Occupational cancer, burden and recognition

Occupational cancer and its burden

Occupational cancer is caused, in whole or in part, by exposure to carcinogens at work, or by a particular set of circumstances at work (IOSH 2022). Occupational exposure is defined as any contact between the human body and a potentially hazardous agent or environment in the workplace. Specific exposures are associated to the type of work people do (i.e., occupation), where they do it (i.e., the economic sector), but also to the direct or indirect measures that are taken to limit the exposure to a given carcinogen. Moreover, the total dose of carcinogen received, the potency of the carcinogen, the presence of other exposures (including smoking), and individual susceptibility are also important factors that influence the likelihood that a worker will develop cancer (Driscoll et al. 2004).

Occupational cancer has been shown to be associated with a significant disease burden at the global, regional, and national levels (Stanaway et al. 2018). New estimates of the GBD have stressed that the population impact of occupational exposures appears to exceed that of other important risk factors, including ambient air and household pollution, high body mass index, passive smoking outside the workplace, and each individual dietary component assessed in recent GBD reports (GBD 2018; GBD 2020; Loomis 2020). In 2016, 349’000 (95%-IC: 282’000-414’000) was the estimated number of cancer deaths attributable to exposure to the occupational carcinogens worldwide (GBD 2020). This represented 3.9% of all cancer deaths, 79% of which were in men. The majority of deaths occurred in Western Europe, East Asia, and North America. The highest mortality rates were observed in Western Europe, Australasia, North America, and high-income Asia-Pacific, while Western, Central, and Eastern sub-Saharan Africa were regions with the lowest mortality rates.

As shown in Figure 5, the number of death per 100’000 persons mainly occurred in high SDI countries. However, exposures to occupational carcinogens in middle- and low-income countries may be less controlled and more widespread than the figures showed, due to the lack of automatic monitoring and self-protection equipment in the workplace (Li et al. 2021).

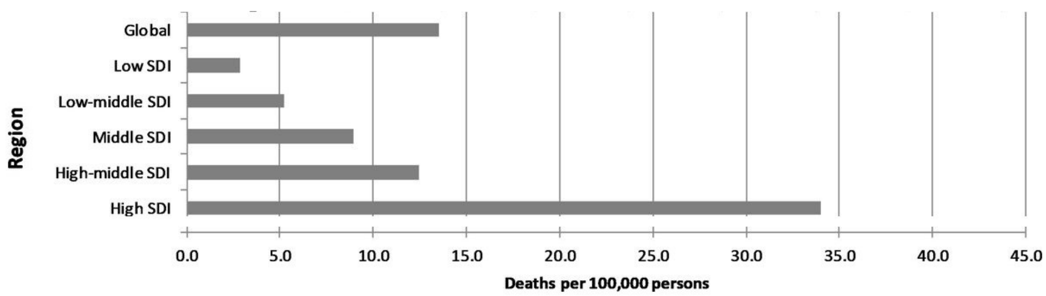


Figure 5: occupation-attributable cancer deaths by SDI, 2016 (per 100 000 persons) (adapted from (GBD, 2020))

Of all the chemical or biological agents classified by the International Agency for Research on Cancer as known (Group 1) or probable human carcinogens (Group 2A), many occur in occupational settings (Driscoll et al. 2004). A review of occupational exposures and cancer showed that out of 118 Group 1 and 75 Group 2A carcinogens, 37 exposures and 73 exposure-cancer site pairs were relevant. This means that a given occupational carcinogen can be linked to several cancer sites, while, similarly, a cancer site may be associated with many occupational carcinogens (Marant Micallef et al. 2018). Occupational lung cancer accounted for the majority of deaths, with 86% of total occupational cancer mortality (Table 2). This represented 299’998 deaths worldwide, with an estimated population attributable fraction (PAF) of lung cancers due to occupational exposures of 17.6%. In comparison, mesothelioma and laryngeal cancer, the second and third leading causes of occupational cancer death, showed 27’612 and 7’213 deaths, respectively. Their PAFs related to occupational exposures were 91.4% and 6.5%, respectively (GBD 2020).

Table 2 Global occupation-attributable cancer deaths and PAFs by cancer type, 2016 (adapted from (GBD 2020))

Type of cancer	Number of deaths	% of deaths	PAF
Breast cancer	4864 (1195–8401)	1.4 (0.3–2.4)	0.9 (0.2–1.6)
Kidney cancer	58 (13–108)	0.0 (0.0–0.0)	0.0 (0.0–0.1)
Larynx cancer	7213 (4437–10 462)	2.1 (1.3–3.0)	6.5 (4.1–9.5)
Leukaemia	2495 (1181–3734)	0.7 (0.3–1.1)	0.8 (0.4–1.2)
Lung cancer	299 998 (233 708–365 251)	86.0 (67.0–100.0)	17.6 (13.8–21.3)
Mesothelioma	27 612 (25 559–29 341)	7.9 (7.3–8.4)	91.4 (89.2–93.2)
Nasopharynx cancer	448 (330–685)	0.1 (0.1–0.2)	0.8 (0.5–1.1)
Ovary cancer	6022 (2984–9404)	1.7 (0.9–2.7)	3.7 (1.8–5.7)
Total	348 741 (269 406–427 386)	100	3.9 (3.2–4.6)

Although occupational exposures on cancer burden are a pressing health issue for many countries, the occupational risk is often overlooked as a contributor to burden of cancer (Labrèche et al. 2019). In 2017, a study on the cost of occupational cancer in the EU-28 was conducted to quantify the monetary value of the burden of occupational cancer in Europe. It was aiming at assessing the economic or social costs, but did not take into account the financial impacts reflecting transfers between different groups in society (ETUI contributors 2020). The cost analysis was based on three main criteria:

- **direct costs**: the medical costs related to the treatment and its context, such as the cost of hospitalization, surgery, physician visits, radiation therapy and chemotherapy/ immunotherapy (Jongeneel et al. 2016);
- **indirect costs**: the monetary losses during the treatment, including productivity losses due to sick leave or other usual activities and lost productivity due to premature death. It also encompassed informal care that is the working and/or leisure time that relatives provide;
- **intangible or human costs**: all the non-financial human losses associated with cancer, such as reduced quality of life, pain, suffering or grief. Authors defined intangible or human costs as the sum of value of statistical life (VSL) and value of cancer morbidity

(VCM). VSL is used to measure both the public's willingness to pay for fatality risk reduction and the marginal cost of improving safety (Kniesner and Viscusi 2019) and VCM is the individual stated willingness to pay for reducing the chance of getting cancer (Jongeneel et al. 2016). In this study, the authors used a VSL of €4 million, which was an approximate midpoint of prior studies and a VCM of €400’000 (ETUI contributors 2020).

Table 3 shows the total costs in value of annual occupational cancer registrations for the central-core scenario. They were estimated between 348 and 438 billion euros, or between 1.8 and 4.1 of EU gross domestic product (GDP), depending on the data used. While the intangible or human costs were the most significant driver of the economic cost, direct cost (healthcare) and indirect costs (loss of working days and informal care) only accounted for less than 2%. Occupational cancer therefore carries significant financial and health costs.

Table 3 Total cost in billions euros of annual occupational cancer in Europe (ETUI contributors, 2020)[1]

Scenario/ Source of data for calculation of AN	Type of cost	Group bearing the cost	Total present value costs	Share of total costs
Central-core EUREG+GCO+UK	Healthcare	Government/taxpayers	5	1.4%
	Lost working days	Worker/ family	0.3	0.1%
	Informal care	Worker/ family	1	0.3%
	VSL	Worker/ family	311	89.3%
	VCM	Worker/ family	31	8.9%
	TOTAL		348	
Central-core/ EUCAN+UK	Healthcare	Government/taxpayers	6	1.3%
	Lost working days	Worker/ family	0.4	0.1%
	Informal care	Worker/ family	1	0.3%
	VSL	Worker/ family	394	90.3%
	VCM	Worker/ family	35	8%
	TOTAL		436	

[1] EUREG : European Network of Cancer Registries
UK: United Kingdom
GCO : Global Cancer Observatory
EUCAN: European Cancer Estimates

In Switzerland, such estimates do not exist. To our knowledge, the only figure available is the one on the costs of disability pensions and death due to occupational cancers recognized by the Swiss National Accident Insurance Fund (Suva). For the period 2015-2019, the total average annual costs were estimated at 92.2 million for 9 pensions and 124 deaths together (SUVA 2021).

Occupational cancer recognition

The link between work and cancer is not easy to establish, since a tumor caused by occupational exposures is indistinguishable from another (ETUI contributors 2021). The long latency period between exposure and first symptoms also complicates the identification of any occupational exposures and other risk factors. The recognition of a cancer as an occupational cancer is further hindered by the fact that physicians often give little importance to the patient's work history (ETUI contributors 2021). From the patient’s perspective, the context of the disease is a big obstacle to claiming the entitlement. The persons fighting cancer often have other priorities than trying to access a right with a very uncertain outcome (Marchand 2016). However, even a reported cancer that meets all the criteria will not necessarily be recognized as an occupational cancer. Occupational cancer is not a distinct medical category, but a disease negotiated in a highly conflictive framework (ETUI contributors 2021). Moreover, there is also an unequal balance of power between representatives of employers, employees and the state in the conditions for the construction of occupational disease lists. Listing of some cancer and/or carcinogens is one of the first structural obstacles to the recognition of occupational cancers, with a large gap between scientific and medical knowledge and what is considered in these lists (Marchand 2016). In France, for example, about 15 carcinogens are included in the list of occupational diseases, while IARC identifies more than 100 agents in Group 1 and more than 60 in Group 2 A (ETUI contributors 2021). In addition, the occupational disease lists are unsuited to the real world of work, as they do not take into account the character of multi-exposure, but generally consider only a single carcinogen. All of this leads to a significant rate of "under-reporting" of occupational diseases that has been emphasized repeatedly for over 30 years in a series of studies and administrative reports. Health insurance data illustrate remarkably well the social invisibility of carcinogenic risks in the workplace with less than 2’000 cancers recognized as occupational diseases each year in France, whereas, according to data from the Santé publique France, between 14’000 and 30’000 new cases are attributable each year to occupational exposure (Marchand 2016).

Occupational cancer in Switzerland

In Switzerland, according to the Federal Law on Accident Insurance (LAA), occupational diseases are exclusively or mainly due to harmful substances or to certain occupational activities in the workplace. The Federal Council is responsible for establishing the list of hazardous substances and diseases related to occupational activities (Ordinance on Accident Insurance (OLAA)). Occupational diseases are listed in annex 1, under article 9.1 of LAA and are recognized as such if they are exclusively or predominantly due to the exercise of professional activity, or exposure to certain harmful work situations. This means that the disease is caused by working conditions by 50% at least, or that the relative risk is equal or superior to 2. Under the article 9.2 of the LAA, there is the possibility for diseases not included in the list to be recognized as occupational, but the causation threshold is higher. The exclusive or predominantly preponderant causation implies that the disease is caused by working conditions by 75% at least, or that relative risk is equal or superior to 4 (Graczyk et al. 2021). Although the list of hazardous substances and diseases related to occupational activities is fairly comprehensive, it has been shown that a number of occupational diseases including cancer, even if listed, are likely to be non-recognized. Currently, the Swiss National Accident Insurance Fund (Suva) recognizes less than 200 cases yearly as occupational cancer, most of which are mesotheliomas (Suva 2017; Suva 2019). In 2016, an international report showed that Switzerland had a ratio of recognized occupational cancers of 4.41 per 100’000 insured workers, far behind Germany (15.1) and

France (11.39) (EUROGIP 2018). However, the extent of underreporting is difficult to assess in Switzerland, as no comprehensive research has been conducted (Graczyk et al. 2021).

In addition to the lack of comprehensive, publicly available reporting on occupational cancers and exposures, the way cancer data are collected has not always been consistent. In Switzerland, the cantonal cancer registers are responsible to gather data of adults with cancer. Each registry is required to register all new cases of cancer diagnosed in the population of its canton. To retrieve data on cancer, cancer registries work closely with hospitals, anatomy and pathology laboratories and all other organizations that can provide information on cancers. However, each registry has its own organizational structure (ONEC 2022). Moreover, data collection began at different points in time depending on the registries. The oldest cancer registry created was the one in Basel in 1969, while other registers, like the one in Jura or Bern, were only created in the years 2000-2010. There is, though, a national institute, the National Institute for Cancer Epidemiology and Registration (NICER), that is responsible for national coordination and harmonization of data from cantonal registries (NICER 2022).

While some Swiss cancer registries have conducted some research on occupation-related cancers and collected information on patients' occupations, the latter was mainly used for investigating socioeconomic differences in incidence, in stage at diagnosis and in survival for breast and colorectal cancers from public health and healthcare perspectives (Feller et al. 2017; Feller et al. 2018). No information other than the occupation has been collected by cancer registries. To our knowledge, the last epidemiological study on occupation and cancer risk using cancer registry data was conducted 20 years ago and provided only odds ratios by occupation and socioeconomic group for men aged 25 to 65 years (Bouchardy et al. 2002).

Another important source for which information on occupation and economic activity is available is the Swiss National Cohort (SNC). The SNC is a long-term, population based multipurpose cohort and research platform and it is based on federal census data from 1990 and 2000. Censuses were mandatory, with population coverage estimated at 98.6% (SFSO 2004). These data were linked to mortality, life birth and emigration records until 2019. All death records contain socio-demographic information as well as information about causes of death (OFS). Regarding occupation, the initial coding in both censuses was based on the Swiss classification of occupations (abbreviated as NSP, from Nomenclature Suisse des Professions), subsequently recoded using the four-digit codes of the International Standard Classification of Occupations, version 1988 (ISCO-88). For the economic activity, the coding was based on the National Classification of Economic Activities (abbreviated as WART from Allgemeine Systematik der Wirtschaftszweige), version 1985 in German in the 1990 census and on the National Classification of Economic Activities (abbreviated as NOGA from Nomenclature Générale des Activités) version 1995 in the 2000 census. Although the SNC provides information on work-related variables, information was only available at two different points in time (1990 and 2000).

Apart from these data sources, Switzerland does not have a systematic data collection strategy to address the issues of occupational exposures and diseases. This hinders the development of Swiss research in occupational cancers. For this research, the occupational history of each individual must be reconstructed , listing all occupations, their duration and the calendar period over the entire career to enable the assessment of occupational exposures (Plys et al. 2022).

I.III. Lung cancer

Lung cancer usually has a poor prognosis. The five-year survival varies considerably across countries with estimates between 10% and 20% (Allemani et al. 2018). In countries with a high and very high human development index (HDI), lung cancer is the most frequent cancer in men, with an incidence of 39 cases per 100’000 people, and the one with the highest mortality with 31.6 deaths (per 100’000 people). In women, it ranks third with 18.2 new cases (per 100’000) and first in mortality (13.7 deaths per 100’000 people) (Sung et al. 2021). However, regional differences exist. While IARC statistics showed that lung cancer mortality was similar among men in Europe and the US, accounting for 24.2% and 23.1% of total cancer mortality, respectively, it was much higher among women in Europe (22.9%) than in the US (14.3%) (IARC 2022d). Within the EU, the overall lung cancer mortality rate was about 54 per 100’000 people, but there were variations between countries of more than threefold or fourfold in women (Fig. 6) (OECD 2020).

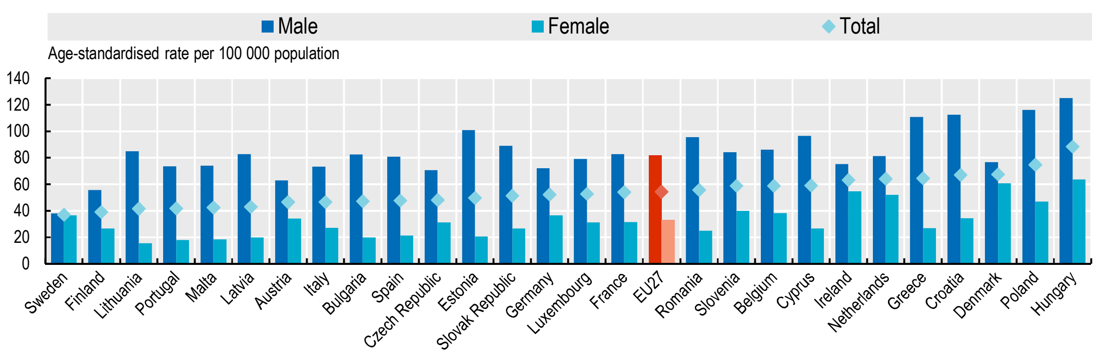


Figure 6 : lung cancer mortality rates by sex in EU, estimates for 2020 (OECD 2020)

Until recently, there has been a steady increase in overall lung cancer mortality in women in most European countries, as well as worldwide. Conversely, men have experienced a decline in lung cancer mortality in most countries and this trend is expected to continue in the near future (Malhotra et al. 2016). In terms of incidence, it has been higher in men than in women in all European countries, although the gender gap has narrowed with incidence declining faster in men in most countries in the last decades (Fidler-Benaoudia et al. 2020). Overall, trends in lung cancer can be interpreted according to changes in smoking prevalence, meaning that an increase in tobacco use is accompanied by an increase in lung cancer incidence and mortality a few decades later, and a decrease in use is followed by a decrease in incidence. Similarly, the difference in lung cancer mortality between women and men mostly reflects historical differences in smoking habits (Malhotra et al. 2016).

Lung cancer in Switzerland

Compared to other European countries, Switzerland has lower incidence and mortality rates for lung cancer. A report comparing several European countries showed that only Sweden had lower estimates in men (Figure 7). Among women, Italy and Sweden had lower incidence than Switzerland, whereas for mortality, only Italy had lower rates.

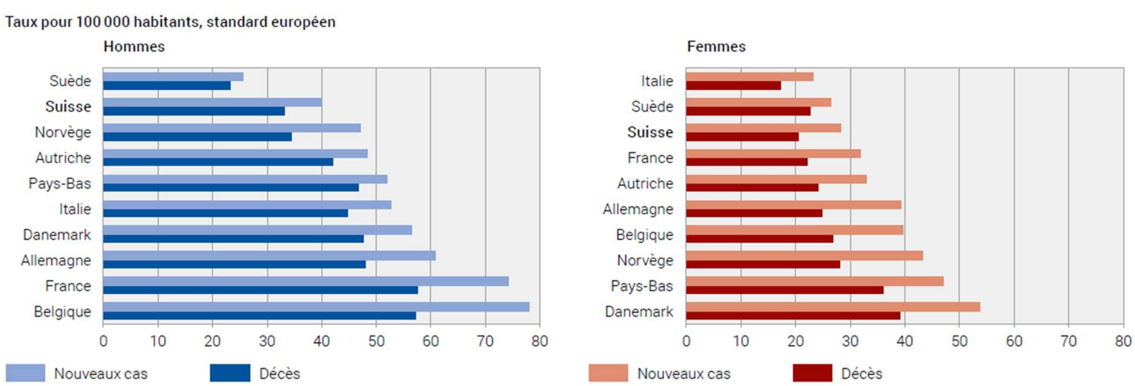


Figure 7: international comparison of lung cancer incidence and mortality, 2018 (Cirillo et al. 2021)

Between 2013 and 2017, an average of just over 2’700 new cases of lung cancer were diagnosed each year in men and just over 1’800 in women. This represented 11.9% of cancers in men and 9.3% of cancers in women. It was the second most frequently diagnosed cancer in men and the third in women, with men being 1.6 times more likely to develop lung cancer. Half of new cases were diagnosed before age 71 in men and before age 70 in women. During the same period, lung cancer caused an average of nearly 2’000 deaths per year among men and about 1’200 among women, which makes it the leading cause of cancer death in men

(21.3% of cancer deaths) and second in women (16.2%). Half deaths occurred before 72 years of age in both sexes (Cirillo et al. 2021).

Between 1988 and 2017, lung cancer incidence and mortality continuously decreased in men, by 34% and 47%, respectively. In women, the incidence rate nearly doubled from approximately 16 to 30 cases per 100'000 people (Fig. 8). Mortality also increased with a rise of 75% compared to the period 1988-1992 (Cirillo et al. 2021).

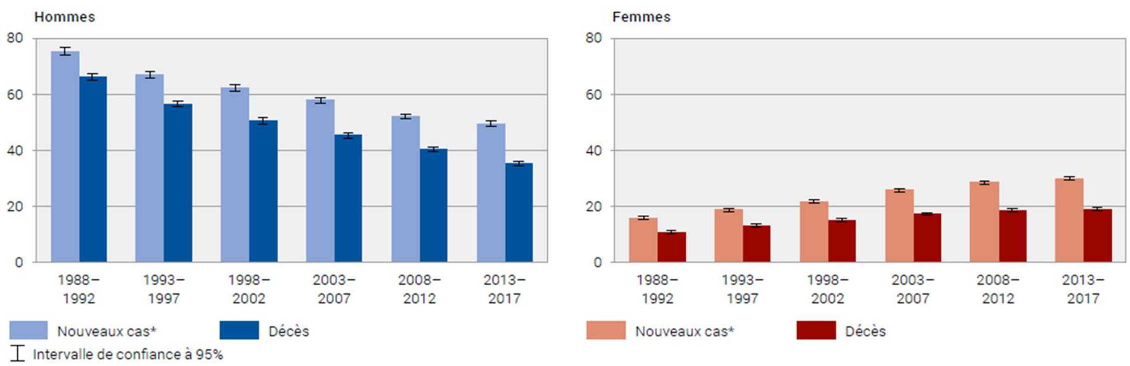


Figure 8: lung cancer in Switzerland: time trend (1988-2017) (Cirillo et al. 2021)

Classifications of lung cancer

In cancer epidemiology, it is essential that the collection and recording of cancer data be as complete and accurate as possible. It is also necessary to standardize the recording of cancer cases so that the data can be compared. There are several standardized classifications for tumor diseases, the two most commonly used of which are presented below: the International Classification of Diseases for Oncology and the TNM staging system. These are also the ones used by the Swiss cancer registries.

International Classification of Diseases for Oncology (ICD-O)

Principally used in cancer registries, the ICD-O has been used for nearly 35 years to code the site (topography) and the morphology of the neoplasm in a standardized way (WHO 2013).

The topography code indicates the site of origin of a neoplasm; in other words, where the tumor originated. In addition, the structure of the morphology code records the type of cell that has become neoplastic and its biological activity (i.e. the type of tumor that has developed and its behavior). It is a 6-digit code composed of three distinct parts: histology, behavior and grade (Fig. 9) (NIH 2022b). Histology, a 4-digit code, gives an indication of the microscopic structure of cells and tissues. The behavior of a tumor is how it acts in the body and can be coded as no risk of spread (0, benign); uncertain if benign or malignant (1) malignant but growing in place (2, noninvasive or in situ); it can invade surrounding tissues (3, malignant, primary site); or it can even spread from its point of origin and begin to grow at another site (6, metastatic). Lastly, the tumor grade describes a tumor based on how abnormal the tumor cells and the tumor tissue look under a microscope. It is an indicator of how quickly a tumor is likely to grow and spread. If the cells of the tumor and the organization of the tumor's tissue are close to those of normal cells and tissue, the tumor is called "well-differentiated." These tumors tend to grow and spread at a slower rate than tumors that are "undifferentiated" or "poorly differentiated," which have abnormal-looking cells and may lack normal tissue structures (NIH 2022c).

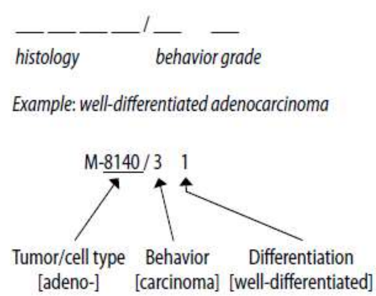


Figure 9: structure of a morphology code (adapted from (WHO 2013))

For lung cancer, the topography code is C34. There are two main histological types, namely small cell lung carcinoma (SCLC) and non-small cell lung carcinoma (NSCLC) (Inamura 2017). About 80% to 85% of lung cancer are NSCLC and are subcategorized into adenocarcinoma, squamous cell carcinoma (SqCC), and large cell carcinoma. The remaining 10% to 15% are SCLC (Houston et al. 2018).

TNM staging system

The TNM staging system is a second classification used for the evaluation of any patient with cancer. This is a standardized nomenclature that aims to define the anatomical extent of the disease (Feng and Yang 2019) and provides a common language for consistent communication (Tanoue 2020). Accurate tumor staging is of paramount importance for patient treatment, as incorrect clinical staging may lead to definitive non-surgical therapy and inappropriate palliative treatment options (Jantz 2019).

For lung cancer, the T (Tumor) component describes the extent of the primary tumor and includes five categories (T0-T4), with the tumor size being the major factor (T1 (≤3 cm) / T2 (>3 and ≤5 cm) / T3 (>5 and ≤7) / T4 (>7 cm)) (Tanoue 2020). Both the location and the satellite lesions have also significant impact on assigning the T component. The N (Node) describes whether the cancer has spread to the lymph nodes and goes from N0 to NX (N0-no regional lymph node involvement / N1-involvement of ipsilateral intrapulmonary or hilar nodes / N2-involvement of ipsilateral mediastinal or subcarinal nodes / N3-involvement of contralateral hilar or mediastinal nodes or supraclavicular nodes / NX-status not able to be assessed). Lastly, the M component (Metastasis) describes whether the cancer has spread to a different part of the body (M0 – no-distance metastases / M1a – Malignant pleural/pericardial effusion or malignant pleural-pericardial nodules, separate tumor nodule(s) in a contralateral lobe / M1b - single extrathoracic metastasis (oligometastasis) / M1c - multiple extrathoracic metastases (1 or >1 organ)) (Feng and Yang 2019).

Overall, there are 64 different TNM combinations for lung cancer (Tanoue 2020), but those that share similar survival outcome with treatment are often grouped into four main stages (Cancer Research UK 2020; OFS 2011):

- **stage I** - the tumor is usually small and has not grown out of the organ in which it originated;
- **stages II** - the tumor is larger than stage 1, but the cancer has not started to spread to the surrounding tissue;
- **stages III** - the cancer is larger. It may have started to spread into the surrounding tissue;
- **stage IV** - the cancer has spread through the blood or lymphatic system to a distant location (metastatic spread).

Major risks for lung cancer

In addition to the ability to define the stage and classify the tumor in a standardized manner, it is also essential to be able to recognize the risk factors leading to cancer. While smoking is considered as the main factor in lung carcinogenesis, there are other important risk factors including environmental and occupational exposures or genetic susceptibility (Malhotra et al. 2016). In the following section, we will focus on the major preventable risks regarding the onset of lung cancer.

Tobacco consumption

A global review on the fractions of cancer attributable to modifiable factors estimated that smoking is the leading risk factor for lung cancer, with estimated PAFs of 81% and 58% for men and women, respectively (Whiteman and Wilson 2016). A pooled analysis of case-control studies showed that age-adjusted odds ratios (ORs) were elevated for all metrics of cigarette smoke (Pesch et al. 2012). The authors demonstrated that men smoking more than 30 cigarettes a day had an OR of 103.5 (95% CI 74.8-143.2) for squamous cell carcinoma, 111.3 (95% CI 69.8-177.5) for small cell lung cancer, and 21.9 (95% CI 16.6-29.0) for adenocarcinoma. In women, odds ratios were 62.7 (95% CI 31.5-124.6), 108.6 (95% CI 50.7-232.8), and 16.8 (95% CI 9.2-30.6), respectively. Although the ORs declined after quitting smoking, the risk was still higher than that observed in never smokers, even after 35 years of cessation. In addition, the duration of smoking should be considered as the strongest determinant of lung cancer risk in smokers (Doll et al. 2004). For second-hand smoke, epidemiological evidence and biological plausibility also support a causal association with lung cancer risk in non-smokers, with primarily spousal and workplace exposure (Malhotra et al. 2016). However, other risks besides smoking are also to be considered. Estimates of worldwide burden of cancer showed that about 25% of all cases occur in non-smokers (Torres-Durán et al. 2015).

Radon

Radon, a colorless, odorless and tasteless noble radioactive gas, often called "the silent killer", is produced by the natural radioactive decay of uranium, which is found in all rocks and soils, and sometimes in water (Lorenzo-González et al. 2019). As it decays in the air, it produces other radioactive particles, which, when inhaled, can be deposited on the cells lining the airways, where they can damage DNA and potentially cause lung cancer. It is considered as the second leading cause of lung cancer in smokers after tobacco use and as the leading cause in non-smokers (Torres-Durán et al. 2015; WHO 2009b). Outdoors radon dilutes quickly to very low levels and is generally not a problem, with averages radon level ranging from 5 to 15 Becquerel per cubic metre (Bq/m3). However, indoor radon concentrations can be much higher, especially in locals with minimal ventilation. In buildings, radon concentrations can vary widely from 10 Bq/m3 to over 10’000 Bq/m3. A collaborative analysis of individual data from 13 European case-control studies showed that the risk of lung cancer increases by about 16% for every 100 Bq/m3 increase over a long period of time, with a linear dose-response relationship (Darby et al. 2005). Moreover, radon is much more likely to cause lung cancer in people who smoke. They are 25 times more at risk from radon than non-smokers (WHO 2021). This agent is classified by IARC as a Group 1 carcinogen for lung cancer (IARC 1988) and is responsible to cause between 3% and 15% of all lung cancers worldwide according to WHO. This percentage may even be higher in regions with high radon concentrations (WHO 2009a).

Air pollution

Outdoor pollution is another risk factor for lung cancer. As defined by IARC, outdoor air pollution is a complex mixture of pollutants from natural and anthropogenic sources, including transportation, power generation, industrial activity, biomass burning, home heating and cooking (IARC 2016). Particulate matter (PM) 2.5 and PM 10 concentration are often used as an indicator of air pollution levels. Results of a systematic review and meta-analysis of 15 studies on PM 2.5 exposure showed a relative risk (RR) of lung cancer of 1.16 (95% CI 1.09-1.23) for an increase of 10 µg/m3 (Ciabattini et al. 2021). In addition, of seven studies with results on PM10 exposure, the risk was of 1.23 (95% CI 1.05-1.40) for comparable increase in PM10 exposure. Authors also identified that the risk for exposure to both PM 2.5 and PM 10 was higher in studies on lung cancer mortality (RR 1.17; 95% CI 1.10-1.25) than incidence (RR 1.11; 95% CI 0.85-1.37). If this is confirmed, it could indicate a possible effect of air pollutants on disease severity or response to treatment. Another explanation could be confounding by factors, such as socioeconomic status, that may be associated with both air pollution exposure and lung cancer outcome (Ciabattini et al. 2021).

Occupational exposures

Of all the chemical or biological agents classified by IARC as known or probable human carcinogens, many occur in occupational settings. A recent study updated the list of occupational carcinogens identified by IARC (Loomis et al. 2018). Included were the IARC monographs from 1971 to 2017 that used specific criteria to ensure occupational relevance and provide high confidence in the causality of the observed exposure-disease associations. IARC Group 1 agents were selected from studies of exposed workers and with documented evidence of occupational exposure in exposed workers in the relevant monograph. Twenty-three percent of all occupational carcinogens were associated with lung cancer, making it the cancer associated with the largest number of occupational carcinogens. In comparison, skin, bone, and bladder cancers, the three other cancers most associated with occupational carcinogens, were linked to 10%, 9%, and 6% of all occupational carcinogens, respectively. Occupational pulmonary carcinogens can be different in nature, including metals and metal compounds, airborne particles, chemicals or chemical mixtures, and radiation and radionuclides (Loomis et al. 2018). Because the occupational risk is often overlooked (Labrèche et al. 2019), the following section will further describe the impact of occupational carcinogens and its burden on lung cancer.

Occupational lung cancer

Lung cancer is the cancer with the second highest PAF related to occupational exposures. The PAF is higher in men with an estimate ranging between 19.3% and 24.4% compared to 2.6% to 5.3% in women. In both sexes combined, about 15% of lung cancer cases are due to occupational lung carcinogens (Olsson and Kromhout 2021).Occupational exposure to asbestos is the largest contributor to occupational lung cancer and was recognized as a carcinogen in 1973 by IARC (Loomis et al. 2018). Exposures to respirable crystalline silica, diesel exhaust, and welding fumes also have a significant impact and together account for half of the occupational PAF for lung cancer (Olsson and Kromhout 2021). Silica dust was recognized as a carcinogen in 1997. However, diesel exhaust and welding fumes have only recently been added by IARC, in 2013 for the former and in 2017 for the latter (Loomis et al. 2018) (Table 4).

Whereas many carcinogens have been identified in mining industry, other occupational settings can be affected (Loomis et al., 2018). As described in Table 4, people working in medical or veterinary industry, as well as in agriculture may be exposed to arsenic. Workers in manufacture of electrical equipment, electronic components, aerospace materials or dental laboratories may be exposed to beryllium. Railway workers, truck drivers and mechanics may be exposed to diesel exhaust. Workers in foundries, ceramics or cement, and construction workers may be exposed to silica dust. These few examples illustrate the extend of potential

Table 4 Occupational lung carcinogens evaluated in the IARC Monographs volumes 1–120 (adapted from (Loomis et al. 2018))

Agent	Year	Occupational exposure settings
Arsenic and inorganic arsenic compounds	1973	Manufacture of glass, pesticides and other chemicals; agricultural settings; mining, smelting and refining of metals; medical and veterinary procedures
Asbestos	1973	Mining, processing, transportation and handling of asbestos; work in shipyards; manufacture and use of asbestos-containing products
Beryllium and beryllium compounds	1993	Beryllium extraction, processing and fabrication; manufacture of electrical equipment, electronic components, aerospace materials; dental laboratory procedures
Bis(chloromethyl)ether; chloromethyl methyl ether (technical grade)	1974	Manufacture of chemicals; laboratory procedures
Cadmium and cadmium compounds	1993	Production, refining, and processing of cadmium and its alloys; manufacture of batteries and pigments
Chromium (VI) compounds	1987	Production and use of chromate pigments and paints; chrome plating; work in chrome-alloy foundries
Coal-tar pitch	1985	Production of coal-tar products; roofing and surface coating activities
Engine exhaust, diesel	2013	Rail, truck, and bus operation and mechanical maintenance; mining; firefighting
Nickel compounds	1990	Mining, smelting and refining of nickel; production of nickel alloys, stainless steel and batteries; electroplating; paint production and use
Outdoor air pollution	2016	Where majority of working time is spent in polluted outdoor environments (eg, urban traffic police, professional drivers, street vendors)
Particulate matter in outdoor air pollution	2016	
Plutonium	2001	Nuclear industry workers
Radon-222 and its decay products	1988	Mining and other underground work; mineral processing
Silica dust, crystalline, in the form of quartz or cristobalite	1997	Mining and quarrying operations; foundries; ceramics, cement and glass industries; construction activities
Soot	1973	Industries and tasks with exposure to combustion products (eg, coke-making, chimney cleaning, incineration)
Sulfur mustard (see also mustard gas)	1975	Manufacture of mustard gas; military service in WWI
Tobacco smoke, secondhand	2004	Work in public settings where smoking occurs (eg, restaurants, bars, casinos, planes)
Welding fumes	2017	Various work environments where welding is performed
X-radiation and gamma-radiation	2000	Nuclear industry workers; human and veterinary medicine; workers involved in nuclear accident clean-up

occupational exposures to carcinogens. It is noteworthy that the impact of an exposure on lung cancer varies between occupational carcinogens. A review on occupational carcinogens and risk relations to cancer in high-income countries, using France as a reference, showed that the highest risk was for exposure to bis(chloromethyl) ether (RR: 7.6 (95%-IC: 4.3-13.5) (Table 5) (Marant Micallef et al. 2018). For other agents, authors demonstrated that the risk of lung cancer increased in line with the dose of carcinogen received. For example, workers exposed to beryllium at a level between 2.0 and 50.0 µg/m3 had a risk of 4.9 (95%-IC: 2.6-9.6) higher compared with those exposed at a level <0.6 µg/m 3. Those exposed to arsenic had a risk of 1.02 (95%-IC: 0.9-1.2) higher for an exposure of 0.29 mg/m3, whereas the risk increased to 2 (95%-IC: 1.7-2.4) with an exposure level of ≥50 mg/m3. Women who worked in the rubber industry also showed an elevated relative risk (1.8, 95%-IC: 1.1-2.8).

Table 5 Relative risk estimates (RR) for occupational carcinogenic agents with sufficient evidence in humans for lung cancer (adapted from (Marant Micallef et al. 2018))

Agents	Exposure definition	RR estimates	95% CI
Engine exhaust diesel	Increase of 100 µg/m3 in elemental carbon	1.1	1.06 to 1.2
Nickel	Any exposure	1.3	1.03 to 1.7
PAHs	<0.01µg/m3	1.0	1.0 to 1.0
	0.01–0.75µg/m3	1.0	1.01 to 1.03
	0.75–2.00µg/m3	1.1	1.04 to 1.1
	≥2.00µg/m3	1.3	1.1 to 1.4
Painters	Ever exposed as painter	1.4	1.2 to 1.5
Rubber industry	Men ever worked in rubber industry	1.2	1.1 to 1.4
	Women ever worked in rubber industry	1.8	1.1 to 2.8
Iron and steel founding	Any exposure	1.4	1.3 to 1.5
Silica	All estimates combined	1.2	1.1 to 1.3
	0.4 – 2.0 mg/m3	1.0	0.9 to 1.3
	2.0–5.4 mg/m3	1.3	1.1 to 1.7
	5.4 – 12.8 mg/m3	1.5	1.2 to 1.9
	>12.8 + mg /m3	1.6	1.3 to 2.1
Asbestos	All combined, Europe	1.6	1.4 to 1.9
Arsenic	0.29 mg/m3	1.02	0.9 to 1.2
	0.30-0.39 mg/m3	1.3	1.1 to 1.7
	0.40-0.49 mg/m3	1.5	1.0 to 2.1
	≥50 mg/m3	2.0	1.7 to 2.4
Beryllium	< 0.6 µg/m3	1.0	
	0.6–2.0 µg/m3	2.3	1.3 to 4.3
	2.0–8.0 µg/m3	2.8	1.5 to 5.5
	8.0–12.0 µg/m3	5.7	2.7 to 12.4
	12.0− 50.0 µg/m 3	4.9	2.6 to 9.6
	≥ 50 µg/m3	4.1	2.1 to 8.4
Bis(chloromethyl)ether	Any exposure	7.6	4.3 to 13.5
Cadmium	250–500 µg/m3 year	1.0	
	Ever exposed to >500 µg/m3 year	1.2	1.1 to 1.3
Chromium VI	Risk increase by mg/m3	0.6	0.2 to 1.3

Of the more than 2 million people dying from lung cancer worldwide ever year, 299'998 deaths are estimated to be associated to occupational exposures (95% CI 233'708-365'251). About 60% of them (181'450 deaths) were due to exposure to asbestos, 16 % (47'999) to silica and 15% to secondhand smoke. Other carcinogens such diesel engine exhaust, nickel and arsenic were responsible for 17'500, 8'101 and 8'073 lung cancer deaths, respectively (GBD 2020), while the impact on morality for beryllium (259) and cadmium (605) was lower.

Using Swiss data form NICER for the period 2011-2015, 12'946 men and 8'314 women were diagnosed with lung cancer, 11.9% and 8.9% of the overall cancer cases, respectively. Within 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=5'872) (NICER 2021). If we assume that the proportion of people exposed to occupational carcinogens in the population is the same as in France, we can apply the French PAFs of lung cancer related to occupational exposures to the Swiss cancer statistics for the period 2011-2015 (Marant Micallef et al. 2019). Doing so, we observed that the lung cancer burden would have diminished by 2'500 and 740 cases of lung cancer in men and women, respectively, in absence of occupational exposures to lung carcinogens. These expected numbers contrast with those of Suva that recognizes less than 200 cases (mainly mesotheliomas) ever year as occupational cancers (Suva 2017; Suva 2019). To our knowledge, SUVA only classifies exposure to nickel, crystalline silica, asbestos, bis(chloromethyl)ether and chromium VI compounds as lung carcinogens to humans (SUVA 2022).

Therefore, further studies should be undertaken to update and better develop estimates of occupational lung cancer. This is especially paramount, since a 2006 report on occupational health showed that Switzerland lagged behind other European countries in terms of research in occupational health (Bauer et al. 2006). The main explanation for this situation is the quasi absence of occupational and industrial cohorts and data on occupational exposures, even for very common occupational hazards, including IARC Group 1 carcinogens (Bovio et al. 2019).

Occupation and lung cancer survival after diagnosis

Overall survival, also known as all-cause survival, estimates the probability of remaining alive a certain time after diagnosis. The five-year overall lung survival has been shown to vary across countries with estimates ranging from 10% to 20% (Allemani et al. 2018). In countries with similar health care structures, differences in survival have also been observed (Coleman et al. 2011). Because it uses all-cause death as a criterion, overall survival, while reliable, is not specific enough to provide information about survival associated with a cancer diagnosis, such as lung cancer. Differences in survival following a diagnosis may be due to other causes than the diagnosed cancer. The net survival is used to estimate the chances of surviving cancer while eliminating possible distortions due to competing causes of death (Mariotto et al. 2014). It measures the net effect of a cancer diagnosis after removing the effects of competing causes of death. Differences in cancer survival will reflect differences in cancer rather than competing causes of death.

A recent meta-analysis explored the effect on lung survival of different socioeconomic measures including occupation, but this variable could not be assessed because of the heterogeneity of the measures across studies (Finke et al. 2018). In this meta-analysis, only two studies used net survival to investigate the influence of occupational context on lung cancer survival. The first was a Danish study that assessed the social class of patients (creative core, creative professional, bohemian, service, manual and agricultural workers). Authors found no statistically significant difference for both 1-year and 5-year net lung cancer survival (Dalton et al. 2008). The second study identified was conducted in Sweden and found that blue collar and low level white collar workers had a lower net lung cancer survival compared to intermediate and high level white collar workers and self-employed (Berglund et al. 2010). The 1- and 5-year survival for blue collar and low level white collar workers was 20% and 41%, respectively, while those with a higher position presented a net survival of 22% and 46%. Nevertheless, the proportional hazard model adjusted for age, sex and stage at diagnosis yielded no statistically significant differences in lung cancer survival, with a hazard ratio of 0.93 (IC-95%: 0.85-1.01) for those with a higher position compared to blue collar and low level white collar workers. A more recent study conducted on occupational disparities in survival in Japan showed that manual workers had statistically significant lower 5-year net lung cancer survival, with a rate ratio of 1.23 (95%-IC: 1.02–1.49), compared to upper non-manual worker and manual workers (Zaitsu et al. 2022). However, after adjusting for stage and treatment, this result turned out non-significant.

In Switzerland, the five-year net survival of lung cancer was 24% for women and 19% for men, compared with 15% and 11% at ten years after diagnosis, respectively (Galli et al. 2019). The higher the stage at diagnosis, and the older the patient, the lower was the survival, in both men and women. As with mortality, further research is needed to understand whether and to what extent occupational factors can significantly influence survival after a lung cancer diagnosis in the Swiss working population, with or without adjustment for stage at diagnosis.

II. Thesis aims and specific objectives

The large differences between international PAFs and the number of cases recognized as occupational lung cancer in Switzerland raised questions. This suggested either a difference in the incidence pattern of lung cancer among Swiss workers, due, for example, to very effective prevention and exposure control measures in Swiss workplaces, or a failure of the Swiss system of occupational disease reporting and recognition. Because "we act on what we know" (Espina et al. 2015), launching an occupational epidemiological study on lung cancer risk according to occupational settings in Switzerland was paramount and urgent to generate reliable epidemiological data and hypotheses on their etiology, and protective and risk factors.

Therefore, my thesis aimed at producing sex-specific lung cancer mortality risk and survival estimates by work-related variables in Switzerland. In addition, a preliminary work focused on the approximation of unavailable data on occupational exposures and on the need and quality of occupation registration in Swiss cancer registries. Ultimately, we hope that this work will help to target the most at-risk occupational groups and allow tailoring effective interventions.

To assess the sex-specific mortality risk and the survival with lung cancer across work-related variables, we

- evaluated whether the distribution of mortality rates is homogeneous according to both occupation and economic activity by comparing three risk estimates of lung cancer mortality: the Standardized Mortality Ratio (SMR), the Causal Mortality Ratio (CMR) and the relative SMR;
- estimated the effect of occupational exposures on lung cancer mortality in Switzerland after adjustment for non-occupational lung carcinogen, using the occupation as a proxy for occupational exposures to lung carcinogens;
- determined whether the occupation–related variables were associated with lung cancer survival, using net survival settings.

III. Studies of lung cancer mortality

III.I. Preparatory work – automatic re/coding of occupations and industries

In Switzerland, data on most occupational exposures are rare and not publically available. Thus, a preliminary work to find solutions to approximate individual exposure data using more easily available data was necessary. The Swiss National Cohort (SNC) was identified as the most informative source, providing data on occupation and economic activity for 82% of Swiss population (5'628'965 adults).

The initial coding of occupations in both censuses was based on the Swiss classification of occupations (abbreviated as NSP, from Nomenclature Suisse des Professions), subsequently recoded using the four-digit codes of the International Standard Classification of Occupations, version 1988 (ISCO-88) by the Swiss Federal Statistical Office (SFSO). As occupations were in German, we first translated them into English. In addition, since ISCO-88 is a multi-tiered classification, we also created new variables for both censuses for each level (Major Group (one digit), Sub-major Group (two digits) and Minor Group (three digits). The coding of economic activity/industry was initially based on the National Classification of Economic Activities (abbreviated as WART from Allgemeine Systematik der Wirtschaftszweige), version 1985 in German in the 1990 census and on the National Classification of Economic Activities (abbreviated as NOGA from Nomenclature Générale des Activités) version 1995 in the 2000 census. To harmonize the coding, we recoded economic activity of 1990 into NOGA-1995, using a computer algorithm based on the crosswalk between the two systems. For both censuses, we then created two variables with the first and second major groups of the multi-tiered NOGA-95 classification. These new standardized variables on occupation and economic activity were not only valuable for this project, but were also used in studies on suicide among Swiss workers (Guseva Canu et al. 2021; Guseva Canu et al. 2019b; Schmid et al. 2020; Wild et al. 2021).

However, manual recoding is time-consuming. In order to be more efficient and to be able to use other sources of occupational data in the future, we developed a software, named Procode. This is a free of charge web-tool that allows automatic coding of occupational data (free-texts) by implementing Complement Naïve Bayes (CNB) as a machine-learning technique. We published an article on this work in Annals of Work Exposures and Health in January 2022.

Own contribution: performed the data management (searched for crosswalks between standardized classifications of occupation or economic activity and provided data sets), tested the tool and revised the manuscript.

Article: Procode: a machine-learning tool to support (re-)coding of free-texts of occupations and industries

Nenad Savic[1*], Nicolas Bovio[1], Fabian Gilbert[2] and Irina Guseva Canu[1]

*The corresponding author:
Nenad Savic
Centre for primary care and public health – Unisanté
Route de la Corniche 2
1066 Epalinges – Lausanne
nenad.savic@unisante.ch

[1] Centre for Primary Care and Public Health (Unisanté), University of Lausanne, Route de la Corniche 2, CH-1066 Epalinges-Lausanne, Switzerland
[2] Research Institute for Environmental and Occupational Health, 28 rue Roger Amsler, CS 74521, 49045 Angers, France

Keywords: epidemiology, occupational classifications, machine learning, Naïve Bayes, cross-validation

Abstract

This paper describes the algorithm, performance evaluation and future goals regarding the development for Procode. The tool incorporates Complement Naïve Bayes as a machine-learning technique to support automatic coding of free-texts against classifications established for occupations and industries. Almost 30'000 free-text entries with manually assigned classification codes of French classification of occupations (PCS) and French classification of activities (NAF) were available. 5-fold cross-validation found 57-81% and 63-83% predictions agreed with the manually assigned codes for PCS and NAF, respectively, depending on the level of classification codes. Procode support also recoding between two classifications. For its first release, however, focus was mainly on the free-text coding. Regarding both operations, more data available for different classification and in different languages is curtail for future development and testing of the tool's performance.

Introduction

Large occupational exposure databases and job exposure matrices (JEM) exist and could be of a meaningful value in studies that associate different exposures (e.g. chemical) to specific occupations, industries or populations worldwide (Fadel et al. 2020). Their use, however, is limited due to prerequisite of translating the data into a usable format. JEMs include free-text entries, which must be in alignment with the job or industry titles defined in different national or international classifications. This task, however, is time-consuming, expensive and requires adequate skills (Koeman et al. 2013; Peters 2020).

Several tools have been developed to provide support to the users coding the free-texts (De Matteis et al. 2017; Patel et al. 2012; Remen et al. 2018; Russ et al. 2016; Warwick Institute for Employment Research 2018). Some of these tools assign classification code to the job entries automatically, while the others are rather (manual) search assistants. For example, OSCAR (De Matteis et al. 2017) is a web-tool for coding the workers' job history, which provides a tree structure of UK SOC (Standard Occupational Classification) to help the users in selecting the appropriate job titles. Another tool, CAPS-Canada (Remen et al. 2018), assign automatically the most likely classification code and title for a free-text entry designating a job. This tool supports seven classifications, i.e. four occupational and three of industries. For each job title defined in a classification, CAPS-Canada calculates a score depending if it finds the word(s) of a free-text in the job title, its definition or synonyms. SOCcer (Russ et al. 2016) and CASCOT (Warwick Institute for Employment Research 2018) apply more advanced approaches. SOCcer, for example, combines multiple classifiers based on training datasets to derive the most probable outcome for the entered free-text criteria. CASCOT was trained to automatically assign job titles of SOC and ISCO-08 (International Standard Classification of Occupations) and industry of SIC (Standard Industrial Classification). The tool also supports a variety of languages (e.g. English, French, Finish, Slovak, etc.).

The authors of this manuscript aimed at designing a new approach, which is expected to overcome the limitations identified for the existing tools. Also, the special efforts were done to mitigate issue of small or unavailable training data for certain classifications. This was embodied in a tool named Procode (available at URL: http://www.pro-code.ch) that is offered to the users free of charge for unlimited time.

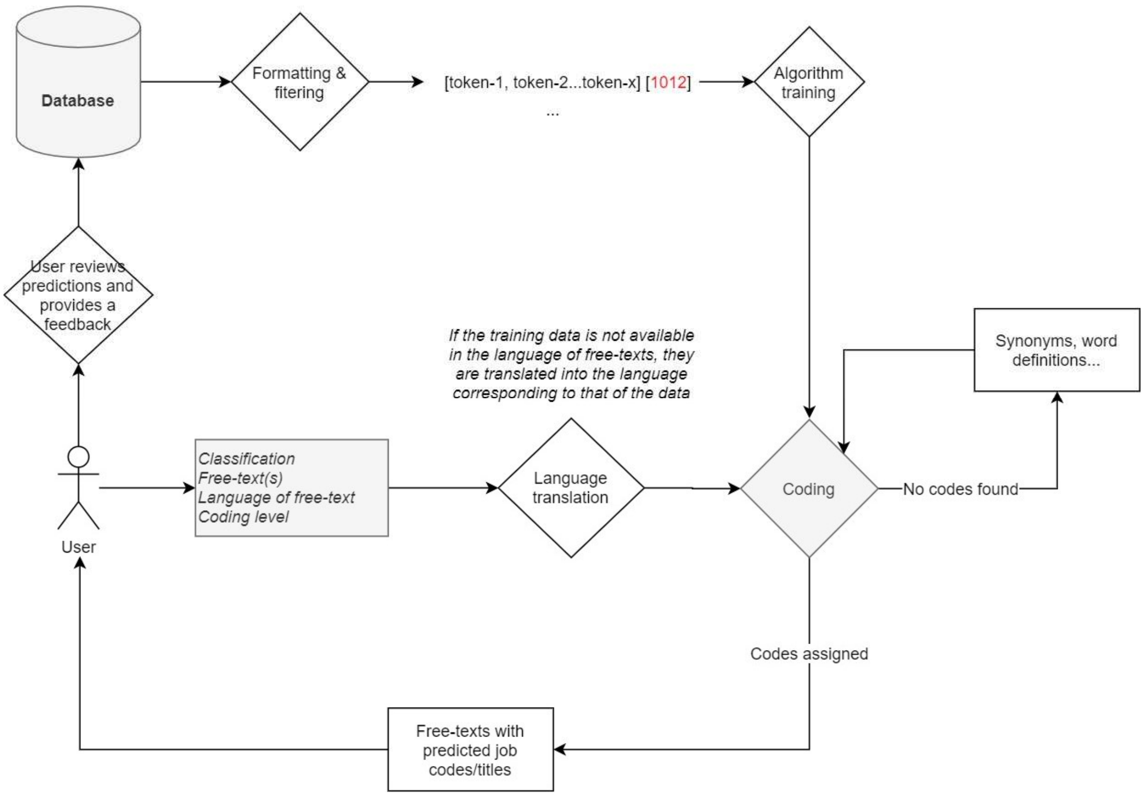
Methodology

Procode is intended to support both coding (free-text assignment to job title) and recoding (job title translation from one to another classification). For the first release, the focus was on the former, while the later was integrated in a simplified manner.

Coding algorithm

Figure 1 illustrates the workflow of the coding algorithm integrated in Procode. A training dataset must include free-text entries with corresponding manually assigned job codes. The first task is data preparation, which includes a formatting operation known as lemmatization and word filtering by importance. Lemmatization (Bird et al. 2009) is a linguistic operation that is used to group together different forms of a word (i.e. lemma) in order to facilitate their analysis. For example, “walk” and “walking” have the same lemma, i.e. “walk”. In this study, the goal is to reduce the number of these predictors or, in other words, to increase frequency of the given lemmas. If an entered free-text is misspelled (e.g. “enginner” instead of “engineer”), the algorithm fails to find lemma and a warning message is displayed in Procode. Not all lemmas are processed. For example, those of no importance, such as “and”, “although”, “or”, “anyone”, etc, which are known as stop words, are discarded. For others, their importance was evaluated using the method called *term-frequency – inverse-document-frequency* (id-idf). For example, word “assistant” likely appears in many free-texts, while it can be associated with a variety of job titles. This word is thus bad predictor and was thus discarded. The formatted data is then used to train a machine-learning algorithm, which is used to predict job code/title for a new free-text entry. The lemmas in free-texts are used as independent predictors (x) of assigned job codes–depending variable (y).

Figure 1. Coding algorithm workflow



Procode is designed to support four languages, i.e. English, German, French and Italian. If no data exists to train the algorithm in the language of the free-text entries, the contained words are translated (e.g. English "restaurant manager" to French "gérant de restaurant"). This is done automatically in the background without consulting the end-user.

It is unlikely to expect that a training dataset may cover the whole universe of different possibilities. Therefore, Procode may fail to assign a job code/title to a given "exotic" free-text entry. In these situations, the algorithm would create a longer string including synonyms and the definitions of those words in the given free-text entry. After formatting this new entry, the coding is repeated. It is assumed that the new text would include important words that appear as well in the training dataset.

Finally, the predictions are displayed to the user. In case of multiple job codes assigned to a given entry, they are ordered by the probability that they match the coded criteria. Their probabilities outputted by the algorithm are used to calculate the corresponding scores depicting the prediction uncertainties. The users of Procode are then provided with the possibility to judge the displayed predictions. Biased or incorrect predictions can be reported together with providing “the best match” jobs manually. This information is then added to the training data and used to improve future prediction. The system thus constantly learns from its mistakes.

Machine-learning classifiers

Procode integrated Complement Naïve Bayes (CNB) (Bird et al. 2009; Ikonomakis et al. 2005) as a machine-learning classifier due to its performance evaluated in this study. Alongside CNB, the authors evaluated performance of Support Vector Classifier (SVC) (Ikonomakis et al. 2005) and Random Forest Classifier (RFC) (Cutler et al. 2011).

The authors considered the three mentioned methods due to their domain of application that fits the text classification intention of this project (Bird et al. 2009; Ikonomakis et al. 2005; Korde 2012). All three methods are supervised learning models, which use the lemmas defined above as predictors of job titles/classes. They are suitable imbalanced datasets (Rennie et al. 2003)– training dataset contains unequal distribution of records per outcome (e.g. job code). CNB applies the Bayesian inference to calculate likelihoods that different words of a free-text determine jobs of a classification. While SVC tries to separate the defined universe of words with a dimensional hyperplane, RFC establishes a set of random decision trees that contribute differently to the final prediction.

Technologies applied

Procode is designed to be a web application. Its back- and front-end sides are decoupled, where the former was developed using Django (Foundation 2020)–Python web framework, while the later using ReactJS (Facebook 2020)–JavaScript library. Natural Language Took Kit (NLTK) (Bird et al. 2009) was used for text formatting (e.g. lemmatization), while the language translations were enabled by using "translate" package of Python (Yin and Henter 2020). Finally, the text-classifiers (e.g. CNB) are part of "sklearn" package of Python (Pedregosa et al. 2011).

Evaluation

Cross-validation

A 5-fold cross-validation used 30'000 free-text entries from Constance cohort (Goldberg et al. 2017; Zins et al. 2015). The data was in French language and included manually assigned occupational job codes of PCS-2003 (fr. *Professions et catégories socioprofessionnelles*) and industry codes of NAF (fr. *Nomenclature d'activités française*). Because the data included job/industry codes of different precision level (i.e. from major groups to subgroups holding different level of detail; usually different number of code digits), the evaluation was performed for each of them separately. The prediction results were compared with the previously manually assigned codes and the percentage agreement was calculated.

End-user test

The authors invited an external tester, who had experience in the occupational coding, to perform a coding operation using own dataset. Using Procode, the tester performed the task on 10'000 free-texts. The dataset was again in French and had already PCS and NAF codes assigned manually. It is important to note that the data was not part of the previous cross-validation. The tester thus calculated percentage accuracy and reported the results.

Language translation test

To test the agreement between coding of free-texts given in different languages (see Figure 1), the authors generated two lists, i.e. in English and in French, each with 200 job free-texts. The data in one corresponded to that in the second list. Since the first release of Procode is based only on the data in French, the entries in other languages must thus be translated to French prior to the coding operation. Both lists were coded and the agreement between the predicted outputs calculated.

Results

Table 1 summarizes the percentage agreement between the predicted and manually coded jobs obtained for the cross-validation and external text. Depending on the coding level, 57-81% of PCS predictions and 63-83% of those for NAF agreed with manually coded jobs. As expected, the best agreement was when predicting the major groups (i.e. top-level codes or those with one digit in their codes) of these two classifications. The external tester reported results (given in brackets in Table 1) that were very similar to those from the cross-validation test.

Table 1. Percentage agreement between predicted and manually coded outputs

Code level	PCS 2003		NAF 2008	
	Number of different codes	Accuracy, %	Number of different codes	Accuracy, %
Cross-validation based on 30'000 entries (external test on 10'000 entries)				
1	8	81 (83)	21	83 (83)
2	24	73 (72)	88	79 (80)
3	42	70 (71)	272	68 (80)
4	497	57 (60)	615	66 (71)
5	-	-	732	63 (71)

The obtained results for the other two considered classifiers, i.e. support vector and random forest, are given in supplementary material. Somewhat lower values (1-2%) were observed for the former (Table S1). The later (Table S2), however, showed much lower performance, where, in the best case, it accurately predicted 31% classification codes.

Finally, for 200 job free-texts in English and French, the coded PCS predictions agreed 95%. In other words, Procode assigned different job codes/titles only for ten entries, which designated the same occupations, but in the two different languages.

Discussion

The "gold standard" is the manual coding and manually coded data, which can be used to train different machine-learning classifiers. Such data are usually unavailable due to confidentiality issues or simply lack of willingness of different institutes to share their data voluntarily. The available data, however, are usually limited in size or variability of free-text records. Moreover, the entries are often given in one language (e.g. English). To overcome to some extent the mentioned issues, Procode was designed with a special focus on the lack of good data.

Currently, CNB classifier of Procode is trained on currently available data (i.e. 30'000 records for PCS and NAF). Using corresponding crosswalks, assigned PCS job codes/titles can be easily translated to ISCO-88. Procode integrates also re-coding of jobs between classifications for which crosswalks are available. In its first release, the tool supports also re-coding between ISCO-88 and NSP (Swiss national occupational classification).

The use of the tools that are not based on a training data, such as, for example, CAPS-Canada, is limited to the free-texts containing terms existing in job titles or additional job information (e.g. their descriptions). For the tools trained on dataset features (e.g. SOCcer), their predictions are strongly affected by the given data collected upon to the tool's development. By keeping the training data constant, a prediction bias that occurs once for one user would thus repeat for the others whenever similar entries are coded. Finally, CASCOT, which is the most comprehensive tool, is not a freeware, except its online version that lacks the features of the standalone version. The online version of CASCOT, for example supports only English and cannot be used to code files containing multiple free-text entries.

Unlike these tools, Procode is freeware with a modern interface (see Supplementary material, Figures S1-S3) that operates in multiple languages and allow the users to code up to 10'000 entries in a single iteration. Support of the users' feedbacks is expected to make its internal database constantly increasing. This is especially important for those coding outcomes when Procode must consult dictionary (see Figure 1). Although using this approach, a coding result is guaranteed in most cases, the validity of this approach is unknown. The erroneous predictions observed once, if reported, may not appear in the next integration. To prevent biased feedbacks, Procode differentiates "trusted end-users" from the others. For a given user, the administrator periodically verifies the received feedback data and, if valid, the user is labelled as trusted.

Limitations and Outlook

Procode is not finalized and more efforts are needed to improve different aspects of the tool and perform additional validation tests. As already mentioned, the focus in the first release was on coding. Only 100% agreement between predictions and the manually coded jobs would mean an automatic coding approach in its full picture. This, however, is not the case with the current version of Procode and additional studies are expected to reveal in which domains the data must be additional enriched or which parts of the coding algorithm should be revised. When more data becomes available in different languages, the use of the language translations and the dictionary sub-algorithm (Figure 1) will be less used. For the moment, these two are necessary to mitigate the lack of data. An in-depth investigation of their performance is thus essential.

Re-coding between two classifications, although supported, is only possible if a crosswalk exists online or can be established based on a dataset. This is, however, only the case for a limited number of crosswalks. An idea that has not yet been embodied is to create a semi-automatic system that would, based on similarity between the job titles in two classifications, define translation links. The users would then score different outputs based on their validity. Some translations would thus become more valid (i.e. less uncertain) than others. Simultaneously, the recoding algorithm would then learn on how different job titles should be linked and would improve its performance.

References

Bird, S., Klein, E. & Loper, E. 2009. *Natural Language Processing with Python*, O'Reilly Media, Inc.

Cutler, A., Cutler, D. & Stevens, J. 2011. Random Forests.

De Matteis, S., Jarvis, D., Young, H., et al. 2017. Occupational self-coding and automatic recording (OSCAR): a novel web-based tool to collect and code lifetime job histories in large population-based studies. *Scand J Work Environ Health,* 43**,** 181-186.

Facebook. 2020. *React - A JavaScript library for building user interfaces* [Online]. Available: https://reactjs.org/ [Accessed 11 April 2020].

Fadel, M., Evanoff, B. A., Andersen, J. H., et al. 2020. Not just a research method: If used with caution, can job-exposure matrices be a useful tool in the practice of occupational medicine and public health? *Scand J Work Environ Health*.

Foundation, D. S. 2020. *The Django Project* [Online]. Available: https://www.djangoproject.com/ [Accessed].

Goldberg, M., Carton, M., Descatha, A., et al. 2017. CONSTANCES: a general prospective population-based cohort for occupational and environmental epidemiology: cohort profile. *Occup Environ Med,* 74**,** 66-71.

Ikonomakis, E., Kotsiantis, S. & Tampakas, V. 2005. Text classification: a recent overview. 125.

Koeman, T., Offermans, N. S., Christopher-De Vries, Y., et al. 2013. JEMs and incompatible occupational coding systems: effect of manual and automatic recoding of job codes on exposure assignment. *Ann Occup Hyg,* 57**,** 107-14.

Korde, V. 2012. Text Classification and Classifiers:A Survey. *International Journal of Artificial Intelligence & Applications,* 3**,** 85-99.

Patel, M. D., Rose, K. M., Owens, C. R., et al. 2012. Performance of automated and manual coding systems for occupational data: a case study of historical records. *Am J Ind Med,* 55**,** 228-31.

Pedregosa, F., Varoquaux, G., Gramfort, A., et al. 2011. Scikit-learn: Machine Learning in Python. 12**,** 2825–2830.

Peters, S. 2020. Although a valuable method in occupational epidemiology, job-exposure -matrices are no magic fix. *Scandi J Work Environ Health***,** 231-234.

Remen, T., Richardson, L., Pilorget, C., et al. 2018. Development of a Coding and Crosswalk Tool for Occupations and Industries. *Ann Work Expo Health,* 62**,** 796-807.

Rennie, J. D. M., Shih, L., Teevan, J., et al. 2003. Tackling the poor assumptions of naive bayes text classifiers. *Proceedings of the Twentieth International Conference on International Conference on Machine Learning.* Washington, DC, USA: AAAI Press.

Russ, D. E., Ho, K. Y., Colt, J. S., et al. 2016. Computer-based coding of free-text job descriptions to efficiently identify occupations in epidemiological studies. *Occup Environ Med,* 73**,** 417-24.

Warwick Institute for Employment Research, U. O. W., Coventry, Cv4 7al, United Kingdom. 2018. *Cascot: Computer Assisted Structured Coding Tool* [Online]. Available: https://warwick.ac.uk/fac/soc/ier/software/cascot/#:~:text=Cascot%20is%20a%20computer%20program,UK%20Office%20for%20National%20Statistics. [Accessed 14.12.2020 2020].

Yin, T. & Henter, R. 2020. Translate Python Documentation.

Zins, M., Goldberg, M. & Team, C. 2015. The French CONSTANCES population-based cohort: design, inclusion and follow-up. *European journal of epidemiology,* 30**,** 1317-1328.

Supplemental Material

Procode: a machine-learning tool to support (re-)coding of free-texts of occupations and industries

Nenad Savic, Nicolas Bovio, Fabian Gilbert and Irina Guseva Canu

Table S1. Performance overview for PCS and NAF obtained using SVC

Level of precision	PCS 2003		NAF 2008	
	Number of different codes	Accuracy (%)	Number of different codes	Accuracy (%)
1	8	79	21	83
2	24	72	88	80
3	42	70	272	68
4	497	55	615	65
5	-	-	732	62

Table S2. Performance overview for PCS and NAF obtained using RFC

Level of precision	PCS 2003		NAF 2008	
	Number of different codes	Accuracy (%)	Number of different codes	Accuracy (%)
1	8	26	21	31
2	24	17	88	21
3	42	14	272	16
4	497	14	615	15
5	-	-	732	9

Figure 1. Coding of a single free-text

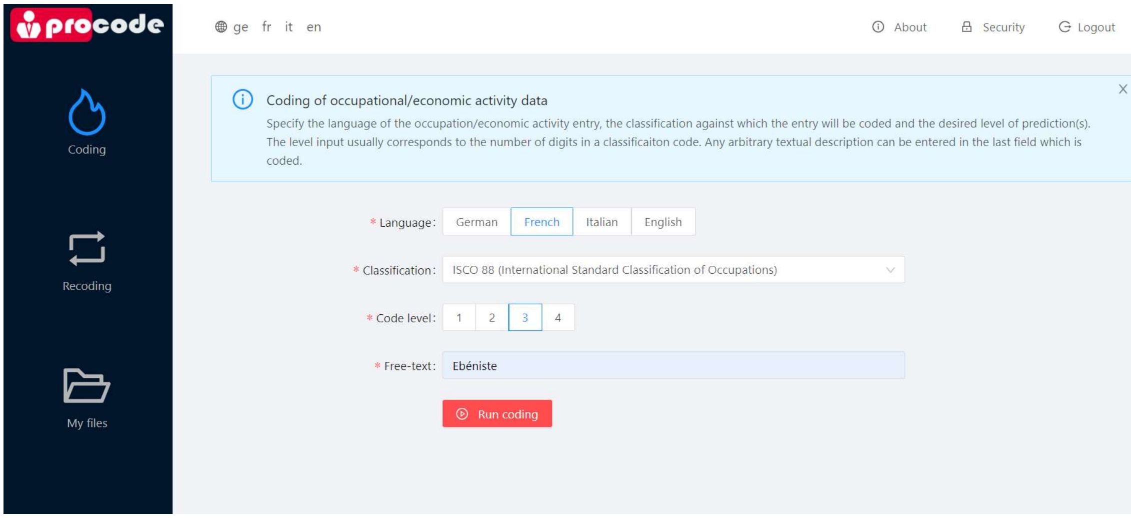


Figure 2. Coding results against PCS 2003 for a file containing three free-text entries. The entered free-text in English was correctly coded using PCS jobs in French

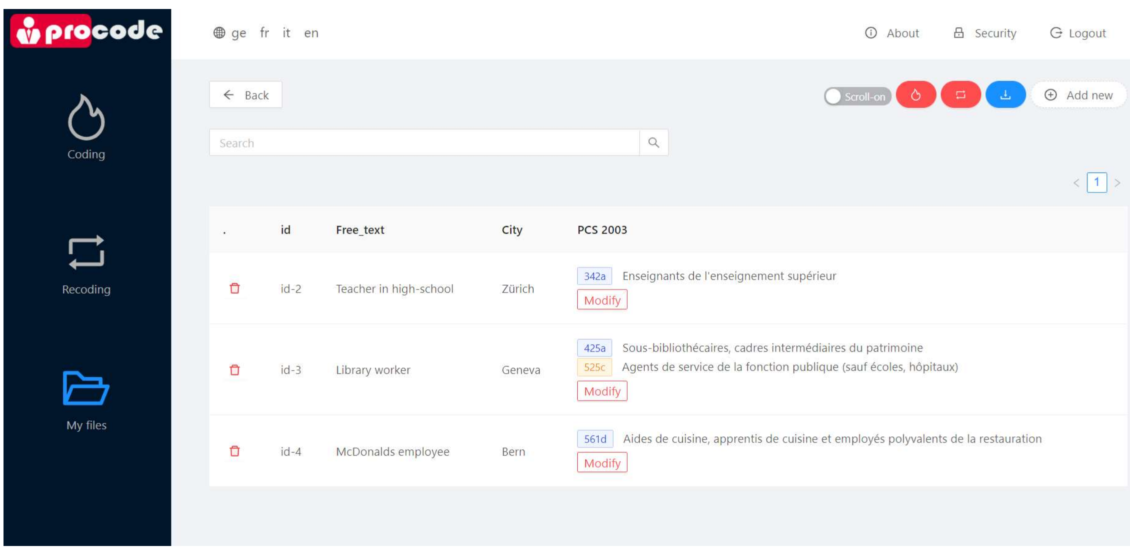
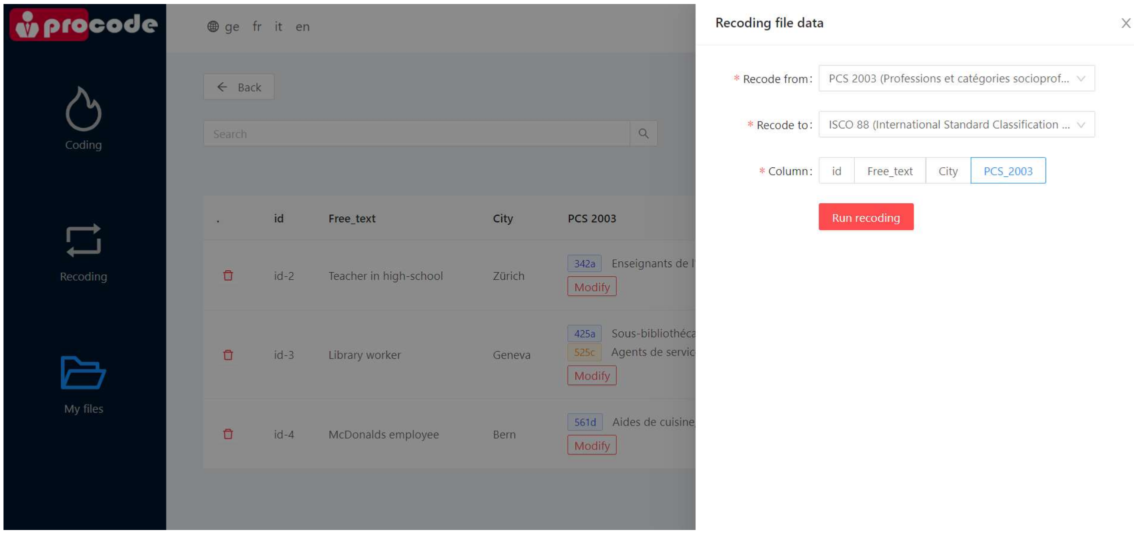


Figure 3. Recoding the PCS results shown in Figure 2 to ISCO-88



III.II. Descriptive study of lung cancer mortality per occupation and economic activity in Switzerland – comparison of three different methods

To our knowledge, no public reporting on occupational lung cancer incidence was available at the national level in Switzerland. In addition, the number of lung cancer cases recognized as occupational diseases by SUVA (OFSP 2015), about 50 cases per year, was much lower than the figures observed internationally (Olsson and Kromhout 2021). Based on these findings, the launch of a national study was strongly needed to better understand the risk of occupational lung cancer. We therefore conducted a first descriptive study to estimate the risk of lung cancer across occupations and economic activities/industries in Switzerland, using three complementary indicators. We published this work in Occupational & Environment Medicine in April 2020.

Own contribution: co-authored the research protocol according to the Human Research Law (project-ID 2018-02077), performed the data management, performed the statistical analyses and wrote the manuscript.

Article: Sex-specific risks and trends in lung cancer mortality across occupations and economic activities in Switzerland (1990-2014)

Nicolas Bovio[1*], David B. Richardson[2], and Irina Guseva Canu[1] for the Swiss National Cohort (SNC).

Running title: lung cancer mortality and occupations in Switzerland

[1] Department of Occupational and Environmental Health, Center for Primary Care and Public Health (unisanté), University of Lausanne, Lausanne, Switzerland.

[2] Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599

**Corresponding author:* Bovio N.

Center for Primary Care and Public Health (unisanté), University of Lausanne

Department of Occupational and Environmental Health

BIOPÔLE Secteur Croisette - Bâtiment SC-B

Rte de la Corniche 2

CH-1066 Epalinges-Lausanne

+41 21 314 47 72

nicolas.bovio@unisante.ch

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COMPETING INTERESTS STATEMENT: This work was conducted in frame of the SNC nested study contract No 180036. The authors have no conflicts of interest to declare.

COMPLIANCE WITH ETHICAL STANDARDS: The SNC 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 manuscript does not contain clinical studies or patient data.

ABSTRACT

Objectives: To assess lung cancer mortality across occupations and economic activities/industries in Switzerland using three statistical estimates.

Methods: All Swiss residents aged 18-65 during the 1990 or 2000 censuses were followed through 2014 to ascertain information on date and cause of death. For every occupation and economic activity/industry, Causal Mortality Ratios (CMR) and Standardized Mortality Ratios (SMR) were computed using national cause-specific mortality rates. We also calculated relative SMR (rSMR) and conducted analyses stratified by socio-economic variables, job-skill level, and calendar periods.

Results: The study sample comprised 5’834’618 participants (111’162’348 person-years). SMR and CMR led to similar results, while rSMR were generally higher. We found 18 occupations in men, 10 occupations in women and 3 industries in each sex with an excess of lung cancer mortality. Among men, rubber- and plastic-products machine operators, and workers in mining and quarrying, and construction industries were at high risk. Among women, motor vehicle drivers and workers in trade, repair of motor vehicles and of domestic articles, and manufacture of goods industries showed the highest risks. In both sexes, hotel and restaurant workers presented an excess of lung cancer mortality.

Conclusion:

Most of the activities and occupations in which we observed excess lung cancer mortality have previously been observed to involve occupational exposure to lung carcinogens. These findings suggest that the number of occupational lung cancer is likely underestimated by the official Swiss statistics. Further research should address this question and the exposure-effect relationships in the most at-risk occupational groups.

Key messages

What is already known about this subject?

- Lung cancer is the most common cause of cancer death worldwide;
- The population attributable fraction of lung cancer due to occupational exposures is estimated at 19.3% in men and 2.6% in women;
- In Switzerland, there is no relevant data on the burden of occupational lung cancer

What are the new findings?

- The occupational activities at highest risk of lung cancer mortality in Switzerland are construction, mining and quarrying industries, and rubber- and plastic-products machine operations for men, and trade, repair of motor vehicles, manufacture of goods industries, and motor vehicle driving for women;
- Using CMR and rSMR, in addition to SMR, enables more consistent estimates of occupational lung cancer mortality;
- Our estimation of the number of occupation-related lung cancer differs from the official statistics on the lung cancer recognized as occupational disease in Switzerland.

How might it impact on policy or clinical practice in the foreseeable future?

- These findings question the effectiveness of the current Swiss system for reporting and recognizing lung cancer cases as occupational disease;
- The occupational groups at high risk of lung cancer mortality, identified in this study, should be targeted for further investigation and tailored prevention.

Introduction

Lung cancer was the leading cause of cancer in 2016, accounting for 2.0 million incident cases and 1.7 million deaths worldwide (GBD 2018). In Switzerland, 12'946 men and 8'314 women were diagnosed with lung cancer between 2011 and 2015, representing respectively 11.9% and 8.9% of the overall cancer cases. Over the same period, 21.6% of all cancer deaths among men (n=10'017) and 15.7% among women (n=5'872) were from lung cancer (NICER 2021). While smoking is a leading cause of lung cancer, the International Agency for Research on Cancer (IARC) recently estimated that the population attributable fraction (PAF) of lung cancers due to occupational exposures was 19.3% in men and 2.6% in women (Jung et al. 2018; Rushton et al. 2012). To date, Switzerland has no public reporting on occupational lung cancer incidence (Bouchardy et al. 2002). By applying the PAF estimated by IARC to the number of lung cancer which occurred between 2011-2015 in Switzerland, about 2500 and 740 lung cancer cases should be considered occupational among men and women, respectively. However, the Swiss National Accident Insurance Fund (Suva) in charge of compensation and prevention of occupational injuries and diseases only recognized around 50 occupational lung cancer cases over this period (OFSP 2015). Such a difference may suggest either a difference in incidence profile from lung cancer among Swiss workers, due, for example, to highly effective preventive measures and exposure control in Swiss workplaces, or a failure in the Swiss system of declaration and recognition of occupational diseases (Guillemin 2018; Guseva Canu et al. 2019b).

Since lung cancer is associated with a poor prognosis and has an estimated 5-year relative survival of only 18%, mortality is as relevant as incidence to study lung cancer risk (de Groot et al. 2018). Therefore, the goal of this study was to estimate the risk of lung cancer across occupations and economic activities/industries in Switzerland using three complementary indicators.

Methods

Data sources

The data of the Swiss National Cohort (SNC) were used to examine lung cancer rates in the Swiss adult population. The SNC is a national longitudinal research platform of 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 (Spoerri et al. 2010). Censuses were mandatory, with population coverage estimated at 98.6% (SFSO 2004). National mortality rates were obtained from the Swiss Federal Statistical Office (SFSO).

Study sample

All active or former Swiss workers were considered at risk with respect to occupation-related lung cancer. In Switzerland, the minimum legal age of employment is 15 and the age of majority is 18. The statutory retirement age is 65 for men and 64 for women. Since employment start and end dates were unavailable, our study sample included all adults aged 18-65 years registered either in the 1990 or 2000 census.

Coding of occupation and economic activity/industry

Occupations were coded using the International Standard Classification of Occupations, version 1988 (ISCO-88) by the SFSO. Economic activities/industries were coded based on the Statistical classification of economic activities in the European Communities (NACE) in the 1990 census and on the General Classification of Economic Activities (NOGA-95), in the 2000 census, a Swiss adaptation of the NACE, 1st revision. A more detailed description of coding and transcoding of these variables is available elsewhere (Guseva Canu et al. 2019a).

Follow-up and identification of lung cancer deaths

Mortality follow-up started either on December 4th 1990 (for the 1990 census) or on December 4th 2000 (for the 2000 census). We followed all participants aged 18 to 65 at the beginning of follow-up up to the earliest date of their 85th birthday, emigration, death or end of the study (December 31st 2014). As occupation and economic activity/industry are time-dependent variables, we assigned person-years as follows:

- participants with a single occupation/industry contributed to this occupation/industry for the entire period of their follow-up;
- participants who changed occupation/industry between 1990 and 2000 census, contributed to the first occupation/industry between 1900 and 2000, and to the second one after 2000.

Depending on the socio-professional status, we also distinguished the unemployed/job-seekers from those with unknown occupation and considered the former as an additional occupational category.

Cases were identified as deaths from lung cancer based on the death certificate. Causes of death were recoded using ICD8 before 1995 and ICD10 thereafter. Only deaths with initial causes coded 162 and primary causes coded C33-C34 according to the International Classification of Disease 8th and 10th edition, respectively, were selected.

Statistical analysis

To identify occupations or economic activities/industries with lung cancer mortality statistically different from that of the general Swiss population, we computed Standardized Mortality Ratios (SMR) and Causal Mortality Ratios (CMR) in men and women. Both methods have the same interpretation and compare the observed deaths in the occupational cohort with the one expected in the absence of occupational exposure(s). The main difference lies in the way expected deaths are calculated. In SMR, expected deaths are the result of a product of constant hazard rates of the reference population (in our case the general Swiss population) and the person-times accrued in the exposed occupation cohort. In CMR, expected deaths are also the product of rates of the reference population and person-times, but they are adjusted at an individual level with the survival probability throughout the follow-up (Richardson et al. 2017). Therefore, CMR are considered less biased compared to SMR as it does not assume that occupational exposures do not influence the cohort's person time, unlike SMR (Richardson et al. 2017; Shrestha et al. 2019). For both methods, 95% confidence intervals were calculated using the exact Poisson formula (Breslow and Day 1987). The national cause-specific rates stratified by age and calendar period (both 5-year groups) were applied to the person-years of every occupation and economic activity/industry. In addition, we calculated relative SMR (rSMR), defined as the ratio of the SMR for lung cancer to the SMR for all causes other than lung cancer using Poisson regression. Assuming a comparable bias for all causes, this measure may reduce bias of the true mortality rate ratio and, thus, the healthy worker effect (Shrestha et al. 2019). CMR, SMR and rSMR were computed over the entire study period.

Moreover, SMR were computed for five calendar periods (1990-1994, 1995-1999, 2000-2004, 2005-2009, 2010-2014) and compared using heterogeneity and trend tests (Breslow and Day 1987). Lastly, we computed SMR and CMR stratified by work-related variables – nationality, socio-professional status (SPS) defined in the SNC as an 8-class variable (OFS 2016), number of workings hours per week, occupation skill-level (ILO 2012), marital status and linguistic region. All analyses were run on STATA version 15 (StataCorp LP; TX, USA).

Results

Cohort description

In total, 5'834'618 Swiss residents were included in this study (111'162'348 person-years), 49% of whom were women. A total of 558'098 individuals died (9.6%) during the follow-up. Men were twice as likely to die from lung cancer as women with 32'910 and 14'447 deaths, respectively. The mean age at death from lung cancer was 64.9 ± 10.2 years in women and 65.6 ± 9.4 years in men. The mean duration of follow-up was 19.5 ± 6.5 years and 18.6 ± 9.4 years in women and men, respectively (Table 1). At study end-point, 20 % of men and 16 % of women were lost to follow-up. Participants lost to follow-up were younger at enrolment, with a mean age at baseline of 33.0 ± 11.8 years in men and 32.3 ± 12.0 years in women, compared to 37.5 ± 12.9 years and 38.0 ± 12.0 years, respectively, for the rest of the cohort. Moreover, elementary occupations in both sexes were overrepresented with a frequency four times higher for those lost to follow-up, compared to those with a complete follow-up.

Table 1 Characteristics of the study sample and number of deaths due to lung cancer : the Swiss National Cohort (1990-2014)

Characteristics	Female				Male			
	n	(%)	*No. of lung cancer deaths*	(%)	*n*	(%)	*No. of lung cancer deaths*	(%)
Total	*2,876,625*	*(100)*	14,477	*(100)*	2,957,993	*(100)*	32,910	*(100)*
Person-years (in 100,000)	560.31				551.31			
Nationality (binary)								
Swiss	2,287,618	*(80)*	13,244	*(91)*	2,197,892	*(74)*	27,105	*(82)*
Non-Swiss	589,007	*(20)*	1,233	*(9)*	760,101	*(26)*	5,805	*(18)*
Socio-professional category								
Top management and independent professions	30,124	*(1)*	73	*(1)*	103,434	*(3)*	593	*(2)*
Other self-employed	103,812	*(4)*	505	*(3)*	262,966	*(9)*	3,108	*(9)*
Professionals and senior management	87,334	*(3)*	228	*(2)*	247,788	*(8)*	1,319	*(4)*
Supervisors/low level management and skilled labour	829,073	*(29)*	2,497	*(17)*	1,000,766	*(34)*	8,232	*(25)*
Unskilled employees and workers	264,046	*(9)*	1,330	*(9)*	283,168	*(10)*	3,159	*(10)*
In paid employment, not classified elsewhere	437,975	*(15)*	1,477	*(10)*	475,647	*(16)*	3,723	*(11)*
Unemployed/job-seeking	90,812	*(3)*	300	*(2)*	77,181	*(3)*	748	*(2)*
Not in paid employment	1,032,828	*(36)*	8,066	*(56)*	506,491	*(17)*	12,028	*(37)*
Unknown	621	*(0)*	1	*(0)*	552	*(0)*	0	*(0)*
1-digit ISCO-88								
0 Armed forces	63	*(0)*	0	*(0)*	2,367	*(0)*	17	*(0)*
1 Legislators, senior officials and managers	73,883	*(3)*	368	*(3)*	245,778	*(8)*	1,860.	*(6)*
2 Professionals	128,431	*(4)*	286	*(2)*	277,934	*(9)*	1,293	*(4)*
3 Technicians and associate professionals	320,958	*(11)*	752	*(5)*	316,521	*(11)*	2,421	*(7)*
4 Clerks	278,755	*(10)*	1,148	*(8)*	129,867	*(4)*	1,393	*(4)*
5 Service workers and shop and market sales workers	278,598	*(10)*	1,114	*(8)*	140,681	*(5)*	974	*(3)*
6 Skilled agricultural and fishery workers	23,560	*(1)*	48	*(0)*	78,861	*(3)*	890	*(3)*
7 Craft and related trades workers	42,916	*(1)*	144	*(1)*	415,594	*(14)*	3,845	*(12)*
8 Plant and machine operators and assemblers	18,383	*(1)*	95	*(1)*	140,088	*(5)*	1,883	*(6)*
9 Elementary occupations	100,573	*(3)*	559	*(4)*	116,164	*(4)*	1,957	*(6)*
Unemployed/job-seeking	90,812	*(3)*	300	*(2)*	77,181	*(3)*	748	*(2)*
Unknown	1,519,693	*(53)*	9,663	*(67)*	1,016,957	*(34)*	15,629	*(47)*
Skill level (based on ISCO)								
Lowest	100,573	*(3)*	559	*(4)*	116,164	*(4)*	1,957	*(6)*
Second lowest	642,212	*(22)*	2,549	*(18)*	905,091	*(31)*	8,985	*(27)*
Second highest	320,958	*(11)*	752	*(5)*	316,521	*(11)*	2,421	*(7)*
Highest	202,314	*(7)*	654	*(5)*	523,712	*(18)*	3,153	*(10)*
Unknown	1,610,568	*(56)*	9,963	*(69)*	1,096,505	*(37)*	16,394	*(50)*

Table 1 continued

Characteristics	Female n	(%)	No. of lung cancer deaths	(%)	Male n	(%)	No. of lung cancer deaths	(%)
Weekly working hours								
1 to 5 hours per week	72,085	*(3)*	247	*(2)*	12,235	*(0)*	171	*(1)*
6 to 19 hours per week	261,797	*(9)*	947	*(7)*	36,613	*(1)*	420	*(1)*
20 to 27 hours per week	234,092	*(8)*	976	*(7)*	45,249	*(2)*	646	*(2)*
28 to 35 hours per week	171,602	*(6)*	644	*(4)*	54,282	*(2)*	414	*(1)*
36 to 39 hours per week	49,534	*(2)*	171	*(1)*	35,729	*(1)*	190	*(1)*
40 to 45 hours per week	709,850	*(25)*	2,119	*(15)*	1,580,518	*(53)*	13,105	*(40)*
46 and more hours per week	110,340	*(4)*	434	*(3)*	447,302	*(15)*	3,294	*(10)*
Unknown	1,267,325	*(44)*	8,939	*(62)*	746,065	*(25)*	14,670	*(45)*
Language region								
German	2,042,499	*(71)*	9,733	*(67)*	2,120,386	*(72)*	22,695	*(69)*
French	694,517	*(24)*	3,931	*(27)*	699,753	*(24)*	8,274	*(25)*
Italian	130,461	*(5)*	766	*(5)*	127,912	*(4)*	1,806	*(5)*
Rhaeto Romansch	9,148	*(0)*	47	*(0)*	9,942	*(0)*	135	*(0)*
Vital status at end-point								
Alive	2,187,271	*(76)*			2,030,220	*(68)*		
Lost to follow-up	472,074	*(16)*			586,955	*(20)*		
Dead	217,280	*(8)*			340,818	*(12)*		
From lung cancer			14,477	*(100)*			32,910	*(100)*
Age (years) : mean ± standard deviation								
At study entry	37.1 ± 13.1				36.6 ± 12.8			
At study end	56.6 ± 15.3				55.2 ± 14.8			
At death from lung cancer	64.9 ± 10.2				65.6 ± 9.4			
Duration (years) : mean ± standard deviation								
Follow-up	19.5 ± 6.2				18.6 ± 6.6			
Between the last occupational information and death from lung cancer	7.5 ± 3.8				6.8 ± 3.8			

Risk of lung cancer by occupational group

Table S1 presents CMR and SMR for each occupation (3-digit ISCO-88) with at least 10 observed deaths due to lung cancer in both sexes. Overall, CMR and SMR results were very similar. The absolute difference (Δ) between CMR and SMR never exceeded 0.03, except for unemployed/job-seekers (Δ=0.11), garbage collectors and related labourers (ISCO-88=916) (Δ=0.05) and manufacturing labourers (ISCO-88=932) (Δ=0.05) in men.

In men, 46 occupations out of 95 presented a statistically significant deficit in mortality from lung cancer (Fig. 1), compared to the general Swiss male population. Physicists, chemists and related professionals (ISCO=211), religious professionals (ISCO=246), and college, university and higher education teaching professionals (ISCO=231) were identified as the most protected occupations. In contrast, rubber- and plastic-products machine operators (ISCO=823), other machine operators (ISCO=829), unemployed/job-seeking men, garbage collectors and related labourers (ISCO=916) and plant and machine operators and assemblers (ISCO=800) were the five occupational groups with the highest excess of lung cancer mortality. Comparisons of SMR across the five calendar periods by 2-digit ISCO-88 showed a statistically significant decreasing trend in lung cancer mortality in sales and services elementary occupations (ISCO=91), with the highest SMR found over 1990-1994 (SMR=1.34, 95%-CI=1.11-1.61) (Table S2).

In women, a statistically significant deficit in lung cancer-mortality was observed in 13 out of 55 occupations (Fig. 3). Crop and animal producers (ISCO=613), primary education teaching associate professionals (ISCO=331) and other teaching associate professionals (ISCO=334) presented the lowest CMR. The five occupations with the highest risk of lung cancer mortality were motor vehicle drivers (ISCO=832), computer associate professionals (ISCO=312), precision workers in metal and related materials (ISCO=731), material-recording and transport clerks (ISCO=413) and unemployed/job seeking women. Corporate managers (ISCO=12) were identified with an increasing trend in lung cancer mortality over the study period with the highest statistically significant SMR found over 1995-1999 (SMR=1.88, 95%-CI=1.54-2.30); afterwards an important decrease was observed in 2000-2004, followed by a slight increase of lung cancer mortality (Table S3).

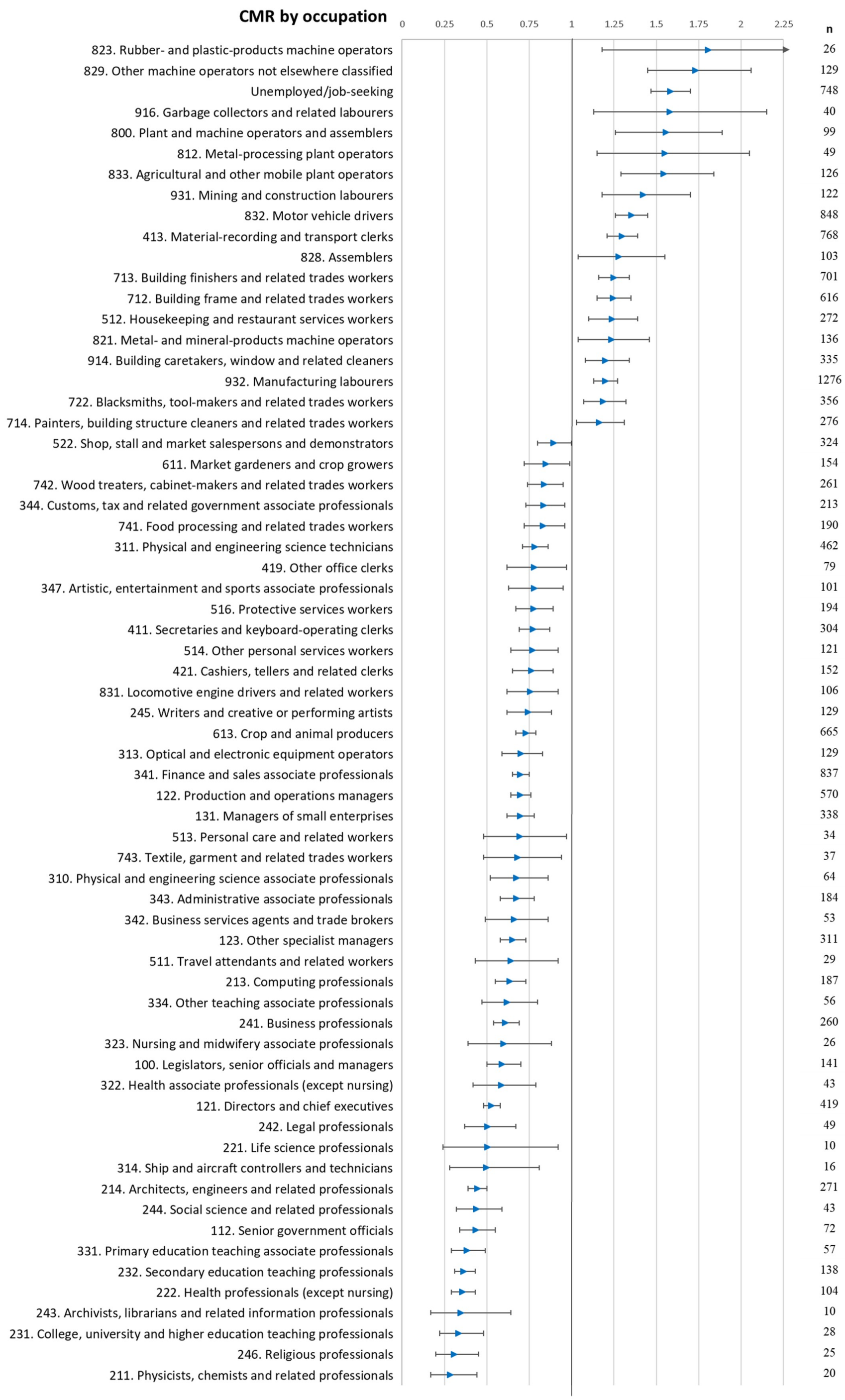

Figure 1: Causal Mortality Ratios (CMR) for mortality due to lung cancer by occupation (3-digit ISCO-88) among males aged 18-85 in the Swiss National Cohort (1990-2014). Only statistically significant results based on at least 10 deaths are presented.

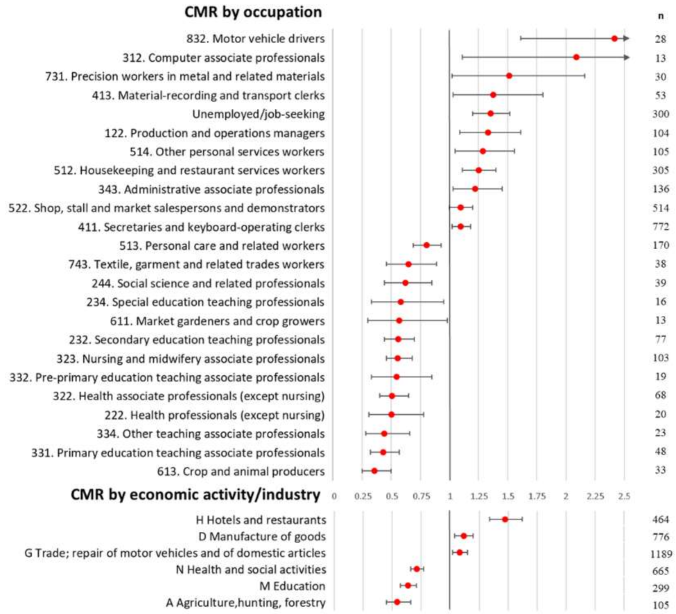

Figure 2: Causal Mortality Ratios (CMR) for mortality due to lung cancer by economic activity/industry (ISCI 3rd and NACE 1st revision) among females aged 18-85 in the Swiss National Cohort (1990-2014). Only statistically significant results based on at least 10 deaths are presented.

Results on rSMR (2-digit ISCO-88) were generally higher than CMR and SMR in both sexes (Table 2). Among men, plant and machine operators, and drivers (ISCO=80-83) were identified with the highest rSMR. Among women, drivers and plant operators (ISCO=83) presented the highest risk (rSMR=2.34, 95%-CI=1.62-3.39). Relative SMR also brought to light some aspects potentially masked by SMR in women. We identified female managers of small enterprises (ISCO=13), physical and engineering science associate professionals (ISCO=32) and other precision, handicraft, craft printing and related traded workers (ISCO=73) with increased risks of lung cancer mortality of 43%, 50% and 50%, respectively, compared to the general population.

Table 2 Standardized mortality ratios[a] (SMR), causal mortality ratios[a] (CMR), relative SMR (rSMR) for lung cancer* by occupation[b] in both sexes aged 18-85 : the Swiss National Cohort (1990-2014)

2-digit ISCO 88 (COM)	O	SMR	(95%CI)[c]	CMR	(95%CI)	rSMR	(95%CI)
Male							
01. Soldiers	17	0.77	(0.45-1.23)	0.77	(0.45-1.24)	1.00	(0.62-1.61)
10. Legislators, senior officials and managers	141	0.59	(0.50-0.69)	0.59	(0.50-0.70)	0.82	(0.70-0.97)
11. Legislators and senior officials	78	0.42	(0.33-0.52)	0.43	(0.34-0.53)	0.84	(0.67-1.05)
12. Corporate managers	1303	0.62	(0.58-0.65)	0.62	(0.59-0.66)	0.93	(0.88-0.98)
13. Managers of small enterprises	338	0.69	(0.62-0.77)	0.70	(0.62-0.78)	1.00	(0.90-1.11)
21. Physical, mathematical and engineering science professionals	481	0.48	(0.43-0.52)	0.49	(0.45-0.54)	0.78	(0.71-0.85)
22. Life science and health professionals	114	0.35	(0.29-0.42)	0.37	(0.30-0.44)	0.67	(0.56-0.81)
23. Teaching professionals	181	0.35	(0.31-0.41)	0.37	(0.31-0.42)	0.71	(0.61-0.82)
24. Other professionals	517	0.56	(0.51-0.61)	0.57	(0.52-0.62)	0.80	(0.73-0.87)
31. Physical and engineering science associate professionals	789	0.76	(0.71-0.82)	0.77	(0.72-0.83)	1.04	(0.97-1.12)
32. Life science and health associate professionals	81	0.58	(0.46-0.72)	0.59	(0.47-0.73)	0.78	(0.63-0.97)
33. Teaching associate professionals	113	0.46	(0.38-0.55)	0.47	(0.39-0.56)	0.79	(0.66-0.95)
34. Other associate professionals	1437	0.71	(0.68-0.75)	0.72	(0.68-0.76)	0.95	(0.90-1.00)
41. Office clerks	1214	1.06	(1.01-1.13)	1.06	(1.00-1.12)	1.14	(1.08-1.21)
42. Customer services clerks	171	0.77	(0.66-0.89)	0.77	(0.66-0.90)	0.99	(0.85-1.15)
51. Personal and protective services workers	650	0.90	(0.83-0.97)	0.90	(0.83-0.97)	1.01	(0.94-1.09)
52. Models, salespersons and demonstrators	324	0.89	(0.80-1.00)	0.89	(0.80-1.00)	1.07	(0.96-1.20)
61. Skilled agricultural and fishery workers	890	0.75	(0.70-0.80)	0.77	(0.72-0.82)	0.96	(0.90-1.02)
71. Extraction and building trades workers	1620	1.23	(1.17-1.29)	1.23	(1.17-1.29)	1.33	(1.27-1.40)
72. Metal, machinery and related trades workers	1430	1.04	(0.98-1.09)	1.04	(0.99-1.09)	1.17	(1.11-1.24)
73. Precision, handicraft, craft printing and related trades workers	276	0.90	(0.80-1.02)	0.92	(0.81-1.03)	1.16	(1.03-1.31)
74. Other craft and related trades workers	512	0.81	(0.75-0.89)	0.82	(0.75-0.90)	0.97	(0.89-1.06)
80. Plant and machine operators and assemblers	99	1.58	(1.30-1.93)	1.56	(1.26-1.89)	1.64	(1.35-2.00)
81. Stationary plant and related operators	110	1.17	(0.97-1.42)	1.17	(0.96-1.41)	1.26	(1.04-1.52)
82. Machine operators and assemblers	592	1.23	(1.13-1.33)	1.22	(1.12-1.32)	1.35	(1.24-1.46)
83. Drivers and mobile plant operators	1082	1.27	(1.20-1.35)	1.27	(1.20-1.35)	1.34	(1.27-1.43)
91. Sales and services elementary occupations	494	1.18	(1.08-1.29)	1.17	(1.07-1.28)	1.25	(1.14-1.36)
92. Agricultural,fishery and related labourers	62	1.30	(1.01-1.66)	1.27	(0.97-1.63)	1.17	(0.92-1.51)
93. Labourers in mining, construction, manufacturing and transport	1401	1.27	(1.20-1.34)	1.22	(1.15-1.28)	0.99	(0.94-1.04)
Unemployed/job-seeking	748	1.69	(1.58-1.82)	1.58	(1.47-1.70)	0.95	(0.88-1.02)

Table 2 continued

2-digit ISCO 88 (COM)	O	SMR	(95%CI)[c]	CMR	(95%CI)	rSMR	(95%CI)
Female							
10. Legislators, senior officials and managers	43	0.95	(0.70-1.28)	0.95	(0.69-1.28)	1.20	(0.89-1.61)
11. Legislators and senior officials	12	0.94	(0.49-1.64)	0.94	(0.49-1.64)	1.11	(0.63-1.95)
12. Corporate managers	202	1.29	(1.12-1.48)	1.29	(1.12-1.48)	1.52	(1.32-1.74)
13. Managers of small enterprises	111	1.17	(0.97-1.41)	1.16	(0.96-1.40)	1.43	(1.19-1.73)
23. Teaching professionals	106	0.57	(0.47-0.69)	0.58	(0.48-0.70)	0.94	(0.78-1.13)
24. Other professionals	132	0.68	(0.58-0.81)	0.69	(0.58-0.82)	0.93	(0.79-1.11)
31. Physical and engineering science associate professionals	97	1.18	(0.96-1.43)	1.18	(0.96-1.44)	1.50	(1.23-1.84)
32. Life science and health associate professionals	171	0.53	(0.46-0.62)	0.54	(0.46-0.62)	0.75	(0.65-0.88)
33. Teaching associate professionals	90	0.45	(0.37-0.55)	0.45	(0.36-0.56)	0.75	(0.61-0.92)
34. Other associate professionals	394	1.02	(0.93-1.13)	1.03	(0.93-1.13)	1.31	(1.19-1.45)
41. Office clerks	969	1.06	(1.00-1.13)	1.07	(1.00-1.14)	1.35	(1.27-1.44)
42. Customer services clerks	177	1.10	(0.95-1.28)	1.11	(0.95-1.28)	1.33	(1.15-1.54)
51. Personal and protective services workers	600	1.06	(0.97-1.14)	1.06	(0.98-1.15)	1.25	(1.16-1.36)
52. Models, salespersons and demonstrators	514	1.09	(1.00-1.19)	1.10	(1.00-1.20)	1.32	(1.21-1.44)
61. Skilled agricultural and fishery workers	48	0.40	(0.30-0.53)	0.40	(0.30-0.53)	0.56	(0.43-0.75)
72. Metal, machinery and related trades workers	29	1.16	(0.78-1.66)	1.16	(0.78-1.67)	1.46	(1.01-2.10)
73. Precision, handicraft, craft printing and related trades workers	54	1.33	(1.02-1.73)	1.33	(1.00-1.73)	1.50	(1.15-1.95)
74. Other craft and related trades workers	54	0.69	(0.53-0.90)	0.70	(0.52-0.91)	0.93	(0.71-1.21)
82. Machine operators and assemblers	62	1.10	(0.86-1.41)	1.10	(0.84-1.40)	1.21	(0.94-1.55)
83. Drivers and mobile plant operators	28	2.15	(1.43-3.10)	2.14	(1.42-3.09)	2.34	(1.62-3.39)
91. Sales and services elementary occupations	293	1.02	(0.91-1.15)	1.02	(0.91-1.15)	1.25	(1.12-1.40)
93. Labourers in mining, construction, manufacturing and transport	264	1.15	(1.02-1.30)	1.14	(1.01-1.29)	1.05	(0.93-1.18)
Unemployed/job-seeking	300	1.38	(1.24-1.55)	1.35	(1.20-1.52)	0.91	(0.81-1.01)

*Only results based on at least 10 deaths from lung cancer for each category are presented.[a] Based on the mortality rates of Swiss population (15-85y), [b] based on the International Standard Classification of Occupations (3-digit ISCO 88), [c] 95%-Confidence interval.
O, observed number of deaths, rSMR, relative SMR

Risk of lung cancer by economic activity/industry

Table S4 presents CMR, rSMR and SMR for each economic activity/industry in both sexes. Our results showed that working in hotel and restaurant was associated with a higher risk of death by lung cancer in both sexes (Fig. 2-3). Among men, working in construction industry was identified with an excess of lung cancer mortality, though the highest risk was observed in mining and quarrying industry (CMR=1.68, 95%-CI=1.36-2.06). A statistically significant trend was also observed in men working in construction, with the highest statistically significant SMR found over the period 1990-1994 (SMR=1.27, 95%-CI=1.17-1.39) (Table S2). Among women, industries of trade, repair of motor vehicles and of domestic articles, and manufacture of goods were observed with CMR and SMR significantly higher than one (Table S4).

Moreover, rSMR identified men working in manufacture of goods, and in transport and communication at higher risk of lung cancer mortality with, respectively, a 14% and 12% increased risk, compared to the general Swiss male population. Female workers in construction (rSMR=1.33, 95%-CI=1.11-1.58) and in domestic services (rSMR=1.72, 95%-CI=1.18-2.51) were also found to have significantly increased rSMR.

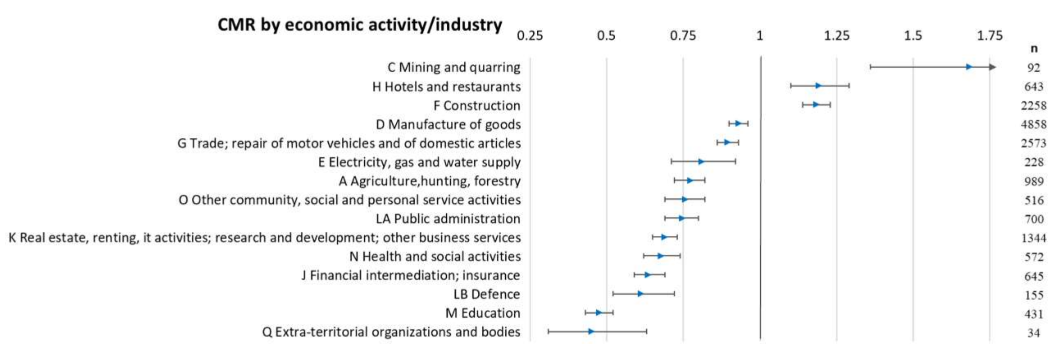

Figure 3: Causal Mortality Ratios (CMR) for mortality due to lung cancer by occupation (3-digit ISCO-88) and economic activity/industry (ISCI 3rd and NACE 1st revision) among men aged 18-85 in the Swiss National Cohort (1990-2014). Only statistically significant results based on at least 10 deaths are presented.

Risk of lung cancer by work-related variables

The stratified analyses showed that non-Swiss men had a higher risk of mortality from lung cancer compared to the general Swiss population (CMR=1.10, 95%- CI= 1.07-1.13) (Table S5). Conversely, non-Swiss women presented a deficit of mortality (CMR=0.77, 95%-CI=0.73-0.82), while Swiss women were identified with an excess (CMR=1.07, 95%-CI=1.06-1.09). In men, we observed an increased risk of lung cancer mortality when the occupation's skill-level decreased. In women, only occupations with the second lowest skill-level presented a 4%-increased risk of lung cancer mortality.

Discussion

Nationwide studies comparing the risk of lung cancer mortality across occupations and economic activities/industries were recently conducted in Korea and Japan. Lee et al. (Lee et al. 2020) found that Korean men working in services/sales and blue-collar occupations had the highest lung cancer rates, while in Japan, the highest rates were observed in unemployed men (Eguchi et al. 2017). Occupational inequalities in female were also identified in Japan, with lower risk of lung cancer among women with high socioeconomic status, even after adjusting for smoking (Zaitsu et al. 2018). In Switzerland, the last epi-study (conducted 20 years ago) only provided odd ratios by occupation and socioeconomic group for males aged 25 to 65 (Bouchardy et al. 2002). In our study, we used three risk estimates of lung cancer mortality; the SMR – to enable comparison of the results with other national and international studies; the CMR – to enable a less bias estimation of mortality; and the rSMR – to control for the healthy worker effect often present in occupational cohorts.

Occupational groups at risk

Our results confirmed an invert socio-economic gradient in lung cancer mortality (Hovanec et al. 2018; Pukkala et al. 2009). In both sexes, the risk increased as the skill level decreased. Previous studies showed that this gradient remained after adjusting for smoking and education, although the effect was greater among men than women (Hovanec et al. 2018). Prior findings (Vanthomme et al. 2017) also showed that unemployed individuals were at higher risk of lung cancer mortality than the general population.

In line with previous reports (EU-OSHA 2014a; Jung et al. 2018), male and female motor vehicle drivers were identified with an excess of lung cancer mortality. A more detailed analysis by 4-digit ISCO-88 identified female car, taxi and van drivers with the highest mortality excess. Despite a relatively small number of observed deaths (n=10), lung cancer mortality was more than three times higher than in the general population (CMR=3.34, 95%-CI=1.60-6.14) (Table S6). This may partly be explained by exposure to diesel exhaust (Silverman 2017), classified as Group 1 human carcinogens by IARC but as group 2A (probable human carcinogens) by SUVA (Shankar et al. 2019; SUVA 2018). We found no studies assessing risk for female workers in metal and related materials. Further investigation would be necessary. In men, the highest excess of lung cancer mortality found in rubber- and plastic-products machine operators is also consistent with prior studies, although the evidence of aromatic amines carcinogenicity in humans is still limited (Brown et al. 2012). In addition, four other occupational groups of operators were identified in the ten most at-risk groups (Fig. 1). Previous studies revealed that the risk remained in these groups even after adjusting for sex, age, smoking, and socio-economic status, except for motorised farm machinery operators identified with a non-significant deficit of lung cancer mortality (Corbin et al. 2011; Pukkala et al. 2009). Thus, the 54%-increased risk of lung cancer mortality we found in agricultural and other mobile operators (ISCO=833) deserves further analyses. Lastly, the extent to which garbage collectors are exposed to carcinogens is less clear. There is considerable potential for hazardous exposure through waste management (Rushton 2003).

Economic activities/industries at risk

Each industry/economic activity is likely to have its own combination of potentially carcinogenic exposures, which can be related to the excess of lung cancer mortality identified in this study.

For instance, the high prevalence of smoking among men and women working in hotels and restaurants might explained the increased risk of lung cancer mortality compared to the general population (Daly et al. 2010; Lopez et al. 2006). In contrast, the deficit of lung cancer mortality observed among workers in agriculture, hunting and forestry might be related to a low smoking frequency in this industry (Boulanger et al. 2018).

The significant excess of lung cancer mortality identified in men working in mining, quarrying and construction is probably due to workplace exposures to carcinogens such as silica dust, asbestos, radon and diesel engine exhaust (Brown et al. 2012; Jung et al. 2018; Pukkala et al. 2009). Moreover, the decreasing trend of lung cancer mortality we observed across calendar periods in men working in construction, especially after asbestos prohibition in 1990 in Switzerland is in line with previous findings showing that construction workers at higher risk of asbestos-related lung cancer presented the same risk as the general population a few decades after cessation of exposure (Jarvholm and Astrom 2014). However, male construction workers remained at risk over 2010-2014, which deserves further analysis.

In women, the excess of lung cancer mortality observed in trade, repair of motor vehicles and of domestic articles was in line with prior reports (EU-OSHA 2014a; Pukkala et al. 2009). Moreover, a more detailed analysis of the economic activity of manufacture of goods revealed that manufacture of electrical and electronic equipment, manufacture of machinery and equipment, and manufacture of chemicals and chemical products presented statistically significant increased risks of lung cancer mortality of 22%, 31% and 65%, respectively. Exposures to IARC Group 1 carcinogens, including strong inorganic acid mists, hexavalent chromium, cobalt, crystalline silica, lead or benzo(a)pyrene and beryllium, were previously identified in these activities and may partially explain this finding (Brown et al. 2012).

Potential underreporting of lung cancer for recognition as occupational disease

Although the Swiss Ordinance of Accident Insurance lists quite exhaustively occupational carcinogenic agents, mesothelioma constitutes the large majority of cancers recognized as occupational by Suva (OFSP 2015). No study has ever evaluated the extent of underreporting and resulting underestimation of number occupational diseases, including lung cancer. However, Swiss physicians acknowledge an underreporting of cases, namely because of too stringent conditions enabling Suva to recognize a case as occupational disease. Swiss physicians also ignore or underestimate the Suva recognition rates (Graczyk et al. 2021). Despite a descriptive nature of this study, we showed that the most at-risk occupations are those, where exposure to lung carcinogens were consistently documented. Therefore, the underreporting of lung cancers to Suva raises a concern, which should be addressed.

Limitations and strengths

One of the main strengths of this study lies in the use of standardized national and international classifications, which allowed us to compare our results with other studies (Guseva Canu et al. 2019a). Moreover, using one of the largest longitudinal datasets worldwide with a 24-year long follow-up at the population level was another strength of this study. We defined occupational settings to approximate the exposure to occupational carcinogens before the outcome of interest occurred, limiting any information bias. Lastly, information on Swiss death certificates was found to be satisfactory with most of malignant neoplasms (Spoerri et al. 2010).

In terms of limitations, we were not able to classify 34% and 53% of occupations in men and women, corresponding to 67% and 47% of all lung cancer deaths, respectively. A prior report comparing participants with known and unknown occupations by main sociodemographic variables did not find any potential for selection bias (Guseva Canu et al. 2019a). This bias might, though, come from the overrepresentation of elementary occupations in participants lost to follow-up. However, a potential underestimation of the number of lung cancer deaths in this occupational group is unlikely, as participants lost to follow-up were on average too young to die from lung cancer, with a mean age at baseline of 33.0 ± 11.8 years in men and 32.3 ± 12.0 years in women. Having only two time points for defining occupations is another limitation, which raises the concern of exposure misclassification. Indeed, information on the longest-held occupation might better reflect long-term exposure to carcinogens (Zaitsu et al. 2019), although information on occupation and industry, when available, was found to be accurate (Vienneau et al. 2017). Lastly, our results should be interpreted with caution as no adjustment for smoking was applied in the analyses, which may have led to an overestimation of lung cancer mortality in occupational or industrial groups with a high smoking prevalence. A job-exposure matrix (JEM) of the lifestyle factors in different occupations was recently developed in Denmark (Bondo Petersen et al. 2018). However, Danish estimates of smoking prevalence differ from those in Switzerland (OFS 2018). Therefore, the need of prior validation of this JEM for Switzerland precluded its use in this study. Given the PAF of lung cancer due to occupational exposures (19.3% in men and 2.6% in women) (Jung et al. 2018; Rushton et al. 2012), improving data quality on occupation and potential confounders is particularly important to identify more accurately the most at-risk occupational groups.

Concluding remarks

This study reports the risk of lung cancer mortality across occupational and industrial groups by sex at a national level. It is descriptive in nature but provides some important insights from both methodological and public health perspectives. It demonstrates that SMR remains a good approximation of mortality in both occupational and general cohorts, though rSMR helped to correct the healthy worker effect, which is usually present in SMR.

Our results, based on both SMR and CMR estimates, demonstrate that 18 out of 95 occupations in men, 10 out of 55 occupations in women and 3 economic activities/industries in each sex present significantly higher risk of lung cancer mortality than the general Swiss population. Occupational exposures to lung carcinogens were consistently documented in most of these activities and occupations. Moreover, our study demonstrated that Swiss workers had no particular profile of mortality from lung cancer by occupational group and sex, compared to other developed countries (Corbin et al. 2011; EU-OSHA 2014a; Hovanec et al. 2018; Jung et al. 2018; Pukkala et al. 2009; Silverman 2017). This suggests that part of the excessive lung cancer mortality observed in these groups could be due to occupational carcinogens. However, further analyses are needed to examine the extent to which the excess of mortality observed in most at-risk occupational groups is due to active smoking, second hand smoking, occupational or environmental exposures. This would allow tailoring effective interventions targeted at the most at-risk groups and the assessment of the efficacy of the current system of reporting and recognizing occupational lung cancers.

References

Collaborators GBDRF. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet (London, England). 2017;390(10100):1345-422.

NICER. Cancer Incidence and Mortality in Switzerland 2019 [Available from: https://www.nicer.org/NicerReportFiles2018/EN/report/atlas.html?&geog=0.

Jung JKH, Feinstein SG, Palma Lazgare L, Macleod JS, Arrandale VH, McLeod CB, et al. Examining lung cancer risks across different industries and occupations in Ontario, Canada: the establishment of the Occupational Disease Surveillance System. Occupational and environmental medicine. 2018;75(8):545-52.

Rushton L, Hutchings SJ, Fortunato L, Young C, Evans GS, Brown T, et al. Occupational cancer burden in Great Britain. British journal of cancer. 2012;107 Suppl 1:S3-7.

Bouchardy C, Schuler G, Minder C, Hotz P, Bousquet A, Levi F, et al. Cancer risk by occupation and socioeconomic group among men--a study by the Association of Swiss Cancer Registries. Scandinavian journal of work, environment & health. 2002;28 Suppl 1:1-88.

OFSP. Amiante : aspects cliniques et mesures préventives. In: Publique OFdlS, editor. 2015. p. 2.

Guillemin M. Santé au travail : le déni des politiques publiques. REISO, Revue d'information sociale. 2018.

Guseva Canu I, Francois M, Graczyk H, Vernez D. Healthy worker, healthy citizen: the place of occupational health within public health research in Switzerland. International journal of public health. 2019.

de Groot PM, Wu CC, Carter BW, Munden RF. The epidemiology of lung cancer. Transl Lung Cancer Res. 2018;7(3):220-33.

Spoerri A, Zwahlen M, Egger M, Bopp M. The Swiss National Cohort: a unique database for national and international researchers. International journal of public health. 2010;55(4):239-42.

SFSO. Methodology report—coverage estimation for the Swiss population census 2000. Swiss Federal Statistical Office, Neuchâtel, pp 1–147. Available from https://www.bfs.admin.ch/bfsstatic/dam/assets/341896/master. Accessed 27 August 2018. 2004.

Guseva Canu I, Bovio N, Mediouni Z, Bochud M, Wild P, Swiss National C. Suicide mortality follow-up of the Swiss National Cohort (1990-2014): sex-specific risk estimates by occupational socio-economic group in working-age population. Soc Psychiatry Psychiatr Epidemiol. 2019.

Richardson DB, Keil AP, Cole SR, MacLehose RF. Observed and Expected Mortality in Cohort Studies. American journal of epidemiology. 2017;185(6):479-86.

Shrestha S, Parks CG, Keil AP, Umbach DM, Lerro CC, Lynch CF, et al. Overall and cause-specific mortality in a cohort of farmers and their spouses. Occupational and environmental medicine. 2019;76(9):632-43.

Breslow NE, Day NE. Statistical methods in cancer research. Volume II--The design and analysis of cohort studies. IARC Sci Publ. 1987(82):1-406.

OFS. Catégories socioprofessionnelles (CSP) 2010 Opérationnalisation des CSP dans le système des variables-clés SHAPE dès 2010. Neuchâtel2016. p. 19.

ILO. International Standard Classification of Occupations 2008 (ISCO-08): Structure, group definitions and correspondence tables2012. 476 p.

Lee H-E, Zaitsu M, Kim E-A, Kawachi I. Occupational Class and Cancer Survival in Korean Men: Follow-Up Study of Nation-Wide Working Population. International journal of environmental research and public health. 2020;17(1):303.

Eguchi H, Wada K, Prieto-Merino D, Smith DR. Lung, gastric and colorectal cancer mortality by occupation and industry among working-aged men in Japan. Scientific Reports. 2017;7(1):43204.

Zaitsu M, Kaneko R, Takeuchi T, Sato Y, Kobayashi Y, Kawachi I. Occupational inequalities in female cancer incidence in Japan: Hospital-based matched case-control study with occupational class. SSM - population health. 2018;5:129-37.
Hovanec J, Siemiatycki J, Conway DI, Olsson A, Stucker I, Guida F, et al. Lung cancer and socioeconomic status in a pooled analysis of case-control studies. PLoS One. 2018;13(2):e0192999.
Pukkala E, Martinsen JI, Lynge E, Gunnarsdottir HK, Sparen P, Tryggvadottir L, et al. Occupation and cancer - follow-up of 15 million people in five Nordic countries. Acta oncologica (Stockholm, Sweden). 2009;48(5):646-790.
Vanthomme K, Van den Borre L, Vandenheede H, Hagedoorn P, Gadeyne S. Site-specific cancer mortality inequalities by employment and occupational groups: a cohort study among Belgian adults, 2001-2011. BMJ Open. 2017;7(11):e015216.
EU-OSHA. Exposure to carcinogens and work-related cancer: A review of assessment methods. Executive summary. Luxembourg: European Agency for Safety and Health at Work (EU-OSHA); 2014.
Silverman DT. Diesel exhaust causes lung cancer: now what? Occupational and environmental medicine. 2017;74(4):233-4.
Shankar A, Dubey A, Saini D, Singh M, Prasad CP, Roy S, et al. Environmental and occupational determinants of lung cancer. Transl Lung Cancer Res. 2019;8(Suppl 1):S31-S49.
SUVA. Valeurs limites Valeurs actuelles VME/VLE 2018 [Available from: https://www.suva.ch/fr-CH/materiel/directives-et-textes-de-lois/grenzwerte-am-arbeitsplatz-mak-werte-applikation/#59317A47178F431595269A7BB5018B2A=%2F%3Flang%3Dfr-CH.
Brown T, Darnton A, Fortunato L, Rushton L, British Occupational Cancer Burden Study G. Occupational cancer in Britain. Respiratory cancer sites: larynx, lung and mesothelioma. British journal of cancer. 2012;107 Suppl 1:S56-70.
Corbin M, McLean D, Mannetje A, Dryson E, Walls C, McKenzie F, et al. Lung cancer and occupation: A New Zealand cancer registry-based case-control study. American journal of industrial medicine. 2011;54(2):89-101.
Rushton L. Health hazards and waste management. Br Med Bull. 2003;68:183-97.
Lopez MJ, Nebot M, Juarez O, Ariza C, Salles J, Serrahima E. [Estimation of the excess of lung cancer mortality risk associated to environmental tobacco smoke exposure of hospitality workers]. Med Clin (Barc). 2006;126(1):13-4.
Daly BJ, Schmid K, Riediker M. Contribution of fine particulate matter sources to indoor exposure in bars, restaurants, and cafes. Indoor Air. 2010;20(3):204-12.
Boulanger M, Tual S, Lemarchand C, Guizard AV, Delafosse P, Marcotullio E, et al. Lung cancer risk and occupational exposures in crop farming: results from the AGRIculture and CANcer (AGRICAN) cohort. Occupational and environmental medicine. 2018;75(11):776-85.
Jarvholm B, Astrom E. The risk of lung cancer after cessation of asbestos exposure in construction workers using pleural malignant mesothelioma as a marker of exposure. Journal of occupational and environmental medicine. 2014;56(12):1297-301.
Graczyk H, Francois M, Krief P, Guseva Canu I. Recognition of occupational diseases in Switzerland: A critical review of the Swiss occupational disease list. 2020 (submitted)
Zaitsu M, Kaneko R, Takeuchi T, Sato Y, Kobayashi Y, Kawachi I. Occupational class and male cancer incidence: Nationwide, multicenter, hospital-based case-control study in Japan. Cancer medicine. 2019;8(2):795-813.
Vienneau D, de Hoogh K, Hauri D, Vicedo-Cabrera AM, Schindler C, Huss A, et al. Effects of Radon and UV Exposure on Skin Cancer Mortality in Switzerland. Environmental health perspectives. 2017;125(6):067009. 2020 (submitted)
Bondo Petersen S, Flachs EM, Prescott EIB, Tjonneland A, Osler M, Andersen I, et al. Job-exposure matrices addressing lifestyle to be applied in register-based occupational health studies. Occupational and environmental medicine. 2018;75(12):890-7.

OFS. Consommation de tabac par âge, sexe, région linguistique, niveau de formation 2018 [Available from: https://www.bfs.admin.ch/bfs/fr/home/statistiques/sante/determinants/tabac.assetdetail.6466022.html.

Supplemental Material

SEX-SPECIFIC RISKS AND TRENDS IN LUNG CANCER MORTALITY ACROSS OCCUPATIONS AND ECONOMIC ACTIVITIES IN SWITZERLAND (1990-2014)

Nicolas Bovio[1], David B. Richardson[2], and Irina Guseva Canu[1] for the Swiss National Cohort (SNC).

[1] Department of Occupational and Environmental Health, Center for Primary Care and Public Health (unisanté), University of Lausanne, Lausanne, Switzerland.

[2] Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA

SUPPLEMENTARY MATERIAL TABLES

Table S1 CMR[a] and SMR[b] for lung cancer* by occupation[c]: the Swiss National Cohort (1990-2014)

3-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
010. Armed forces	-	-	-	-	-	17	0.77	(0.45-1.24)	0.77	(0.45-1.23)
100. Legislators, senior officials and managers, nos[e]	43	0.95	(0.69-1.28)	0.95	(0.69-1.28)	141	0.59	(0.50-0.70)	0.59	(0.49-0.69)
112. Senior government officials	-	-	-	-	-	72	0.44	(0.34-0.55)	0.43	(0.33-0.54)
121. Directors and chief executives	49	1.35	(1.00-1.78)	1.35	(1.00-1.78)	419	0.53	(0.48-0.58)	0.52	(0.47-0.57)
122. Production and operations managers	104	1.33	(1.09-1.61)	1.33	(1.09-1.62)	570	0.70	(0.64-0.76)	0.69	(0.64-0.75)
123. Other specialist managers	49	1.16	(0.86-1.54)	1.17	(0.86-1.54)	311	0.65	(0.58-0.73)	0.65	(0.58-0.72)
131. Managers of small enterprises	111	1.16	(0.96-1.40)	1.17	(0.96-1.40)	338	0.70	(0.62-0.78)	0.69	(0.62-0.77)
211. Physicists, chemists and related professionals	-	-	-	-	-	20	0.28	(0.17-0.44)	0.27	(0.17-0.42)
213. Computing professionals	21	1.45	(0.90-2.21)	1.45	(0.90-2.21)	187	0.64	(0.55-0.73)	0.62	(0.54-0.72)
214.Architects, engineers and related professionals	-	-	-	-	-	271	0.44	(0.39-0.50)	0.43	(0.38-0.48)
221. Life science professionals	-	-	-	-	-	10	0.50	(0.24-0.92)	0.49	(0.24-0.90)
222. Health professionals (except nursing)	20	0.50	(0.31-0.78)	0.49	(0.30-0.76)	104	0.36	(0.29-0.43)	0.34	(0.28-0.41)
231. College, university and higher education teaching professionals	-	-	-	-	-	28	0.33	(0.22-0.48)	0.32	(0.21-0.47)
232. Secondary education teaching professionals	77	0.56	(0.44-0.70)	0.56	(0.44-0.70)	138	0.36	(0.31-0.43)	0.35	(0.30-0.42)
234. Special education teaching professionals	16	0.58	(0.33-0.95)	0.58	(0.33-0.94)	-	-	-	-	-
241. Business professionals	46	0.86	(0.63-1.14)	0.86	(0.63-1.14)	260	0.61	(0.54-0.69)	0.60	(0.53-0.68)
242. Legal professionals	10	1.14	(0.55-2.10)	1.14	(0.55-2.09)	49	0.50	(0.37-0.67)	0.48	(0.36-0.64)
243. Archivists, librarians and related information professionals	-	-	-	-	-	10	0.35	(0.17-0.64)	0.34	(0.16-0.63)
244. Social science and related professionals	39	0.62	(0.44-0.85)	0.62	(0.44-0.84)	43	0.44	(0.32-0.59)	0.43	(0.31-0.58)
245. Writers and creative or performing artists	28	0.72	(0.48-1.04)	0.72	(0.48-1.03)	129	0.74	(0.62-0.88)	0.73	(0.61-0.87)
246. Religious professionals	-	-	-	-	-	25	0.31	(0.20-0.45)	0.29	(0.19-0.43)
310. Physical and engineering science associate professionals, nos	-	-	-	-	-	64	0.68	(0.52-0.86)	0.67	(0.52-0.86)
311. Physical and engineering science technicians	45	1.04	(0.76-1.39)	1.03	(0.75-1.38)	462	0.78	(0.71-0.86)	0.77	(0.70-0.84)
312. Computer associate professionals	13	2.09	(1.11-3.57)	2.10	(1.12-3.59)	30	0.90	(0.60-1.28)	0.90	(0.61-1.29)
313. Optical and electronic equipment operators	20	1.35	(0.82-2.08)	1.34	(0.82-2.07)	129	0.70	(0.59-0.83)	0.70	(0.58-0.83)
314. Ship and aircraft controllers and technicians	-	-	-	-	-	16	0.50	(0.28-0.81)	0.49	(0.28-0.79)
315. Safety and quality inspectors	12	0.91	(0.47-1.58)	0.90	(0.47-1.58)	88	0.95	(0.76-1.17)	0.95	(0.76-1.17)
321. Life science technicians and related associate professional	-	-	-	-	-	12	0.57	(0.30-1.00)	0.56	(0.29-0.98)
322. Health associate professionals (except nursing)	68	0.51	(0.40-0.65)	0.51	(0.39-0.64)	43	0.59	(0.42-0.79)	0.58	(0.42-0.78)
323. Nursing and midwifery associate professionals	103	0.56	(0.46-0.68)	0.55	(0.45-0.67)	26	0.60	(0.39-0.88)	0.59	(0.38-0.86)
331. Primary education teaching associate professionals	48	0.43	(0.32-0.57)	0.43	(0.31-0.57)	57	0.38	(0.29-0.49)	0.37	(0.28-0.48)
332. Pre-primary education teaching associate professionals	19	0.55	(0.33-0.85)	0.54	(0.33-0.85)	-	-	-	-	-
334. Other teaching associate professionals	23	0.44	(0.28-0.66)	0.44	(0.28-0.66)	56	0.62	(0.47-0.80)	0.61	(0.46-0.79)
340. Other associate professionals, nos	18	0.75	(0.44-1.18)	0.75	(0.44-1.18)	30	0.98	(0.66-1.40)	0.98	(0.66-1.39)
341. Finance and sales associate professionals	169	1.06	(0.91-1.23)	1.06	(0.90-1.23)	837	0.70	(0.65-0.75)	0.69	(0.64-0.74)
342. Business services agents and trade brokers	-	-	-	-	-	53	0.66	(0.49-0.86)	0.66	(0.49-0.86)
343. Administrative associate professionals	136	1.22	(1.03-1.45)	1.22	(1.02-1.44)	184	0.67	(0.58-0.78)	0.67	(0.57-0.77)
344. Customs, tax and related government associate professionals	28	1.07	(0.71-1.54)	1.07	(0.71-1.55)	213	0.84	(0.73-0.96)	0.84	(0.73-0.96)
347. Artistic, entertainment and sports associate professionals	20	0.73	(0.45-1.13)	0.73	(0.44-1.12)	101	0.78	(0.63-0.95)	0.76	(0.62-0.93)
348. Religious associate professionals	-	-	-	-	-	15	0.73	(0.41-1.20)	0.71	(0.40-1.17)
411. Secretaries and keyboard-operating clerks	772	1.10	(1.02-1.18)	1.09	(1.01-1.17)	304	0.77	(0.69-0.87)	0.78	(0.69-0.87)
412. Numerical clerks	15	1.25	(0.70-2.06)	1.25	(0.70-2.06)	-	-	-	-	-
413. Material-recording and transport clerks	53	1.38	(1.03-1.80)	1.38	(1.03-1.80)	768	1.30	(1.21-1.39)	1.31	(1.22-1.41)
414. Library, mail and related clerks	13	1.03	(0.55-1.76)	1.03	(0.55-1.76)	58	1.00	(0.76-1.29)	1.00	(0.76-1.29)

Table S1 continued

3-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
419. Other office clerks	116	0.84	(0.69-1.00)	0.84	(0.69-1.00)	79	0.78	(0.62-0.97)	0.78	(0.62-0.97)
421. Cashiers, tellers and related clerks	110	1.17	(0.96-1.41)	1.17	(0.96-1.41)	152	0.76	(0.65-0.89)	0.76	(0.64-0.89)
422. Client information clerks	67	1.01	(0.78-1.28)	1.01	(0.78-1.28)	19	0.88	(0.53-1.37)	0.89	(0.53-1.38)
511. Travel attendants and related workers	-	-	-	-	-	29	0.64	(0.43-0.92)	0.63	(0.42-0.91)
512. Housekeeping and restaurant services workers	305	1.25	(1.11-1.40)	1.25	(1.11-1.40)	272	1.24	(1.10-1.39)	1.25	(1.11-1.41)
513. Personal care and related workers	170	0.80	(0.69-0.93)	0.80	(0.68-0.93)	34	0.69	(0.48-0.97)	0.69	(0.48-0.97)
514. Other personal services workers	105	1.29	(1.05-1.56)	1.28	(1.05-1.55)	121	0.77	(0.64-0.92)	0.76	(0.63-0.90)
516. Protective services workers	17	1.06	(0.62-1.70)	1.06	(0.62-1.70)	194	0.78	(0.67-0.89)	0.77	(0.66-0.88)
522. Shop, stall and market salespersons and demonstrators	514	1.10	(1.00-1.20)	1.09	(1.00-1.19)	324	0.89	(0.80-1.00)	0.89	(0.80-1.00)
611. Market gardeners and crop growers	13	0.57	(0.30-0.98)	0.57	(0.30-0.97)	154	0.85	(0.72-0.99)	0.83	(0.71-0.98)
612. Animal producers and related workers	-	-	-	-	-	31	1.12	(0.76-1.58)	1.13	(0.77-1.60)
613. Crop and animal producers	33	0.36	(0.25-0.50)	0.35	(0.24-0.50)	665	0.73	(0.67-0.79)	0.71	(0.66-0.77)
614. Forestry and related workers	-	-	-	-	-	34	1.29	(0.90-1.81)	1.31	(0.90-1.82)
711. Miners, shotfirers, stone cutters and carvers	-	-	-	-	-	27	1.11	(0.73-1.62)	1.13	(0.74-1.64)
712. Building frame and related trades workers	-	-	-	-	-	616	1.25	(1.15-1.35)	1.25	(1.15-1.35)
713. Building finishers and related trades workers	-	-	-	-	-	701	1.25	(1.16-1.34)	1.25	(1.16-1.34)
714. Painters, building structure cleaners and related trades workers	-	-	-	-	-	276	1.16	(1.03-1.31)	1.16	(1.03-1.30)
720. Metal, machinery and related trades workers, nos	-	-	-	-	-	140	1.00	(0.84-1.18)	1.01	(0.85-1.19)
721. Metal moulders, welders, sheet-metal workers, structural-metal preparers, and related trades workers	-	-	-	-	-	91	1.14	(0.92-1.40)	1.15	(0.92-1.41)
722. Blacksmiths, tool-makers and related trades workers	-	-	-	-	-	356	1.19	(1.07-1.32)	1.19	(1.07-1.32)
723. Machinery mechanics and fitters	11	1.52	(0.76-2.72)	1.52	(0.76-2.73)	623	0.98	(0.90-1.06)	0.98	(0.90-1.06)
724. Electrical and electronic equipment mechanics and fitters	10	1.35	(0.65-2.48)	1.35	(0.65-2.48)	220	0.97	(0.84-1.10)	0.97	(0.84-1.10)
731. Precision workers in metal and related materials	30	1.51	(1.02-2.16)	1.51	(1.02-2.16)	171	1.01	(0.86-1.17)	0.99	(0.85-1.15)
732. Potters, glass-makers and related trades workers	-	-	-	-	-	11	0.78	(0.39-1.39)	0.78	(0.39-1.39)
733. Handicraft workers in wood, textile, leather and related materials	-	-	-	-	-	12	0.78	(0.41-1.37)	0.77	(0.40-1.34)
734. Craft printing and related trades workers	14	1.04	(0.57-1.74)	1.04	(0.57-1.74)	82	0.82	(0.65-1.01)	0.80	(0.64-1.00)
741. Food processing and related trades workers	-	-	-	-	-	190	0.83	(0.72-0.96)	0.82	(0.71-0.95)
742. Wood treaters, cabinet-makers and related trades workers	-	-	-	-	-	261	0.84	(0.74-0.95)	0.83	(0.73-0.94)
743. Textile, garment and related trades workers	38	0.65	(0.46-0.89)	0.64	(0.46-0.88)	37	0.68	(0.48-0.94)	0.67	(0.47-0.93)
744. Pelt, leather and shoemaking trades workers	-	-	-	-	-	24	0.82	(0.53-1.22)	0.81	(0.52-1.21)
800. Plant and machine operators and assemblers, nos	-	-	-	-	-	99	1.56	(1.26-1.89)	1.58	(1.29-1.93)
812. Metal-processing plant operators	-	-	-	-	-	49	1.55	(1.15-2.05)	1.58	(1.17-2.08)
815. Chemical-processing-plant operators	-	-	-	-	-	17	1.16	(0.68-1.86)	1.17	(0.68-1.87)
816. Power-production and related plant operators	-	-	-	-	-	35	0.96	(0.67-1.33)	0.95	(0.66-1.33)
821. Metal- and mineral-products machine operators	-	-	-	-	-	136	1.24	(1.04-1.46)	1.25	(1.05-1.48)
822. Chemical-products machine operators	-	-	-	-	-	29	1.38	(0.93-1.98)	1.40	(0.94-2.01)
823. Rubber- and plastic-products machine operators	-	-	-	-	-	26	1.81	(1.18-2.65)	1.84	(1.20-2.70)
825. Printing-, binding- and paper-products machine operators	14	1.76	(0.96-2.96)	1.77	(0.97-2.97)	94	0.92	(0.75-1.13)	0.92	(0.74-1.12)
826. Textile-, fur- and leather-products machine operators	27	0.87	(0.58-1.27)	0.87	(0.58-1.27)	33	0.83	(0.57-1.17)	0.84	(0.58-1.18)
827. Food and related products machine operators	-	-	-	-	-	37	0.94	(0.66-1.30)	0.94	(0.67-1.30)
828. Assemblers	-	-	-	-	-	103	1.28	(1.04-1.55)	1.30	(1.06-1.57)
829. Other machine operators not elsewhere classified	-	-	-	-	-	129	1.73	(1.45-2.06)	1.78	(1.48-2.11)
831. Locomotive engine drivers and related workers	-	-	-	-	-	106	0.76	(0.62-0.92)	0.76	(0.62-0.91)
832. Motor vehicle drivers	28	2.42	(1.61-3.49)	2.43	(1.62-3.51)	848	1.35	(1.26-1.45)	1.36	(1.27-1.45)

Table S1 continued

3-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
833. Agricultural and other mobile plant operators	-	-	-	-	-	126	1.54	(1.29-1.84)	1.58	(1.31-1.88)
913. Domestic and related helpers, cleaners and launderers	133	0.93	(0.78-1.11)	0.94	(0.78-1.11)	30	1.34	(0.91-1.92)	1.38	(0.93-1.97)
914. Building caretakers, window and related cleaners	131	1.11	(0.93-1.31)	1.11	(0.93-1.32)	335	1.20	(1.08-1.34)	1.20	(1.08-1.34)
915. Messengers, porters, doorkeepers and related workers	28	1.10	(0.73-1.59)	1.10	(0.73-1.59)	89	0.95	(0.76-1.16)	0.96	(0.77-1.18)
916. Garbage collectors and related labourers	-	-	-	-	-	40	1.58	(1.13-2.15)	1.63	(1.16-2.22)
921. Agricultural, fishery and related labourers	-	-	-	-	-	62	1.27	(0.97-1.63)	1.30	(0.99-1.66)
931. Mining and construction labourers	-	-	-	-	-	122	1.42	(1.18-1.70)	1.45	(1.20-1.73)
932. Manufacturing labourers	258	1.13	(1.00-1.28)	1.14	(1.01-1.29)	1,276	1.20	(1.13-1.27)	1.25	(1.18-1.32)
Unemployed/job-seeking	300	1.35	(1.20-1.52)	1.38	(1.23-1.55)	748	1.58	(1.47-1.70)	1.69	(1.57-1.82)

*Only results based on at least 10 deaths from lung cancer for each category are presented.[a] Causal mortality ratios, based on the mortality rates of Swiss population (15-85y), [b] standardized mortality ratios, based on the mortality rates of Swiss population (15-85y), [c] based on the International Standard Classification of Occupations (3-digit ISCO 88), [d] 95%-Confidence interval, [e] not otherwise specified.

Table S2 Trend and heterogeneity test on SMR[a] from lung cancer* by occupation[b] and economic activity/industry[c] in men aged 15-85 : the Swiss National Cohort (1990-2014)

Characteristics	No. of deaths	SMR 1990-1994	(95%CI)[d]	SMR 1995-1999	(95%CI)	SMR 2000-2004	(95%CI)	SMR 2005-2009	(95%CI)	SMR 2010-2014	(95%CI)	P_H[d]	P_T[e]
2-digit ISCO 88													
1. Soldiers	17	0.86	(0.23-2.20)	1.12	(0.45-2.30)	-	-	0.71	(0.15-2.08)	0.71	(0.15-2.07)	0.53	0.52
11. Legislators and senior officials	78	0.42	(0.25-0.67)	0.44	(0.28-0.65)	0.43	(0.21-0.80)	0.48	(0.27-0.77)	0.31	(0.15-0.57)	0.87	0.62
12. Corporate managers	1303	0.63	(0.56-0.70)	0.72	(0.66-0.79)	0.51	(0.43-0.61)	0.54	(0.47-0.62)	0.55	(0.47-0.63)	0.00	0.00
13. Managers of small enterprises	338	0.88	(0.18-2.57)	0.43	(0.05-1.57)	0.58	(0.46-0.72)	0.68	(0.57-0.81)	0.79	(0.67-0.94)	0.23	0.04
21. Physical, mathematical and engineering science professionals	481	0.44	(0.35-0.55)	0.46	(0.38-0.55)	0.46	(0.37-0.59)	0.49	(0.40-0.59)	0.52	(0.43-0.62)	0.81	0.21
22. Life science and health professionals	114	0.37	(0.23-0.57)	0.51	(0.37-0.70)	0.24	(0.13-0.41)	0.37	(0.24-0.53)	0.24	(0.14-0.38)	0.05	0.06
23. Teaching professionals	181	0.32	(0.21-0.46)	0.37	(0.27-0.49)	0.45	(0.32-0.62)	0.28	(0.19-0.39)	0.38	(0.28-0.52)	0.36	0.88
24. Other professionals	517	0.61	(0.50-0.76)	0.65	(0.54-0.78)	0.44	(0.35-0.56)	0.55	(0.46-0.65)	0.54	(0.45-0.65)	0.12	0.18
31. Physical and engineering science associate professionals	789	0.81	(0.70-0.95)	0.85	(0.75-0.97)	0.64	(0.53-0.79)	0.70	(0.60-0.82)	0.75	(0.64-0.87)	0.13	0.12
32. Life science and health associate professionals	81	0.46	(0.22-0.85)	0.74	(0.46-1.13)	0.64	(0.36-1.06)	0.47	(0.27-0.76)	0.58	(0.35-0.90)	0.62	0.79
33. Teaching associate professionals	113	0.40	(0.23-0.67)	0.43	(0.27-0.65)	0.30	(0.15-0.52)	0.60	(0.44-0.84)	0.48	(0.32-0.69)	0.25	0.26
34. Other associate professionals	1437	0.64	(0.57-0.72)	0.77	(0.70-0.84)	0.65	(0.56-0.76)	0.75	(0.67-0.84)	0.72	(0.64-0.81)	0.08	0.31
41. Office clerks	1214	1.03	(0.91-1.16)	1.18	(1.06-1.30)	0.91	(0.77-1.08)	1.13	(0.99-1.28)	0.98	(0.85-1.13)	0.05	0.47
42. Customer services clerks	171	0.83	(0.63-1.10)	0.75	(0.58-0.97)	0.84	(0.50-1.33)	0.51	(0.29-0.83)	0.90	(0.60-1.30)	0.41	0.72
51. Personal and protective services workers	650	0.68	(0.56-0.83)	0.92	(0.79-1.07)	0.81	(0.66-1.00)	1.04	(0.89-1.21)	1.00	(0.85-1.18)	0.01	0.00
52. Models, salespersons and demonstrators	324	0.84	(0.66-1.07)	1.00	(0.82-1.21)	0.96	(0.73-1.28)	0.62	(0.46-0.84)	1.04	(0.82-1.31)	0.06	0.95
61. Skilled agricultural and fishery workers	890	0.71	(0.62-0.81)	0.84	(0.75-0.95)	0.66	(0.54-0.80)	0.82	(0.71-0.95)	0.65	(0.55-0.77)	0.03	0.45
71. Extraction and building trades workers	1620	1.31	(1.19-1.45)	1.23	(1.12-1.34)	1.07	(0.93-1.24)	1.22	(1.09-1.37)	1.24	(1.10-1.39)	0.30	0.42
72. Metal, machinery and related trades workers	1430	1.00	(0.90-1.12)	1.10	(1.00-1.21)	1.03	(0.89-1.19)	0.96	(0.85-1.09)	1.05	(0.93-1.19)	0.51	0.77
73. Precision, handicraft, craft printing and related trades workers	276	0.98	(0.76-1.25)	0.86	(0.68-1.08)	0.73	(0.51-1.03)	0.84	(0.64-1.11)	1.09	(0.85-1.40)	0.34	0.63
74. Other craft and related trades workers	512	0.76	(0.63-0.91)	0.85	(0.73-0.99)	0.70	(0.54-0.92)	0.85	(0.70-1.05)	0.87	(0.70-1.07)	0.64	0.42
81. Stationary plant and related operators	110	0.88	(0.48-1.48)	1.51	(1.01-2.17)	0.92	(0.50-1.54)	1.41	(0.99-2.00)	1.03	(0.65-1.56)	0.26	0.89
82. Machine operators and assemblers	592	1.16	(0.98-1.37)	1.37	(1.19-1.58)	0.91	(0.70-1.18)	1.20	(0.99-1.45)	1.35	(1.12-1.63)	0.06	0.71
83. Drivers and mobile plant operators	1082	1.17	(1.02-1.33)	1.45	(1.30-1.60)	1.09	(0.91-1.31)	1.29	(1.12-1.48)	1.26	(1.09-1.45)	0.04	0.96
91. Sales and services elementary occupations	494	1.34	(1.11-1.61)	1.30	(1.09-1.55)	1.21	(0.98-1.51)	0.96	(0.78-1.18)	1.10	(0.90-1.35)	0.13	0.03
92. Agricultural,fishery and related labourers	62	1.27	(0.71-2.10)	1.40	(0.85-2.19)	1.30	(0.59-2.47)	1.41	(0.73-2.46)	0.99	(0.40-2.05)	0.95	0.70
Unemployed/job-seeking	748	1.62	(1.26-2.09)	1.89	(1.53-2.34)	1.54	(1.32-1.79)	1.46	(1.27-1.67)	2.07	(1.82-2.35)	0.00	0.13

Table S2 Continued

Characteristics	No. of deaths	SMR 1990-1994	(95%CI)[d]	SMR 1995-1999	(95%CI)	SMR 2000-2004	(95%CI)	SMR 2005-2009	(95%CI)	SMR 2010-2014	(95%CI)	P_H[d]	P_T[e]
ISIC Rev.3/NACE Rev.1/NOGA 95													
A Agriculture,hunting, forestry	989	0.69	(0.59-0.79)	0.84	(0.74-0.94)	0.62	(0.52-0.74)	0.85	(0.75-0.97)	0.72	(0.62-0.83)	0.01	0.68
C Mining and quarrying	92	1.04	(0.56-1.78)	1.96	(1.37-2.80)	1.41	(0.67-2.58)	2.23	(1.40-3.38)	1.84	(1.07-2.94)	0.21	0.14
D Manufacture of goods	4858	0.89	(0.84-0.95)	0.97	(0.92-1.02)	0.83	(0.77-0.90)	0.89	(0.83-0.95)	0.97	(0.91-1.03)	0.01	0.62
E Electricity, gas and water supply	228	0.81	(0.61-1.07)	0.85	(0.67-1.09)	0.69	(0.45-1.02)	0.88	(0.66-1.17)	0.71	(0.52-0.97)	0.77	0.62
F Construction	2258	1.27	(1.17-1.39)	1.25	(1.15-1.35)	1.05	(0.93-1.17)	1.12	(1.02-1.23)	1.14	(1.04-1.25)	0.03	0.02
G Trade; repair of motor vehicles and of domestic articles	2573	0.83	(0.76-0.91)	1.00	(0.93-1.07)	0.78	(0.70-0.87)	0.86	(0.79-0.94)	0.89	(0.82-0.97)	0.00	0.74
H Hotels and restaurants	643	1.14	(0.93-1.40)	1.19	(1.00-1.42)	1.03	(0.84-1.26)	1.30	(1.12-1.51)	1.25	(1.07-1.47)	0.40	0.29
I Transport and communication	1477	0.92	(0.82-1.02)	0.98	(0.89-1.08)	0.95	(0.82-1.10)	0.96	(0.85-1.08)	0.90	(0.80-1.02)	0.83	0.73
J Financial intermediation; insurance	645	0.60	(0.50-0.73)	0.68	(0.58-0.79)	0.52	(0.42-0.65)	0.68	(0.58-0.80)	0.59	(0.50-0.70)	0.23	0.82
K Real estate, renting, it activities; research and development; other business services	1344	0.69	(0.61-0.79)	0.74	(0.66-0.83)	0.60	(0.53-0.69)	0.60	(0.54-0.68)	0.73	(0.66-0.81)	0.02	0.68
LA Public administration	700	0.70	(0.60-0.81)	0.81	(0.72-0.92)	0.68	(0.53-0.86)	0.69	(0.57-0.84)	0.75	(0.62-0.90)	0.44	0.83
M Education	431	0.41	(0.32-0.52)	0.54	(0.45-0.65)	0.46	(0.36-0.58)	0.46	(0.37-0.56)	0.44	(0.35-0.54)	0.42	0.68
N Health and social activities	572	0.63	(0.51-0.78)	0.67	(0.56-0.81)	0.59	(0.48-0.73)	0.73	(0.62-0.86)	0.67	(0.56-0.79)	0.59	0.50
O Other community, social and personal service activities	516	0.61	(0.48-0.76)	0.78	(0.65-0.93)	0.65	(0.52-0.82)	0.84	(0.71-0.99)	0.80	(0.67-0.96)	0.13	0.07
Q Extra-territorial organizations and bodies	34	0.38	(0.15-0.79)	0.55	(0.29-0.94)	0.18	(0.02-0.64)	0.43	(0.17-0.89)	0.69	(0.23-1.62)	0.46	0.68

*Only results based on at least 10 deaths from lung cancer for each category are presented, [a] Standardized mortality ratio, based on the mortality rates of Swiss working-age (15-68y) population, [b] based on the International Standard Classification of Occupations (3-digit ISCO 88 (COM)), [c] based on the main categories of the International Standard Industrial Classification of All Economic Activities (ISIC Rev.3), the Statistical classification of economic activities in the European Community (NACE Rev.1) and the General Classification of Economic Activities (NOGA 95), [d] 95% Confidence interval, [d] p-value for heterogeneity test across SMR (1990-2014), p-value for trend test across SMR (1990-2014)

Table S3 Trend and heterogeneity test on SMR[a] for lung cancer* by occupation[b] and economic activity/industry[c] in women aged 18-85 : the Swiss National Cohort (1990-2014)

Characteristics	No. of deaths	SMR 1990-1994	(95%CI)[d]	SMR 1995-1999	(95%CI)	SMR 2000-2004	(95%CI)	SMR 2005-2009	(95%CI)	SMR 2010-2014	(95%CI)	P_H[e]	P_T[f]
2-digit ISCO 88													
11. Legislators and senior officials	12	1.71	(0.21-6.16)	0.55	(0.01-3.06)	-	-	1.40	(0.45-3.26)	1.00	(0.27-2.56)	0.42	0.82
12. Corporate managers	202	1.33	(0.99-1.79)	1.88	(1.54-2.30)	0.68	(0.34-1.21)	0.92	(0.60-1.36)	0.92	(0.61-1.33)	0.00	0.00
13. Managers of small enterprises	111	-	-	1.37	(0.28-3.99)	1.05	(0.66-1.60)	1.31	(0.97-1.76)	1.13	(0.84-1.53)	0.64	0.59
21. Physical, mathematical and engineering science professionals	27	1.25	(0.26-3.65)	1.20	(0.39-2.80)	0.77	(0.16-2.26)	1.02	(0.41-2.11)	1.14	(0.52-2.17)	0.97	0.93
22. Life science and health professionals	21	1.12	(0.31-2.88)	0.34	(0.04-1.22)	0.68	(0.22-1.59)	0.24	(0.05-0.71)	0.50	(0.20-1.03)	0.26	0.29
23. Teaching professionals	106	0.67	(0.36-1.15)	0.82	(0.54-1.20)	0.40	(0.21-0.70)	0.45	(0.28-0.68)	0.60	(0.42-0.84)	0.16	0.27
24. Other professionals	132	0.86	(0.46-1.48)	0.98	(0.63-1.46)	0.68	(0.43-1.01)	0.59	(0.42-0.83)	0.62	(0.45-0.85)	0.29	0.07
31. Physical and engineering science associate professionals	97	0.64	(0.26-1.33)	1.37	(0.88-2.04)	1.00	(0.52-1.75)	1.36	(0.90-1.98)	1.20	(0.79-1.75)	0.39	0.34
32. Life science and health associate professionals	171	0.58	(0.33-0.94)	0.54	(0.35-0.80)	0.30	(0.17-0.48)	0.57	(0.44-0.75)	0.60	(0.46-0.76)	0.14	0.39
33. Teaching associate professionals	90	0.37	(0.12-0.87)	0.65	(0.36-1.07)	0.45	(0.26-0.73)	0.49	(0.33-0.70)	0.36	(0.23-0.53)	0.46	0.29
34. Other associate professionals	394	1.25	(0.94-1.65)	0.93	(0.72-1.21)	1.02	(0.80-1.30)	0.97	(0.80-1.18)	1.04	(0.87-1.24)	0.62	0.62
41. Office clerks	969	0.98	(0.81-1.18)	1.26	(1.10-1.43)	1.06	(0.90-1.25)	1.01	(0.88-1.14)	1.02	(0.91-1.15)	0.10	0.25
42. Customer services clerks	177	1.00	(0.60-1.57)	1.10	(0.79-1.55)	0.97	(0.62-1.44)	1.25	(0.95-1.65)	1.08	(0.82-1.43)	0.84	0.66
51. Personal and protective services workers	600	0.97	(0.75-1.26)	1.23	(1.02-1.47)	1.00	(0.81-1.22)	0.96	(0.82-1.13)	1.11	(0.96-1.28)	0.28	0.95
52. Models, salespersons and demonstrators	514	1.32	(1.06-1.63)	1.06	(0.87-1.29)	0.97	(0.77-1.23)	1.12	(0.94-1.33)	1.05	(0.88-1.24)	0.37	0.30
61. Skilled agricultural and fishery workers	48	0.31	(0.12-0.64)	0.46	(0.26-0.75)	0.36	(0.12-0.84)	0.53	(0.27-0.92)	0.31	(0.13-0.60)	0.67	0.99
72. Metal, machinery and related trades workers	29	0.94	(0.26-2.42)	1.23	(0.53-2.42)	0.31	(0.01-1.74)	1.33	(0.53-2.74)	1.55	(0.71-2.94)	0.54	0.38
73. Precision, handicraft, craft printing and related trades workers	54	2.10	(1.01-3.87)	0.93	(0.37-1.92)	1.10	(0.44-2.26)	2.02	(1.25-3.08)	0.77	(0.35-1.47)	0.05	0.32
74. Other craft and related trades workers	54	0.47	(0.17-1.03)	0.59	(0.29-1.05)	0.74	(0.32-1.46)	0.76	(0.41-1.31)	0.85	(0.49-1.38)	0.73	0.16
82. Machine operators and assemblers	62	0.43	(0.12-1.10)	1.16	(0.66-1.88)	1.04	(0.45-2.05)	1.39	(0.81-2.23)	1.26	(0.74-2.02)	0.27	0.08
83. Drivers and mobile plant operators	28	2.38	(0.49-6.96)	1.99	(0.54-5.11)	2.26	(0.73-5.26)	1.95	(0.78-4.02)	2.27	(1.04-4.30)	1.00	1.00
91. Sales and services elementary occupations	293	0.97	(0.70-1.34)	1.24	(0.98-1.57)	0.73	(0.52-1.03)	1.05	(0.84-1.32)	1.03	(0.83-1.28)	0.17	0.87
Unemployed/job-seeking	300	2.40	(1.52-3.59)	1.18	(0.71-1.84)	1.22	(0.94-1.60)	1.35	(1.11-1.65)	1.42	(1.18-1.72)	0.07	0.52

Table S3 Continued

Characteristics	No. of deaths	SMR 1990-1994	(95%CI)[d]	SMR 1995-1999	(95%CI)	SMR 2000-2004	(95%CI)	SMR 2005-2009	(95%CI)	SMR 2010-2014	(95%CI)	P_H[e]	P_T[f]
ISIC Rev.3/NACE Rev.1/NOGA 95													
A Agriculture,hunting, forestry	105	0.34	(0.16-0.65)	0.52	(0.32-0.80)	0.56	(0.32-0.90)	0.69	(0.49-0.98)	0.51	(0.34-0.74)	0.41	0.29
D Manufacture of goods	776	0.96	(0.78-1.18)	1.21	(1.04-1.40)	0.97	(0.80-1.18)	1.11	(0.97-1.29)	1.19	(1.05-1.36)	0.20	0.26
E Electricity, gas and water supply	16	0.68	(0.02-3.79)	1.74	(0.48-4.47)	1.16	(0.24-3.40)	0.71	(0.15-2.08)	1.05	(0.34-2.45)	0.78	0.72
F Construction	123	1.04	(0.52-1.86)	1.14	(0.68-1.77)	1.46	(0.98-2.10)	0.93	(0.65-1.33)	0.93	(0.67-1.31)	0.39	0.32
G Trade; repair of motor vehicles and of domestic articles	1189	1.28	(1.10-1.48)	1.08	(0.94-1.23)	0.94	(0.81-1.10)	1.11	(0.99-1.24)	1.04	(0.93-1.15)	0.08	0.15
H Hotels and restaurants	464	1.14	(0.83-1.57)	1.78	(1.45-2.18)	1.47	(1.17-1.84)	1.58	(1.33-1.87)	1.33	(1.12-1.59)	0.10	0.7
I Transport and communication	205	0.68	(0.37-1.14)	1.09	(0.78-1.51)	0.82	(0.54-1.20)	1.04	(0.80-1.35)	1.13	(0.90-1.43)	0.34	0.14
J Financial intermediation; insurance	289	1.08	(0.75-1.54)	1.16	(0.88-1.52)	1.17	(0.89-1.56)	1.01	(0.80-1.28)	1.16	(0.94-1.43)	0.91	0.98
K Real estate, renting, it activities; research and development; other business services	412	0.88	(0.62-1.24)	1.30	(1.04-1.63)	0.90	(0.71-1.15)	0.94	(0.78-1.13)	0.93	(0.78-1.11)	0.11	0.28
LA Public administration	159	0.68	(0.38-1.11)	1.06	(0.76-1.46)	1.03	(0.69-1.48)	0.80	(0.58-1.10)	0.77	(0.57-1.05)	0.4	0.54
M Education	299	0.86	(0.62-1.18)	0.89	(0.69-1.13)	0.52	(0.38-0.70)	0.54	(0.43-0.69)	0.57	(0.46-0.70)	0.00	0.00
N Health and social activities	665	0.74	(0.58-0.96)	0.80	(0.66-0.97)	0.62	(0.51-0.75)	0.70	(0.61-0.81)	0.72	(0.63-0.82)	0.45	0.67
O Other community, social and personal service activities	320	0.88	(0.59-1.26)	1.22	(0.95-1.56)	0.92	(0.69-1.22)	1.01	(0.82-1.25)	1.02	(0.83-1.24)	0.53	0.94
P Domestic services	27	1.57	(0.81-2.74)	1.35	(0.75-2.22)	-	-	-	-	-	-	0.99	0.66
Q Extra-territorial organizations and bodies	15	1.94	(0.63-4.54)	0.50	(0.06-1.79)	1.25	(0.34-3.19)	0.38	(0.05-1.39)	0.54	(0.07-1.94)	0.14	0.09

*Only results based on at least 10 deaths from lung cancer for each category are presented, [a] Standardized mortality ratio, based on the mortality rates of Swiss working-age (15-85y) population, [b] based on the International Standard Classification of Occupations (3-digit ISCO 88), [c] based on the main categories of the International Standard Industrial Classification of All Economic Activities (ISIC Rev.3), the Statistical classification of economic activities in the European Community (NACE Rev.1) and the General Classification of Economic Activities (NOGA 95), [d] 95% Confidence interval, [e] p-value for heterogeneity test across SMR (1990-2014), [f] p-value for trend test across SMR (1990-2014).

Table S4 Standardized mortality ratios[a] (SMR), causal mortality ratios[a] (CMR), relative SMRs (rSMR) for lung cancer* by economic activity/industry[b]: the Swiss National Cohort (1990-2014)

ISIC Rev.3/NACE Rev.1/NOGA 95	O	E_s	SMR	(95%CI)[c]	E_c	CMR	(95%CI)	rSMR	(95%CI)
Female									
A Agriculture, hunting, forestry	105	195	0.54	(0.45-0.65)	193	0.54	(0.45-0.66)	0.77	(0.63-0.93)
D Manufacture of goods	776	697	1.11	(1.04-1.20)	693	1.12	(1.04-1.20)	1.32	(1.23-1.42)
E Electricity, gas and water supply	16	15	1.05	(0.60-1.70)	15	1.05	(0.60-1.70)	1.37	(0.84-2.23)
F Construction	123	116	1.06	(0.89-1.27)	115	1.07	(0.89-1.27)	1.33	(1.11-1.58)
G Trade; repair of motor vehicles and of domestic articles	1189	1105	1.08	(1.02-1.14)	1098	1.08	(1.02-1.15)	1.32	(1.25-1.40)
H Hotels and restaurants	464	314	1.48	(1.35-1.62)	314	1.48	(1.34-1.62)	1.59	(1.45-1.74)
I Transport and communication	205	204	1.01	(0.88-1.15)	203	1.01	(0.88-1.16)	1.24	(1.08-1.42)
J Financial intermediation; insurance	289	259	1.12	(0.99-1.25)	258	1.12	(0.99-1.26)	1.35	(1.20-1.51)
K Real estate, renting, it activities; research and development; other business services	412	423	0.97	(0.88-1.07)	421	0.98	(0.89-1.08)	1.24	(1.13-1.37)
LA public administration	159	185	0.86	(0.74-1.01)	184	0.86	(0.74-1.01)	1.11	(0.95-1.30)
LB Defence	36	43	0.84	(0.61-1.17)	43	0.84	(0.59-1.16)	1.06	(0.76-1.46)
LC Compulsory social security	10	10	0.97	(0.47-1.79)	10	0.97	(0.47-1.79)	1.18	(0.63-2.19)
M Education	299	476	0.63	(0.56-0.70)	470	0.64	(0.57-0.71)	0.97	(0.87-1.09)
N Health and social activities	665	938	0.71	(0.66-0.76)	931	0.71	(0.66-0.77)	0.90	(0.84-0.97)
O Other community, social and personal service activities	320	314	1.02	(0.91-1.14)	312	1.02	(0.92-1.14)	1.32	(1.18-1.47)
P Domestic services	27	19	1.44	(0.95-2.09)	19	1.43	(0.94-2.08)	1.72	(1.18-2.51)
Q Extra-territorial organizations and bodies	15	19	0.80	(0.45-1.32)	19	0.80	(0.45-1.33)	1.05	(0.63-1.75)
Male									
A Agriculture, hunting, forestry	989	1311	0.75	(0.71-0.80)	1281	0.77	(0.72-0.82)	0.94	(0.89-1.00)
C Mining and quarring	92	54	1.70	(1.39-2.09)	55	1.68	(1.36-2.06)	1.74	(1.42-2.14)
D Manufacture of goods	4858	5287	0.92	(0.89-0.95)	5219	0.93	(0.90-0.96)	1.14	(1.11-1.17)
E Electricity, gas and water supply	228	285	0.80	(0.70-0.91)	281	0.81	(0.71-0.92)	1.05	(0.92-1.20)
F Construction	2258	1919	1.18	(1.13-1.23)	1908	1.18	(1.14-1.23)	1.32	(1.27-1.38)
G Trade; repair of motor vehicles and of domestic articles	2573	2916	0.88	(0.85-0.92)	2875	0.89	(0.86-0.93)	1.07	(1.02-1.11)
H Hotels and restaurants	643	537	1.20	(1.11-1.29)	540	1.19	(1.10-1.29)	1.17	(1.08-1.26)
I Transport and communication	1477	1564	0.94	(0.90-0.99)	1554	0.95	(0.90-1.00)	1.12	(1.07-1.18)
J Financial intermediation; insurance	645	1036	0.62	(0.58-0.67)	1017	0.63	(0.59-0.69)	0.91	(0.84-0.98)
K Real estate, renting, it activities; research and development; other business services	1344	1996	0.67	(0.64-0.71)	1953	0.69	(0.65-0.73)	0.92	(0.87-0.97)
LA Public administration	700	946	0.74	(0.69-0.80)	938	0.75	(0.69-0.80)	1.01	(0.94-1.09)
LB Defence	155	254	0.61	(0.52-0.71)	253	0.61	(0.52-0.72)	0.85	(0.73-1.00)
LC Compulsory social security	18	25	0.73	(0.43-1.15)	25	0.73	(0.43-1.16)	0.98	(0.62-1.55)
M Education	431	932	0.46	(0.42-0.51)	905	0.48	(0.43-0.52)	0.80	(0.73-0.88)
N Health and social activities	572	860	0.67	(0.61-0.72)	845	0.68	(0.62-0.74)	0.81	(0.75-0.88)
O Other community, social and personal service activities	516	692	0.75	(0.68-0.81)	683	0.76	(0.69-0.82)	0.93	(0.85-1.01)
Q Extra-territorial organizations and bodies	34	77	0.44	(0.32-0.62)	75	0.45	(0.31-0.63)	0.81	(0.58-1.14)

*Only results based on at least 10 deaths from lung cancer for each category are presented.[a] Based on the mortality rates of Swiss population (15-85y), [b]based on the main categories of the International Standard Industrial Classification of All Economic Activities (ISIC Rev.3), the Statistical classification of economic activities in the European Community (NACE Rev.1) and the General Classification of Economic Activities (NOGA 95), [c]95%-Confidence interval.
O, observed number of deaths, E_s, expected number of deaths for SMR calculation, E_c, expected number of deaths for CMR calculation, rSMR, relative SMR

Table S5 Mortality from lung cancer* by selected socio-economic factors and by sex: the Swiss National Cohort (1990-2014)

Characteristics	Female					Male				
	n	CMR[a]	(95%CI)[b]	SMR[c]	(95%CI)	n	CMR	(95%CI)	SMR	(95%CI)
Skill level										
Lowest	559	1.07	(0.98-1.16)	1.07	(0.98-1.16)	1,957	1.21	(1.15-1.26)	1.25	(1.19-1.30)
Second lowest	2,549	1.04	(1.00-1.08)	1.04	(1.00-1.08)	8,985	1.03	(1.01-1.05)	1.02	(1.00-1.04)
Second highest	752	0.76	(0.71-0.82)	0.76	(0.71-0.81)	2,421	0.71	(0.69-0.74)	0.70	(0.68-0.73)
Highest	654	0.87	(0.81-0.94)	0.86	(0.80-0.93)	3,153	0.56	(0.54-0.58)	0.54	(0.52-0.56)
Unknown	9,963	1.06	(1.04-1.08)	1.05	(1.03-1.08)	16,394	1.10	(1.08-1.11)	1.14	(1.12-1.16)
Weekly working hours										
1 to 5 hours per week	247	0.79	(0.70-0.90)	0.79	(0.69-0.89)	171	1.04	(0.89-1.21)	1.05	(0.90-1.22)
6 to 19 hours per week	947	0.78	(0.73-0.83)	0.78	(0.73-0.83)	420	0.88	(0.80-0.97)	0.89	(0.80-0.97)
20 to 27 hours per week	976	0.87	(0.81-0.92)	0.86	(0.81-0.92)	646	1.01	(0.93-1.09)	1.03	(0.95-1.11)
28 to 35 hours per week	644	0.92	(0.85-0.99)	0.92	(0.85-0.99)	414	0.84	(0.76-0.92)	0.84	(0.76-0.93)
36 to 39 hours per week	171	0.98	(0.84-1.14)	0.98	(0.84-1.14)	190	0.76	(0.65-0.87)	0.76	(0.65-0.87)
40 to 45 hours per week	2,119	1.20	(1.15-1.25)	1.19	(1.14-1.25)	13,105	0.92	(0.90-0.93)	0.91	(0.89-0.92)
46 and more hours per week	434	0.99	(0.90-1.09)	0.99	(0.90-1.09)	3,294	0.68	(0.65-0.70)	0.66	(0.64-0.68)
Unknown	8,939	1.07	(1.04-1.09)	1.06	(1.04-1.08)	14,670	1.13	(1.11-1.15)	1.17	(1.15-1.19)
Nationality (binary)										
Swiss	13,244	1.07	(1.06-1.09)	1.05	(1.04-1.07)	27,105	0.99	(0.98-1.00)	0.95	(0.94-0.96)
Non-Swiss	1,233	0.77	(0.73-0.82)	0.76	(0.72-0.81)	5,805	1.10	(1.07-1.13)	1.07	(1.04-1.10)
Region language										
German	9,733	0.98	(0.96-1.00)	0.96	(0.94-0.98)	22,695	0.96	(0.95-0.98)	0.93	(0.91-0.94)
French	3,931	1.22	(1.18-1.26)	1.20	(1.16-1.23)	8,274	1.11	(1.09-1.14)	1.08	(1.05-1.10)
Italian	766	1.12	(1.04-1.20)	1.09	(1.02-1.17)	1,806	1.15	(1.10-1.20)	1.11	(1.06-1.16)
Rhaeto-Romansch	47	0.91	(0.67-1.21)	0.89	(0.66-1.19)	135	1.05	(0.88-1.25)	1.03	(0.86-1.22)
Civil status										
Divorced	2,527	1.68	(1.61-1.74)	1.69	(1.62-1.76)	3,828	1.43	(1.39-1.48)	1.47	(1.43-1.52)
Widowed	2,086	1.28	(1.22-1.33)	1.29	(1.23-1.34)	1,150	1.17	(1.11-1.24)	1.23	(1.16-1.30)
Single	1,488	1.12	(1.06-1.18)	1.12	(1.07-1.18)	3,472	1.16	(1.12-1.20)	1.19	(1.15-1.23)
Married	8,376	0.88	(0.86-0.90)	0.86	(0.84-0.88)	24,460	0.93	(0.92-0.95)	0.89	(0.88-0.90)
Highest education achieved										
Compulsory education or less	5,836	1.15	(1.12-1.18)	1.14	(1.11-1.17)	9,188	1.39	(1.36-1.42)	1.38	(1.35-1.41)
Upper secondary level education	7,301	1.01	(0.98-1.03)	0.99	(0.97-1.01)	17,798	1.05	(1.03-1.06)	1.01	(1.00-1.03)
Tertiary level education	1,142	0.76	(0.72-0.81)	0.75	(0.71-0.80)	5,494	0.61	(0.60-0.63)	0.58	(0.57-0.60)
Unknown	198	1.33	(1.15-1.53)	1.36	(1.18-1.57)	430	1.57	(1.43-1.73)	1.67	(1.51-1.83)

*Only results based on at least 10 deaths from lung cancer for each category are presented. [a] causal mortality ratios, based on the mortality rates of Swiss population (15-85y), [b] 95%-Confidence interval; [c] standardized mortality ratios, based on the mortality rates of Swiss population (15-85y).

Table S6 CMR[a] and SMR[b] for lung cancer* by 4-digit ISCO[c] codes in both sexes aged 18-85: the Swiss National Cohort (1990-2014)

4-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
Unemployed/job-seeking	300	1.35	(1.20-1.52)	1.38	(1.23-1.55)	748	1.58	(1.47-1.70)	1.69	(1.57-1.82)
0100. Armed forces	-	-	-	-	-	17	0.77	(0.45-1.24)	0.77	(0.45-1.23)
1000. Legislators, senior officials and managers, nos[e]	43	0.95	(0.69-1.28)	0.95	(0.69-1.28)	141	0.59	(0.50-0.70)	0.59	(0.49-0.69)
1120. Senior government officials	-	-	-	-	-	72	0.44	(0.34-0.55)	0.43	(0.33-0.54)
1210. Directors and chief executives	49	1.35	(1.00-1.78)	1.35	(1.00-1.78)	419	0.53	(0.48-0.58)	0.52	(0.47-0.57)
1222. Production and operations managers in manufacturing	12	1.56	(0.81-2.72)	1.57	(0.81-2.75)	275	0.70	(0.62-0.79)	0.70	(0.62-0.78)
1223. Production and operations managers in construction	-	-	-	-	-	28	0.85	(0.56-1.22)	0.84	(0.56-1.21)
1224. Production and operations managers in wholesale and retail trade	-	-	-	-	-	32	0.61	(0.42-0.86)	0.60	(0.41-0.85)
1225. Production and operations managers in restaurants and hotels	70	1.75	(1.36-2.21)	1.75	(1.37-2.22)	122	1.09	(0.90-1.30)	1.11	(0.92-1.32)
1226. Production and operations managers in transport, storage and communications	-	-	-	-	-	48	0.62	(0.46-0.82)	0.61	(0.45-0.82)
1227. Production and operations managers in business services enterprises	-	-	-	-	-	29	0.38	(0.26-0.55)	0.38	(0.25-0.54)
1229. Production and operations managers not elsewhere classified	-	-	-	-	-	29	0.46	(0.31-0.67)	0.46	(0.31-0.66)
1230. Other specialist managers, nos	36	1.58	(1.11-2.19)	1.59	(1.11-2.20)	200	0.71	(0.61-0.81)	0.70	(0.61-0.81)
1231. Finance and administration managers	-	-	-	-	-	23	0.61	(0.38-0.91)	0.60	(0.38-0.90)
1233. Sales and marketing managers	-	-	-	-	-	52	0.58	(0.43-0.76)	0.58	(0.43-0.75)
1312. Managers of small enterprises in manufacturing	-	-	-	-	-	44	0.59	(0.43-0.79)	0.59	(0.43-0.79)
1313. Managers of small enterprises in construction	-	-	-	-	-	29	0.69	(0.46-0.99)	0.68	(0.46-0.98)
1314. Managers of small enterprises in wholesale and retail trade	27	1.04	(0.69-1.52)	1.04	(0.69-1.52)	87	0.70	(0.56-0.87)	0.70	(0.56-0.86)
1315. Managers of small enterprises in restaurants and hotels	50	1.45	(1.08-1.92)	1.46	(1.09-1.93)	85	1.21	(0.96-1.49)	1.22	(0.98-1.51)
1316. Managers of small enterprises in transport, storage and communications	-	-	-	-	-	23	0.92	(0.58-1.38)	0.92	(0.58-1.38)
1317. Managers of small enterprises in business services enterprises	-	-	-	-	-	43	0.50	(0.36-0.67)	0.49	(0.35-0.66)
1318. Managers of small enterprises in personal care, cleaning and related services	-	-	-	-	-	11	0.62	(0.31-1.11)	0.61	(0.31-1.10)
1319. Managers of small enterprises not elsewhere classified	13	0.94	(0.50-1.61)	0.94	(0.50-1.60)	15	0.37	(0.21-0.62)	0.37	(0.21-0.61)
2113. Chemists	-	-	-	-	-	15	0.36	(0.20-0.59)	0.35	(0.20-0.58)
2131. Computer systems designers, analysts and programmers	13	1.67	(0.89-2.86)	1.68	(0.89-2.87)	109	0.56	(0.46-0.67)	0.55	(0.45-0.66)
2139. Computing professionals not elsewhere classified	-	-	-	-	-	77	0.81	(0.64-1.01)	0.80	(0.63-1.00)
2140. Architects, engineers and related professionals, nos	-	-	-	-	-	53	0.32	(0.24-0.42)	0.32	(0.24-0.42)
2141. Architects, town and traffic planners	-	-	-	-	-	111	0.50	(0.41-0.60)	0.48	(0.40-0.58)
2142. Civil engineers	-	-	-	-	-	33	0.43	(0.30-0.61)	0.42	(0.29-0.58)
2143. Electrical engineers	-	-	-	-	-	16	0.35	(0.20-0.57)	0.35	(0.20-0.56)
2145. Mechanical engineers	-	-	-	-	-	22	0.46	(0.29-0.70)	0.45	(0.29-0.69)
2149. Architects, engineers and related professionals not elsewhere classified	-	-	-	-	-	22	0.68	(0.43-1.04)	0.67	(0.42-1.01)
2221. Medical doctors	14	0.55	(0.30-0.93)	0.55	(0.30-0.92)	65	0.31	(0.24-0.40)	0.30	(0.23-0.38)
2222. Dentists	-	-	-	-	-	24	0.47	(0.30-0.70)	0.44	(0.28-0.66)
2224. Pharmacists	-	-	-	-	-	10	0.58	(0.28-1.07)	0.56	(0.27-1.02)
2310. College, university and higher education teaching professionals	-	-	-	-	-	28	0.33	(0.22-0.48)	0.32	(0.21-0.47)
2320. Secondary education teaching professionals	77	0.56	(0.44-0.70)	0.56	(0.44-0.70)	138	0.36	(0.31-0.43)	0.35	(0.30-0.42)
2340. Special education teaching professionals	16	0.58	(0.33-0.95)	0.58	(0.33-0.94)	-	-	-	-	-
2411. Accountants	-	-	-	-	-	80	0.64	(0.51-0.80)	0.63	(0.50-0.78)
2412. Personnel and careers professionals	14	0.76	(0.42-1.28)	0.76	(0.41-1.27)	21	0.49	(0.31-0.75)	0.49	(0.30-0.75)
2419. Business professionals not elsewhere classified	22	0.80	(0.50-1.22)	0.81	(0.51-1.22)	158	0.61	(0.52-0.72)	0.61	(0.52-0.71)
2420. Legal professionals, nos	-	-	-	-	-	19	0.64	(0.38-1.00)	0.64	(0.38-0.99)
2421. Lawyers	-	-	-	-	-	13	0.30	(0.16-0.51)	0.29	(0.15-0.50)

Table S6 Continued

4-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
2422. Judges	-	-	-	-	-	15	0.79	(0.44-1.30)	0.77	(0.43-1.26)
2444. Philologists, translators and interpreters	12	1.06	(0.55-1.86)	1.05	(0.54-1.84)	10	0.55	(0.27-1.02)	0.55	(0.26-1.01)
2446. Social work professionals	18	0.69	(0.41-1.09)	0.68	(0.41-1.08)	17	0.65	(0.38-1.03)	0.63	(0.37-1.01)
2451. Authors, journalists and other writers	10	0.64	(0.31-1.18)	0.64	(0.31-1.17)	46	0.63	(0.46-0.84)	0.62	(0.45-0.82)
2452. Sculptors, painters and related artists	-	-	-	-	-	40	1.17	(0.83-1.59)	1.17	(0.83-1.59)
2453. Composers, musicians and singers	-	-	-	-	-	16	0.47	(0.27-0.76)	0.46	(0.26-0.74)
2455. Film, stage and related actors and directors	-	-	-	-	-	18	0.79	(0.47-1.25)	0.78	(0.46-1.23)
2460. Religious professionals	-	-	-	-	-	25	0.31	(0.20-0.45)	0.29	(0.19-0.43)
3100. Physical and engineering science associate professionals, nos	-	-	-	-	-	64	0.68	(0.52-0.86)	0.67	(0.52-0.86)
3110. Physical and engineering science technicians, nos	-	-	-	-	-	113	0.73	(0.60-0.88)	0.73	(0.60-0.87)
3111. Chemical and physical science technicians	16	0.91	(0.52-1.47)	0.90	(0.52-1.47)	26	0.70	(0.46-1.03)	0.70	(0.45-1.02)
3112. Civil engineering technicians	-	-	-	-	-	105	0.83	(0.68-1.00)	0.82	(0.67-0.99)
3113. Electrical engineering technicians	-	-	-	-	-	11	0.61	(0.31-1.10)	0.61	(0.30-1.09)
3114. Electronics and telecommunications engineering technicians	-	-	-	-	-	10	0.57	(0.27-1.04)	0.56	(0.27-1.03)
3115. Mechanical engineering technicians	-	-	-	-	-	10	0.53	(0.26-0.98)	0.52	(0.25-0.96)
3116. Chemical engineering technicians	15	1.41	(0.79-2.33)	1.41	(0.79-2.33)	44	1.02	(0.74-1.37)	1.02	(0.74-1.38)
3118. Draughts persons	-	-	-	-	-	86	0.97	(0.77-1.20)	0.96	(0.77-1.19)
3119. Physical and engineering science technicians not elsewhere classified	-	-	-	-	-	57	0.64	(0.49-0.83)	0.64	(0.48-0.82)
3122. Computer equipment operators	10	1.88	(0.90-3.46)	1.89	(0.91-3.48)	27	0.91	(0.60-1.33)	0.92	(0.61-1.34)
3131. Photographers and image and sound recording equipment operators	-	-	-	-	-	27	0.74	(0.49-1.08)	0.73	(0.48-1.06)
3139. Optical and electronic equipment operators not elsewhere classified	-	-	-	-	-	89	0.67	(0.54-0.82)	0.67	(0.54-0.83)
3152. Safety, health and quality inspectors	12	0.95	(0.49-1.66)	0.95	(0.49-1.65)	80	0.98	(0.78-1.23)	0.99	(0.78-1.23)
3221. Medical assistants	27	0.72	(0.47-1.04)	0.71	(0.47-1.04)	-	-	-	-	-
3226. Physiotherapists and related associate professionals	14	0.39	(0.21-0.65)	0.38	(0.21-0.64)	12	0.47	(0.24-0.82)	0.46	(0.24-0.81)
3231. Nursing associate professionals	101	0.57	(0.46-0.69)	0.56	(0.46-0.68)	26	0.60	(0.39-0.88)	0.59	(0.38-0.86)
3310. Primary education teaching associate professionals	48	0.43	(0.32-0.57)	0.43	(0.31-0.57)	57	0.38	(0.29-0.49)	0.37	(0.28-0.48)
3320. Pre-primary education teaching associate professionals	19	0.55	(0.33-0.85)	0.54	(0.33-0.85)	-	-	-	-	-
3340. Other teaching associate professionals	23	0.44	(0.28-0.66)	0.44	(0.28-0.66)	56	0.62	(0.47-0.80)	0.61	(0.46-0.79)
3400. Other associate professionals, nos	18	0.75	(0.44-1.18)	0.75	(0.44-1.18)	30	0.98	(0.66-1.40)	0.98	(0.66-1.39)
3410. Finance and sales associate professionals, nos	85	1.08	(0.87-1.34)	1.08	(0.87-1.34)	343	0.68	(0.61-0.75)	0.68	(0.61-0.75)
3412. Insurance representatives	-	-	-	-	-	64	0.78	(0.60-0.99)	0.78	(0.60-0.99)
3413. Estate agents	12	1.13	(0.59-1.98)	1.13	(0.58-1.97)	45	0.70	(0.51-0.94)	0.69	(0.50-0.93)
3415. Technical and commercial sales representatives	15	0.90	(0.50-1.49)	0.90	(0.50-1.48)	199	0.83	(0.71-0.95)	0.82	(0.71-0.94)
3416. Buyers	-	-	-	-	-	35	0.56	(0.39-0.78)	0.55	(0.38-0.77)
3419. Finance and sales associate professionals not elsewhere classified	42	1.11	(0.80-1.51)	1.11	(0.80-1.50)	144	0.61	(0.52-0.72)	0.61	(0.52-0.72)
3420. Business services agents and trade brokers, nos	-	-	-	-	-	18	0.73	(0.44-1.16)	0.74	(0.44-1.16)
3422. Clearing and forwarding agents	-	-	-	-	-	11	0.80	(0.40-1.43)	0.79	(0.40-1.42)
3429. Business services agents and trade brokers not elsewhere classified	-	-	-	-	-	20	0.53	(0.32-0.81)	0.53	(0.32-0.81)
3430. Administrative associate professionals, nos	39	1.16	(0.82-1.58)	1.16	(0.82-1.59)	82	0.77	(0.61-0.96)	0.77	(0.61-0.95)
3433. Bookkeepers	87	1.32	(1.06-1.63)	1.32	(1.06-1.63)	93	0.66	(0.53-0.81)	0.65	(0.53-0.80)
3440. Customs, tax and related government associate professionals, nos	26	1.07	(0.70-1.57)	1.08	(0.70-1.58)	162	0.83	(0.71-0.97)	0.84	(0.71-0.98)
3441. Customs and border inspectors	-	-	-	-	-	34	0.86	(0.60-1.20)	0.85	(0.59-1.18)
3449. Customs, tax and related government associate professionals not elsewhere classified	-	-	-	-	-	15	1.23	(0.69-2.03)	1.26	(0.70-2.08)
3471. Decorators and commercial designers	20	0.87	(0.53-1.35)	0.86	(0.53-1.33)	92	0.80	(0.64-0.98)	0.78	(0.63-0.95)

Table S6 Continued

4-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
3480. Religious associate professionals	-	-	-	-	-	15	0.73	(0.41-1.20)	0.71	(0.40-1.17)
4110. Secretaries and keyboard-operating clerks, nos	576	1.10	(1.02-1.20)	1.10	(1.01-1.19)	285	0.79	(0.70-0.88)	0.79	(0.70-0.89)
4113. Data entry operators	10	2.33	(1.12-4.29)	2.36	(1.13-4.35)	-	-	-	-	-
4115. Secretaries	186	1.03	(0.89-1.19)	1.03	(0.89-1.19)	16	0.55	(0.31-0.89)	0.54	(0.31-0.88)
4121. Accounting and book-keeping clerks	14	1.39	(0.76-2.34)	1.39	(0.76-2.34)	-	-	-	-	-
4130. Material-recording and transport clerks, nos	-	-	-	-	-	29	0.98	(0.66-1.40)	0.98	(0.66-1.41)
4131. Stock clerks	28	1.20	(0.79-1.73)	1.20	(0.80-1.73)	546	1.32	(1.22-1.44)	1.35	(1.23-1.46)
4133. Transport clerks	22	1.59	(1.00-2.41)	1.60	(1.00-2.42)	193	1.28	(1.11-1.48)	1.30	(1.12-1.50)
4142. Mail carriers and sorting clerks	-	-	-	-	-	45	1.14	(0.83-1.53)	1.15	(0.84-1.53)
4143. Coding, proof-reading and related clerks	-	-	-	-	-	10	0.67	(0.32-1.22)	0.66	(0.32-1.21)
4190. Other office clerks	116	0.84	(0.69-1.00)	0.84	(0.69-1.00)	79	0.78	(0.62-0.97)	0.78	(0.62-0.97)
4210. Cashiers, tellers and related clerks, nos	-	-	-	-	-	12	1.12	(0.58-1.95)	1.12	(0.58-1.95)
4211. Cashiers and ticket clerks	71	1.43	(1.11-1.80)	1.43	(1.11-1.80)	-	-	-	-	-
4212. Tellers and other counter clerks	33	0.84	(0.58-1.18)	0.83	(0.57-1.17)	128	0.75	(0.62-0.89)	0.74	(0.62-0.88)
4222. Receptionists and information clerks	26	1.31	(0.86-1.92)	1.31	(0.85-1.91)	12	0.93	(0.48-1.63)	0.94	(0.49-1.64)
4223. Telephone switchboard operators	40	0.92	(0.66-1.25)	0.92	(0.65-1.25)	-	-	-	-	-
5112. Transport conductors	-	-	-	-	-	19	0.58	(0.35-0.91)	0.58	(0.35-0.90)
5120. Housekeeping and restaurant services workers, nos	22	1.60	(1.00-2.41)	1.60	(1.00-2.42)	11	1.31	(0.66-2.35)	1.33	(0.67-2.38)
5121. Housekeepers and related workers	86	1.03	(0.82-1.27)	1.03	(0.82-1.27)	25	1.32	(0.85-1.94)	1.35	(0.87-1.99)
5122. Cooks	44	0.87	(0.63-1.17)	0.87	(0.63-1.17)	160	1.12	(0.96-1.31)	1.14	(0.97-1.33)
5123. Waiters, waitresses and bartenders	153	1.59	(1.35-1.87)	1.59	(1.35-1.87)	76	1.52	(1.20-1.90)	1.53	(1.21-1.92)
5130. Personal care and related workers, nos	50	0.82	(0.61-1.08)	0.82	(0.61-1.08)	15	0.65	(0.36-1.08)	0.65	(0.36-1.07)
5131. Child-care workers	15	0.71	(0.40-1.18)	0.71	(0.40-1.17)	-	-	-	-	-
5132. Institution-based personal care workers	78	0.83	(0.66-1.04)	0.83	(0.65-1.03)	11	0.80	(0.40-1.43)	0.80	(0.40-1.43)
5133. Home-based personal care workers	24	0.70	(0.45-1.05)	0.70	(0.45-1.04)	-	-	-	-	-
5140. Other personal services workers, nos	11	1.29	(0.64-2.30)	1.29	(0.64-2.30)	59	0.66	(0.50-0.85)	0.65	(0.50-0.84)
5141. Hairdressers, barbers, beauticians and related workers	85	1.29	(1.03-1.59)	1.28	(1.02-1.58)	49	0.84	(0.62-1.11)	0.81	(0.60-1.07)
5160. Protective services workers, nos	-	-	-	-	-	35	1.06	(0.74-1.48)	1.08	(0.75-1.50)
5162. Police officers	-	-	-	-	-	85	0.61	(0.49-0.75)	0.59	(0.47-0.73)
5169. Protective services workers not elsewhere classified	-	-	-	-	-	64	1.04	(0.80-1.32)	1.05	(0.81-1.34)
5220. Shop, stall and market salespersons and demonstrators	514	1.10	(1.00-1.20)	1.09	(1.00-1.19)	324	0.89	(0.80-1.00)	0.89	(0.80-1.00)
6110. Market gardeners and crop growers, nos	-	-	-	-	-	21	1.03	(0.64-1.58)	1.04	(0.64-1.59)
6111. Field crop and vegetable growers	-	-	-	-	-	12	0.43	(0.22-0.76)	0.43	(0.22-0.74)
6112. Gardeners, horticultural and nursery growers	10	0.57	(0.27-1.04)	0.56	(0.27-1.03)	121	0.90	(0.74-1.07)	0.89	(0.74-1.06)
6120. Animal producers and related workers, nos	-	-	-	-	-	18	1.33	(0.79-2.10)	1.37	(0.81-2.17)
6130. Crop and animal producers	33	0.36	(0.25-0.50)	0.35	(0.24-0.50)	665	0.73	(0.67-0.79)	0.71	(0.66-0.77)
6141. Forestry workers and loggers	-	-	-	-	-	34	1.29	(0.90-1.81)	1.31	(0.90-1.82)
7113. Stone splitters, cutters and carvers	-	-	-	-	-	17	0.84	(0.49-1.34)	0.85	(0.49-1.36)
7120. Building frame and related trades workers, nos	-	-	-	-	-	167	1.13	(0.96-1.31)	1.13	(0.97-1.32)
7122. Bricklayers and stonemasons	-	-	-	-	-	341	1.40	(1.26-1.56)	1.41	(1.26-1.57)
7123. Concrete placers, concrete finishers and related workers	-	-	-	-	-	20	1.70	(1.04-2.63)	1.75	(1.07-2.70)
7124. Carpenters and joiners	-	-	-	-	-	84	0.97	(0.78-1.20)	0.97	(0.77-1.20)
7130. Building finishers and related trades workers, nos	-	-	-	-	-	62	1.25	(0.96-1.60)	1.26	(0.97-1.62)
7131. Roofers	-	-	-	-	-	24	1.11	(0.71-1.65)	1.10	(0.71-1.64)
7132. Floor layers and tile setters	-	-	-	-	-	96	1.39	(1.13-1.70)	1.39	(1.12-1.69)

Table S6 Continued

4-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
7133. Plasterers	-	-	-	-	-	78	1.48	(1.17-1.85)	1.48	(1.17-1.85)
7134. Insulation workers	-	-	-	-	-	30	1.61	(1.08-2.29)	1.62	(1.09-2.31)
7135. Glaziers	-	-	-	-	-	13	1.44	(0.76-2.46)	1.43	(0.76-2.45)
7136. Plumbers and pipe fitters	-	-	-	-	-	214	1.19	(1.04-1.36)	1.19	(1.03-1.36)
7137. Building and related electricians	-	-	-	-	-	152	1.08	(0.92-1.27)	1.08	(0.92-1.27)
7139. Building finishers and related trade workers not elsewhere classified	-	-	-	-	-	32	1.45	(0.99-2.05)	1.46	(1.00-2.06)
7141. Painters and related workers	-	-	-	-	-	251	1.13	(1.00-1.28)	1.13	(0.99-1.27)
7143. Building structure cleaners	-	-	-	-	-	24	1.59	(1.02-2.36)	1.57	(1.01-2.34)
7200. Metal, machinery and related trades workers, nos	-	-	-	-	-	140	1.00	(0.84-1.18)	1.01	(0.85-1.19)
7211. Metal moulders and coremakers	-	-	-	-	-	16	2.39	(1.36-3.87)	2.38	(1.36-3.87)
7212. Welders and flame cutters	-	-	-	-	-	38	1.07	(0.76-1.47)	1.08	(0.76-1.48)
7213. Sheet-metal workers	-	-	-	-	-	25	0.97	(0.63-1.43)	0.97	(0.63-1.44)
7222. Tool-makers and related workers	-	-	-	-	-	249	1.25	(1.10-1.42)	1.26	(1.11-1.42)
7223. Machine-tool setters and setter-operators	-	-	-	-	-	42	0.99	(0.72-1.34)	1.00	(0.72-1.35)
7224. Metal wheel-grinders, polishers and tool sharpeners	-	-	-	-	-	47	1.35	(0.99-1.79)	1.37	(1.00-1.82)
7230. Machinery mechanics and fitters, nos	-	-	-	-	-	441	1.07	(0.97-1.17)	1.08	(0.98-1.18)
7231. Motor vehicle mechanics and fitters	-	-	-	-	-	150	0.79	(0.67-0.93)	0.78	(0.66-0.92)
7233. Agricultural- or industrial-machinery mechanics and fitters	-	-	-	-	-	29	0.99	(0.67-1.43)	0.99	(0.66-1.41)
7240. Electrical and electronic equipment mechanics and fitters, nos	-	-	-	-	-	10	0.55	(0.27-1.02)	0.56	(0.27-1.04)
7241. Electrical mechanics fitters and services	-	-	-	-	-	133	1.05	(0.88-1.24)	1.05	(0.88-1.25)
7242. Electronics mechanics, fitters and servicers	-	-	-	-	-	42	0.86	(0.62-1.17)	0.86	(0.62-1.16)
7244. Telegraph and telephone installers and servicers	-	-	-	-	-	15	0.92	(0.51-1.51)	0.92	(0.51-1.51)
7245. Electrical line installers, repairers and cable jointers	-	-	-	-	-	20	1.07	(0.65-1.65)	1.07	(0.65-1.65)
7311. Precision-instrument makers and repairers	29	1.73	(1.16-2.49)	1.74	(1.16-2.50)	142	1.05	(0.88-1.23)	1.03	(0.87-1.22)
7313. Jewellery and precious-metal workers	-	-	-	-	-	22	0.87	(0.54-1.32)	0.84	(0.53-1.27)
7341. Compositors, typesetters and related workers	-	-	-	-	-	35	0.85	(0.59-1.18)	0.84	(0.59-1.17)
7343. Printing engravers and etchers	-	-	-	-	-	11	0.74	(0.37-1.32)	0.73	(0.36-1.30)
7345. Bookbinders and related workers	-	-	-	-	-	22	1.02	(0.64-1.55)	1.01	(0.63-1.53)
7411. Butchers, fishmongers and related food preparers	-	-	-	-	-	102	0.99	(0.81-1.20)	0.98	(0.80-1.19)
7412. Bakers, pastry-cooks and confectionery makers	-	-	-	-	-	69	0.79	(0.61-1.00)	0.78	(0.61-0.99)
7413. Dairy-products workers	-	-	-	-	-	17	0.46	(0.27-0.74)	0.46	(0.27-0.73)
7420. Wood treaters, cabinet-makers and related trades workers, nos	-	-	-	-	-	111	0.77	(0.63-0.93)	0.78	(0.64-0.93)
7422. Cabinetmakers and related workers	-	-	-	-	-	111	0.79	(0.65-0.95)	0.78	(0.64-0.94)
7423. Woodworking machine setters and setter-operators	-	-	-	-	-	28	1.19	(0.79-1.72)	1.21	(0.80-1.74)
7433. Tailors, dressmakers and hatters	16	0.59	(0.34-0.96)	0.59	(0.33-0.95)	-	-	-	-	-
7436. Sewers, embroiderers and related workers	12	0.62	(0.32-1.09)	0.62	(0.32-1.09)	-	-	-	-	-
7437. Upholsterers and related workers	-	-	-	-	-	18	1.13	(0.67-1.79)	1.11	(0.66-1.76)
7442. Shoe-makers and related workers	-	-	-	-	-	17	0.69	(0.40-1.11)	0.68	(0.40-1.09)
8000. Plant and machine operators and assemblers, nos	-	-	-	-	-	99	1.56	(1.26-1.89)	1.58	(1.29-1.93)
8122. Metal melters, casters and rolling-mill operators	-	-	-	-	-	17	1.24	(0.72-1.99)	1.26	(0.73-2.02)
8123. Metal heat-treating-plant operators	-	-	-	-	-	23	1.60	(1.01-2.39)	1.62	(1.03-2.43)
8150. Chemical-processing-plant operators, nos	-	-	-	-	-	17	1.32	(0.77-2.11)	1.33	(0.77-2.13)
8160. Power-production and related plant operators, nos	-	-	-	-	-	22	1.06	(0.67-1.61)	1.07	(0.67-1.62)
8210. Metal- and mineral-products machine operators, nos	-	-	-	-	-	10	1.15	(0.55-2.12)	1.18	(0.56-2.16)
8211. Machine-tool operators	-	-	-	-	-	109	1.15	(0.94-1.38)	1.16	(0.95-1.40)

Table S6 Continued

4-digit ISCO 88	Female					Male				
	No. of deaths	CMR	(95%CI)[d]	SMR	(95%CI)	No. of deaths	CMR	(95%CI)	SMR	(95%CI)
8212. Cement and other mineral products machine operators	-	-	-	-	-	17	2.65	(1.54-4.24)	2.67	(1.55-4.27)
8229. Chemical-products machine operators not elsewhere classified	-	-	-	-	-	26	1.39	(0.91-2.04)	1.41	(0.92-2.06)
8231. Rubber-products machine operators	-	-	-	-	-	11	3.49	(1.74-6.24)	3.59	(1.79-6.42)
8232. Plastic-products machine operators	-	-	-	-	-	15	1.34	(0.75-2.20)	1.36	(0.76-2.24)
8251. Printing-machine operators	13	1.92	(1.02-3.29)	1.93	(1.03-3.30)	88	0.94	(0.76-1.16)	0.93	(0.75-1.15)
8262. Weaving- and knitting-machine operators	-	-	-	-	-	19	0.80	(0.48-1.25)	0.81	(0.49-1.26)
8264. Bleaching-, dyeing- and cleaning-machine operators	20	0.88	(0.54-1.36)	0.88	(0.54-1.36)	11	0.87	(0.43-1.56)	0.88	(0.44-1.58)
8270. Food and related products machine operators, nos	-	-	-	-	-	11	1.65	(0.82-2.96)	1.67	(0.83-2.99)
8278. Brewers, wine and other beverage machine operators	-	-	-	-	-	23	1.14	(0.72-1.71)	1.15	(0.73-1.72)
8280. Assemblers, nos	-	-	-	-	-	98	1.27	(1.03-1.54)	1.28	(1.04-1.56)
8290. Other machine operators not elsewhere classified	-	-	-	-	-	129	1.73	(1.45-2.06)	1.78	(1.48-2.11)
8311. Locomotive engine drivers	-	-	-	-	-	36	0.67	(0.47-0.93)	0.66	(0.46-0.91)
8312. Railway brakers, signallers and shunters	-	-	-	-	-	65	0.80	(0.61-1.01)	0.80	(0.62-1.02)
8320. Motor vehicle drivers, nos	12	2.11	(1.09-3.69)	2.12	(1.09-3.70)	638	1.37	(1.27-1.48)	1.38	(1.28-1.49)
8322. Car, taxi and van drivers	10	3.34	(1.60-6.14)	3.45	(1.66-6.35)	55	1.35	(1.02-1.76)	1.38	(1.04-1.80)
8323. Bus and tram drivers	-	-	-	-	-	38	0.88	(0.62-1.21)	0.89	(0.63-1.22)
8324. Heavy truck and lorry drivers	-	-	-	-	-	117	1.43	(1.18-1.71)	1.45	(1.20-1.73)
8330. Agricultural and other mobile plant operators, nos	-	-	-	-	-	70	1.74	(1.36-2.20)	1.79	(1.39-2.26)
8333. Crane, hoist and related plant operators	-	-	-	-	-	46	1.31	(0.96-1.74)	1.33	(0.97-1.77)
9130. Domestic and related helpers, cleaners and launderers, nos	105	0.92	(0.75-1.11)	0.92	(0.75-1.11)	28	1.42	(0.94-2.05)	1.46	(0.97-2.12)
9132. Helpers and cleaners in offices, hotels and other establishments	23	0.96	(0.61-1.44)	0.96	(0.61-1.44)	-	-	-	-	-
9140. Building caretakers, window and related cleaners, nos	92	1.15	(0.92-1.41)	1.15	(0.93-1.41)	186	1.26	(1.09-1.45)	1.28	(1.11-1.48)
9141. Building caretakers	38	1.00	(0.71-1.38)	1.01	(0.71-1.38)	148	1.11	(0.94-1.30)	1.12	(0.95-1.31)
9151. Messengers, package and luggage porters and deliverers	17	1.01	(0.59-1.61)	1.01	(0.59-1.61)	69	0.97	(0.75-1.22)	0.98	(0.77-1.25)
9152. Doorkeepers, watchpersons and related workers	-	-	-	-	-	19	1.00	(0.60-1.56)	1.00	(0.60-1.57)
9161. Garbage collectors	-	-	-	-	-	19	1.26	(0.76-1.97)	1.29	(0.77-2.01)
9162. Sweepers and related labourers	-	-	-	-	-	16	1.70	(0.97-2.77)	1.79	(1.02-2.91)
9211. Farm-hands and labourers	-	-	-	-	-	60	1.23	(0.94-1.59)	1.26	(0.96-1.62)
9310. Mining and construction labourers, nos	-	-	-	-	-	40	1.58	(1.13-2.15)	1.61	(1.15-2.19)
9312. Construction and maintenance labourers: roads, dams and similar constructions	-	-	-	-	-	76	1.35	(1.06-1.69)	1.37	(1.08-1.71)
9320. Manufacturing labourers	258	1.13	(1.00-1.28)	1.14	(1.01-1.29)	1276	1.20	(1.13-1.27)	1.25	(1.18-1.32)

*Only results based on at least 10 deaths from lung cancer for each category are presented.[a] causal mortality ratios, based on the mortality rates of Swiss population (15-85y), [b] standardized mortality ratios, based on the mortality rates of Swiss population (15-85y), [c] based on the International Standard Classification of Occupations (4-digit ISCO 88), [d] 95%-Confidence interval, [e] not otherwise specified.

III. III. Modelling of lung cancer mortality rates in Swiss workers according to occupational and non-occupational exposures

In our first study, we found significant differences in lung cancer mortality between certain occupational groups and the general Swiss population. However, this study was purely descriptive. Therefore, to have a better understanding of these results, we initiated a second study that aimed at examining the effect of occupational and non-occupational exposures together on lung cancer mortality. Since smoking and radon exposure are currently the two most important risk factors for lung cancer, we adjusted our results for occupation by taking these two factors into account. The occupation was used as a proxy of all potential occupational exposures, given the unavailability of public occupational exposure data in Switzerland. We published this work in Journal of Occupational and Environmental Medicine in December 2021.

Own contribution: performed the data management, performed the statistical analyses and wrote the manuscript.

Article: Lung cancer mortality in the Swiss working population: the effect of occupational and non-occupational factors

Nicolas Bovio, MA [1], Pascal Wild, PhD [1-2], and Irina Guseva Canu, PhD [1] for the Swiss National Cohort (SNC)

[1]Department of Occupational and Environmental Health, Center for Primary Care and Public Health (unisanté), University of Lausanne, Lausanne, Switzerland
[2]INRS, Vandoeuvre Les Nancy Cedex, France

**Corresponding author:* Bovio N.
Center for Primary Care and Public Health (unisanté), University of Lausanne
Department of Occupational and Environmental Health
Rte de la Corniche 2
CH-1066 Epalinges-Lausanne
+41 21 314 47 72

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Ethics approval and consent to participate: 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.

Running title: Risk of lung cancer by occupation in Switzerland

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ABSTRACT

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, watchmaking, 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.

Keyword: longitudinal study; lung cancer; occupational exposures; Switzerland, gender differences, 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 (IARC 2021a; IARC 2021c). 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 population attributable fractions (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 (Olsson and Kromhout 2021). Accounting for 86% of all occupational cancers (GBD 2020), 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, second-hand smoke (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=5’872) (NICER). Applying the French PAF estimated at 19.3% for males and 2.6 for females(Marant Micallef et al. 2019), 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 (Suva 2017; Suva 2019), 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 (Guseva Canu et al. 2019b). 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 (Menzler et al. 2008). For smoking, data showed that 29% of Swiss adult males and 21% of females were smokers in 2015 (Gmel et al. 2016). 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 (Jakob et al. 2017).

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 (Bovio et al. 2020). 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 (Spoerri et al. 2010). Censuses were mandatory, with population coverage estimated at 98.6%(SFSO 2004). No data on smoking or radon exposure were 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 (OFS 1998), and the household radon concentration measured in 2013 by the Federal Office of Public Health (FOPH) for the latter.

Study population

The study sample comprised adults aged 18-65 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.

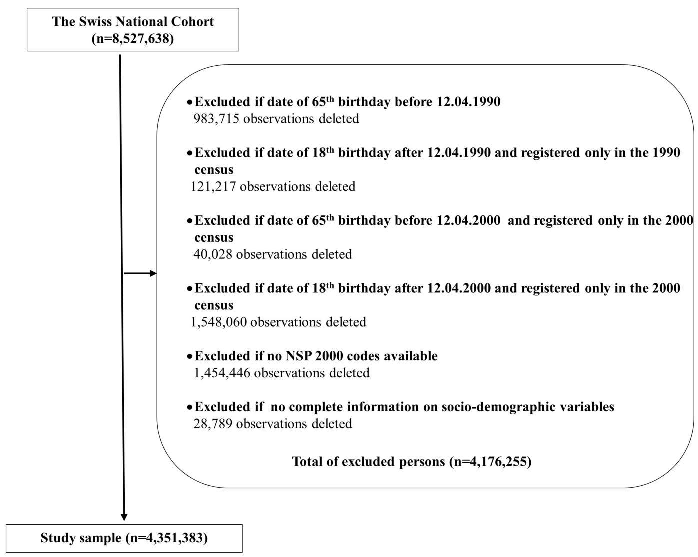

Fig. 1: Flowchart of study population selection

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 Swiss Federal

Statistical Office (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 (Greene 2012). 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 correspondent1-digit NSP code.

Concerning radon, we used the risk of exposure based on the household radon concentration in Bq/m3 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 (1990-1995, 1995-2000, 2000-2005, 2005-2010, and 2010-2014) and age group (18-35, 35-45, 45-55, 55-65 and 65+). The lung cancer mortality rate per 100'000 person-years was assessed using negative binomial regression in order to account for overdispersion (Hilbe 2011). 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 sociodemographic variables (geographical regions, marital status, education level and nationality) to assess whether these variables, previously identified as being associated with smoking (Laaksonen et al. 2005; Ramsey et al. 2019), 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) (Judge et al. 1985). 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 (Jung et al. 2018). The statistical analyses were run on STATA version 16 (StataCorp LP; TX, USA).

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 4’818 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 radon 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 (Table S1-S2). While the risk decreased over time in men, we found an opposite trend in women with the highest risk in the last calendar period (2010-2014). In both sexes, all socio-demographic 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 vs. 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.

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)*	4,818	*(100)*
Person-years (in 100,000)	386.04				293.19			
Nationality (binary)								
Swiss	1,865,423	*(78)*	13,360	*(83)*	1,636,679	*(84)*	4,415	*(92)*
Non-Swiss	537,803	*(22)*	2,715	*(17)*	311,478	*(16)*	403	*(8)*
Language region								
German and Rhaeto-Romansch	1,756,963	*(73)*	11,446	*(71)*	1,416,669	*(73)*	3,401	*(71)*
French	546,069	*(23)*	3,849	*(24)*	454,766	*(23)*	1,215	*(25)*
Italian	100,194	*(4)*	780	*(5)*	76,722	*(4)*	202	*(4)*
Civil status								
Single	707,098	*(29)*	1,649	*(10)*	599,919	*(31)*	678	*(14)*
Married	1,532,055	*(64)*	12,270	*(76)*	1,103,268	*(57)*	2,636	*(55)*
Widowed	18,413	*(1)*	1,804	*(11)*	61,036	*(3)*	404	*(8)*
Divorced	145,660	*(6)*	352	*(2)*	183,934	*(9)*	1,100	*(23)*
Highest education achieved								
Compulsory education or less	421,356	*(18)*	3,838	*(24)*	434,894	*(22)*	1,372	*(28)*
Upper secondary level education	1,304,783	*(54)*	9,246	*(58)*	1,227,791	*(63)*	2,927	*(61)*
Tertiary level education	677,087	*(28)*	2,991	*(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)*			4,818	*(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 informatio and death by lung cancer	6.9±3.8				7.6±3.8			

Adding socio-demographic variables in model 2, we observed that most of the relative risks (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 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%-IC: 2.83-3.95) to 2.42 (95%-IC: 2.05-2.87) and 2.99 (95%-IC: 2.15-4.14) to 2.08 (95%-IC: 1.50-2.89), 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 and toolmaking (from 2.69 (95%-IC: 2.02-3.57) to 2.33 (95%-IC: 1.75-3.10)) and transport and traffic occupations (from 2.43 (95%-IC: 1.91-3.09) to 2.23 (95%-IC: 1.75-2.83)). 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%).

Table 2 Relative risk (RR) and confidence interval (IC-95%) for lung cancer mortality by occupation among males aged 18-85 in the Swiss National Cohort (1990-2014)

2-digit NSP 2000[a]	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	1,009	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	1,399	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	1,847	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	4,383	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	1,460	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	1,281	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)

[a] Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits

Table 3 Relative risk (RR) and confidence interval (IC-95%) for lung cancer mortality by occupation among females aged 18-85 in the Swiss National Cohort (1990-2014)

2-digit NSP 2000[a]	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	9,902	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	5,716	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	6,554	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	1,288	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	7,024	19	1.02	1.69	[1.06,2.68]	1.52	[0.96,2.41]	1.47	[0.93,2.34]
75. Judicial occupations	6,734	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	9,449	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)

[a] Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits

Discussion

Three models were compared to estimate the effect of occupation after accounting for sociodemographic 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 (Guseva Canu et al. 2019a). 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 (EU-OSHA 2014a), 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 (Malhotra et al. 2016). 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 (Lillard 2018). 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 (Jones et al. 2010; Laaksonen et al. 2005; Lindström 2010; Ramsey et al. 2019).

Contrary to previous reports suggesting an 8%-increase in lung cancer mortality per 100 Bq/m3 (Menzler et al. 2008; Zeeb et al. 2009) 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 (Seki et al. 2013). This histologic type is less sensitive to smoking than squamous cell carcinoma, small cell carcinoma, and large cell lung cancer (Khuder 2001; Seki et al. 2013) and occurs at a young age(Kreuzer et al. 1999; Seki et al. 2013). 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 (Loomis 2020). 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 (i.e. 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 (Axelson 1989; Blair et al. 2007; Kriebel et al. 2004). 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 odds ratio (OR) of 1.61 among plant and machine operators and assemblers, after adjusting for sex, age, ethnicity, smoking, and socio-economic status (Corbin et al. 2011). 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 (Dement et al. 2020) 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 (Jung et al. 2018), 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 1.59-2.74 to 1.18-2.34, when smoking-adjusted (Taeger et al. 2015). 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 (Brown et al. 2012; Jung et al. 2018; Pukkala et al. 2009). 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 (Atramont et al. 2016; Garshick et al. 2008; Garshick et al. 2004).

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 (Bovio et al. 2020). 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 (Garshick et al. 2008; Garshick et al. 2004), 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 (EU-OSHA 2014a). 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 (Pearson et al. 2007). 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 (Lillard 2018). 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 (Spoerri et al. 2010), 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 (EU-OSHA 2014b).

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 results in some misclassification of occupational exposures. Nevertheless, the information on occupation was found to be correct (Vienneau et al. 2017) 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 (Bovio et al. 2019). As latency of solid cancers is generally 10-12 years (Kim et al. 2010) and even longer for some occupational carcinogens (up to 40 years for asbestos), a 24-y 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 (Galli et al. 2019), 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 (Turner and Mehlum 2018), 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.

References

IARC. Age-standardized 1-,5-year net survival (15–99 years) in 2010-2014, Lung, both sexes. 2021. https://gco.iarc.fr/survival/survmark/ (accessed 03.06.2021).

IARC. Estimated number of new cases in 2020, worldwide, both sexes, all ages. 2021. https://gco.iarc.fr/today/home (accessed 03.06.2021).

Olsson A, Kromhout H. Occupational cancer burden: the contribution of exposure to process-generated substances at the workplace. *Molecular oncology* 2021; **15**(3): 753-63.

Collaborators GBDOC. Global and regional burden of cancer in 2016 arising from occupational exposure to selected carcinogens: a systematic analysis for the Global Burden of Disease Study 2016. *Occupational and environmental medicine* 2020; **77**(3): 151-9.

NICER. Cancer Incidence and Mortality in Switzerland https://www.nicer.org/NicerReportFiles2018/EN/report/atlas.html?&geog=0 (accessed 03.06.2021).

Marant Micallef C, Shield KD, Vignat J, et al. Cancers in France in 2015 attributable to occupational exposures. *Int J Hyg Environ Health* 2019; **222**(1): 22-9.

Suva. Statistique des accidents LAA 2019. Lucerne, suisse, 2019.

Suva. Statistique des accidents LAA 2017. Lucerne, suisse, 2017.

Guseva Canu I, François M, Graczyk H, Vernez D. Healthy worker, healthy citizen: the place of occupational health within public health research in Switzerland. *International journal of public health* 2020; **65**(1): 111-20.

Menzler S, Piller G, Gruson M, Rosario AS, Wichmann HE, Kreienbrock L. POPULATION ATTRIBUTABLE FRACTION FOR LUNG CANCER DUE TO RESIDENTIAL RADON IN SWITZERLAND AND GERMANY. *Health Physics* 2008; **95**(2).

Gmel G, Kuendig H, Notari L, Gmel C. Monitorage suisse des addictions - Consommation d'alcool, de tabac et de drogues illégales en Suisse en 2015. *Addiction Suisse, Lausanne, Suisse* 2016.

Jakob J, Cornuz J, Diethelm P. Prevalence of tobacco smoking in Switzerland: do reported numbers underestimate reality? *Swiss medical weekly* 2017; **147**: w14437.

Bovio N, Richardson DB, Guseva Canu I. Sex-specific risks and trends in lung cancer mortality across occupations and economic activities in Switzerland (1990-2014). *Occupational and environmental medicine* 2020.

Spoerri A, Zwahlen M, Egger M, Bopp M. The Swiss National Cohort: a unique database for national and international researchers. *International journal of public health* 2010; **55**(4): 239-42.

SFSO. Methodology report—coverage estimation for the Swiss population census 2000. Swiss Federal Statistical Office. 2004. https://www.bfs.admin.ch/bfsstatic/dam/assets/341896/master (accessed 03.06.2021).

OFS. Enquête suisse sur la santé - Santé et comportements vis-à-vis de la santé en Suisse - Résultats détaillés de la première enquête suisse sur la santé 1992/93. 1998. https://www.bfs.admin.ch/bfs/fr/home/statistiques/catalogues-banques-donnees/publications.assetdetail.341000.html (accessed 03.06.2021).

Greene WH. Econometric analysis. Boston; London: Pearson; 2012.

Hilbe JM. Negative Binomial Regression. 2 ed. Cambridge: Cambridge University Press; 2011.

Laaksonen M, Rahkonen O, Karvonen S, Lahelma E. Socioeconomic status and smoking: Analysing inequalities with multiple indicators. *European journal of public health* 2005; **15**(3): 262-9.

Ramsey MW, Jr., Chen-Sankey JC, Reese-Smith J, Choi K. Association between marital status and cigarette smoking: Variation by race and ethnicity. *Preventive medicine* 2019; **119**: 48-51.

Judge GG, Griffiths WE, Hill RC, Lütkepohl H, Lee T-C. The Theory and Practice of Econometrics. 2nd ed.; 1985.

Jung JKH, Feinstein SG, Palma Lazgare L, et al. Examining lung cancer risks across different industries and occupations in Ontario, Canada: the establishment of the Occupational

Disease Surveillance System. *Occupational and environmental medicine* 2018; **75**(8): 545-52.
Guseva Canu I, Bovio N, Mediouni Z, Bochud M, Wild P, Swiss National C. Suicide mortality follow-up of the Swiss National Cohort (1990-2014): sex-specific risk estimates by occupational socio-economic group in working-age population. *Soc Psychiatry Psychiatr Epidemiol* 2019.
EU-OSHA. Exposure to carcinogens and work-related cancer: A review of assessment methods. Executive summary. Luxembourg: European Agency for Safety and Health at Work (EU-OSHA), 2014.
Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P. Risk factors for lung cancer worldwide. *Eur Respir J* 2016; **48**(3): 889-902.
Lillard DR. The Evolution of Smoking in Switzerland. In: Tillmann R, Voorpostel M, Farago P, eds. Social Dynamics in Swiss Society: Empirical Studies Based on the Swiss Household Panel. Cham: Springer International Publishing; 2018: 3-16.
Jones A, Gulbis A, Baker EH. Differences in tobacco use between Canada and the United States. *International journal of public health* 2010; **55**(3): 167-75.
Lindström M. Social capital, economic conditions, marital status and daily smoking: a population-based study. *Public health* 2010; **124**(2): 71-7.
Zeeb H, Shannoun F, World Health O. WHO handbook on indoor radon: a public health perspective. World Health Organization; 2009.
Seki T, Nishino Y, Tanji F, et al. Cigarette smoking and lung cancer risk according to histologic type in Japanese men and women. *Cancer science* 2013; **104**(11): 1515-22.
Khuder SA. Effect of cigarette smoking on major histological types of lung cancer: a meta-analysis. *Lung Cancer* 2001; **31**(2-3): 139-48.
Kreuzer M, Kreienbrock L, Müller KM, Gerken M, Wichmann E. Histologic types of lung carcinoma and age at onset. *Cancer* 1999; **85**(9): 1958-65.
Loomis D. Estimating the global burden of disease from occupational exposures. *Occupational and environmental medicine* 2020; **77**(3): 131-2.
Axelson O. Editorial: Confounding from Smoking in Occupational Epidemiology. *British Journal of Industrial Medicine* 1989; **46**(8): 505-7.
Kriebel D, Zeka A, Eisen EA, Wegman DH. Quantitative evaluation of the effects of uncontrolled confounding by alcohol and tobacco in occupational cancer studies. *International journal of epidemiology* 2004; **33**(5): 1040-5.
Blair A, Stewart P, Lubin JH, Forastiere F. Methodological issues regarding confounding and exposure misclassification in epidemiological studies of occupational exposures. *American journal of industrial medicine* 2007; **50**(3): 199-207.
Corbin M, McLean D, Mannetje A, et al. Lung cancer and occupation: A New Zealand cancer registry-based case-control study. *American journal of industrial medicine* 2011; **54**(2): 89-101.
Dement JM, Ringen K, Hines S, Cranford K, Quinn P. Lung cancer mortality among construction workers: implications for early detection. *Occupational and environmental medicine* 2020; **77**(4): 207.
Taeger D, Pesch B, Kendzia B, et al. Lung cancer among coal miners, ore miners and quarrymen: smoking-adjusted risk estimates from the synergy pooled analysis of case–control studies. *Scandinavian journal of work, environment & health* 2015; (5): 467-77.
Brown T, Darnton A, Fortunato L, Rushton L, British Occupational Cancer Burden Study G. Occupational cancer in Britain. Respiratory cancer sites: larynx, lung and mesothelioma. *British journal of cancer* 2012; **107 Suppl 1**: S56-70.
Pukkala E, Martinsen JI, Lynge E, et al. Occupation and cancer - follow-up of 15 million people in five Nordic countries. *Acta oncologica (Stockholm, Sweden)* 2009; **48**(5): 646-790.
Garshick E, Laden F, Hart JE, et al. Lung cancer and vehicle exhaust in trucking industry workers. *Environmental health perspectives* 2008; **116**(10): 1327-32.
Garshick E, Laden F, Hart JE, et al. Lung cancer in railroad workers exposed to diesel exhaust. *Environmental health perspectives* 2004; **112**(15): 1539-43.

Atramont A, Guida F, Mattei F, et al. Professional Cleaning Activities and Lung Cancer Risk Among Women: Results From the ICARE Study. *Journal of occupational and environmental medicine* 2016; **58**(6): 610-6.
Pearson D, Angulo A, Bourcier E, Freeman E, Valdez R. Hospitality workers' attitudes and exposure to secondhand smoke, hazardous chemicals, and working conditions. *Public Health Rep* 2007; **122**(5): 670-8.
EU-OSHA. Priorities for occupational safety and health research in Europe for the years 2013-2020. Summary report. Luxembourg: European Agency for Safety and Health at Work (EU-OSHA), 2014.
Vienneau D, de Hoogh K, Hauri D, et al. Effects of Radon and UV Exposure on Skin Cancer Mortality in Switzerland. *Environmental health perspectives* 2017; **125**(6): 067009.
Bovio N, Vienneau D, Canu IG. O3D.6 Inventory of occupational, industrial and population cohorts in switzerland. *Occupational and environmental medicine* 2019; **76**(Suppl 1): A29.
Kim T-W, Koh D-H, Park C-Y. Decision Tree of Occupational Lung Cancer Using Classification and Regression Analysis. *Safety and Health at Work* 2010; **1**(2): 140-8.
Galli F, Rohrmann S, Lorez M. Lung cancer survival in Switzerland by histology, TNM stage and age at diagnosis. 2019; **39**.
Turner MC, Mehlum IS. Greater coordination and harmonisation of European occupational cohorts is needed. *Occupational and environmental medicine* 2018; **75**(7): 475.

Supplemental material

Table S1 Relative risk (RR) and confidence interval (IC-95%) for lung cancer mortality among males aged 18-85 in the Swiss National Cohort (1990-2014)

Characteristics	n of lung cancer deaths	Model 1*		Model 2**		Model 3***	
Age group at lung cancer death		p<0.001[a]		p<0.001		p<0.001	
18-34	38	0.01	[0.01,0.02]	0.01	[0.01,0.02]	0.02	[0.01,0.02]
35-44	429	0.15	[0.14,0.17]	0.15	[0.13,0.17]	0.16	[0.14,0.18]
45-54	2,647	1.00	Ref.	1.00	Ref.	1.00	Ref.
55-64	6,861	3.42	[3.26,3.57]	3.39	[3.24,3.54]	3.82	[3.64,4.01]
65+	6,100	7.49	[7.15,7.85]	7.42	[7.07,7.78]	8.75	[8.31,9.21]
Calendar period at lung cancer death		p<0.001		p<0.001		p<0.001	
1990-1994	3,573	1.00	Ref.	1.00	Ref.	1.00	Ref.
1995-1999	4,789	0.89	[0.85,0.93]	0.89	[0.85,0.93]	0.89	[0.85,0.93]
2000-2004	1,879	0.63	[0.60,0.67]	0.66	[0.63,0.70]	0.64	[0.60,0.67]
2005-2009	2,975	0.64	[0.61,0.68]	0.68	[0.64,0.71]	0.65	[0.62,0.68]
2010-2014	2,859	0.58	[0.55,0.61]	0.61	[0.58,0.65]	0.59	[0.56,0.62]
2-digit NSP 2000[b]		p<0.001		p<0.001		p<0.001	
11. Occupations in agriculture, forestry, animal husbandry and care of animals	1,009	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	256	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	99	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	1,399	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	463	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	305	1.84	[1.55,2.19]	1.46	[1.22,1.74]	1.76	[1.48,2.10]
27. Graphic Arts occupations	177	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	164	2.55	[2.08,3.13]	2.03	[1.65,2.49]	2.14	[1.74,2.62]
29. Other processing and manufacturing occupations	722	2.78	[2.39,3.23]	2.01	[1.72,2.35]	2.23	[1.91,2.60]
31. Engineers	295	0.97	[0.82,1.16]	1.04	[0.87,1.24]	1.00	[0.84,1.19]
32. Technicians	248	1.61	[1.34,1.93]	1.45	[1.21,1.74]	1.62	[1.35,1.94]
33. Occupations in technical drawing	88	2.03	[1.58,2.60]	1.59	[1.24,2.04]	2.13	[1.66,2.72]
34. Technical staff	530	1.64	[1.40,1.92]	1.42	[1.21,1.66]	1.68	[1.43,1.97]
35. Machine operators	382	3.35	[2.83,3.95]	2.42	[2.05,2.87]	2.79	[2.35,3.30]
36. Computer occupations	221	1.43	[1.18,1.72]	1.28	[1.06,1.54]	1.44	[1.19,1.73]
41. Construction occupations	1,847	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	43	2.99	[2.15,4.14]	2.08	[1.50,2.89]	2.63	[1.90,3.65]
51. Commercial and sales occupations	993	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	230	1.30	[1.08,1.56]	1.22	[1.01,1.47]	1.20	[1.00,1.45]
53. Transport and traffic occupations	1,460	2.53	[2.20,2.92]	1.82	[1.57,2.11]	2.35	[2.03,2.71]
54. Postal and Telecommunications occupations	215	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	583	2.82	[2.41,3.29]	2.16	[1.84,2.53]	2.54	[2.17,2.97]

Table S1 Continued

Characteristics	n of lung cancer deaths	Model 1*		Model 2**		Model 3***	
62. Cleaning, hygiene and personal care professionals	523	2.65	[2.26,3.10]	2.03	[1.73,2.39]	2.46	[2.10,2.88]
71. Contractors, directors and senior officials	1,281	1.21	[1.05,1.40]	1.13	[0.98,1.30]	1.21	[1.05,1.40]
72. Commercial and administrative occupations	941	1.68	[1.45,1.95]	1.38	[1.19,1.60]	1.66	[1.43,1.93]
73. Banking professionals and insurance employees	258	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	267	1.71	[1.43,2.04]	1.37	[1.14,1.64]	1.61	[1.34,1.92]
75. Judicial occupations	58	1.03	[0.77,1.37]	1.11	[0.83,1.49]	1.10	[0.82,1.47]
81. Media occupations and related occupations	142	1.49	[1.20,1.83]	1.29	[1.04,1.60]	1.50	[1.21,1.85]
82. Artistic occupations	215	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	93	1.06	[0.83,1.35]	1.02	[0.80,1.30]	1.10	[0.86,1.40]
84. Teaching and education occupations	286	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	53	0.76	[0.57,1.03]	0.82	[0.60,1.10]	0.79	[0.59,1.07]
86. Health occupations	220	1.00	Ref.	1.00	Ref.	1.00	Ref.
Linguistic region				p<0.001			
German and Rhaeto-Romansch	11,446			1.00	Ref.		
French	3,849			1.14	[1.10,1.18]		
Italian	780			1.12	[1.04,1.21]		
Civil status				p<0.001			
Single	1,649			1.20	[1.14,1.27]		
Married	12,270			1.00	Ref.		
Divorced	352			1.57	[1.49,1.65]		
Widowed	1,804			1.36	[1.22,1.51]		
Nationality				p<0.001			
Swiss	13,360			1.00	Ref.		
Non-Swiss	2,715			0.91	[0.87,0.95]		
Highest education achieved				p<0.001			
Compulsory education or less	3,838			1.30	[1.24,1.35]		
Upper secondary level education	9,246			1.00	Ref.		
Tertiary level education	2,991			0.71	[0.67,0.74]		
Smoking probability (median = 54%)						p<0.001	
Lower than the median	8,917					1.00	Ref.
Higher than the median	7,159					1.33	[1.27,1.38]
Radon environmental exposure						p=0.601	
Low	10,294					1.00	Ref.
Medium	5,041					0.99	[0.96,1.03]
High	740					1.03	[0.96,1.11]

*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)

[a] Wald test
[b] Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits

Table S2 Relative risk (RR) and confidence interval (IC-95%) for lung cancer mortality among females aged 18-85 in the Swiss National Cohort (1990-2014)

Characteristics	n of lung cancer deaths	Model 1*		Model 2**		Model 3***	
Age group at lung cancer death		p<0.001[a]		p<0.001		p<0.001	
18-34	12	0.01	[0.01,0.02]	0.01	[0.01,0.02]	0.01	[0.01,0.02]
35-44	244	0.20	[0.18,0.23]	0.21	[0.18,0.24]	0.18	[0.15,0.20]
45-54	1,143	1.00	Ref.	1.00	Ref.	1.00	Ref.
55-64	2,096	2.42	[2.25,2.60]	2.31	[2.15,2.49]	2.59	[2.41,2.79]
65+	1,323	3.99	[3.68,4.33]	3.65	[3.36,3.97]	4.51	[4.13,4.92]
Calendar period at lung cancer death		p<0.001		p<0.001		p<0.001	
1990-1994	760	1.00	Ref.	1.00	Ref.	1.00	Ref.
1995-1999	1,188	1.08	[0.99,1.18]	1.10	[1.00,1.21]	1.08	[0.98,1.18]
2000-2004	601	1.08	[0.97,1.20]	1.08	[0.97,1.21]	1.06	[0.96,1.19]
2005-2009	1,074	1.29	[1.17,1.41]	1.32	[1.21,1.46]	1.28	[1.16,1.40]
2010-2014	1,195	1.38	[1.25,1.51]	1.44	[1.31,1.59]	1.37	[1.24,1.50]
2-digit NSP 2000[b]		p<0.001		p<0.001		p<0.001	
11. Occupations in agriculture, forestry, animal husbandry and care of animals	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	21	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	76	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	28	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	55	2.69	[2.02,3.57]	2.33	[1.75,3.10]	2.13	[1.59,2.85]
27. Graphic Arts occupations	27	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	41	1.57	[1.13,2.16]	1.49	[1.08,2.06]	1.28	[0.92,1.77]
29. Other processing and manufacturing occupations	74	1.99	[1.55,2.56]	1.84	[1.43,2.37]	1.80	[1.40,2.32]
34. Technical staff	20	2.19	[1.40,3.44]	2.05	[1.31,3.22]	2.24	[1.42,3.51]
36. Computer occupations	36	2.48	[1.76,3.49]	2.38	[1.69,3.35]	2.18	[1.54,3.07]
41. Construction occupations	13	1.93	[1.11,3.36]	1.82	[1.05,3.17]	1.64	[0.94,2.86]
51. Commercial and sales occupations	755	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	42	1.31	[0.95,1.80]	1.29	[0.94,1.78]	1.23	[0.89,1.69]
53. Transport and traffic occupations	83	2.43	[1.91,3.09]	2.23	[1.75,2.83]	2.38	[1.87,3.02]
54. Postal and Telecommunications occupations	99	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	585	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	363	1.74	[1.50,2.02]	1.72	[1.48,2.00]	1.70	[1.47,1.97]
71. Contractors, directors and senior officials	243	1.74	[1.48,2.05]	1.71	[1.45,2.01]	1.56	[1.32,1.84]
72. Commercial and administrative occupations	1,288	1.76	[1.56,1.98]	1.67	[1.48,1.88]	1.67	[1.48,1.88]
73. Banking professionals and insurance employees	91	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	19	1.69	[1.06,2.68]	1.52	[0.96,2.41]	1.47	[0.93,2.34]
75. Judicial occupations	11	1.31	[0.72,2.38]	1.43	[0.78,2.62]	1.21	[0.66,2.21]
81. Media occupations and related occupations	48	1.16	[0.86,1.57]	1.22	[0.90,1.65]	1.12	[0.83,1.51]
82. Artistic occupations	50	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	98	1.08	[0.87,1.36]	1.08	[0.86,1.35]	1.08	[0.86,1.35]
84. Teaching and education occupations	201	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	13	0.85	[0.49,1.48]	0.97	[0.56,1.69]	0.87	[0.50,1.51]
86. Health occupations	355	1.00	Ref.	1.00	Ref.	1.00	Ref.
Linguistic region				p<0.001			
German and Rhaeto-Romansch	3,401			1	Ref.		
French	1,215			1.157	[1.08,1.24]		
Italian	202			1.216	[1.05,1.40]		

Table S2 Continued

Characteristics	n of lung cancer deaths	Model 1**	Model 2**	Model 3***
Civil status			p<0.001	
Single	678		1.27 [1.17,1.39]	
Married	2,636		1.00 Ref.	
Divorced	404		1.83 [1.70,1.96]	
Widowed	1,100		1.482 [1.33,1.65]	
Nationality			p<0.001	
Swiss	4,415		1.00 Ref.	
Non-Swiss	403		0.691 [0.62,0.77]	
Highest education achieved			p<0.001	
Compulsory education or less	1,372		1.184 [1.10,1.27]	
Upper secondary level education	2,927		1.00 Ref.	
Tertiary level education	519		0.805 [0.73,0.89]	
Smoking probability (median = 34%)				p<0.001
Lower than the median	3,590			1.00 Ref.
Higher than the median	1,228			1.37 [1.26,1.48]
Radon environmental exposure				p=0.019
Low	3,261			1.00 Ref.
Medium	1,355			0.92 [0.86,0.98]
High	202			1.03 [0.89,1.19]

*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)

[a] Wald test

[b] Occupation is coded using the Swiss classification of occupations, version 2000 (NSP 2000), coded on 2 digits

IV. Study of lung cancer survival

IV. I. Preparatory work – need for and quality of occupation registration in cancer registries of Western Switzerland

Unlike our studies on lung cancer mortality, for which data on occupation and work-related variables were available only in the SNC, for this chapter on cancer survival, we also had access to data from the French-speaking cancer registries. Because cancer registries have access to different sources of information and rely on different procedures to record occupation, we first aimed to assess the quality (i.e., completeness, accuracy and precision) of occupation registration in all cancer registries of Western Switzerland. We also aimed to find a relevant and feasible strategy to collect this information in the future. The need of such an evaluation was urged by the recent Cancer Registration Act on the compulsory registration of oncologic diseases in Switzerland, according to which occupation is not included in the national cancer data structure (Bulliard et al. 2020; OFSP 2022). Before this Act came in force (1st January 2020), the perimeter of data registration in cancer registries was more flexible, allowing collection of occupational variables and other variables deemed relevant for epidemiologic research. We published this work in Swiss Medical Weekly in February 2022.

Own contribution: created the SQL query to extract lung cancer data for each cancer registry, performed the data management of data from all cancer registries, performed the statistical analyses and wrote the method part of the manuscript.

Article: Research on occupational diseases in the absence of occupational data: a mixed-method study among cancer registries of western Switzerland

Ekaterina Plys[1], Nicolas Bovio[1], Patrick Arveux[2], Yvan Bergeron[3], Jean-Luc Bulliard[1,2,7], Nadia Elia[4], Evelyne Fournier[5], Isabelle Konzelmann[6], Manuela Maspoli[7], Elisabetta Rapiti Aylward[5], Irina Guseva Canu[1]

[1] Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne ;

[2] Vaud Cancer Registry, Unisanté, Lausanne ;

[3] Fribourg cancer registry;

[4] Division of Anesthesiology, University Hospital of Geneva;

[5] Geneva Cancer Registry, University of Geneva;

[6] Valais cancer registry, Sion;

[7] Neuchâtel and Jura cancer registry, Neuchâtel.

Corresponding author:

Dr. Ekaterina Plys

Centre for Primary Care and Public Health (Unisanté),

Ekaterina.Plys@unisante.ch

SUMMARY

The burden of occupation-related diseases in the global burden of diseases is heavily underestimated, mainly due to a shortage of occupational exposure data. This problem is particularly salient in Switzerland, where no estimates of occupation-related diseases burden exist, even for the well-recognized occupational cancers, such as malignant pleural mesothelioma and lung cancer.

To overcome this situation, we launched a research project “Examining Cancers and Labor Indicators to assess the Burden” (ExCaLIBur). Within this project, we aimed to assess the need for and quality (i.e., completeness, accuracy and precision) of occupation registration in all cancer registries of western Switzerland. Given that the recent Cancer Registration Act restricts the routine collection of occupational data by the Swiss cancer registries, we also aimed to find a relevant and feasible strategy to collect this information in the future.

We applied a mixed research method. We observed that, independently of the level of precision (5-3-2-1-digit aggregation level), the accuracy was better in the registries that were able to actively searched and verified occupational information. Overall, the distinction of occupations based on the 3-digit code presents an acceptable compromise in terms of precision. Having such occupations registered in all, or most, Swiss cancer registries routinely would obviously be valuable for epidemiological surveillance of occupational cancers in Switzerland. However, it seems less obvious how these data could fulfill the research objectives, since a better precision than 3-digit occupational coding is challenging to achieve.

Despite the new legislation, the collection of occupational data by the Swiss cancer registries remains feasible in frame of specific research projects on occupational cancers. However, available data sources as well as lack of financial and human resources will continue affecting quality of the collected occupations. Therefore, the usage of the standardized questionnaire retracing the individual occupational history to enable further assessment of individual exposure to potential occupational hazards is recommended. However, this approach will disable the Swiss registries to insuring their epidemiological surveillance mission with respect to occupational cancers in Switzerland, for which national statistics remain limited. An adequate solution to this problem is therefore requested from the Swiss public health authority.

KEY WORDS

Surveillance; retrospective exposure assessment; legislation; public health; insurance

Introduction

Occupation is an essential component of adult life and a major determinant of health and healthy ageing (1). Moreover, some occupational exposures also affect the offspring health (2, 3). The burden of occupation-related diseases in the global burden of diseases (GBD) is heavily underestimated, mainly due to a shortage of occupational exposure data (4). This problem is particularly salient in Switzerland, where no estimates of occupation-related diseases burden exist, even for the well-recognized occupational cancers, such as malignant pleural mesothelioma and lung cancer (5, 6). The reasons for it include: a low interest for occupational medicine (7, 8), little research in the field of occupational health (9), and lack of accessible information on occupation and occupational exposure history in the medico-administrative databases (10). Apart from statistics produced by the Federal Statistical Office (FSO) from the Swiss Health Surveys and the Swiss Labour Force Survey, Switzerland does not have a systematic data collection strategy to address the issues of occupational exposures and diseases. This hampers etiological research development, for which occupational history (also called *curriculum laboris*) of each individual should be assessed prospectively or retrospectively, by listing all occupations, their duration and calendar period over the entire career.

Swiss cancer registries have initiated some research on occupation-related cancers and collected information on patient's occupation. However, the latter mainly served as an adjustment variable or for investigating socioeconomic differences in cancer incidence, in stage at cancer diagnosis, and in cancer survival (11, 12) from a public health and healthcare perspectives. The study by Bouchardy et al. (13), published twenty years ago, constitutes the only reference on occupational cancer in Switzerland. It is worth noting that this study provides no cancer incidence rates by occupation because general population data were not available. A case-control design was thus applied, using the patients with cancer of interest as cases, and patients with all other cancers as controls. Moreover, this study was limited to male cancer cases which occurred during the period 1980-1993. This study suggested increased cancer risk among farmers, butchers, leather and fur workers, founders, electricians, machinists and professional drivers, carpenters, cabinet-makers, hotel and restaurant employees, hairdressers, and chemists. The authors recognized a questionable quality of their occupation information; the occupations were unknown for 23% of cases among men aged 25 to 64 years; and for an even greater proportion among men aged over 65 years (13). However, no further research on occupational cancer has been conducted since except one on the skin cancer in relation with solar UV exposure (14, 15). Moreover, female workers, ageing workers, and young workers remained neglected with respect to their risk of occupational and occupation-related cancer, although these groups are considered ‘particularly sensitive risk groups’, because of the differences in metabolism, pre-existing health problems — including those caused by work (16, 17).

To overcome this situation, we launched a research project entitled “Examining Cancers and Labor Indicators to assess the Burden” (ExCaLIBur) in order to 1) produce sex- and age-specific cancer risk and survival estimates by occupation and by economic activity in Switzerland; 2) assess the need and quality of occupation registration in Swiss registries. This second part of the project aims at evaluating the completeness, accuracy and precision of occupations documented in Swiss cancer registries and the relevance to collect this information for future occupational epidemiology research. The need of such an evaluation was urged by the recent Cancer Registration Act (CRA) on the compulsory registration of oncologic diseases and variables in Switzerland, which removed occupation from the list of variables that can be registered by cancer registries (18, 19).

Because cancer registries have access to different sources of information and rely on different procedures to record occupation, we hypothesized that the sources and procedures for collecting data on occupation would lead to the more accurate coding of occupation as compared to the occupation coded by the FSO in the Swiss National Cohort (SNC) (20).

To investigate this hypothesis and understand the sources/reasons of practice and potential heterogeneity between registries, as well as to consider ways to improve the access to and the quality of occupation variable, we conducted a mixed method research (21) in collaboration with the Cancer Registries of Western Switzerland (CRWS) .This report presents the results of combined quantitative and qualitative analyses, including focus group and mapping approaches (22).

Methods

Data sources

For the quantitative analysis, we used two sources of data: the FSO, which provided the access to the SNC, and the cancer registries of Geneva, Neuchâtel-Jura, Valais, and Vaud. The registry of Fribourg did not register occupation of their patients and was excluded. The data collected by FSO were used for comparison, because these data come from the trustful sources and the FSO can guarantee the veracity of its data (23).

The SNC is a national longitudinal research platform for the entire resident population of Switzerland. It includes the records of the 1990 and 2000 Swiss censuses, linked to mortality, life birth and emigration records until 2015, using a combination of deterministic and probabilistic methods (20). Because federal censuses were mandatory, the SNC covered 98.6% of Swiss population (24). The occupations recorded in 2000 were coded by the FSO using the Swiss Standard Classification of Occupations 2000 (NSP 2000), the most used classification in Switzerland nowadays. Therefore, the SNC is the only available data source, which is relevant to serve as an external reference comparator for occupation for this study purposes.

Occupational data from all cancer cases from the four CRWS over the period 1990-2014 were extracted by each registry and sent to Unisanté, where they were harmonized and centralized into a database. The linkage between these data and the SNC data was then established by the Institute of Social and Preventive Medicine based on a probabilistic linkage procedure.

Besides, each registry provided the description of their practices of occupational data collection and coding, the data sources used, the type of collection (i.e., active versus passive; systematic versus occasional), their quality control procedures, the resources available as well as the challenges related to these practices.

Study sample

The study sample included all cancer records diagnosed between 1996 and 2004 in four CRWS, which collected occupational data, matched with the SNC. This selection was made in order to enable the comparison of the occupations for this calendar period with occupations declared in the 2000 federal census, under the hypothesis that occupation remained constant during this period (25).

Quantitative component

Firstly, we conducted descriptive analyses of registries' data aiming to estimate the proportion of missing values (empty fields) and potentially inaccurate information such as "Non-defined occupation" or "No information". We were also interested in the proportion of records coded as "Retired" and "Housewife" as this information cannot be used for occupational epidemiology.

Secondly, we compared the occupational information coding agreement and precision between occupation coded in the registries and in the SNC. Only occupations coded using NSP 2000 were used for this comparison. Since the registry of Geneva used the Classification of the Swiss Federal census 1979, their data were not included in this analysis. The comparison between the registries' and SNC codes of occupation was performed accounting for the precision of occupation coding in each registry. For this, we stratified the analysis by the NSP 2000 aggregation level, using 5, 3, 2, and 1-digit levels of aggregation, with 5-digit level being the most detailed coding (i.e., distinguishing 383 occupations) and the 1-digit level the less detailed one (with 9 occupation groups only). When the occupation was coded at a more aggregated level, we completed the code by replacing the missing digit(s) with 0.

If the occupation code was identical between the registry and the SNC, we categorized it under "Same occupation". If the code was different between the two data sources, it was classified as "Mismatch." When the information was missing from both the registry and the SNC, we assigned the case to "No information". Finally, we also compared the agreement of coding of retired patients within each registry, using "Retired" code in both sources. All statistical analyses were stratified by registry and performed using STATA statistical software, version 16 (StataCorp LP; TX, USA).

Qualitative component

The qualitative component of the study consisted in a focus group combined with a mapping approach. The focus group aimed at discussing the results of quantitative analysis and better possibilities of occupational data collection. The focus group took place online and included representatives of the five CRWS. It lasted three hours. It started with an open discussion, where the members of the focus group provided possible explanations for the observed results, based on their registry-specific experience. Then, the participants were invited to suggest potential solutions allowing effective and efficient occupational data collection in the context of the new Swiss Cancer Registration Act. One moderator (IGC) and one observer (NB) from the project-team managed the focus group, while another observer (EP) was taking notes. The moderator iteratively summarized the suggested solutions, which were (re)debated in several rounds of discussion until a consensus on their respective relevance could be reached among the CRWS representatives.

Finally, the feasibility of the most relevant strategies was assessed by conducting a mapping study (22). The latter consisted in an iterative review of potential sources of occupational data aimed to reveal qualitative descriptors and linkages between occupation-related data and information flow on the federal level in Switzerland.

This study was approved by the Vaud ethical committee for research (N° 2018-02077), and received funding form the Swiss Cancer Research.

Results

Registry specific practices of occupational data collection and coding

Table 1 summarizes the registries' practices of collection and coding occupation over time. The CRWS have long recognized the importance of occupational data collection for occupational epidemiology but also for the development of effective prevention strategies. Four CRWS out of five collected these data and considered it in accordance with their mission of cancer monitoring in Switzerland. However, some registries (Fribourg and Valais) believe that occupational data serve mostly research rather than surveillance purposes and are less invested. Fribourg registry has not collected occupational data at all. Most registries encounter difficulties in collection of the information about patients' occupation due to a lack of financial and human resources. The registries of Geneva, Valais and Vaud mentioned that they could not afford to hire trained people to collect information on occupation, while the registry of Neuchâtel-Jura is the only registry that had an employee partly in charge of occupational data collection and coding for 12 years.

Identification of the patients' socio-economic status was the main objective of occupational data collection. After adoption of the recent legislation on the compulsory registration of oncologic diseases, only the registry of Neuchâtel-Jura has obtained permission to continue occupational data collection. The other registries had to stop it. All the registries used medical records and mortality data provided by the FSO as data source about occupation. Nevertheless, they also referred to other sources such as oncological reports, cantonal or municipal population office, or cantonal population registry book.

The registries of Neuchâtel-Jura and until 2015 Geneva actively searched and verified occupations. Moreover, the registry of Neuchâtel-Jura assessed the economic activity branch or industry of their patients' employer, based on the company name and accounted for it in their coding of occupations. The registries of Geneva and Neuchâtel also searched and documented the last occupation of the retired patients. Further, the registry of Neuchâtel-Jura compared their documented occupation with the occupation provided by the FOS on the death certificate and applied changes if necessary. Conversely, the registries of Vaud and Valais collected only the occupational information available without any active data search or verification. Regarding data quality, the collected occupational data were occasionally checked by a physician at the registry of Neuchâtel-Jura, while the registry of Vaud performed checks only for data used in research studies.

Currently, all the registries except Geneva code occupations using the Swiss classification of occupations adopted in 2000. In the Geneva registry, occupations were coded based on the classification of occupations of the Swiss Federal Census of 1979. Nevertheless, several other classifications of occupations were used by the registries in the past (Table 1).

Table 1 Coding procedures of the occupational information among the five cancer registries of Western Switzerland

Registry	Source of information (period)	Classification type and objective of data collection	Quality of the collected data
Valais	• Cantonal office of population (1989-2011)[p] • Medical records (2012-2019)[p] • **Mortality data from the FSO (2014-2019)**[p]	Classification • Classification of the ASRT • NSP 2000 Objectives No particular objective	Data occasionally collected between 1989 and 2019 Data collection stopped in 2020 Quality check None
Neuchâtel-Jura	• **Civil registry (Social assistance service)** (1974-1995)[a] • **Medical records (from 1996)**[a] • Oncological reports (form 2005)[a] • Mortality data from the FSO (from 2016)[a]	Classification • 1974-1991: only 3 types of occupations (worker, employee/middle-class, executive) • 1992-1997: Classification of the Swiss Federal census 1980 • 1998-2016: NSP 1990 • From 2016: NSP 2000 • In 2016 all the documented cases was recoded in accordance with the NSP 2000 Objectives • Evaluate socio-economic status of the patients • Use occupational data in epidemiological studies	Data systematically collected from 1974 Data collection still possible after 2020 Specificity of data coding • If the patient is retired but his/her occupation is known, the occupation is coded • Comparison of the collected data with those provided by the FOS; modifications are made if necessary (from 2016) Quality check Occasional check done by a physician
Vaud	• Municipalities' population registry (till 2014)[p] • Medical records (till 2017)[p] • Mortality data from the FSO[p]	Classification NSP 2000 Objective Evaluate risk of cancer incidence depending on socio-economic and occupational status of the patients	Data collection between 1974 and 2017 Data systematically collected till 2010 Data collection stopped in 2020 Quality check Occasional (data used for research studies)
Geneva	• **Cantonal office of population** (from 1970)[p] • Mortality data from the FSO (if occupation field is empty at the time of death) • Population registry book of the Geneva canton (1970-1999)[a] • Medical records (from 1970)[p]	Classification Classification of the Swiss Federal census 1979 Objective Evaluate socio-economic status of the patients	Data systematically collected between 1980 and 2015 Data occasionally collected between 2015 and 2020 Data collection stopped in 2020 Specificity of data coding • If the occupation is unknown, the case is coded as « No occupation » or « Occupation is unknown » • If the patient is retired at the time of diagnosis, the last occupation is coded Quality check None

Note: In bold: main source of the occupational information; [a] active data collection (some specific steps are undertaken to collect data, for instance, search for the occupation in a population registry book, search of the information on exposures to environmental carcinogens, check of the available information); [p] passive data collection (coding of the occupational information as it was transmitted). ASRT: Swiss association of cancer registries; FSO: Federal Statistical Office; ISCO 88 (COM): International standard classification of occupations; NSP 1990: Swiss standard classification of occupations 1990; NSP 2000: Swiss standard classification of occupations 2000

Registries acknowledged that their occupational data might be incomplete and inaccurate as their sources of information are not always reliable. For instance, several registries reported lack of data on women's occupations. The registries also expressed their concern about being able to collect only the last occupation of their patients, which is insufficient for research in occupational epidemiology.

Description of registries' occupational data and data provided by FSO

In total, the four registries registered 97 571 cancer cases between 1996 and 2004. All data were used for descriptive statistics. Table 2 shows that the proportion of missing values in registries' data is small, ranging between 0% and 5.22%. We observed the same result for housewives, whose missing value proportion ranged between 0.01% and 1.61%. Records coded as "No information" were particularly rare in registries of Geneva and Neuchâtel (0.04% and 3.73% respectively). However, they accounted for 59.16% in the data provided by Valais. Data presented by Neuchâtel and Vaud contained few records with non-defined occupation (2.98% and 2.45% respectively), whereas they accounted for 12.62% and 14.51% of records in Valais and Geneva, respectively.

Table 2 Completeness of occupational information in Cancer Registries of Western Switzerland and SNC

Note: [a] Empty field; [b] Unknown or unclassified occupations; [c] No information was collected about the occupation.

Registry	Number of recorded cases	Missing values [a]		Non-defined occupation [b]		No information [c]		Retired		Housewife	
		n	%	n	%	n	%	n	%	n	%
Neuchâtel-Jura	9 662	1	0	289	3	360	3.7	5 711	59.1	7	0.1
Vaud	45 264	22	0.1	110	2.45	8 696	19.21	18 765	41.5	4	0
Valais	14 832	722	4.9	1 872	12.6	8 774	59.2	0	0	239	1.6
Geneva	27 813	1 452	5.2	4 035	14.5	11	0	-	-	-	-
Total	**97 571**	**2 197**	**2.3**	**6 306**	**6.5**	**17 841**	**18.3**	**24 476**	**25.1**	**250**	**0.3**

Comparison of occupation codes between registries and the SNC

Table 3 shows that differences in agreement varies depending on the levels of precision in the occupation coding. We observed that the finer the level of aggregation, the lower the percentage of concordance. For example, in the registry of Neuchâtel-Jura 11% of the records had the same occupational code at 1 digit, while this number decreased to 7% when occupation was coded at 5-digits. Based on these findings, it seems that using the 3-digit code can be an acceptable compromise. Therefore all subsequent results are presented at the 3-digit level.

Regarding the mismatch in occupation codes, we identified that occupational information differed by at least 50% between the two data sources. Data from the registry of Neuchâtel-Jura had the lowest level of mismatch (46%) followed by the registry of Vaud (55%). The registry of Valais had 81% of mismatch, which was largely due to the fact it coded retired patients as “No information”.

Since we aimed at comparing the agreement of occupation coding by the registers with that by the FSO, we considered concordant when the occupational information was missing or when the patient was coded “Retired” in both sources. Thus, most often occupations matched in the data of the Vaud registry (11%), followed by Neuchâtel-Jura (9%), and Valais (5%). However, when we took into account the percentage of mismatch or data on retired patients, we see that the most accurate information was collected by the registry of Neuchâtel-Jura (Table 3). Thus, Neuchâtel-Jura had 46% of mismatch data, whereas Vaud and Valais had 55% and 81% of mismatch respectively. Regarding accuracy of coding for retired status, Neuchâtel-Jura had 44% of match with SNC data, whereas Vaud and Valais had 29% and 0%.

Table 3 Comparison of coded occupational information in the Cancer Registries of Western Switzerland between 1996 and 2004 with that of the Swiss National Cohort in the 2000 federal census

Registry *	Neuchâtel-Jura		Vaud		Valais	
	n	%	n	%	n	%
NSP 2000 1 digit						
Mismatch	3 391	44	19 356	52	9 156	79
Same occupation	870	11	4937	13	745	6
Retired	3 389	44	10 658	29	0	0
No information	114	1	2 003	5	1 693	15
NSP 2000 2 digits						
Mismatch	3 516	45	19 996	54	9 250	80
Same occupation	745	10	4 297	12	651	6
Retired	3 389	44	10 658	29	0	0
No information	114	1	2 003	5	1 693	15
NSP 2000 3 digits						
Mismatch	3 580	46	20 354	55	9 338	81
Same occupation	681	9	3 939	11	563	5
Retired	3 389	44	10 658	29	0	0
No information	114	1	2 003	5	1 693	15
NSP 2000 5 digits						
Mismatch	3 732	48	21 236	57	9 517	82
Same occupation	529	7	3 057	8	384	3
Retired	3 389	44	10 658	29	0	0
No information	114	1	2 003	5	1 693	15
Total	7 764	100	36 954	100	11 594	100

Note: NSP 2000: Swiss standard classification of occupations 2000.

* Only occupations coded using NSP 2000 were used in this analysis. Since the registry of Geneva coded their occupations according to the Classification of the Swiss Federal census 1979, their data were excluded.

Strategies for occupational data collection defined within the focus group

During the Focus group meeting, the participants commented the results of quantitative analysis. The observed differences in data quality between the registries seems determined by the data collection practices. Thus, registry of Neuchâtel-Jura systematically documented if their patients were retired and actively searched for information about patients' occupation, whereas those of Valais and Vaud did not. This situation also reflects differences in availability of human and financial resources and stresses the importance to provide the registries with reliable occupational information that can be easily coded. The high percentage of occupations matched with the FSO coded occupations observed in the Vaud registry explained by the fact that the latter used data provided by the FSO as main source of occupation is a reliable illustration of it.

Regarding the strategies aiming to improve the collection of occupational information on patients, cancer registries representatives agreed unanimously on the usefulness of data directly transmitted by a competent institution, such as the Cantonal compensation office. This option was judged optimal as the registries have the identification number of the Old-age and survivors' insurance (OASI) of their patients that facilitates the linkage of data from different sources. The registries also suggested some steps aiming to provide all of them the permission to collect patients' occupation trough this source. In order to remove the restrictions imposed by the new legislation, the registries suggested that a request to the legislator is submitted on behalf of the CRWS at a cantonal level or on behalf of the National Institute for Cancer Epidemiology and Registration (NICER) at the national level. However, this strategy would be successful only if additional resources are provided for insuring a sufficient quality standard of occupational information registered. In fact, the information on occupation gathered by the Cantonal population offices is self-declared and might be inaccurate or imprecise. The registries have also mentioned that if none of the proposed strategies is accepted, it would still be possible to continue collecting occupational data using occupational history questionnaires within the framework of specific research studies. The latter can be done in two different manners: either the registries collect the occupation of all new registered patients diagnosed with studied cancer during a limited period (e.g., two years) or they participate in the occupational history data collection by sending a standardized questionnaire to patients or their families. The latter solution seems more appropriate as using different methods of occupation and exposure assessment in cancer cases and controls would introduce a differential exposure misclassification bias.

Discussion

The first aim of this study was to evaluate the agreement of occupational information documented in Swiss cancer registries compared with the FSO data. We hypothesized that the sources and procedures for collecting data on occupation would affect the agreement or coding of occupation as compared to the occupation in the SNC. Our results allow to conclude that discrepancies in occupational coding are related to the different procedures of data collection used by the registries. Thus, unsurprisingly, we observed that, independently of the level of precision (5-3-2-1-digit aggregation level), the percentage of mismatch was lesser in the registries that were able to actively searched and verified occupational information.

Our results suggest that using the 3-digit code can be a compromise between accuracy and precision. In fact, it allows clearly identifying the occupation of the patient and avoiding excluding those patients whose occupation was coded slightly differently as compared to the occupation code at 5-digit precision assigned by the FSO in the SNC. For example, in the NSP 2000, at the 1-digit level, the code 8 corresponds to a large group of occupations related to health, teaching, culture and science. At the 2-digit level, it allows distinguishing smaller groups such as Occupations related to media (NSP 2000 code 81) or Health professionals (NSP 2000 code 86). At the 3-digit level, the occupation is even more specific, distinguishing for instance Occupations related to human medicine and pharmaceutics (NSP 2000 code 861) among the Health professionals. Finally, the 5-digit level allows distinguishing specific occupations such as physician (861.01) or pharmacist (861.03) among the latter.

Our second aim was to evaluate the relevance of the further collection of occupational information by the registries. We identified many current important barriers to further occupational data collection. The Cancer Registration Act imposes restriction on the occupational data collection by the Swiss cancer registries. Currently, only the registry of Neuchâtel-Jura has obtained cantonal legal authorizations to continue collecting these data. However, even if this restriction is withdrawn, available data sources as well as lack of financial and human resources will continue affecting quality of the collected occupational information.

Having occupation registered in all, or most, Swiss cancer registries routinely would obviously be valuable for epidemiological surveillance of occupational cancers in Switzerland. However, it seems less obvious how these data could fulfill the research objectives, since a better precision than 3-digit occupational coding is challenging to achieve. Although a 3-digit occupation is relevant for surveillance purposes, it would not suffice when a linkage with exposure database (e.g., job exposure matrix for night shift work (26, 27), lung carcinogens (28), or radioactive materials (29)) based on a 4 or 5-digit occupation classification is necessary. In this case, occupational history should be reconstructed very precisely, based on the data coming for a centralized source, able to gather them within a regulatory frame, such as insurance or federal census.

The OASI emerged as a potentially relevant data source from our focus group investigation. The use of OASI data is expected to be the most cost-effective strategy as all occupational history could be reconstructed thanks to the employer's declarations of their workers. Moreover, such unique personal identifiers are widely used in Scandinavian countries (30-32) and since recently in France (33). Therefore, in collaboration with the Federal office of public health, OASI, and FSO we investigated the relevance and feasibility of a direct transmission of OASI data to the cancer registries thanks to the OASI ID number and the translation of these data in the occupational histories. Our investigation revealed that in Switzerland, OASI does not collect information neither on occupation of the insured person nor about his/her occupational activity branch or working conditions, but only the enterprise number and the worker's salary for calculation of the contribution amount. It is thus impossible to retrace the patients' occupational history using OASI data. Nevertheless, the FSO is able to link the enterprise number to the Swiss enterprises registry and assess its economic activity branch. Using the latter along with the salary information from the OASI it could be possible to deduce the socioeconomic status of the worker in each enterprise and perhaps, the occupation, although imprecisely. Thus, the routine collection of occupational data given the existent sources, the current legislative context, resources available, and our findings, seems challenging and inefficient. Consequently, such a data collection should be limited to the specific research studies and conducted according to the research plan approved by relevant ethical committees.

In such a research context, the strategy of collection and coding occupation for a specific cancer location during a limited calendar period by the cancer registries also seems suboptimal. In fact, it would only inform on the occupation in incident cancer cases but not in the controls (e.g., patients with other cancer locations or healthy people) or external comparison group (e.g., general (sub-)population). Retrieving their occupation would request additional, potentially differential investigation; consequently, such a strategy is prone to a high risk of introducing differential exposure classification bias in the research results. Conversely, the retrospective reconstruction of *curriculum laboris* using a standardized questionnaire provided to both cancer patients and controls remains a relevant and feasible solution for continuing research on occupational cancer in Switzerland. Indeed, it is the only possible strategy in the current context. This approach was shown reliable in many epidemiological studies and allowed dose-response relationship assessment for many occupational carcinogens in national and international studies (34-36). The coding of the occupations during the entire career is a burdensome and time-consuming task and constitutes the main limitation of this approach. However, the automation of the coding of occupations thanks to a new software “PROCODE” allows alleviating this limitation (38). The second drawback is that such a questionnaire significantly elongates the study questionnaire and the time requested for its completeness, which could bother the participant and lead to a dropout. To remedy this issue, a simplified questionnaire on occupational history can be used, as one currently tested within the Swiss Health Study (SHeS) Pilot Project (39) as well as more interactive on-line questionnaires which could be filled in using a smartphone or a tablet. Indeed, the collaboration of Swiss cancer registries in the administration of such a questionnaire to their patients is an additional key-point in this strategy.

Study strengths and limitations

This study is the first to examine the quality of occupational data using a systemic research protocol applied to five population-based Swiss cancer registries. The study findings confirmed the research hypothesis that the quality of data estimated as completeness and precision of registries’ occupational data depends on the sources used for data collection and the methodological rigour of registration and coding procedures, the latter being determined by the resources available. The original study findings were produced timely, given the new regulation on cancer registration in Switzerland, entered into operation in January 2020.

The study was limited to all cancer registries of Western Switzerland, raising the concern of the findings generalisation to all the other Swiss registries. Nevertheless, we covered most administrative sources available and these sources are largely comparable across cantons. Therefore, the diversity observed in data collection procedures in our study is likely representative of the procedures used in a broader sample of Swiss cancer registries. The unavailability of occupations coded using NSP 2000 in Geneva registry and no occupational data in Fribourg registry precluded accuracy and precision analysis of these registries. However, it is unlikely that inclusion of them in the analysis would change the study results and conclusions.

The strategies discussed within the focus group and investigated by mapping are federal-level strategies. Consequently, they are relevant for all Swiss registries of diseases. The conclusion of the studies regarding the most relevant approach to collect patients' occupation and promote the research on occupational diseases and occupational health are therefore generalizable to all health outcomes in the country, given its particularities in data availability, flow, interoperability and linkages.

Conclusion

This study is the first investigating the quality of occupational data collected by Swiss cancer registries. The usage of a mixed method protocol added to its originality. The study confirmed the research hypothesis that the quality of occupational data estimated in terms of data completeness, accuracy and precision, depends on the sources used by the registry for data collections and the methodological rigour of registration and coding procedures, the latter being strongly determined by the local legislation and resources available. Given that the Cancer Registration Act restricts the routine collection of occupational data by the Swiss cancer registries, the collection of such data remains feasible in frame of specific research projects on occupational cancers. However, available data sources as well as lack of financial and human resources will continue affecting quality of the collected occupational information. Therefore, the usage of the standardized questionnaire retracing the individual occupational history to enable further assessment of individual exposure to potential occupational carcinogens and hazards will be more relevant than using routinely available data. However, this approach will disable the Swiss registries to insuring their epidemiological surveillance mission with respect to occupational cancers in Switzerland, for which national statistics remain limited. An adequate solution to this problem is therefore requested from the Swiss public health authority.

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Conflicts of interest

The authors declare no conflict of interest.

References

GBD. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet (London, England). 2018;392(10159):1923-94.

Adachi S, Sawaki J, Tokuda N, Tanaka H, Sawai H, Takeshima Y, et al. Paternal occupational exposure to chemicals and secondary sex ratio: results from the Japan Environment and Children's Study. The Lancet Planetary health. 2019;3(12):e529-e38.

Pape K, Svanes C, Sejbæk CS, Malinovschi A, Benediktsdottir B, Forsberg B, et al. Parental occupational exposure pre- and post-conception and development of asthma in offspring. International Journal of Epidemiology. 2020.

Loomis D. Estimating the global burden of disease from occupational exposures. Occupational and environmental medicine. 2020;77(3):131-2.

Bovio N, Richardson DB, Guseva Canu I. Sex-specific risks and trends in lung cancer mortality across occupations and economic activities in Switzerland (1990-2014). Occupational and environmental medicine. 2020;77(8):540-8.

Bovio N, Wild P, Guseva Canu I. Lung Cancer Mortality in the Swiss Working Population: The Effect of Occupational and Non-Occupational Factors. Journal of occupational and environmental medicine. 2021.

Danuser B. Comment soigner la santé au travail ? REISO. 2014(23 juin 2014):1-4.

Graczyk H, François M, Krief P, Guseva Canu I. The role of the Swiss list of occupational diseases in the protection of workers' health. Swiss Med Weekly. 2021;(in press).

Guseva Canu I, François M, Graczyk H, Vernez D. Healthy worker, healthy citizen: the place of occupational health within public health research in Switzerland. International journal of public health. 2020;65(1):111-20.

OECD. Health Data Governance: Privacy, Monitoring and Research. Paris; 2015.

Feller A, Schmidlin K, Bordoni A, Bouchardy C, Bulliard JL, Camey B, et al. Socioeconomic and demographic disparities in breast cancer stage at presentation and survival: A Swiss population-based study. Int J Cancer. 2017;141(8):1529-39.

Feller A, Schmidlin K, Bordoni A, Bouchardy C, Bulliard JL, Camey B, et al. Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: evidence from a Swiss population-based study. Cancer Med. 2018;7(4):1498-510.

Bouchardy C, Schuler G, Minder C, Hotz P, Bousquet A, Levi F, et al. Cancer risk by occupation and socioeconomic group among men--a study by the Association of Swiss Cancer Registries. Scandinavian journal of work, environment & health. 2002;28 Suppl 1:1-88.

Backes C, Religi A, Moccozet L, Vuilleumier L, Vernez D, Bulliard JL. Facial exposure to ultraviolet radiation: predicted sun protection effectiveness of various hat styles. Photodermatol Photoimmunol Photomed. 2018;34:330-7.

Milon A, Bulliard JL, Vuilleumier L, Danuser B, Vernez D. Estimating the contribution of occupational solar UV exposure to skin cancer. Br J Dermatol. 2014;170:157-64.

EU-OSHA. Exposure to carcinogens and work-related cancer: A review of assessment methods. Executive summary. Luxembourg: European Agency for Safety and Health at Work (EU-OSHA); 2014.

EU-OSHA. Priorities for occupational safety and health research in Europe for the years 2013-2020. Summary report. Luxembourg: European Agency for Safety and Health at Work (EU-OSHA); 2014.

(OFSP) Ofdlsp. Législation sur l'enregistrement des cancers Bern, Suisse2021 [updated 28.04.2021. Available from : https://www.bag.admin.ch/bag/fr/home/gesetze-und-bewilligungen/gesetzgebung/gesetzgebung-mensch-gesundheit/gesetzgebung-krebsregistrierung.html]

Bulliard JL, Ducros C, Germann S, Arveux P, Bochud M. Nouvelles exigences légales dans le domaine de l'enregistrement du cancer: opportunités et défis. Rev Med Suisse. 2020; 6(713):2099-2103.
Spoerri A, Zwahlen M, Egger M, Bopp M. The Swiss National Cohort: a unique database for national and international researchers. International journal of public health. 2010;55(4):239-42.
Johnson RB, Onwuegbuzie AJ. Mixed Methods Research: A Research Paradigm Whose Time Has Come. Educational Researcher. 2004;33(7):14-26.
Cooper ID. What is a “mapping study"? J Med Libr Assoc. 2016;104(1):76–8.
Lorenz H. The Data Innovation Project “NOGAuto”. SWISS FEDERAL STATISTICAL OFFICE; 2021.
SFSO. Methodology report—coverage estimation for the Swiss population census 2000. Swiss Federal Statistical Office Neuchâtel2004 [Available from: https://www.bfs.admin.ch/bfsstatic/dam/assets/341896/master.
Guseva Canu I, Bovio N, Mediouni Z, Bochud M, Wild P. Suicide mortality follow-up of the Swiss National Cohort (1990-2014): sex-specific risk estimates by occupational socio-economic group in working-age population. Social psychiatry and psychiatric epidemiology. 2019;54(12):1483-95.
Sok V, Tvardik N, Cordina E, Pelletan JB, Houot M, Pilorget C, et al. Création d'une matrice emplois-expositions sur le travail à horaires atypiques. Archives des Maladies Professionnelles et de l'Environnement. 2018;79(3):400.
Fernandez RC, Peters S, Carey RN, Davies MJ, Fritschi L. Assessment of exposure to shiftwork mechanisms in the general population: the development of a new job-exposure matrix. Occupational and environmental medicine. 2014;71(10):723-9.
Peters S, Vermeulen R, Portengen L, Olsson A, Kendzia B, Vincent R, et al. SYN-JEM: A Quantitative Job-Exposure Matrix for Five Lung Carcinogens. The Annals of occupational hygiene. 2016;60(7):795-811.
Guseva Canu I, Faust S, Knieczak E, Carles M, Samson E, Laurier D. Estimating historic exposures at the European Gaseous Diffusion plants. International journal of hygiene and environmental health. 2013;216(4):499-507.
Foss L, Gravseth HM, Kristensen P, Claussen B, Mehlum IS, Skyberg K. “Inclusive working life in Norway”: a registry-based five-year follow-up study. Journal of Occupational Medicine and Toxicology. 2013;8(1):19.
Ludvigsson JF, Håberg SE, Knudsen GP, Lafolie P, Zoega H, Sarkkola C, et al. Ethical aspects of registry-based research in the Nordic countries. Clin Epidemiol. 2015;7:491-508.
Kristensen P, Hanvold TN, Hasting RL, Merkus SL, Hoff R, Mehlum IS. Work participation in young Norwegians: a 19-year follow up in a registry-based life-course cohort. Scandinavian journal of public health. 2021;49(2):176-87.
(Irdes) Idredeédls. HYGIE Project: Information system on daily allowances Paris, France: Irdes; 2021 [Available from: https://www.irdes.fr/recherche/partenariats/hygie-systeme-d-information-sur-les-indemnites-journalieres/presentation-de-la-base.html.
Hall AL, Kromhout H, Schüz J, Peters S, Portengen L, Vermeulen R, et al. Laryngeal cancer risks in workers exposed to lung carcinogens: Exposure-effect analyses using a Quantitative job exposure matrix. Epidemiology (Cambridge, Mass). 2020;31(1):145-54.
Guha N, Bouaoun L, Kromhout H, Vermeulen R, Brüning T, Behrens T, et al. Lung cancer risk in painters: results from the SYNERGY pooled case-control study consortium. Occupational and environmental medicine. 2021;78(4):269-78.
Ge C, Peters S, Olsson A, Portengen L, Schüz J, Almansa J, et al. Respirable Crystalline Silica Exposure, smoking, and lung cancer subtype risks. A Pooled Analysis of Case-Control Studies. American journal of respiratory and critical care medicine. 2020;202(3):412-21.
Ge C, Peters S, Olsson A, Portengen L, Schüz J, Almansa J, et al. Diesel engine exhaust exposure, smoking, and lung cancer subtype risks. A Pooled Exposure-response

analysis of 14 case-control studies. American journal of respiratory and critical care medicine. 2020;202(3):402-11.
Savic N, Bovio N, Gilbert F, Paz J, Guseva Canu I. Procode: A Machine-learning tool to support (re-)coding of free-texts of occupations and industries. Annals of work exposures and health. 2021.
Unisanté. Swiss Health Study (SHeS, pilot phase) Lausanne, Switzerland2021 [Available from: https://www.unisante.ch/fr/formation-recherche/recherche/groupes-recherche/swiss-health-study-shes-pilot-phase.

Supplemental material

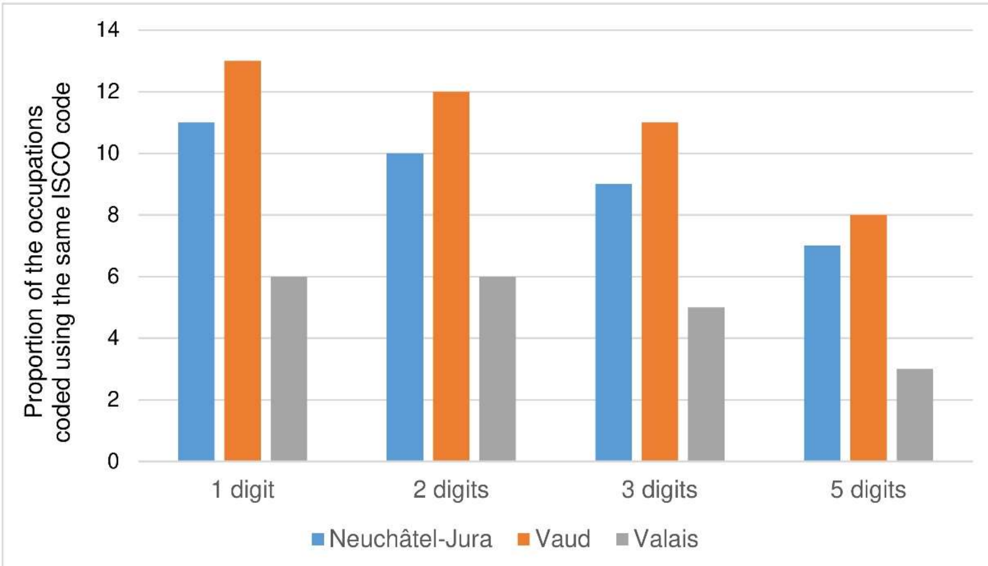

Figure S1: Proportions of the occupations coded using the same International standard classification of occupations (ISCO) code as in the Swiss National Cohort between 1996 and 2004.

IV. II. Work-related factors and sex-specific lung cancer survival

As we observed differences in lung cancer mortality across occupations in chapter III, we wanted to go further and try to understand whether survival after lung cancer diagnosis could also be affected by occupation or occupational conditions. A meta-analysis analyzed the effect on lung survival of different measures, including occupation, but because of heterogeneity, this measure could not be explored (Finke et al. 2018). Moreover, most of the studies on occupation included in this meta-analysis were several years to several decades old. To overcome this, we launched the first Swiss study that aimed at assessing the relation between occupation or work-related variables measures and lung cancer survival in Switzerland. Our main hypothesis was that the survival after cancer diagnosis vary across occupations are dependent of working conditions before and/or after cancer diagnosis, in both sexes. The objective of this study was therefore to investigate this association by focusing on 1-occupation, 2-skill level required for the occupation and 3-socio-professional category independently, using relative survival settings. This work is about to be submitted in Cancers.

Own contribution: performed the data management, performed the statistical analyses and wrote the manuscript.

Manuscript: Work-related factors and sex-specific lung cancer survival: an analysis of cancer registry data in Switzerland (1990-2014)

Nicolas Bovio[1], Michel Grzebyk[2], Patrick Arveux[3], Yvan Bergeron[4], Jean-Luc Bulliard[1,3,5], Arnaud Chiolero[6,7,9,10], Evelyne Fournier[8], Isabelle Konzelmann[7], Manuela Maspoli[5], Elisabetta Rapiti[8], Irina Guseva Canu[1]

[1] Center for Primary Care and Public Health (Unisanté), University of Lausanne, Lausanne, Switzerland;

[2] Institut National de Recherche et Sécurité (INRS), Vandoeuvre lès Nancy, France.

[3] Vaud Cancer Registry, Unisanté, Lausanne, Switzerland;

[4] Fribourg Cancer registry, Fribourg, Switzerland;

[5] Neuchâtel and Jura Cancer Registry, Neuchâtel, Switzerland;

[6] Population Health Laboratory (#PopHealthLab), University of Fribourg, Fribourg, Switzerland.

[7] Valais Cancer Registry, Sion, Switzerland;

[8] Geneva Cancer Registry, University of Geneva, Switzerland.

[9] Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland.

[10] Department of Epidemiology, Biostatistics and Occupational Health, McGill University, Montréal, Quebec, Canada.

Corresponding author:

Nicolas Bovio

Center for Primary Care and Public Health (unisanté), University of Lausanne
Department of Occupational and Environmental Health
BIOPÔLE Secteur Croisette - Bâtiment SC-B
Rte de la Corniche 2
CH-1066 Epalinges-Lausanne

+41 21 314 47 72
nicolas.bovio@unisante.ch

ABSTRACT

Objective: To investigate whether occupation, skill level required for the occupation, and socio-professional category were associated with lung cancer survival.

Methods: Using data from 5,773 patients from cancer registries in French-speaking Switzerland between 1990 and 2014, we selected three work-related measures to assess their association with lung cancer survival. The first measure was occupation and was coded according to the International Standard Classification of Occupations. The second measure was the skill level required for the occupation, ranging from occupations requiring simple, routine physical or manual tasks to occupations involving complex problem solving and decision-making. The third measure was the socio-professional category, a composite of occupation, occupational status, highest level of education attained, and legal form of business. For each measure, we applied non-parametric and parametric methods to estimate net lung cancer survival, controlling for age, calendar period, and tumor stage at diagnosis.

Results: After adjustment, the instantaneous risk of dying from lung cancer among male workers with a paid employment but without precise information on socio-professional category was 36% higher than among top management workers and self-employed. In women, technicians and associate professionals had a 23% lower risk compared to legislators, senior officials and managers. We observed no statistically significant differences in net survival across skill levels in both sexes.

Conclusions: Our results need further analyses, taking into account the patients' smoking habits and the treatments received. Information on past occupational exposures, as well as occupational conditions after diagnosis, is also needed for a better understanding of the differences in net survival between occupational groups.

Keyword: net survival; lung cancer; occupation; Switzerland, gender differences, workers

Introduction

Lung cancer usually has a poor prognosis and results in the highest mortality among all cancers, with 1.8 million deaths worldwide in 2020 (IARC 2021a; IARC 2021c). Its five-year survival varies considerably across countries with estimates between 10% and 20% (Allemani et al. 2018). A recent meta-analysis explored the effect on survival of different measures including education, income and area-based socio-economic status most often used an index (Finke et al. 2018). The effect of occupation could not be explored in this study because of the heterogeneity of the measures on occupation across studies. Hence, among eight studies using individual data, four designated occupational status by collar color or similar categories (Berglund et al. 2010; Chirikos et al. 1984; Pastorino et al. 1990; Vågerö and Persson 1987). One was based on socio-professional category (Grivaux et al. 2011). The last three studies identified provided more details on occupation, but only specific groups were analyzed (Dalton et al. 2015; Fujino 2007; Kravdal 2000). Because most of these studies are several years or even decades old, there is a need not only to update survival estimates but also to analyze survival using standardized occupational measures.

In Switzerland, the five year survival of lung cancer was 24% for women and 19% for men, compared with 15% and 11% at ten years after diagnosis, respectively (Galli et al. 2019). The higher the stage at diagnosis, and the older the patient, the lower was the survival, in both men and women. To our knowledge, there is no studies assessing the relation between occupation or work-related variables measures and lung cancer survival in Switzerland. Because previous Swiss studies have demonstrated differences in lung cancer mortality between occupational groups (Bovio et al. 2020; Bovio et al. 2021), we aimed at determining whether occupation and occupation-related factors were also associated with lung cancer survival. The objective of this study was therefore to investigate this association by focusing on 1-occupation, 2-skill level required for the occupation and 3-socio-professional category independently, using relative survival settings.

Materials & Methods

Sources of data

We used data from the cancer registries of Western Switzerland (cantons of Geneva, Neuchâtel, Vaud, and Valais) for the period 1990-2014. In order to retrieve information on occupation and mortality, we used data from the Swiss National Cohort (SNC), with an estimated population coverage of 98.6% (SFSO 2004). The SNC is based on data from the 1990 and 2000 federal censuses, which were linked to mortality, birth and emigration records. In order to have a single database of the cancer registries and SNC data, the registries responsible for recording all incident cases of cancer diagnosed in their resident population transmitted data on their lung cancer cases to the Center for Primary Care and Public Health (Unisanté). Unisanté centralized the registries' data and harmonized their format to enable linkage with SNC data. The linkage was carried out by the Institute of Social and Preventive Medicine of the University of Bern and almost all patients in cancer registries could be linked with the SNC data (94.4%).

Study sample and follow-up

In Switzerland, the minimum legal working age is 15 and the age of majority is 18. The legal retirement age is 65 for men and 64 for women. Therefore, our study sample included lung cancer cases aged between 18 and 65 years at the time of either of the census with an available occupation. Patients were followed from the date of lung cancer diagnosis until the earliest of the following events: date of emigration, 85th birthday, death, or study termination (December 31, 2014).

Definition of predictor variables

We selected three different work-related variables to assess their association with lung cancer survival. The first is the occupation, which was coded according to the International Standard

Classification of Occupations, 1988 version (ISCO-88). This multi-tiered classification was used in both censuses and coded using four-digit codes by the Swiss Federal Statistical Office (SFSO). For this study, we used the one-digit ISCO-88 aggregated into 9 major occupational groups. The second variable is the skill level required for the occupation. It was defined according to (Milner et al. 2013), based on ISCO codes aggregated into four different levels. It ranges from occupations that require simple, routine physical or manual tasks, at low skill level, or level one, to occupations involving the performance of tasks requiring complex problem solving and decision making, at high skill level, or level four. The third measure was the socio-professional category, a composite of occupation, occupational status, highest education completed, and legal form of business, defined according to (SFSO 2016). Since the start and end dates of employment were not known, we assigned the earliest available occupational information to each participant (1990 census information first and 2000 census information second). This allowed us to retrieve occupational information for those retired at the age of cancer diagnosis.

Case selection and tumour stage

We considered incident primary malignant lung cancer (C33-C34) based on the International Classification of Diseases for Oncology (ICD-O), 3rd edition. We identified cases using the four Western Swiss cancer registries and selected them according to the International Agency for Research on Cancer (IARC) rules for multiple primary cancers (IARC 2005).

Tumour stage at diagnosis was coded by cancer registries according to the classification of malignant tumours (TNM) (Sobin et al. 2011). Tumours localized to the organ of origin constituted stages I and II, locally extensive spread, particularly to regional lymph nodes, stage III, and tumours with distant metastasis, stage IV. Stage at diagnosis was imputed, when missing, with multivariate imputation by chained equations (van Buuren and Groothuis-Oudshoorn 2011) using the following variables as predictors : age at diagnosis, survival time, skill level required for the occupation, socio-professional category, cancer registry, language region and civil status. We run all models with 25 imputations, in order to reduce the impact of the random sampling inherent in multiple imputation procedures (Spratt et al. 2010). Comparison of the proportions of each category of stage between the observed and imputed data showed a better match by grouping stage III and IV in one category. Consequently, we grouped stages III and IV and considered stage as a three-class variable.

Statistical analyses

Net survival can be used to estimate the survival that would be observed if the only possible underlying cause of death was the disease under study (Berkson and Gage 1952). It can be calculated using either the cause-specific or relative survival (RS) approach. Prior findings showed that the latter was more robust and recommended for net survival analysis (Schaffar et al. 2017). In this setting, net survival is estimated using life tables and can be defined as the ratio of the observed survival to the one expected from the life tables. In other words, it approximates the net survival probability and can be seen as the survival probability from the disease under study after all other risk have been removed (Estève et al. 1994).

In this study, we applied two different methods based on RS settings : the Pohar-Perme non parametric method (Perme et al. 2012) with the log-rank type test to compare the net survival curves between groups (Grafféo et al. 2016) and a parametric method that models the excess hazard in a framework of multivariable proportional hazard regression model (Remontet et al. 2007). Both analyses were conducted separately for men and women.

Non-parametric survival analysis

For the non-parametric approach, we used the STNS package (Clerc-Urmès et al. 2014) developed in STATA. It requires the all causes mortality rate table, which is used to compute the expected hazard and survival of each subject at each event time in the dataset. We calculated it using the mortality rates of the population of the cantons of Geneva, Neuchâtel, Vaud and Valais stratified by 5-year age group (18-85 years) and 5-year calendar period (1990-2014). These categories were chosen to smooth the rates and avoid large differences in mortality by age or calendar year. Because we were mainly interested in the survival by occupation, we also stratified our rates by ISCO-88 1-digit code. This allowed us to account for differences in overall mortality between occupational groups. Net lung cancer survival was computed at 5 years for occupation (ISCO-88 1-digit code), skill level and socio-professional category and we applied a log-rank test stratified by stage to compare the net survival curves between groups.

Multivariate parametric survival analysis

For the parametric approach, we used the flexrsurv R package (Clerc-Urmès et al. 2021). A cubic spline with 3 knots (1, 5 and 10 years of follow-up), the internal breakpoints that define the spline used to estimate the baseline hazard, were fitted. Background mortality rates were the same than in the non-parametric survival analysis. Again, we calculated the excess hazards by occupation (ISCO-88 1-digit), skill level and socio-professional category. For each of these variables, we fitted a model adjusted for age and calendar period at diagnosis. Furthermore, we adjusted all models for stage at diagnosis, and also tested the non-proportional effect of stage using B-Splines (Giorgi et al. 2003). In order to compare the fit of our models, we used the Akaike Information Criterion (AIC) (Akaike et al. 1973).

Results

Cohort description

Of the 13'427 lung cancer cases, we excluded 48% of men and 67% of women because of lack of information on occupation. Unemployed or job-seeking people, who represented 3% of the total sample, were also excluded. The final sample consisted of 5'773 cases, 76% of which were men. (Table 1). Most of participants were Swiss, with only 22% and 16% of non-Swiss in men and women, respectively. More than half of the study participants were married and about one third were single. The mean age at the study entry was 60.7 ± 8.0 years in men and 58.4 ± 8.5 years in women and the mean duration of follow-up was 2.5 ± 4.0 and 2.8 ± 4.1, respectively. The most represented occupational group differed between men and women. In men, it was craft and related trades workers, with 24% of them belonging to this group (versus 4% of women). In women, the most represented occupational group was clerks, with 26% of women in this group compared to only 8% of men. About half of the study participants had occupation requiring the second lowest level of skills. In addition, both male and female participants were more likely to be in the supervisors/low level management and skilled labor socio-professional categories. In contrast, participants with top management and independent occupations accounted for only 5% in men and 2 % in women.

Table 1 Characteristics of the study sample of lung cancer incidence cases in French-speaking Switzerland (1990-2014)

Characteristics	Male		Female	
	n of lung cancer	*(%)*	n of lung cancer	*(%)*
Total	4'360	*(100)*	1'413	*(100)*
Nationality (binary)				
Swiss	3,298	*(78)*	1,226	*(84)*
Non-Swiss	1,062	*(22)*	187	*(16)*
Civil status				
Single	409	*(29)*	219	*(31)*
Married	3'330	*(64)*	735	*(57)*
Widowed	90	*(1)*	108	*(3)*
Divorced	531	*(6)*	351	*(9)*
Occupation [a]*				
Legislators, senior officials and managers	480	*(11)*	101	*(7)*
Professionals	392	*(9)*	112	*(8)*
Technicians and associate professionals	721	*(17)*	287	*(20)*
Clerks	340	*(8)*	374	*(26)*
Service workers and shop and market sales workers	276	*(6)*	318	*(23)*
Skilled agriculture and fishery workers	178	*(4)*	15	*(1)*
Craft and related trades workers	1'043	*(24)*	59	*(4)*
Plant and machine operators and assemblers	399	*(9)*	13	*(1)*
Elementary occupations	531	*(12)*	134	*(9)*
Skill level required for the occupation				
Low	531	*(12)*	134	*(9)*
Intermediate low	2'236	*(51)*	779	*(55)*
Intermediate high	721	*(17)*	287	*(20)*
High	872	*(20)*	213	*(15)*
Socio-professional category				
Top management and independent professions	229	*(5)*	23	*(2)*
Other self-employed	827	*(19)*	174	*(12)*
Professionals and senior management	371	*(9)*	91	*(6)*
Supervisors/low level management and skilled labour	1'927	*(44)*	744	*(53)*
Unskilled employees and workers	868	*(20)*	345	*(24)*
In paid employment, not classified elsewhere	138	*(3)*	36	*(3)*
Tumour stage				
Stage 1	464	*(11)*	184	*(13)*
Stage 2	222	*(5)*	79	*(6)*
Stage 3	575	*(13)*	191	*(14)*
Stage 4	1420	*(33)*	546	*(39)*
Missing information	1679	*(39)*	413	*(29)*
Calendar periods				
1990-1994	758	*(17)*	146	*(10)*
1995-1999	1268	*(29)*	297	*(21)*
2000-2004	691	*(16)*	222	*(16)*
2005-2009	752	*(17)*	312	*(22)*
2010-2014	891	*(20)*	436	*(31)*
Age at entry (years) : mean ± standard deviation	60.7 ± 8.0		58.4 ± 8.5	
Duration of follow-up (years) : mean ± standard deviation	2.5 ± 4.0		2.8 ± 4.1	

[a] Occupation is coded using the International Standard Classification of Occupations, version 1988 (ISCO-88), coded on 1 digit

Five-year net survival per occupational group

In non-parametric setting, the overall log rank test showed that the survival differences across occupational groups were not statistically significant (p=0.13). However, when we compared the survival observed in male legislators, senior officials, and managers, identified with the highest 5-year survival (0.25 % 95%-IC: 0.22-0.28), we found significant differences with other occupational groups. Farmers, observed with the lowest survival (0.17%, 95%-IC: 0.11-0.23), craft and related trades workers (0.20%, 95%-IC: 0.17-0.23), and workers in elementary occupations (0.21%, 95%-IC: 0.17-0.24) had statistically lower survival (Fig.1). In parametric setting, considering legislators, senior officials and managers as reference category, we found that all occupations had a hazard ratios (HR) higher than 1. The instantaneous risk of dying from lung cancer in men working in elementary occupations and in skilled agriculture and fishery male workers were 22% and 20% higher than the reference group (Table 2). However, after adjustment for tumour stage at diagnosis, the estimated HRs corresponding to the occupational group decreased, ranging from 0.99 to 1.09 and were not statistically significant.

Among women, female technicians and associate professionals were identified as having the highest net survival (0.29%, 95%-IC: 0.23-0.36). We observed that this result was statistically significantly different from that of legislators, senior officials, and executives, who showed the lowest survival (0.20%, 95%-IC: 0.12-0.29). Technicians and associate professionals had higher survival at almost all time points (Fig. 2). The corresponding HRs were 0.72 (95%-IC: 0.55-0.94) and 0.72 (95%-IC: 0.54-0.95), respectively, and were not affected by the adjustment for stage at diagnosis (Table 3).

Five-year net survival per skill level required for the occupation

In the non-parametric approach, we found statistically significant differences in net survival across skill levels in men (p-value=0.02). Men with the highest skill level demonstrated the highest survival at each time point (0.22%, 95%-IC: 0.19-0.25), while those with the lowest skill level the lowest net survival (0.19%, 95%-IC: 0.16-0.23). We confirmed this results in parametric analyses as well, observing a protective effect of the high skill level (HR=0.86 (95%-IC: 0.76-0.98)) compared to men with the lowest skill level, in the model not adjusted for tumour stage (Table 2). After adjustment for tumour stage, this result turned out non-significant (HR=0.91 (95%-IC: 0.80-1.04). In women, we also found statistically significant differences in net survival across skill levels (p-value 0.013) and we observed that workers with the second highest skill level presented the highest survival at any time point (0.29%, 95%-IC: 0.23-0.36), whereas the lowest level demonstrated the lowest net survival (0.19%, 95%-IC: 0.12-0.27). This was also confirmed in the parametric analyses (HR = 0.75 (95%-IC: 0.59-0.97) in the model not adjusted for tumour stage. After adjustment, this result became statistically non-significant, with an upper bound of the confidence interval slightly greater than 1 (HR: 0.79 (95%-IC: 0.61-1.02)).

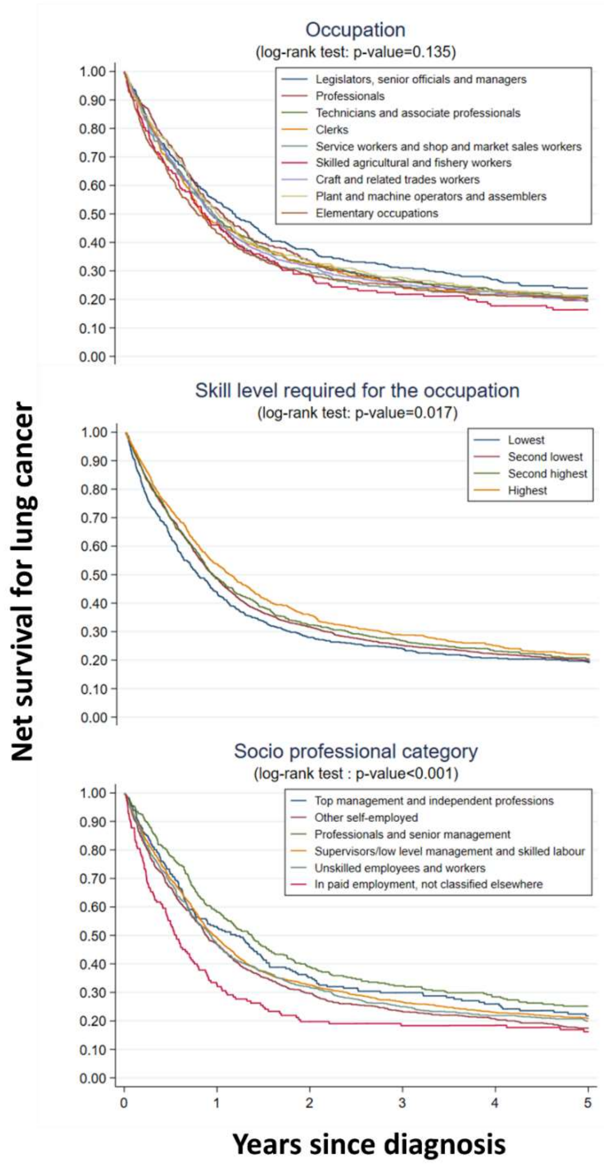

Figure 1: non-parametric net survival of lung cancer across occupation (1-digit ISCO-88), skill level required for the occupation and socio-professional category in men

Five-year net survival per socio-professional category

In non-parametric analysis, among men, professionals and senior managers had the highest five-year net survival (0.25%, 95%-IC: 0.20-0.30), followed by top management and independent professionals (0.21%, 95%-IC: 0.16-0.28) (Fig. 1). In opposite, men in paid employment (not classified elsewhere) had a survival of 16.19% (95%-IC: 0.10-0.22), the lowest net survival estimated. We also identified this category as having the highest risk in the parametric analysis, with HR=1.46 (95%-IC, 1.15-1.86). This risk remained statistically significant even after adjusting for tumour stage at diagnosis (HR=1.36 (95%-IC, 1.05-1.76) (Table 2). Among women, we found no significant differences between socio-professional categories.

Table 2 Hazard ratios (HR) and Confidence Interval (95%-IC) for Lung Cancer relative survival by work-related variables among males aged 18-85 in French-speaking Switzerland

Characteristics	Model 1*		Model 2**	
Occupation				
Legislators, senior officials and managers	Ref.		Ref.	
Professionals	1.09	0.93-1.27	0.99	0.84-1.16
Technicians and associate professionals	1.14	1.00-1.30	1.04	0.90-1.20
Clerks	1.11	0.94-1.30	1.01	0.85-1.20
Service workers and shop and market sales workers	1.18	1.00-1.41	1.15	0.96-1.37
Skilled agricultural and fishery workers	1.22	1.01-1.49	1.04	0.85-1.28
Craft and related trades workers	1.15	1.01-1.30	1.02	0.89-1.16
Plant and machine operators and assemblers	1.07	0.91-1.25	1.01	0.85-1.19
Elementary occupations	1.20	1.04-1.39	1.09	0.94-1.27
Skill level required for the occupation				
Low	Ref.		Ref.	
Intermediate low	0.94	0.84-1.05	0.94	0.84-1.06
Intermediate high	0.95	0.83-1.08	0.95	0.83-1.09
High	0.86	0.76-0.98	0.91	0.80-1.04
Socio-professional category				
Top management and independent professions	Ref.		Ref.	
Other self-employed	1.18	0.99-1.40	1.09	0.91-1.31
Professionals and senior management	0.91	0.75-1.11	0.91	0.74-1.12
Supervisors/low level management and skilled labour	1.08	0.92-1.27	1.06	0.89-1.26
Unskilled employees and workers	1.09	0.91-1.29	1.04	0.87-1.25
In paid employment, not classified elsewhere	1.43	1.13-1.82	1.36	1.05-1.76

*Model 1 is adjusted for age and calendar period;**Model 2 is adjusted for age, calendar period and stage at diagnosis

[a] Occupation is coded using the International Standard Classification of Occupations, version 1988 (ISCO-88), coded on 1 digit

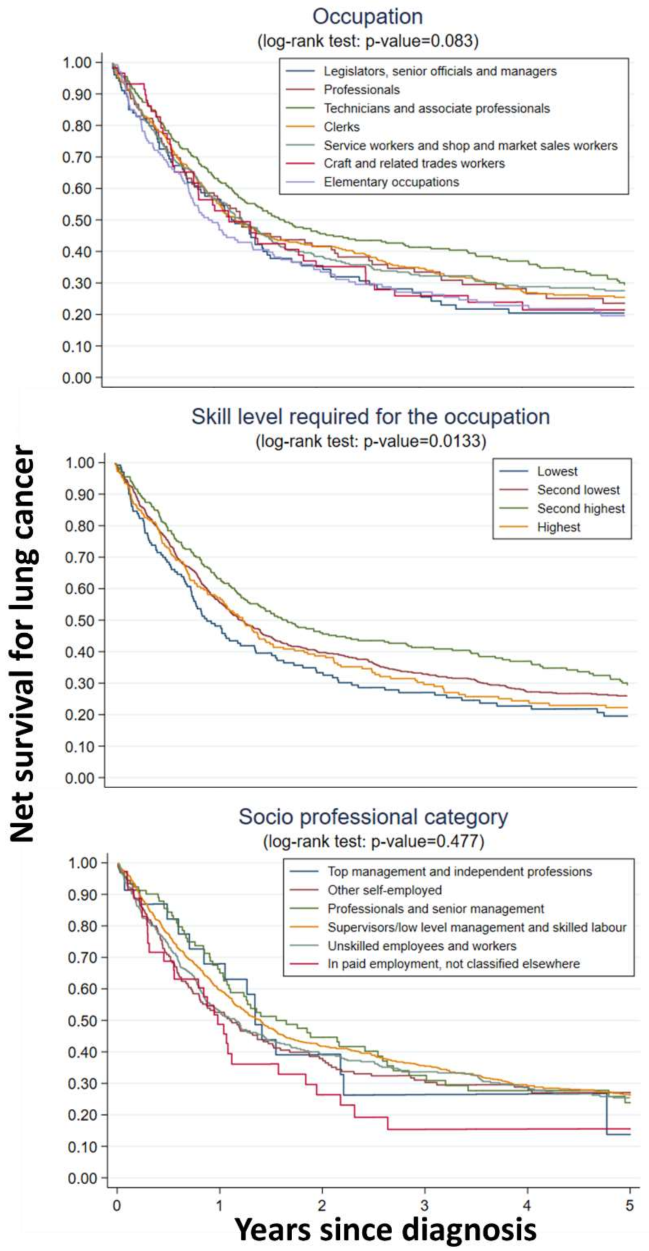

Figure 2: non-parametric net survival of lung cancer across occupation (1-digit ISCO-88), skill level required for the occupation and socio-professional category in women

Table 3 Hazard ratios (HR) and Confidence Interval (95%-IC) for Lung Cancer relative survival by work-related variables among females aged 18-85 in French-speaking Switzerland

Characteristics	Model 1*		Model 2**	
Occupation[a]				
Legislators, senior officials and managers	Ref.		Ref.	
Professionals	0.89	0.65-1.22	0.81	0.58-1.12
Technicians and associate professionals	0.72	0.55-0.94	0.72	0.54-0.95
Clerks	0.86	0.67-1.11	0.83	0.64-1.09
Service workers and shop and market sales workers	0.85	0.66-1.11	0.83	0.63-1.09
Skilled agricultural and fishery workers	1.17	0.63-2.17	0.99	0.53-1.85
Craft and related trades workers	0.86	0.59-1.25	0.84	0.57-1.26
Plant and machine operators and assemblers	0.96	0.47-1.94	0.72	0.35-1.48
Elementary occupations	0.96	0.71-1.29	0.92	0.66-1.26
Skill level required for the occupation				
Low	Ref.		Ref.	
Intermediate low	0.90	0.73-1.11	0.91	0.72-1.15
Intermediate high	0.75	0.59-0.97	0.79	0.61-1.02
High	0.98	0.76-1.27	0.98	0.74-1.28
Socio-professional category				
Top management and independent professions	Ref.		Ref.	
Other self-employed	0.93	0.56-1.57	0.99	0.58-1.70
Professionals and senior management	0.81	0.46-1.40	0.84	0.47-1.49
Supervisors/low level management and skilled labour	0.84	0.51-1.38	0.96	0.57-1.59
Unskilled employees and workers	0.87	0.52-1.44	0.99	0.59-1.67
In paid employment, not classified elsewhere	1.08	0.58-2.00	1.18	0.63-2.23

*Model 1 is adjusted for age and calendar period;**Model 2 is adjusted for age, calendar period and stage at diagnosis

[a] Occupation is coded using the International Standard Classification of Occupations, version 1988 (ISCO-88), coded on 1 digit

DISCUSSION

To our knowledge, this study was the first to assess the net survival using three work-related variables: the official ILO standardized classification of occupations (ISCO-88), the skill level required for the occupation and occupation and the socio-professional category. Although Grivaux et al. used a socio-professional category (Grivaux et al. 2011), our categorization was more exhaustive and took into account all levels of the population's social professional structure. We observed that women working as technicians and as associate professionals had a better net survival compared to senior officials and managers. Among men, workers with a paid employment but without precise information on socio-professional category had a worse survival compared to professionals and senior managers. When adjusted for tumour stage, the skill level required for the occupation was not associated with net survival.

Net lung cancer survival in work- related variables

We showed that after the addition of the tumour stage at diagnosis point estimates in men were reduced toward 1 for occupation and socio-professional category. For women, the estimates for occupation and socio-professional slightly changed after adjustment. In both sexes, the estimates for skill level remained unchanged. Using the AIC criterion, we observed that the addition of tumour stage improved the fit of all our models, both in men and women. This is consistent with previous findings that survival is influenced by tumour stage at diagnosis (Coleman et al. 2011), although this factor alone cannot explain all of the difference in survival (Woods et al. 2006). To have a better understanding of the effect of the tumour stage on our results, we compared the distributions of tumour stage at diagnosis across occupations, skill levels and socio-professional categories using a Chi2 test. We found that tumour stage at diagnosis did not depend on occupation or skill level. However, in men, there was a significant association between tumour stage and socio-professional category (p=0.03) (result not shown). Men in paid employment (not classified elsewhere) were diagnosed later (stage III and IV) (81%) than the other socio-professional categories. Because this category remained with an HR of 1.36 (95%-IC: 1.05-1.76) in the model adjusted for stage at diagnosis, we may suppose that net survival in this category is lower than that of workers in top management positions and independent professions. Moreover, other or additional factors that we could not address using the available data could explain this result. For example, previous findings demonstrated that current smoking at diagnosis was a significant independent predictor of reduced lung cancer survival and that the effect of this variable was not explained by sociodemographic factors, stage or treatment (Tammemagi et al. 2004). However, this hypothesis could not be tested. The cancer registries had very little data on smoking, while the SNC had none. Furthermore, treatment differences between social groups has been demonstrated to influence lung cancer survival (Woods et al. 2006). We believe, though, that this hypothesis is small in Switzerland, as health insurance covers most of the expenses related to treatment (Swiss Confederation 2022).

After adjustment for tumour stage, all occupational groups among women had an HR less than 1 compared with the reference category of legislators, senior officials, and managers, but only those estimated on female technicians and associate professionals remained statistically significant. This result raised the question of the impact of occupational factors on lung cancer net survival. However, the heterogeneity of occupations in this group, including engineers, teachers, health care workers, and those working in finance and business, made any hypothesis difficult. In a previous Swiss descriptive study of lung cancer mortality, we showed that female teachers and health care workers had a lower risk of dying from lung cancer compared with the general population (Bovio et al. 2020). For the other groups above, the risk of mortality was higher, but none of these results were adjusted for smoking. We believe therefore that occupation-specific analyses should be conducted. Under the AIC criterion, internal analyses showed that the 1-digit ISCO-88 code fitted the data better than the 2-digit codes. However, the occupational groups at this 1- or 2-digit level may not be specific enough and may incorporate different socioeconomic concepts that are not directly related to occupational exposure. Analyses at 3- or 4-digit level should be tested. Moreover, smoking habits, information exposure and working conditions before and after diagnosis is needed. Lastly, the inclusion of measures such as income, education, or regional socioeconomic status could also help adjusting for the effect of other non-occupational factors. Although correlated with occupation, they measure different phenomena and exploit different causal mechanisms (Geyer et al. 2006).

Finally, the use of relative survival framework in our study was appropriate to investigate inequalities in lung cancer after diagnosis. This allows for disparities in mortality between study groups with respect to multiple causes of death (Redondo-Sánchez et al. 2022). Because of the association between occupational variables and mortality (Redondo-Sánchez et al. 2022), we believe that future studies on occupational factors should also focus on RS methods. We also think further analyses should remained stratified by sex. Although this was not done in the systematic review and meta-analysis by (Finke et al. 2018), we believe that doing so is essential to account for gender specificities, as recommended by the European Agency for Safety and Health at Work (EU-OSHA 2014).

Strengths and limitations

A major strength of our study lies in the use of international classification of occupation that we also used to create the skill level required for the occupation. This allows for a common definition and measurement of occupation-related variables, which can be replicated and compared internationally. In addition, our analyses were stratified by sex, which addressed the recommendation to improve knowledge of occupational exposures and their effects on women (EU-OSHA 2014b). Moreover, the nonparametric method allowed us to calculate net lung cancer survival for each of the three occupational variables without making any specific assumptions, whereas the parametric method allowed us to quantify the differences between groups in terms of hazard ratios and to test the proportional hazards assumption. Although the tumour stage at diagnosis was missing for 23% of women and 38% in men, we were able to complete it using multiple imputation. The comparison of models using listwise deletion (complete case analyses) and those with imputed models yielded similar results. There is no evidence for biased estimates or insufficient precision due to imputation. Because each new cancer case must be reported to the cantonal tumor registry to which the resident is attached, we believe that the incidence information was of very good quality.

In terms of limitations, the occupation information was missing for 67% of women and 48% of men. However, an internal comparison of socio-demographic information showed that excluded participants with missing occupation information were similar to included participants. Assigning occupations as a time-dependent variable based on two time points could result in some misclassification. Nevertheless, the information on occupation at the time of the federal censuses is correct and we believe we assigned it accurately enough, since the majority of participants kept the same between the two censuses (Bovio et al. 2021). Having occupational information at the date of incidence would be more accurate, but it was not available in the SNC. In a study conducted prior to this research, we assessed the quality of occupational data in the six Western-Swiss cancer registries and in the SNC and concluded at heterogeneity issues between registries (Plys et al. 2022). To avoid differential misclassification on occupation, we considered the use of the SNC data more relevant than the registry data. Lastly, information on smoking and occupational exposures at diagnosis and during treatment was not available to study their effect on cancer survival. Information on treatment after diagnosis was also unavailable in this study, but is available in some cancer registries. Collection of this information and its use in future analyses will allow more accurate estimation of factors affecting net lung cancer survival.

Conclusion

This study reports net survival for lung cancer across three different occupation-related variables: occupation, skill level required for the occupation and the socio-professional category of employment. After adjustment for tumour stage at diagnosis, we observed that most of differences were smaller. Men in paid employment not elsewhere classified had the lowest net survival and top management and independent professions the highest. We observed that tumour stage varied significantly between male socio-professional categories and could partly explain this result. Further studies are required, taking into account smoking habits and the treatment received by the patient. The inclusion of potential occupational carcinogens, their dose and potency before and after diagnosis is also paramount to be able to quantify the effect of occupational context, if any. These factors should be applied in more detailed analyses of occupations included in female technicians and associate professionals, which had a higher survival compared to legislators, senior officials and managers. This would allow assessing whether survival with lung cancer differs for engineers, teachers, health care workers and women working in finance and business, and to clarify the factors influencing it. Finally, the use of standardized classifications in our study allowed us to produce results that can be compared internationally. The previously demonstrated association between occupational variables and mortality (Paglione et al. 2020) also showed us the importance of focusing on relative survival methods for future studies on occupational factors.

References

Akaike H, Petrov BN, Csaki F (1973) Second international symposium on information theory. Akademia Kiado

Allemani C, et al. (2018) Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. The Lancet 391(10125):1023-1075 doi:https://doi.org/10.1016/S0140-6736(17)33326-3

Berglund A, Holmberg L, Tishelman C, Wagenius G, Eaker S, Lambe M (2010) Social inequalities in non-small cell lung cancer management and survival: a population-based study in central Sweden. Thorax 65(4):327-33 doi:10.1136/thx.2009.125914

Berkson J, Gage R Calculation of survival rates for cancer. In, 1952.

Bovio N, Richardson DB, Guseva Canu I (2020) Sex-specific risks and trends in lung cancer mortality across occupations and economic activities in Switzerland (1990-2014). Occup Environ Med 77(8):540-548 doi:10.1136/oemed-2019-106356

Bovio N, Wild P, Canu IG, Swiss National C (2021) Lung Cancer Mortality in the Swiss Working Population: The Effect of Occupational and Non-Occupational Factors. J Occup Environ Med doi:10.1097/JOM.0000000000002302

Chirikos TN, Reiches NA, Moeschberger ML (1984) Economic differentials in cancer survival: A multivariate analysis. Journal of Chronic Diseases 37(3):183-193 doi:https://doi.org/10.1016/0021-9681(84)90146-2

Clerc-Urmès I, Grzebyk M, Hédelin G (2014) Net survival estimation with stns. Stata Journal 14(1):87-102

Clerc-Urmès I, Grzebyk M, Hédelin G (2021) flexrsurv: Flexible Relative Survival Analysis.

Coleman MP, et al. (2011) Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. The Lancet 377(9760):127-138 doi:https://doi.org/10.1016/S0140-6736(10)62231-3

Dalton SO, et al. (2015) Socioeconomic position and survival after lung cancer: Influence of stage, treatment and comorbidity among Danish patients with lung cancer diagnosed in 2004–2010. Acta Oncologica 54(5):797-804 doi:10.3109/0284186X.2014.1001037

Estève J, Benhamou E, Raymond L (1994) Statistical methods in cancer research. Volume IV. Descriptive epidemiology. IARC scientific publications(128):1-302

EU-OSHA (2014) Priorities for occupational safety and health research in Europe for the years 2013-2020. Summary report. Occupational Safety and Health Topic. European Agency for Safety and Health at Work (EU-OSHA), Luxembourg, p 23

Finke I, Behrens G, Weisser L, Brenner H, Jansen L (2018) Socioeconomic Differences and Lung Cancer Survival—Systematic Review and Meta-Analysis. Frontiers in Oncology 8(536) doi:10.3389/fonc.2018.00536

Fujino Y (2007) Occupational factors and mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). Asian Pacific journal of cancer prevention : APJCP 8 Suppl:97-104

Galli F, Rohrmann S, Lorez M (2019) Lung cancer survival in Switzerland by histology, TNM stage and age at diagnosis. 39

Geyer S, Hemström O, Peter R, Vågerö D (2006) Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. Journal of epidemiology and community health 60(9):804-810 doi:10.1136/jech.2005.041319

Giorgi R, et al. (2003) A relative survival regression model using B-spline functions to model non-proportional hazards. Stat Med 22(17):2767-84 doi:10.1002/sim.1484

Grafféo N, Castell F, Belot A, Giorgi R (2016) A log-rank-type test to compare net survival distributions. Biometrics 72(3):760-769 doi:https://doi.org/10.1111/biom.12477

Grivaux M, et al. (2011) Five-year survival for lung cancer patients managed in general hospitals. Revue des Maladies Respiratoires 28(7):e31-e38 doi:https://doi.org/10.1016/j.rmr.2008.07.001

IARC (2005) International rules for multiple primary cancers (ICD-0 third edition). European Journal of Cancer Prevention 14(4)
IARC (2021a) Age-standardized 1-,5-year net survival (15–99 years) in 2010-2014, Lung, both sexes. In. https://gco.iarc.fr/survival/survmark/ Accessed 03.06.2021
IARC (2021b) Estimated number of new cases in 2020, worldwide, both sexes, all ages. In. https://gco.iarc.fr/today/home Accessed 03.06.2021
Kravdal O (2000) Social inequalities in cancer survival. Popul Stud (Camb) 54(1):1-18 doi:10.1080/713779066
Milner A, Spittal MJ, Pirkis J, LaMontagne AD (2013) Suicide by occupation: systematic review and meta-analysis. The British journal of psychiatry : the journal of mental science 203(6):409-16 doi:10.1192/bjp.bp.113.128405
Paglione L, Angelici L, Davoli M, Agabiti N, Cesaroni G (2020) Mortality inequalities by occupational status and type of job in men and women: results from the Rome Longitudinal Study. BMJ Open 10(6):e033776 doi:10.1136/bmjopen-2019-033776
Pastorino U, et al. (1990) Incident Lung Cancer Survival. Long-Term Follow-Up of a Population-Based Study in Italy. Tumori Journal 76(2):199-204 doi:10.1177/030089169007600210
Perme MP, Stare J, Estève J (2012) On estimation in relative survival. Biometrics 68(1):113-20 doi:10.1111/j.1541-0420.2011.01640.x
Plys E, et al. (2022) Research on occupational diseases in the absence of occupational data: a mixed-method study among cancer registries of Western Switzerland. Swiss medical weekly 152:w30127 doi:10.4414/smw.2022.w30127
Redondo-Sánchez D, Petrova D, Rodríguez-Barranco M, Fernández-Navarro P, Jiménez-Moleón JJ, Sánchez M-J (2022) Socio-Economic Inequalities in Lung Cancer Outcomes: An Overview of Systematic Reviews. Cancers 14(2):398
Remontet L, Bossard N, Belot A, Estève J, FRANCIM tFnocr (2007) An overall strategy based on regression models to estimate relative survival and model the effects of prognostic factors in cancer survival studies. Statistics in medicine 26(10):2214-2228 doi:https://doi.org/10.1002/sim.2656
Schaffar R, Rachet B, Belot A, Woods LM (2017) Estimation of net survival for cancer patients: Relative survival setting more robust to some assumption violations than cause-specific setting, a sensitivity analysis on empirical data. European journal of cancer (Oxford, England : 1990) 72:78-83 doi:10.1016/j.ejca.2016.11.019
SFSO (2004) Methodology report—coverage estimation for the Swiss population census 2000. Swiss Federal Statistical Office. In. https://www.bfs.admin.ch/bfsstatic/dam/assets/341896/master Accessed 03.06.2021
SFSO (2016) Catégories socioprofessionnelles (CSP) 2010 - Opérationnalisation des CSP dans le système des variables-clés SHAPE dès 2010.19
Sobin LH, Gospodarowicz MK, Wittekind C (2011) TNM classification of malignant tumours. John Wiley & Sons
Spratt M, et al. (2010) Strategies for multiple imputation in longitudinal studies. American journal of epidemiology 172(4):478-87 doi:10.1093/aje/kwq137
Swiss Confederation (2022) Loi fédérale sur l'assurance-maladie (LAMal). In. https://www.fedlex.admin.ch/eli/cc/1995/1328_1328_1328/fr Accessed 01.03.2022
Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P (2004) Smoking and Lung Cancer Survival: The Role of Comorbidity and Treatment. Chest 125(1):27-37 doi:https://doi.org/10.1378/chest.125.1.27
Vågerö D, Persson G (1987) Cancer survival and social class in Sweden. Journal of Epidemiology and Community Health 41(3):204-209 doi:10.1136/jech.41.3.204
van Buuren S, Groothuis-Oudshoorn K (2011) mice: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software 45(3):1 - 67 doi:10.18637/jss.v045.i03
Woods LM, Rachet B, Coleman MP (2006) Origins of socio-economic inequalities in cancer survival: a review. Annals of Oncology 17(1):5-19 doi:https://doi.org/10.1093/annonc/mdj007

V Discussion

Because of the limited data on occupational lung cancer available in Switzerland, the objective of this work was to calculate the first national estimates of lung cancer risk between occupations and other occupational factors. We focused mainly on mortality and net survival analyses. In addition, it was important as a preliminary work to find a way to re/code the occupation or economic activity through an automated process, which was made possible by the creation of the Procode software. Although we initially coded and recoded the occupations manually, the creation of this software saved us considerable time. The same will be true in future studies that need to code from the raw text or recode occupation to a standardized classification.

With respect to lung cancer mortality, the first study we conducted was descriptive in nature but provided some important insights from both methodological and public health perspectives. It demonstrated that SMR remained a good approximation of the excess of mortality in both occupational and general cohorts, though rSMR helped to correct the healthy worker effect, which is usually present in SMR. Occupational exposures to lung carcinogens were consistently documented in most of the activities and occupations that we observed with an excess of lung cancer mortality, which demonstrated that Swiss workers had no particular profile of mortality from lung cancer by occupational group and sex, compared to other developed countries (Corbin et al. 2011; EU-OSHA 2014a; Hovanec et al. 2018; Jung et al. 2018; Pukkala et al. 2009; Silverman 2017). Part of the excessive lung cancer mortality observed in these groups could be due to occupational carcinogens. However, these results should be interpreted with caution because there was no adjustment for smoking, which may have led to an overestimation of lung cancer mortality in occupational or industrial groups with a high smoking prevalence.

After adjustment for smoking, we observed in the second study we conducted that there was little variation in risk between occupations in women. In men, machine operator, construction workers, and hotel and restaurant employees remained with a higher risk of lung cancer mortality, as suggested by our first descriptive study. However, there is still a need to conduct further analysis for women working in transportation and traffic occupations, who had an adjusted risk higher than two compared to health occupations. To our knowledge, this result was original and should be confirmed. The degree of exposure of women working in the electrical engineering, electronics, watchmaking, vehicle and tool manufacturing sectors also needs further confirmation.

To our knowledge, SUVA only recognizes nickel, crystalline silica, asbestos, bis(chloromethyl) ether and chromium VI as carcinogens for the lung cancer (SUVA, 2022). According to the international studies, workers in occupations we identified as high-risk were likely to be exposed to a greater number of IARC carcinogens. Swiss construction workers could be exposed to diesel exhaust diesel exhaust (Jung et al. 2018). Workers in mining, stone working, and building material manufacturing may be exposed to arsenic, PAHs and/or diesel exhaust (Brown et al. 2012; Jung et al. 2018; Pukkala et al. 2009) and those in electrical engineering, electronics, watchmaking, automotive, and tool-making might be exposed to welding fumes, engine exhaust, PAHs, and beryllium (EU-OSHA 2014a). Although exposure to these carcinogens in these occupations remains to be demonstrated by more detailed analyses, it would appear that these occupational carcinogens are not recognized by SUVA. In addition, the differences in lung cancer mortality observed between the occupations also raise questions about the number of occupational lung cancers in Switzerland (Suva 2017; Suva 2019). While SUVA recognizes only a few cases as occupational diseases, there is a further need to assess if the number recognized cases is accurate or if there is an under-recognition or under-reporting. In addition to providing a more reliable estimate of the total number of work-related lung cancers in Switzerland, doing so will allow comparison with international studies.

A major limitation of this thesis is the unavailability of individual smoking data. To circumvent this, it is essential to find a better way to adjust indirectly for this important confounding factor, using the most appropriate methods. To this end, we are conducting with the European network OMEGA-NET a scoping review of adjustment methods for smoking when individual smoking data are completely missing (Turner and Mehlum 2018). Another limitation of our studies was the lack of information on occupational variables, as we were only able to assign occupation based on two points in time (i.e., occupation at the time of the federal censuses). With our study on the quality of professional data collected by Swiss cancer registries, we demonstrated that the lack of financial and human resources will continue to affect the quality of this information. However, access to participants' complete work history is of paramount importance. We believe that for future studies the use of a standardized questionnaire tracing individual work history will be the best option to allow for a more thorough assessment of individual exposure to potential occupational risks. This will be more relevant than using routinely available data.

Regarding lung cancer survival, our study was the first to assess the net survival using the official ILO standardized classification of occupations (ISCO-88), but also the skill level required for the occupation at the individual level. We were able to show the importance of applying multivariate analyses when studying lung cancer survival, as the addition of stage decreased the effect of occupational variables. However, we found that tumour stage alone could not explain all the difference in survival. Men in paid employment (not classified elsewhere) remained with lower net survival that of workers in top management positions and independent professions. We think that other or additional factors that we could not address using the available data could explain this result. Previous findings demonstrated that current smoking at diagnosis was a significant independent predictor of reduced lung cancer survival and that the effect of this variable was not explained by sociodemographic factors, stage or treatment (Tammemagi et al. 2004). Inclusion of this factor is therefore necessary in future studies. In addition, differential treatment between social groups has been demonstrated to influence lung cancer survival (Woods et al. 2006). Although we believe that this hypothesis is unlikely in Switzerland, because health insurance covers most of the expenses related to treatment (Swiss Confederation 2022), it could be easily verified in future analyses, because this information is available in cancer registries. Furthermore, the significant differences in survival observed between women working as technicians and associate professionals and women legislators, senior officials, and managers raised the question of the potential impact of other occupational factors that might influence lung cancer survival. However, the heterogeneity of the occupations in this group including engineers, teachers, health care workers, and people working in finance and business made any assumptions difficult. Because occupational groups at this 1- or 2-digit level may not be specific enough and may incorporate different socioeconomic constructs that are not directly related to occupational exposure, we believe that analyses at a 3- or 4-digit level should be tested. This could not be tested, however, because the number of participants per occupation was too small at this level of aggregation. In addition to smoking habits, it is also necessary to retrieve information on exposure and working conditions before and after for better estimates of their potential effect on net survival.

We think that the use of relative survival framework is more appropriate than overall survival to investigate inequalities in lung cancer after diagnosis. This allows for disparities in mortality between study groups with respect to multiple causes of death (Redondo-Sánchez et al. 2022). Because of the association between occupational variables and mortality (Redondo-Sánchez et al. 2022), we believe that future studies on occupational factors should also focus on relative survival methods.

Finally, for either mortality or survival, we observed differences between men and women. This was expected and reinforces that future studies should be stratified by sex, as recommended by the European Agency for Safety and Health at Work (EU-OSHA 2014). This will allow for the development of appropriate gender-based prevention measures.

VI Conclusion

Occupational lung cancer represents 86% of all occupational cancers and is responsible for approximately 15% of lung cancer deaths worldwide. In addition, the financial and health burden of this disease is significant. However, before this thesis, very little knowledge about occupational lung cancer was available in Switzerland. The objective of this work was therefore to fill this gap by providing the first estimates of mortality risks and net survival of lung cancer across occupation and other work-related variables. In doing so, we demonstrated that even after adjustment for smoking, significant differences remained in both mortality and survival. Our gender-stratified analyses also allowed us to observe significant differences by gender. In addition, our results demonstrated that occupational groups identified as being at risk are likely to be exposed to occupational lung carcinogens. To have a better understanding of the effect of the work environment on lung cancer mortality and survival in these groups, it is necessary to apply analyses at finer levels of occupational aggregation. In our analyses, occupational groups at 1-2 digit level may not be specific enough and may incorporate different socioeconomic concepts that are not directly related to occupational exposure. Use of the 3-4 digit ISCO-88 occupations should provide a more accurate estimate of the risk factors and occupational exposures faced by workers in high-risk groups. As mentioned by (Loomis et al., 2018), many workplace agents have never been evaluated for carcinogenicity, and epidemiological evidence is insufficient or completely lacking for many agents evaluated by IARC. It is therefore essential to undertake this work at the Swiss level, which will subsequently allow the development of more appropriate and specific prevention measures aimed at reducing the impact of occupational lung cancer in Switzerland. It will also allow to estimate the number of workers exposed to occupational lung carcinogens in Switzerland and to generate quantitative data on exposure. In addition to providing a scientific basis, these data will be used as a basis for comparison with current Swiss figures on the recognition of lung cancer as an occupational disease and will allow an analysis of whether there is under-recognition or under-reporting of cases.

VII References

Akaike H, Petrov BN, Csaki F (1973) Second international symposium on information theory. Akademia Kiado

Allemani C, et al. (2018) Global surveillance of trends in cancer survival 2000–14 (CONCORD-3): analysis of individual records for 37 513 025 patients diagnosed with one of 18 cancers from 322 population-based registries in 71 countries. The Lancet 391(10125):1023-1075 doi:https://doi.org/10.1016/S0140-6736(17)33326-3

Atramont A, et al. (2016) Professional Cleaning Activities and Lung Cancer Risk Among Women: Results From the ICARE Study. J Occup Environ Med 58(6):610-6 doi:10.1097/JOM.0000000000000722

Axelson O (1989) Editorial: Confounding from Smoking in Occupational Epidemiology. British Journal of Industrial Medicine 46(8):505-507

Bauer G, et al. (2006) Conditions de travail et santé: une orientation stratégique commune: impulsions, résultats et recommandations issus de la Journée nationale de travail de la politique nationale suisse de la santé le 8 [ie 18] septembre 2003 à Aarau. Office fédéral de la santé publique, Secrétariat exécutif pour la politique …

Berglund A, Holmberg L, Tishelman C, Wagenius G, Eaker S, Lambe M (2010) Social inequalities in non-small cell lung cancer management and survival: a population-based study in central Sweden. Thorax 65(4):327-33 doi:10.1136/thx.2009.125914

Berkson J, Gage R Calculation of survival rates for cancer. In, 1952.

Bird S, Klein E, Loper E (2009) Natural Language Processing with Python. O'Reilly Media, Inc.

Blair A, Stewart P, Lubin JH, Forastiere F (2007) Methodological issues regarding confounding and exposure misclassification in epidemiological studies of occupational exposures. Am J Ind Med 50(3):199-207 doi:10.1002/ajim.20281

Bondo Petersen S, et al. (2018) Job-exposure matrices addressing lifestyle to be applied in register-based occupational health studies. Occup Environ Med 75(12):890-897 doi:10.1136/oemed-2018-104991

Bouchardy C, et al. (2002) Cancer risk by occupation and socioeconomic group among men--a study by the Association of Swiss Cancer Registries. Scandinavian journal of work, environment & health 28 Suppl 1:1-88

Boulanger M, et al. (2018) Lung cancer risk and occupational exposures in crop farming: results from the AGRIculture and CANcer (AGRICAN) cohort. Occup Environ Med 75(11):776-785 doi:10.1136/oemed-2017-104976

Bovio N, Richardson DB, Guseva Canu I (2020) Sex-specific risks and trends in lung cancer mortality across occupations and economic activities in Switzerland (1990-2014). Occupational and environmental medicine doi:10.1136/oemed-2019-106356

Bovio N, Vienneau D, Canu IG (2019) O3D.6 Inventory of occupational, industrial and population cohorts in switzerland. Occupational and Environmental Medicine 76(Suppl 1):A29 doi:10.1136/OEM-2019-EPI.77

Bovio N, Wild P, Canu IG, Swiss National C (2021) Lung Cancer Mortality in the Swiss Working Population: The Effect of Occupational and Non-Occupational Factors. J Occup Environ Med doi:10.1097/JOM.0000000000002302

Breslow NE, Day NE (1987) Statistical methods in cancer research. Volume II--The design and analysis of cohort studies. IARC scientific publications(82):1-406

Brown T, Darnton A, Fortunato L, Rushton L, British Occupational Cancer Burden Study G (2012) Occupational cancer in Britain. Respiratory cancer sites: larynx, lung and mesothelioma. British journal of cancer 107 Suppl 1:S56-70 doi:10.1038/bjc.2012.119

Bulliard J, Ducros C, Germann S, Arveux P, Bochud M (2020) Nouvelles exigences légales dans le domaine de l'enregistrement du cancer : opportunités et défis. Rev Med Suisse volume 6.(no. 713, 2099 - 2103)

Cancer Research UK (2020) Stages of cancer. In. https://www.cancerresearchuk.org/about-cancer/what-is-cancer/stages-of-cancer Accessed 21.03.2022

Chirikos TN, Reiches NA, Moeschberger ML (1984) Economic differentials in cancer survival: A multivariate analysis. Journal of Chronic Diseases 37(3):183-193 doi:https://doi.org/10.1016/0021-9681(84)90146-2
Ciabattini M, Rizzello E, Lucaroni F, Palombi L, Boffetta P (2021) Systematic review and meta-analysis of recent high-quality studies on exposure to particulate matter and risk of lung cancer. Environmental Research 196:110440 doi:https://doi.org/10.1016/j.envres.2020.110440
Cirillo P, et al. (2021) Le cancer en Suisse, rapport 2021 - Etats des lieux et évolutions.
Clerc-Urmès I, Grzebyk M, Hédelin G (2014) Net survival estimation with stns. Stata Journal 14(1):87-102
Clerc-Urmès I, Grzebyk M, Hédelin G (2021) flexrsurv: Flexible Relative Survival Analysis.
Cogliano VJ, et al. (2011) Preventable exposures associated with human cancers. Journal of the National Cancer Institute 103(24):1827-39 doi:10.1093/jnci/djr483
Coleman MP, et al. (2011) Cancer survival in Australia, Canada, Denmark, Norway, Sweden, and the UK, 1995–2007 (the International Cancer Benchmarking Partnership): an analysis of population-based cancer registry data. The Lancet 377(9760):127-138 doi:https://doi.org/10.1016/S0140-6736(10)62231-3
Corbin M, et al. (2011) Lung cancer and occupation: A New Zealand cancer registry-based case-control study. Am J Ind Med 54(2):89-101 doi:10.1002/ajim.20906
Cutler A, Cutler D, Stevens J (2011) Random Forests. vol 45, p 157-176
Dalton SO, Steding-Jessen M, Engholm G, Schüz J, Olsen JH (2008) Social inequality and incidence of and survival from lung cancer in a population-based study in Denmark, 1994-2003. European journal of cancer (Oxford, England : 1990) 44(14):1989-95 doi:10.1016/j.ejca.2008.06.023
Dalton SO, et al. (2015) Socioeconomic position and survival after lung cancer: Influence of stage, treatment and comorbidity among Danish patients with lung cancer diagnosed in 2004–2010. Acta Oncologica 54(5):797-804 doi:10.3109/0284186X.2014.1001037
Daly BJ, Schmid K, Riediker M (2010) Contribution of fine particulate matter sources to indoor exposure in bars, restaurants, and cafes. Indoor Air 20(3):204-12 doi:10.1111/j.1600-0668.2010.00645.x
Darby S, et al. (2005) Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 330(7485):223 doi:10.1136/bmj.38308.477650.63
de Groot PM, Wu CC, Carter BW, Munden RF (2018) The epidemiology of lung cancer. Transl Lung Cancer Res 7(3):220-233 doi:10.21037/tlcr.2018.05.06
De Matteis S, et al. (2017) Occupational self-coding and automatic recording (OSCAR): a novel web-based tool to collect and code lifetime job histories in large population-based studies. Scandinavian journal of work, environment & health 43(2):181-186 doi:10.5271/sjweh.3613
Dement JM, Ringen K, Hines S, Cranford K, Quinn P (2020) Lung cancer mortality among construction workers: implications for early detection. Occupational and Environmental Medicine 77(4):207 doi:10.1136/oemed-2019-106196
Doll R, Peto R, Boreham J, Sutherland I (2004) Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 328(7455):1519 doi:10.1136/bmj.38142.554479.AE
Driscoll T, et al. (2004) Occupational carcinogens : assessing the environmental burden of disease at national and local levels / Tim Driscoll ... [et al.]. Environmental burden of disease series ; no. 6. World Health Organization, Geneva
Eguchi H, Wada K, Prieto-Merino D, Smith DR (2017) Lung, gastric and colorectal cancer mortality by occupation and industry among working-aged men in Japan. Scientific Reports 7(1):43204 doi:10.1038/srep43204
Espina C, et al. (2015) European Code against Cancer 4th Edition: Environment, occupation and cancer. Cancer Epidemiol 39 Suppl 1:S84-92 doi:10.1016/j.canep.2015.03.017
Estève J, Benhamou E, Raymond L (1994) Statistical methods in cancer research. Volume IV. Descriptive epidemiology. IARC scientific publications(128):1-302

ETUI contributors (2020) The cost of occupational cancer in the EU-28 - Executive summary. The European Trade Union Institute
ETUI contributors (2021) Cancer and work: understanding occupational cancers and taking action to eliminate them. ETUI, The European Trade Union Institute
EU-OSHA (2014a) Exposure to carcinogens and work-related cancer: A review of assessment methods. Executive summary. In: Observatory ER (ed). European Agency for Safety and Health at Work (EU-OSHA), Luxembourg, p 27
EU-OSHA (2014b) Priorities for occupational safety and health research in Europe for the years 2013-2020. Summary report. Occupational Safety and Health Topic. European Agency for Safety and Health at Work (EU-OSHA), Luxembourg, p 23
EUROGIP (2018) Incidence and detection of occupational cancers in nine European countries.
Facebook (2020) React - A JavaScript library for building user interfaces. In. https://reactjs.org/ Accessed 11 April 2020
Fadel M, et al. (2020) Not just a research method: If used with caution, can job-exposure matrices be a useful tool in the practice of occupational medicine and public health? Scandinavian journal of work, environment & health doi:10.5271/sjweh.3900
Feller A, et al. (2017) Socioeconomic and demographic disparities in breast cancer stage at presentation and survival: A Swiss population-based study. Int J Cancer 141(8):1529-1539 doi:https://doi.org/10.1002/ijc.30856
Feller A, et al. (2018) Socioeconomic and demographic inequalities in stage at diagnosis and survival among colorectal cancer patients: evidence from a Swiss population-based study. Cancer Med 7(4):1498-1510 doi:https://doi.org/10.1002/cam4.1385
Feng SH, Yang S-T (2019) The new 8th TNM staging system of lung cancer and its potential imaging interpretation pitfalls and limitations with CT image demonstrations. Diagn Interv Radiol 25(4):270-279 doi:10.5152/dir.2019.18458
Fidler-Benaoudia MM, Torre LA, Bray F, Ferlay J, Jemal A (2020) Lung cancer incidence in young women vs. young men: A systematic analysis in 40 countries. Int J Cancer 147(3):811-819 doi:https://doi.org/10.1002/ijc.32809
Finke I, Behrens G, Weisser L, Brenner H, Jansen L (2018) Socioeconomic Differences and Lung Cancer Survival—Systematic Review and Meta-Analysis. Frontiers in Oncology 8(536) doi:10.3389/fonc.2018.00536
Foundation DS (2020) The Django Project. In. https://www.djangoproject.com/
Fujino Y (2007) Occupational factors and mortality in the Japan Collaborative Cohort Study for Evaluation of Cancer (JACC). Asian Pacific journal of cancer prevention : APJCP 8 Suppl:97-104
Galli F, Rohrmann S, Lorez M (2019) Lung cancer survival in Switzerland by histology, TNM stage and age at diagnosis. 39
Garshick E, et al. (2008) Lung cancer and vehicle exhaust in trucking industry workers. Environmental health perspectives 116(10):1327-1332 doi:10.1289/ehp.11293
Garshick E, et al. (2004) Lung cancer in railroad workers exposed to diesel exhaust. Environmental health perspectives 112(15):1539-1543 doi:10.1289/ehp.7195
GBD (2018) Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet (London, England) 392(10159):1923-1994 doi:10.1016/s0140-6736(18)32225-6
GBD (2020) Global and regional burden of cancer in 2016 arising from occupational exposure to selected carcinogens: a systematic analysis for the Global Burden of Disease Study 2016. Occupational and environmental medicine 77(3):151-159 doi:10.1136/oemed-2019-106012
GBD (2022a) High SDI, Both sexes, All ages, 2019, Deaths In. https://vizhub.healthdata.org/gbd-compare/ Accessed 11.03.2022
GBD (2022b) Total cancers - Cause. In. https://www.healthdata.org/results/gbd_summaries/2019/total-cancers-level-2-cause Accessed 08.02.2022

Geyer S, Hemström O, Peter R, Vågerö D (2006) Education, income, and occupational class cannot be used interchangeably in social epidemiology. Empirical evidence against a common practice. Journal of epidemiology and community health 60(9):804-810 doi:10.1136/jech.2005.041319

Giorgi R, et al. (2003) A relative survival regression model using B-spline functions to model non-proportional hazards. Stat Med 22(17):2767-84 doi:10.1002/sim.1484

Gmel G, Kuendig H, Notari L, Gmel C (2016) Monitorage suisse des addictions - Consommation d'alcool, de tabac et de drogues illégales en Suisse en 2015. Addiction Suisse, Lausanne, Suisse

Goldberg M, et al. (2017) CONSTANCES: a general prospective population-based cohort for occupational and environmental epidemiology: cohort profile. Occup Environ Med 74(1):66-71 doi:10.1136/oemed-2016-103678

Graczyk H, François M, Krief P, Guseva Canu I (2021) The role of the Swiss list of occupational diseases in the protection of workers' health. Swiss medical weekly 151:w20538 doi:10.4414/smw.2021.20538

Grafféo N, Castell F, Belot A, Giorgi R (2016) A log-rank-type test to compare net survival distributions. Biometrics 72(3):760-769 doi:https://doi.org/10.1111/biom.12477

Greene WH (2012) Econometric analysis. Pearson, Boston; London

Grivaux M, et al. (2011) Five-year survival for lung cancer patients managed in general hospitals. Revue des Maladies Respiratoires 28(7):e31-e38 doi:https://doi.org/10.1016/j.rmr.2008.07.001

Guillemin M (2018) Santé au travail : le déni des politiques publiques. REISO, Revue d'information sociale

Guseva Canu I, Bovio N, Mediouni Z, Bochud M, Wild P, Swiss National C (2019a) Suicide mortality follow-up of the Swiss National Cohort (1990-2014): sex-specific risk estimates by occupational socio-economic group in working-age population. Soc Psychiatry Psychiatr Epidemiol doi:10.1007/s00127-019-01728-4

Guseva Canu I, Bovio N, Wild P, Bopp M, Swiss National C (2021) Identification of socio-demographic, occupational, and societal factors for guiding suicide prevention: A cohort study of Swiss male workers (2000-2014). Suicide Life Threat Behav 51(3):540-553 doi:10.1111/sltb.12746

Guseva Canu I, Francois M, Graczyk H, Vernez D (2019b) Healthy worker, healthy citizen: the place of occupational health within public health research in Switzerland. Int J Public Health doi:10.1007/s00038-019-01245-w

Hanahan D, Weinberg RA (2000) The Hallmarks of Cancer. Cell 100(1):57-70 doi:https://doi.org/10.1016/S0092-8674(00)81683-9

Hanahan D, Weinberg Robert A (2011) Hallmarks of Cancer: The Next Generation. Cell 144(5):646-674 doi:https://doi.org/10.1016/j.cell.2011.02.013

Hilbe JM (2011) Negative Binomial Regression, 2 edn. Cambridge University Press, Cambridge

Houston KA, Mitchell KA, King J, White A, Ryan BM (2018) Histologic Lung Cancer Incidence Rates and Trends Vary by Race/Ethnicity and Residential County. Journal of Thoracic Oncology 13(4):497-509 doi:https://doi.org/10.1016/j.jtho.2017.12.010

Hovanec J, et al. (2018) Lung cancer and socioeconomic status in a pooled analysis of case-control studies. PLoS One 13(2):e0192999 doi:10.1371/journal.pone.0192999

IARC (1988) Man-made mineral fibres. IARC monographs on the evaluation of carcinogenic risks to humans 43:39-171

IARC (2005) International rules for multiple primary cancers (ICD-0 third edition). European Journal of Cancer Prevention 14(4)

IARC (2016) Outdoor Air Pollution. IARC monographs on the evaluation of carcinogenic risks to humans 109:9-444

IARC (2021a) Age-standardized 1-,5-year net survival (15–99 years) in 2010-2014, Lung, both sexes. In. https://gco.iarc.fr/survival/survmark/ Accessed 03.06.2021

IARC (2021b) Cancer. In. https://www.who.int/news-room/fact-sheets/detail/cancer Accessed 05.01.2002

IARC (2021c) Estimated number of new cases in 2020, worldwide, both sexes, all ages. In. https://gco.iarc.fr/today/home Accessed 03.06.2021
IARC (2022a) Agents Classés par les Monographies du CIRC, Volumes 1–130. In. https://monographs.iarc.who.int/fr/agents-classes-par-les-monographies-du-circ-2/ Accessed 05.01.2022
IARC (2022b) Cancer Today In. https://gco.iarc.fr/today/online-analysis-map?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=total&sex=2&cancer=39&type=0&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=10&group_cancer=1&include_nmsc=1&include_nmsc_other=1&projection=natural-earth&color_palette=default&map_scale=quantile&map_nb_colors=5&continent=0&show_ranking=0&rotate=%255B10%252C0%255D Accessed 05.01.2022
IARC (2022c) Estimated number of deaths in 2020, wordwide, both sexes, all ages In. https://gco.iarc.fr/today/online-analysis-pie?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=total&sex=0&cancer=39&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=7&group_cancer=1&include_nmsc=1&include_nmsc_other=1&half_pie=0&donut=0 19.01.2022
IARC (2022d) Estimated number of deaths in 2020, worldwide, all ages. In. https://gco.iarc.fr/today/online-analysis-pie?v=2020&mode=cancer&mode_population=continents&population=900&populations=900&key=total&sex=1&cancer=39&type=1&statistic=5&prevalence=0&population_group=0&ages_group%5B%5D=0&ages_group%5B%5D=17&nb_items=7&group_cancer=1&include_nmsc=0&include_nmsc_other=1&half_pie=0&donut=0 Accessed 22.02.2022
Ikonomakis E, Kotsiantis S, Tampakas V (2005) Text classification: a recent overview.125
ILO (2012) International Standard Classification of Occupations 2008 (ISCO-08): Structure, group definitions and correspondence tables,
Inamura K (2017) Lung Cancer: Understanding Its Molecular Pathology and the 2015 WHO Classification. Front Oncol 7:193-193 doi:10.3389/fonc.2017.00193
IOSH (2022) Occupational cancer. In. https://iosh.com/resources-and-research/our-resources/occupational-health-toolkit/occupational-cancer/
Jakob J, Cornuz J, Diethelm P (2017) Prevalence of tobacco smoking in Switzerland: do reported numbers underestimate reality? Swiss medical weekly 147:w14437 doi:10.4414/smw.2017.14437
Jantz MA (2019) Lung cancer staging: accuracy is critical. J Thorac Dis 11(Suppl 9):S1322-S1324 doi:10.21037/jtd.2019.04.18
Jarvholm B, Astrom E (2014) The risk of lung cancer after cessation of asbestos exposure in construction workers using pleural malignant mesothelioma as a marker of exposure. J Occup Environ Med 56(12):1297-301 doi:10.1097/JOM.0000000000000258
Jones A, Gulbis A, Baker EH (2010) Differences in tobacco use between Canada and the United States. Int J Public Health 55(3):167-75 doi:10.1007/s00038-009-0101-3
Jongeneel W, Eysink P, Theodori D, Hamberg-van Reenen HH, Verhoeven J (2016) Work-related cancer in the European Union: Size, impact and options for further prevention.
Judge GG, Griffiths WE, Hill RC, Lütkepohl H, Lee T-C (1985) The Theory and Practice of Econometrics. 2nd ed.,
Jung JKH, et al. (2018) Examining lung cancer risks across different industries and occupations in Ontario, Canada: the establishment of the Occupational Disease Surveillance System. Occup Environ Med 75(8):545-552 doi:10.1136/oemed-2017-104926
Khuder SA (2001) Effect of cigarette smoking on major histological types of lung cancer: a meta-analysis. Lung cancer (Amsterdam, Netherlands) 31(2-3):139-48 doi:10.1016/s0169-5002(00)00181-1

Kim T-W, Koh D-H, Park C-Y (2010) Decision Tree of Occupational Lung Cancer Using Classification and Regression Analysis. Safety and Health at Work 1(2):140-148 doi:https://doi.org/10.5491/SHAW.2010.1.2.140

Kniesner TJ, Viscusi WK (2019) The Value of a Statistical Life (April 10, 2019). Oxford Research Encyclopedia of Economics and Finance

Koeman T, et al. (2013) JEMs and incompatible occupational coding systems: effect of manual and automatic recoding of job codes on exposure assignment. The Annals of occupational hygiene 57(1):107-14 doi:10.1093/annhyg/mes046

Korde V (2012) Text Classification and Classifiers:A Survey. International Journal of Artificial Intelligence & Applications 3:85-99 doi:10.5121/ijaia.2012.3208

Kravdal O (2000) Social inequalities in cancer survival. Popul Stud (Camb) 54(1):1-18 doi:10.1080/713779066

Kreuzer M, Kreienbrock L, Müller KM, Gerken M, Wichmann E (1999) Histologic types of lung carcinoma and age at onset. Cancer 85(9):1958-65 doi:10.1002/(sici)1097-0142(19990501)85:9<1958::aid-cncr12>3.0.co;2-u

Kriebel D, Zeka A, Eisen EA, Wegman DH (2004) Quantitative evaluation of the effects of uncontrolled confounding by alcohol and tobacco in occupational cancer studies. International Journal of Epidemiology 33(5):1040-1045 doi:10.1093/ije/dyh151

Laaksonen M, Rahkonen O, Karvonen S, Lahelma E (2005) Socioeconomic status and smoking: Analysing inequalities with multiple indicators. European Journal of Public Health 15(3):262-269 doi:10.1093/eurpub/cki115

Labrèche F, et al. (2019) The current burden of cancer attributable to occupational exposures in Canada. Preventive medicine 122:128-139 doi:10.1016/j.ypmed.2019.03.016

Lee H-E, Zaitsu M, Kim E-A, Kawachi I (2020) Occupational Class and Cancer Survival in Korean Men: Follow-Up Study of Nation-Wide Working Population. Int J Environ Res Public Health 17(1):303 doi:10.3390/ijerph17010303

Li N, et al. (2021) Association of 13 Occupational Carcinogens in Patients With Cancer, Individually and Collectively, 1990-2017. JAMA Network Open 4(2):e2037530-e2037530 doi:10.1001/jamanetworkopen.2020.37530

Lillard DR (2018) The Evolution of Smoking in Switzerland. In: Tillmann R, Voorpostel M, Farago P (eds) Social Dynamics in Swiss Society: Empirical Studies Based on the Swiss Household Panel. Springer International Publishing, Cham, p 3-16

Lindström M (2010) Social capital, economic conditions, marital status and daily smoking: a population-based study. Public health 124(2):71-7 doi:10.1016/j.puhe.2010.01.003

Loomis D (2020) Estimating the global burden of disease from occupational exposures. Occupational and Environmental Medicine 77(3):131-132 doi:10.1136/oemed-2019-106349

Loomis D, Guha N, Hall AL, Straif K (2018) Identifying occupational carcinogens: an update from the IARC Monographs. Occupational and Environmental Medicine 75(8):593-603 doi:10.1136/oemed-2017-104944

Lopez MJ, Nebot M, Juarez O, Ariza C, Salles J, Serrahima E (2006) [Estimation of the excess of lung cancer mortality risk associated to environmental tobacco smoke exposure of hospitality workers]. Med Clin (Barc) 126(1):13-4

Lorenzo-González M, Torres-Durán M, Barbosa-Lorenzo R, Provencio-Pulla M, Barros-Dios JM, Ruano-Ravina A (2019) Radon exposure: a major cause of lung cancer. Expert review of respiratory medicine 13(9):839-850 doi:10.1080/17476348.2019.1645599

Malarkey DE, Hoenerhoff MJ, Maronpot RR (2018) Chapter 6 - Carcinogenesis: Manifestation and Mechanisms. In: Wallig MA, Haschek WM, Rousseaux CG, Bolon B (eds) Fundamentals of Toxicologic Pathology (Third Edition). Academic Press, p 83-104

Malhotra J, Malvezzi M, Negri E, La Vecchia C, Boffetta P (2016) Risk factors for lung cancer worldwide. The European respiratory journal 48(3):889-902 doi:10.1183/13993003.00359-2016

Marant Micallef C, et al. (2018) Occupational exposures and cancer: a review of agents and relative risk estimates. Occupational and Environmental Medicine 75(8):604-614 doi:10.1136/oemed-2017-104858

Marant Micallef C, et al. (2019) Cancers in France in 2015 attributable to occupational exposures. Int J Hyg Environ Health 222(1):22-29 doi:10.1016/j.ijheh.2018.07.015
Marchand A (2016) When Occupational Cancers go Unrecognized. What Hinders Workers'Recourse to Law? Sociétés contemporaines 102(2):103-128
Mariotto AB, et al. (2014) Cancer survival: an overview of measures, uses, and interpretation. Journal of the National Cancer Institute Monographs 2014(49):145-86 doi:10.1093/jncimonographs/lgu024
Menzler S, Piller G, Gruson M, Rosario AS, Wichmann HE, Kreienbrock L (2008) POPULATION ATTRIBUTABLE FRACTION FOR LUNG CANCER DUE TO RESIDENTIAL RADON IN SWITZERLAND AND GERMANY. Health Physics 95(2)
Milner A, Spittal MJ, Pirkis J, LaMontagne AD (2013) Suicide by occupation: systematic review and meta-analysis. The British journal of psychiatry : the journal of mental science 203(6):409-16 doi:10.1192/bjp.bp.113.128405
NICER (2021) Cancer Incidence and Mortality in Switzerland In. https://www.nicer.org/NicerReportFiles2018/EN/report/atlas.html?&geog=0 Accessed 03.06.2021
NICER (2022) Mission and vision. In. https://www.nicer.org/en/background-legal-basis/mission-and-vision Accessed 11.05.2022
NIH (2022a) Carcinogen definition. In. https://www.genome.gov/genetics-glossary/Carcinogen Accessed 05.01.2022
NIH (2022b) Morphology In. https://training.seer.cancer.gov/coding/guidelines/morphology.html Accessed 22.02.2022
NIH (2022c) Tumor Grade.
OECD (2020) Incidence, survival and mortality for lung cancer. In. https://www.oecd-ilibrary.org/sites/547f405e-en/index.html?itemId=/content/component/547f405e-en Accessed 18.01.2022
OFS Swiss National Cohort (SNC). In. https://www.bfs.admin.ch/bfs/en/home/statistics/population/surveys/snc.html Accessed 11.05.2022
OFS (1998) Enquête suisse sur la santé - Santé et comportements vis-à-vis de la santé en Suisse -Résultats détaillés de la première enquête suisse sur la santé 1992/93. In. https://www.bfs.admin.ch/bfs/fr/home/statistiques/catalogues-banques-donnees/publications.assetdetail.341000.html Accessed 03.06.2021
OFS (2011) Cancer in Switzerland: Situation and development from 1983 to 2007.96
OFS (2016) Catégories socioprofessionnelles (CSP) 2010 Opérationnalisation des CSP dans le système des variables-clés SHAPE dès 2010. Neuchâtel, p 19
OFS (2018) Consommation de tabac par âge, sexe, région linguistique, niveau de formation. In. https://www.bfs.admin.ch/bfs/fr/home/statistiques/sante/determinants/tabac.assetdetail.6466022.html Accessed 14.08.2019 2019
OFSP (2015) Amiante : aspects cliniques et mesures préventives. In: Publique OFdlS (ed). p 2
OFSP (2022) Législation sur l'enregistrement des cancers. In. https://www.bag.admin.ch/bag/fr/home/gesetze-und-bewilligungen/gesetzgebung/gesetzgebung-mensch-gesundheit/gesetzgebung-krebsregistrierung.html Accessed 26.01.2022
Oliveira PA, Colaço A, Chaves R, Guedes-Pinto H, De-La-Cruz PL, Lopes C (2007) Chemical carcinogenesis. Anais da Academia Brasileira de Ciencias 79(4):593-616 doi:10.1590/s0001-37652007000400004
Olsson A, Kromhout H (2021) Occupational cancer burden: the contribution of exposure to process-generated substances at the workplace. Molecular Oncology 15(3):753-763 doi:https://doi.org/10.1002/1878-0261.12925

ONEC (2022) Brève histoire de l’enregistrement du cancer en Suisse. In. https://www.onec.ch/fr/population/informations-sur-lenregistrement-des-cancers/ Accessed 11.05.2022
Paglione L, Angelici L, Davoli M, Agabiti N, Cesaroni G (2020) Mortality inequalities by occupational status and type of job in men and women: results from the Rome Longitudinal Study. BMJ Open 10(6):e033776 doi:10.1136/bmjopen-2019-033776
Pastorino U, et al. (1990) Incident Lung Cancer Survival. Long-Term Follow-Up of a Population-Based Study in Italy. Tumori Journal 76(2):199-204 doi:10.1177/030089169007600210
Patel MD, Rose KM, Owens CR, Bang H, Kaufman JS (2012) Performance of automated and manual coding systems for occupational data: a case study of historical records. Am J Ind Med 55(3):228-31 doi:10.1002/ajim.22005
Pearson D, Angulo A, Bourcier E, Freeman E, Valdez R (2007) Hospitality workers' attitudes and exposure to secondhand smoke, hazardous chemicals, and working conditions. Public Health Rep 122(5):670-678 doi:10.1177/003335490712200515
Pedregosa F, et al. (2011) Scikit-learn: Machine Learning in Python. 12(null %J J. Mach. Learn. Res.):2825–2830
Perme MP, Stare J, Estève J (2012) On estimation in relative survival. Biometrics 68(1):113-20 doi:10.1111/j.1541-0420.2011.01640.x
Pesch B, et al. (2012) Cigarette smoking and lung cancer--relative risk estimates for the major histological types from a pooled analysis of case-control studies. Int J Cancer 131(5):1210-1219 doi:10.1002/ijc.27339
Peters S (2020) Although a valuable method in occupational epidemiology, job-exposure -matrices are no magic fix. Scandi J Work Environ Health(3):231-234 doi:10.5271/sjweh.3894
Plys E, et al. (2022) Research on occupational diseases in the absence of occupational data: a mixed-method study among cancer registries of Western Switzerland. Swiss medical weekly 152:w30127 doi:10.4414/smw.2022.w30127
Pukkala E, et al. (2009) Occupation and cancer - follow-up of 15 million people in five Nordic countries. Acta oncologica (Stockholm, Sweden) 48(5):646-790 doi:10.1080/02841860902913546
Ramsey MW, Jr., Chen-Sankey JC, Reese-Smith J, Choi K (2019) Association between marital status and cigarette smoking: Variation by race and ethnicity. Preventive medicine 119:48-51 doi:10.1016/j.ypmed.2018.12.010
Rappaport SM, Smith MT (2010) Epidemiology. Environment and disease risks. Science (New York, NY) 330(6003):460-1 doi:10.1126/science.1192603
Redondo-Sánchez D, Petrova D, Rodríguez-Barranco M, Fernández-Navarro P, Jiménez-Moleón JJ, Sánchez M-J (2022) Socio-Economic Inequalities in Lung Cancer Outcomes: An Overview of Systematic Reviews. Cancers 14(2):398
Remen T, Richardson L, Pilorget C, Palmer G, Siemiatycki J, Lavoue J (2018) Development of a Coding and Crosswalk Tool for Occupations and Industries. Annals of work exposures and health 62(7):796-807 doi:10.1093/annweh/wxy052
Remontet L, Bossard N, Belot A, Estève J, FRANCIM tFnocr (2007) An overall strategy based on regression models to estimate relative survival and model the effects of prognostic factors in cancer survival studies. Statistics in medicine 26(10):2214-2228 doi:https://doi.org/10.1002/sim.2656
Rennie JDM, Shih L, Teevan J, Karger DR (2003) Tackling the poor assumptions of naive bayes text classifiers. Paper presented at the Proceedings of the Twentieth International Conference on International Conference on Machine Learning, Washington, DC, USA,
Richardson DB, Keil AP, Cole SR, MacLehose RF (2017) Observed and Expected Mortality in Cohort Studies. American journal of epidemiology 185(6):479-486 doi:10.1093/aje/kww205
Rushton L (2003) Health hazards and waste management. Br Med Bull 68:183-97 doi:10.1093/bmb/ldg034

Rushton L, et al. (2012) Occupational cancer burden in Great Britain. British journal of cancer 107 Suppl 1:S3-7 doi:10.1038/bjc.2012.112
Russ DE, et al. (2016) Computer-based coding of free-text job descriptions to efficiently identify occupations in epidemiological studies. Occup Environ Med 73(6):417-24 doi:10.1136/oemed-2015-103152
Schaffar R, Rachet B, Belot A, Woods LM (2017) Estimation of net survival for cancer patients: Relative survival setting more robust to some assumption violations than cause-specific setting, a sensitivity analysis on empirical data. European journal of cancer (Oxford, England : 1990) 72:78-83 doi:10.1016/j.ejca.2016.11.019
Schmid M, Michaud L, Bovio N, Guseva Canu I, Swiss National C (2020) Prevalence of somatic and psychiatric morbidity across occupations in Switzerland and its correlation with suicide mortality: results from the Swiss National Cohort (1990-2014). BMC Psychiatry 20(1):324 doi:10.1186/s12888-020-02733-7
Seki T, et al. (2013) Cigarette smoking and lung cancer risk according to histologic type in Japanese men and women. Cancer science 104(11):1515-22 doi:10.1111/cas.12273
SFSO (2004) Methodology report—coverage estimation for the Swiss population census 2000. Swiss Federal Statistical Office. In. https://www.bfs.admin.ch/bfsstatic/dam/assets/341896/master Accessed 03.06.2021
SFSO (2016) Catégories socioprofessionnelles (CSP) 2010 - Opérationnalisation des CSP dans le système des variables-clés SHAPE dès 2010.19
Shankar A, et al. (2019) Environmental and occupational determinants of lung cancer. Transl Lung Cancer Res 8(Suppl 1):S31-S49 doi:10.21037/tlcr.2019.03.05
Shrestha S, et al. (2019) Overall and cause-specific mortality in a cohort of farmers and their spouses. Occup Environ Med 76(9):632-643 doi:10.1136/oemed-2019-105724
Silverman DT (2017) Diesel exhaust causes lung cancer: now what? Occup Environ Med 74(4):233-234 doi:10.1136/oemed-2016-104197
Sobin LH, Gospodarowicz MK, Wittekind C (2011) TNM classification of malignant tumours. John Wiley & Sons
Spoerri A, Zwahlen M, Egger M, Bopp M (2010) The Swiss National Cohort: a unique database for national and international researchers. Int J Public Health 55(4):239-42 doi:10.1007/s00038-010-0160-5
Spratt M, et al. (2010) Strategies for multiple imputation in longitudinal studies. American journal of epidemiology 172(4):478-87 doi:10.1093/aje/kwq137
Stanaway JD, et al. (2018) Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks for 195 countries and territories, 1990–2017: a systematic analysis for the Global Burden of Disease Study 2017. The Lancet 392(10159):1923-1994 doi:https://doi.org/10.1016/S0140-6736(18)32225-6
Sung H, et al. (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA: A Cancer Journal for Clinicians 71(3):209-249 doi:https://doi.org/10.3322/caac.21660
Suva (2017) Statistique des accidents LAA 2017. In: Suva Gdcdsdla-aLCco (ed). Lucerne, suisse, p 66
SUVA (2018) Valeurs limites Valeurs actuelles VME/VLE. In. https://www.suva.ch/fr-CH/materiel/directives-et-textes-de-lois/grenzwerte-am-arbeitsplatz-mak-werte-applikation/#59317A47178F431595269A7BB5018B2A=%2F%3Flang%3Dfr-CH
Suva (2019) Statistique des accidents LAA 2019. In: Suva Gdcdsdla-aLCco (ed). Lucerne, suisse, p 66
SUVA (2021) Statistique des accidents LAA 2021.
SUVA (2022) Valeurs actuelles VME/VLE. In. https://www.suva.ch/fr-CH/materiel/directives-et-textes-de-lois/grenzwerte-am-arbeitsplatz-mak-werte-applikation#gnw-location=%2F Accessed 24.01.2022
Swiss Confederation (2022) Loi fédérale sur l’assurance-maladie (LAMal). In. https://www.fedlex.admin.ch/eli/cc/1995/1328_1328_1328/fr Accessed 01.03.2022

Taeger D, et al. (2015) Lung cancer among coal miners, ore miners and quarrymen: smoking-adjusted risk estimates from the synergy pooled analysis of case–control studies. Scandinavian journal of work, environment & health(5):467-477 doi:10.5271/sjweh.3513
Tammemagi CM, Neslund-Dudas C, Simoff M, Kvale P (2004) Smoking and Lung Cancer Survival: The Role of Comorbidity and Treatment. Chest 125(1):27-37 doi:https://doi.org/10.1378/chest.125.1.27
Tanoue LT (2020) Lung Cancer Staging. Clinics in Chest Medicine 41(2):161-174 doi:https://doi.org/10.1016/j.ccm.2020.02.006
Torres-Durán M, et al. (2015) Residential radon and lung cancer characteristics in never smokers. International Journal of Radiation Biology 91(8):605-610 doi:10.3109/09553002.2015.1047985
Turner MC, Mehlum IS (2018) Greater coordination and harmonisation of European occupational cohorts is needed. Occupational and Environmental Medicine 75(7):475 doi:10.1136/oemed-2017-104955
Vågerö D, Persson G (1987) Cancer survival and social class in Sweden. Journal of Epidemiology and Community Health 41(3):204-209 doi:10.1136/jech.41.3.204
van Buuren S, Groothuis-Oudshoorn K (2011) mice: Multivariate Imputation by Chained Equations in R. Journal of Statistical Software 45(3):1 - 67 doi:10.18637/jss.v045.i03
Vanthomme K, Van den Borre L, Vandenheede H, Hagedoorn P, Gadeyne S (2017) Site-specific cancer mortality inequalities by employment and occupational groups: a cohort study among Belgian adults, 2001-2011. BMJ Open 7(11):e015216 doi:10.1136/bmjopen-2016-015216
Vermeulen R, Schymanski EL, Barabási AL, Miller GW (2020) The exposome and health: Where chemistry meets biology. Science (New York, NY) 367(6476):392-396 doi:10.1126/science.aay3164
Vienneau D, et al. (2017) Effects of Radon and UV Exposure on Skin Cancer Mortality in Switzerland. Environmental health perspectives 125(6):067009 doi:10.1289/ehp825
Vineis P, Wild CP (2014) Global cancer patterns: causes and prevention. The Lancet 383(9916):549-557 doi:https://doi.org/10.1016/S0140-6736(13)62224-2
Warwick Institute for Employment Research UoW, Coventry, CV4 7AL, United Kingdom (2018) Cascot: Computer Assisted Structured Coding Tool. In. https://warwick.ac.uk/fac/soc/ier/software/cascot/#:~:text=Cascot%20is%20a%20computer%20program,UK%20Office%20for%20National%20Statistics. Accessed 14.12.2020 2020
Weston A, C. Harris C (2003) Holland-Frei Cancer Medicine, 6th Edition - Multistage Carcinogenesis. Decker Periodicals Publ Incorporated
Whiteman DC, Wilson LF (2016) The fractions of cancer attributable to modifiable factors: A global review. Cancer Epidemiology 44:203-221 doi:https://doi.org/10.1016/j.canep.2016.06.013
WHO (2009a) WHO Guidelines Approved by the Guidelines Review Committee WHO Handbook on Indoor Radon: A Public Health Perspective. World Health Organization
Copyright © 2009, World Health Organization., Geneva
WHO (2009b) WHO handbook on indoor radon: a public health perspective. World Health Organization
WHO (2013) International Classification of Diseases for Oncology - Third Edition - First Revision.
WHO (2021) Radon and health. In. https://www.who.int/news-room/fact-sheets/detail/radon-and-health Accessed 11.01.2021
Wild CP (2005) Complementing the genome with an "exposome": the outstanding challenge of environmental exposure measurement in molecular epidemiology. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 14(8):1847-50 doi:10.1158/1055-9965.epi-05-0456

Wild CP, Scalbert A, Herceg Z (2013) Measuring the exposome: a powerful basis for evaluating environmental exposures and cancer risk. Environmental and molecular mutagenesis 54(7):480-99 doi:10.1002/em.21777

Wild P, Bovio N, Guseva Canu I, Swiss National C (2021) Part-time work and other occupational risk factors for suicide among working women in the Swiss National Cohort. Int Arch Occup Environ Health 94(5):981-990 doi:10.1007/s00420-020-01629-z

Woods LM, Rachet B, Coleman MP (2006) Origins of socio-economic inequalities in cancer survival: a review. Annals of Oncology 17(1):5-19 doi:https://doi.org/10.1093/annonc/mdj007

Yin T, Henter R (2020) Translate Python Documentation. vol Release 3.5.0,

Zaitsu M, Kaneko R, Takeuchi T, Sato Y, Kobayashi Y, Kawachi I (2018) Occupational inequalities in female cancer incidence in Japan: Hospital-based matched case-control study with occupational class. SSM - population health 5:129-137 doi:10.1016/j.ssmph.2018.06.001

Zaitsu M, Kaneko R, Takeuchi T, Sato Y, Kobayashi Y, Kawachi I (2019) Occupational class and male cancer incidence: Nationwide, multicenter, hospital-based case-control study in Japan. Cancer Med 8(2):795-813 doi:10.1002/cam4.1945

Zaitsu M, Kobayashi Y, Myagmar-Ochir E, Takeuchi T, Kobashi G, Kawachi I (2022) Occupational disparities in survival from common cancers in Japan: Analysis of Kanagawa cancer registry. Cancer Epidemiology 77:102115 doi:https://doi.org/10.1016/j.canep.2022.102115

Zeeb H, Shannoun F, World Health O (2009) WHO handbook on indoor radon: a public health perspective. World Health Organization

Zins M, Goldberg M, team C (2015) The French CONSTANCES population-based cohort: design, inclusion and follow-up. Eur J Epidemiol 30(12):1317-1328 doi:10.1007/s10654-015-0096-4