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# Occupational exposures and skin cancer incidence in six Swiss cantons

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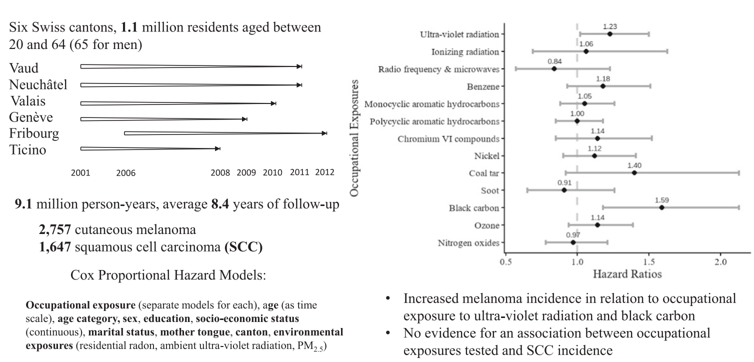
## HIGHLIGHTS

- Occupational exposure to toxins and pollutants may be related to melanoma.
- Exposure was determined using a job-exposure-matrix with two methods.
- Occupational UVR and black carbon exposure were related to melanoma incidence.
- No associations were found for squamous cell carcinoma incidence.

## GRAPHICAL ABSTRACT




## ARTICLE INFO

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## ABSTRACT

*Objectives:* Most studies on occupational risk factors for melanoma have focused on ultra-violet radiation (UVR) exposure from outdoor work. This study investigates a broader range of occupational exposures including UVR, ionizing and non-ionizing radiation, benzene, poly- and monocyclic aromatic hydrocarbons, hexavalent

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Incidence
Job-exposure matrix

chromium, nickel, coal tar, black carbon, ozone, soot and nitrous oxides with skin cancer in a working-age population-based prospective cohort.
*Methods:* Adult residents (20 to 65 years) in the cantons of Fribourg, Ticino, Vaud, Valais, Neuchâtel, and Genève at the 2000 census were included ($n$ = 1,077,487). Incident cases of primary melanoma and squamous cell carcinoma (SCC) of the skin were retrieved from cantonal cancer registries until 2012. Job-exposure matrices were used to assign exposures, using two assessment methods to explore exposure misclassification (i.e. conservative approach for main analyses vs. inclusive approach for sensitivity analyses). Cox proportional hazard models, with age as timescale and adjusted for demographic and environmental factors (residential radon, ambient UVR, and $PM_{2.5}$ concentrations) were used to estimate hazard ratios (HR) in relation to each occupational exposure.
*Results:* 2757 incident melanoma cases were observed during an average of 8.4 years follow-up. Occupational exposure to UVR and black carbon were associated with melanoma incidence (HR = 1.23; 95 % CI: 1.02–1.50 and HR = 1.59; 95 % CI: 1.18–2.13, respectively). Occupational exposure to ionizing radiation and ozone were only associated with melanoma when using the inclusive exposure assessment method. No associations were found for SCC incidence.
*Conclusion:* UVR and air pollution in occupational settings were associated with melanoma incidence. Melanoma related to these risk factors is only recognized as an occupational disease in a few countries, while other occupational risk factors are largely neglected.

## 1. Introduction

Exposure to ultraviolet radiation (UVR) from the sun and artificial sources is a major risk factor for melanoma (Kanavy and Gerstenblith, 2011; IARC, 1992). Family history of melanoma, having lighter skin and eye colour, number of melanocytic nevi (Holly et al., 1987), inability of skin to tan, and suppressed immune system are other known risk factors (Carr et al., 2020). A systematic review and meta-analysis, published in 2021 and conducted jointly by the World Health Organization (WHO) and the International Labour Organization (ILO), reported that any (or high) UVR exposure in outdoor occupational settings was associated with higher melanoma incidence. Their sensitivity analyses comparing studies that included vs. excluded lentigo maligna melanoma (LMM), however, showed larger point estimates when including LMM and an inverse association when excluding LMM. The overall evidence for melanoma incidence was rated as limited (World Health Organization, 2021). By contrast, the same review found sufficient evidence of harmfulness for non-melanoma skin cancer (with higher risk for squamous cell carcinoma (SCC) than basal cell carcinoma (BCC)) from occupational solar UVR exposure (World Health Organization, 2021). Two more recently published systematic reviews also reported no consistent associations between outdoor occupational exposure and melanoma (Maduka et al., 2023; Slavinsky et al., 2024). Additionally, meta-analyses showed increased melanoma risk from indoor tanning devices, especially with early or frequent use (Boniol et al., 2012). Occupational UVR exposure has also previously been associated with SCC incidence (Diepgen and Drexler, 2020; Diepgen et al., 2012; Schmitt et al., 2011). In contrast, evidence for melanoma from ionizing radiation is inconsistent and not considered established in authoritative reviews. Ionizing radiation may be associated with increased risk of melanoma among workers in certain industries and specific occupations (Gawkrodger, 2004; Fortes and De Vries, 2008; Sanlorenzo et al., 2015), including airline crew and pilots (Pukkala et al., 2002), and medical workers including radiologic technologist (Freedman et al., 2003) and x-ray workers (Wakeford, 2009). Other occupational exposures that have been hypothesized to be associated with melanoma include non-ionizing radiation, specifically microwave (MW) and radio frequency (RF) magnetic fields (MF) (Atzmon et al., 2016).

Working in environments with potential exposure to pesticides (Fortes et al., 2016), arsenic and its compounds (Kennedy et al., 2005; Dennis et al., 2010), ambient particulate matter pollution (Kim et al., 2016; An, 2020; Kee et al., 2021) including benzene (Stenehjem et al., 2017; Mehlman, 2006; Dika et al., 2010) and polycyclic aromatic hydrocarbons (PAHs) (Stec et al., 2018), and heavy metals such as thallium, mercury, hexavalent chromium, nickel (Rahman et al., 2023; Meyskens and Sun, 2011; Berwick et al., 2016; Järup et al., 1998) can also potentially induce damage to the skin and may contribute to melanoma (Fortes and De Vries, 2008). PAHs, considered class 1 human carcinogens by International Agency for Research on Cancer (Jameson, 2019), are by-products of carbon-based fuel processing/burning, and certain occupations have high exposure levels. Mono- and poly-cyclic aromatic hydrocarbons, together with coal tar exposures, mainly occur within metal industries, oil refineries, road paving and roofing related industries, and chemical manufacturing plants (Jameson, 2019). Soot has also been associated with increased risk of skin cancers (Gawkrodger, 2004). Autoworkers and those involved in engine maintenance/repair can be exposed to mineral-oil based fluids (Costello et al., 2011), and those working in electronics and metal industries (Nelemans et al., 1993) are at higher risk of cutaneous melanoma. More traditional ambient air pollutants, including particulate matter (PM), black carbon (BC), ozone and nitrogen oxides are also potential environmental risk factors for melanoma development (Abolhasani et al., 2021). PM also exacerbates skin related illnesses, such as atopic dermatitis, acne and psoriasis via inducing oxidative stress and inflammation (Kim et al., 2016).

Most studies are based on industry cohorts within certain specific occupational groups, such as male firefighters and air crew members, using general definitions of job categories or are focused on one type of exposure such as indoor vs. outdoor work, thus representing a broad mixture with limited information about specific risk factors (Fortes and De Vries, 2008). Studies in the general working population, utilizing a prospective design can provide valuable insights into the validity and magnitude of the associations.

We constructed a cohort of working aged adults to investigate the associations between individual potential occupational risk factors and melanoma incidence. As a secondary objective, SCC incidence was investigated. We utilized a job-exposure matrix (JEM) to determine exposures to UVR, ionizing radiation, radio frequency and microwaves, benzene, mononuclear aromatic hydrocarbons (MAHs), polycyclic aromatic hydrocarbons (PAHs), chromium VI compounds, nickel, coal tar, soot, BC, ozone, and nitrogen oxides. We adjusted for three non-occupational, environmental exposures assigned to participants at baseline residential coordinates: ambient UV radiation, residential radon, and particulate matter less than 2.5 μm ($PM_{2.5}$) concentrations. Residential radon has been linked to melanoma outcomes in Swiss cohorts and correlates with geological/altitude features that can also influence UV exposure (Vienneau et al., 2017; Boz et al., 2024; Boz et al., 2022).

## 2. Methods

### 2.1. Data sources, linkage & outcome definitions

We used data from the cantonal cancer registries and the Swiss National Cohort (SNC) to define the study population.

The SNC is a longitudinal database created by linking national censuses with mortality and emigration records. The linkage process for the former decennial censuses relied on a probabilistic approach using variables such as date of birth, sex, marital status, religion, place of residence. Participation in the census is mandatory in Switzerland, and the 2000 census was estimated to cover 98.6 % of the population (Bopp et al., 2009; Spoerri et al., 2010). The SNC contains multi-dimensional data including residential coordinates and building related information, records of cause-specific mortality, emigration/immigration records, occupational codes (International Standard Classification of Occupations [ISCO-88]), as well as demographic information (e.g. birth date, sex, mother tongue, marital status, education). A small-area based socio-economic position index (Swiss-SEP) was also developed and linked to the SNC using information on median rent, household occupancy, and occupation and education (Panczak et al., 2012). Swiss-SEP, shown to strongly associate with household income, was used in this study as a proxy of participants' socio-economic status (Panczak et al., 2012; Spoerri et al., 2010). Approval for the SNC was granted by the Ethics Committees of the Cantons of Zurich and Bern.

Melanoma incidence data were obtained from six cancer registries: Fribourg, Ticino, Vaud, Valais, Neuchâtel and Jura (without cases from canton Jura), and Genève. Previously, the Institute of Social and Preventive Medicine at the University of Bern probabilistically linked these cancer registry data to the decennial census records within the SNC (Feller et al., 2017, 2018). This allowed us to retrieve essential information about the cases and construct a cohort of the working age population in the selected cantons. The melanoma cases were merged into a single database at the Centre for Primary Care and Public Health (Unisanté) with the permission from the National Institute for Cancer Epidemiology and Registration (NICER) and each cancer registry.

Melanoma incidence was defined as the primary outcome; case data were available for all cancer registries included in this study. We identified incident cases of melanoma of the skin (C43) using the International Classification of Disease for Oncology, Third edition (ICD-O-3), codes. Primary melanoma tumours were identified using histology codes (8720–8790). In situ, *benign* and cases of uncertain behaviour were not included. The secondary analysis distinguished incident malignant cases of SCC (C44) using histology codes (8050–8084, 8560–8574). All registries except the Ticino cancer registry, which lacked data on SCC, were included. For both the primary and secondary outcomes, the date of diagnosis was only available in month/year format thus the 15th day of the month was assigned. Basal cell carcinoma (BCC) incidence was not considered, because it was less consistently registered and incomplete in most registries during the study period.

### 2.2. Study population & follow-up periods

The study consisted of working age adults, between 20 and 65 years at baseline, residing in the cantons of Fribourg, Ticino, Vaud, Valais, Neuchâtel, and Genève. People with no residential addresses, or living in non-residential buildings (such as hostels), or missing the socio-economic status index were not included.

Participants were followed from 12.04.2000, except for the Fribourg canton (starting from 01.01.2006), until the retirement age (65 for men, 64 for women,), date of diagnosis, date of death, emigration date, or the end date of the study for each canton, whichever occurred first. We censored participants at retirement age to minimize potential biases related to variations in latency periods, the persistence of risks associated with each exposure, and changes in exposure patterns and behaviours after retirement. A sensitivity analysis where we did not censor at retirement age was also included (described in Section 2.5). Follow-up ended according to each cancer registry: until the last day of the year 2008 for Ticino, 2009 for Genève, 2010 for Valais, 2011 for Vaud, Neuchâtel, and 2012 for Fribourg (Fig. S1).

### 2.3. Occupational exposure assessment

Occupational exposures informed by the literature and hypothesized to be associated with melanoma incidence were UVR (both from the sun and artificial sources), ionizing radiation (Wakeford, 2009; Sanlorenzo et al., 2015), radio frequency and microwaves (RF & MW) (Atzmon et al., 2016), benzene (Stenehjem et al., 2017), mononuclear aromatic hydrocarbons (MAHs), polycyclic aromatic hydrocarbons (PAHs) (Rahman et al., 2023), chromium VI compounds (Berwick et al., 2016), nickel (Järup et al., 1998), coal tar (Moustafa et al., 2015), soot, black carbon (Puntoni et al., 2004), ozone (Kim et al., 2016; Abolhasani et al., 2021), and nitrogen oxides (Yarlagadda et al., 2017).

We used CANJEM, a job exposure matrix (JEM) developed in Montreal, Canada, to assign occupational exposures as binary (exposed, not exposed), at baseline, to participants based on their current profession as recorded in the 2000 census (Siemiatycki and Lavoué, 2018). CANJEM was developed using 4 large case-control studies on cancer and assess occupational exposures with combination of detailed interviews and expert assessments (Sauvé et al., 2018; Siemiatycki and Lavoué, 2018). To reflect the exposure levels most relevant to the study period, the 1970–2005 period was selected as the temporal axis. In CANJEM, exposed occupational codes are listed by agent, with a temporal axis, and a confidence (categorical: definite, probable, possible), intensity (categorical: high, medium, low), frequency (categorical [as hours exposed per week]: 0.5–2, 2–12, 12–40, 40+) and frequency weighted intensity (continuous: 0–1) metrics. We used the default parameters for each aspect (i.e. possible, low, 0.5–2 and 0.05, respectively), which are recommended for general use. Job codes in the U.S. Standard Occupational Classification 2010 (SOC2010) system with 6 digits (U.S. Bureau of Labor Statistics, 2010), were translated to the International Standard Classification of Occupations version 1988 (ISCO-88) to establish the link to the SNC. Translation was implemented in two steps. First, the official crosswalk of the U.S. Bureau of Labor Statistics (2010) was used to convert SOC2010 codes to ISCO-08 (International Labor Office, 2012). Next, the ISCO-08 codes were matched and converted to the older ISCO-88 using a correspondence table obtained from the report published by ILO (International Labor Office, 2012). This two-step process was used to ensure that official correspondence tables were used.

The SOC2010 system has a higher resolution of occupational categories compared to ISCO-08 and ISCO-88, and it collapses some former groups of occupations into single entries. Hence, the complexity of the multi-step translation process from SOC2010 ultimately to ISCO-88 necessitated two occupational exposure assessment approaches to address intrinsic uncertainties. Method 1 (conservative approach), classifies an ISCO-88 code as exposed only when all corresponding codes in the larger SOC2010 group were exposed, minimizing false positives at the cost of increasing false negatives. Method 2 (inclusive approach), assigns the ISCO-88 code as exposed if any corresponding SOC2010 code in the group was exposed. Method 2 thus captures more potentially exposed workers with the risk of increasing exposure misclassification (Fig. S2). We used the interrater agreement and Cohen's kappa to evaluate agreement between the two methods (Table S2). Method 1 was our primary analysis due to its higher specificity (results in the manuscript), while Method 2 was a sensitivity analysis (results in the Supplementary materials).

### 2.4. Environmental exposure assessment

Long-term average residential ambient UV exposure (in $mW/m^2$) and modelled residential radon exposure (in $Bq/m^3$) (Vienneau et al., 2021), both previously applied in the SNC (Boz et al., 2022, 2024), were assigned to each individual's home address at baseline. Satellite-based UV climatology data were available with a spatial resolution of 1 × 1 km and a temporal resolution of one month, covering the period from 2004 to 2016 (Vuilleumier et al., 2021). The annual average of the whole period was calculated and used as ambient UV exposure. Residential radon exposure was derived from a model built with approximately 80,000 radon measurements across Switzerland (Vienneau et al., 2021). The model utilizes a random forest approach and estimates the residential radon concentrations in the dwellings based on parameters related to the building and underlying geology.

As a marker for ambient air pollution, $PM_{2.5}$ from the European-wide land use regression model from the ELAPSE project was used. This model, described in de Hoogh et al. (2018) reflects the annual mean for year 2010. It used concentration data from over 540 monitoring sites across Europe, along with satellite- and chemical transport model-based $PM_{2.5}$, altitude, land use, and roads data. Back extrapolation of the 2010 estimates to 2000 was done using estimates from the 26 × 26 km Danish Eulerian Hemispheric Model (Brandt et al., 2012), downscaled from the original 50 × 50 km, and averaged for Switzerland. The back extrapolated annual mean $PM_{2.5}$ concentrations (in μg/m$^3$) were then assigned to home addresses at baseline.

### 2.5. Statistical methods

Cox proportional hazard models were used to estimate hazard ratios for melanoma and SCC incidence in relation to each occupational exposure separately. Models were constructed with age as time scale. The models were further adjusted for age category (20–34, 35–49, 50–64 [65 for men]), sex (male, female), education level (compulsory or less, upper secondary, tertiary), mother tongue (German and Rhaeto-Romansh, French, Italian, other), marital status (single, married, divorced, widowed), cancer registry, and socio-economic position (continuous). Residential environmental exposures, specifically ambient long-term average UV exposure in mW/m$^2$, residential radon exposure in Bq/m$^3$, and ambient $PM_{2.5}$ in μg/m$^3$, were added to the models as continuous variables. The proportional hazard (PH) assumption for each variable used in the models was tested visually. Education level and marital status were ultimately included as strata variables due to violations of the PH assumption. Hazard ratios (HR) and 95 % confidence intervals were reported for each occupational exposure compared to the unexposed population (i.e. binary exposure).

The main analysis was for melanoma incidence, with the main approach to occupational exposure assessment being method 1. SCC cases were used as outcome in a secondary analysis. For both melanoma and SCC, effect estimates were compared between exposure assessment method 1 and 2. Additional analyses were only conducted for an outcome if an effect was found in the main analysis for method 1. This involved testing for effect modification by introducing interaction terms between occupational exposure and age group and sex (separately). We also conducted three sensitivity analyses: first, keeping the original population, but not censoring at retirement age; second, including people older than 65 years old if they had an occupation at baseline; and third, excluding known workers without a specified job code.

## 3. Results

The study population included 1,077,487 working age adults in six cantons. During an average of 8.4 years of follow-up, we observed 2757 melanoma cases within a total 9.1 million person-years. The mean age of the cohort was 42.4 at baseline. For melanoma cases, the mean age at diagnosis was 49.3 years. While the proportion of men to women was similar in the study population (49.3 % men), 53.7 % of the cases were men. The majority of the cohort individuals were married (64.7 % cohort, 68.2 % cases), French speaking (61.4 %, 70.0 %), and had completed upper secondary or higher education (74.6 %, 88.3 %). Seventy-five percent of participants were employed, of whom 25 % had missing information about their job code (Table 1). Environmental exposures were similar in the cohort and cases. 39 % of the cohort were aged 30 to 49 years at baseline, while 30 % were younger and 31 % were older (Table S1). The secondary analysis on SCC incidence consisted of 904,134 people. During the average 8.7 years of follow-up, we observed 1647 cases of SCC with 7.9 million person-years of analysis time (Table 1).

The interrater agreement and Cohen's kappa values between the two exposure assessment methods indicated that the agreement varied by occupational exposure, from fair to moderate (Table S2). We also compared the top 10 jobs in relation to UVR exposure, and found marked differences depending on the exposure assessment method, with only 3 out of the top 10 within the list for method 1 appearing in the list for method 2 (Table S3).

Using the main method 1 (conservative approach), we found positive statistically significant associations for increased melanoma incidence and working in the jobs with exposure to UVR and BC compared to those not exposed (HR = 1.23; 95 % CI: 1.02–1.50 and HR = 1.59; 95 % CI 1.18–2.13, respectively) (Table 2). With the sensitivity analysis method 2 (inclusive approach) these associations suggested increased risk, but HRs were not significantly elevated. Though not found with method 1, method 2 showed associations for melanoma among workers exposed to ionizing radiation and ozone (HR = 1.18; 95 % CI: 1.03–1.36 and HR = 1.11: 95 % CI: 1.02–1.21, respectively) (Table S4). Otherwise, we observed no clear evidence for associations with the other occupational exposures.

In the stratified analysis, the positive associations with occupational UVR exposure were mainly found in the older two age groups. For BC, increased risks were found in the 20–34 years old and 50–65 years old categories but not the middle age category (Table 3). The analysis stratified by sex revealed that the associations with melanoma incidence were in men only (HR = 1.25, 95 % CI: 1.02–1.53 for UVR, HR = 1.57; 95 % CI: 1.15, 2.12 for BC). In women, none of the occupational exposures were associated with melanoma incidence (Table S5). The results were similar in the three sensitivity analyses compared to the main analysis (Table 2 vs Tables S6 to S8).

Regarding SCC, no association was found in the main analysis with any of the occupational exposures using the method 1 (conservative approach) exposure assessment (Table 4). When using method 2 (inclusive approach), only ionizing radiation was found to be borderline associated with SCC incidence (HR = 1.20; 95 % CI: 0.99–1.45) (Table S9). Given the null findings, we did not test for effect modification nor conduct the three sensitivity analyses.

## 4. Discussion

Our findings suggest positive associations between melanoma incidence and working in occupations with exposure to ultra-violet radiation or black carbon. The association with UVR was strongest in 35–49 year old men, while the association with BC was strongest among 20–34 year old men compared to the study population not occupationally exposed. The findings from the age-stratified analysis should be interpreted with caution, as they might reflect random variations or chance findings rather than actual differences in risk across age groups. Additionally, we observed associations for melanoma and ionizing radiation and ozone using a more inclusive exposure assessment method in the sensitivity analysis. We found no evidence for an association between the occupational exposures and SCC incidence.

Considering that risks from UVR exposure tend to increase with age, it is reasonable to assume that exposure to UV radiation from the sun and artificial sources (Table S10) is a relevant risk factor for melanoma incidence after cumulative occupational exposure. A recent systematic review concluded that melanoma incidence increased among workers exposed to any or high solar UVR compared with no or low solar UVR (World Health Organization, 2021). The association was only observed

**Table 1**
Population characteristics at baseline for the cohort and incident skin cancer cases.

| Characteristics | Study population melanoma | Melanoma cases | Study population SCC | SCC cases |
|---|---|---|---|---|
| Participants | 1,077,487 | 2757 | 904,134 | 1647 |
| Age, mean (SD) | 42.4 (11.9) | 44.2 (10.5) | 42.3 (11.9) | 51.1 (7.1) |
| Age category, *n* (%) | | | | |
| 20–34 | 327,741 (30.4) | 613 (22.2) | 276,171 (30.5) | 51 (3.1) |
| 35–49 | 420,534 (39.0) | 1146 (41.6) | 354,769 (39.2) | 511 (31.0) |
| 50–65 | 329,212 (30.6) | 998 (36.2) | 273,194 (30.2) | 1085 (65.9) |
| Working status | | | | |
| Working – job specified | 608,700 (56.5) | 1760 (63.8) | 519,905 (57.5) | 1022 (62.1) |
| Working – job not specified | 202,475 (18.8) | 419 (15.2) | 170,014 (18.8) | 284 (17.2) |
| Not working | 266,312 (24.7) | 578 (21.1) | 214,215 (23.7) | 341 (20.7) |
| Sex, % (*n*) | | | | |
| Women | 546,026 (50.7) | 1277 (46.3) | 446,239 (50.6) | 713 (43.3) |
| Men | 531,461 (49.3) | 1480 (53.7) | 457,895 (49.4) | 934 (56.7) |
| Marital status, *n* (%) | | | | |
| Single | 273,071 (25.3) | 568 (20.6) | 229,091 (25.3) | 200 (12.1) |
| Married | 697,506 (64.7) | 1889 (68.2) | 585,430 (64.8) | 1236 (75.1) |
| Divorced | 87,727 (8.1) | 252 (9.1) | 74,128 (8.2) | 185 (11.2) |
| Widowed | 19,183 (1.8) | 48 (1.7) | 15,485 (1.7) | 26 (1.6) |
| Mother tongue, *n* (%) | | | | |
| German and Rhaeto-Romansh | 122,086 (11.3) | 291 (10.6) | 107,812 (11.9) | 176 (10.7) |
| French | 661,120 (61.4) | 1930 (70.0) | 658,194 (72.8) | 1288 (78.2) |
| Italian | 172,107 (16.0) | 362 (13.1) | 30,131 (3.3) | 51 (3.1) |
| Other | 122,174 (11.3) | 174 (6.3) | 107,997 (11.9) | 132 (8.0) |
| Completed education, *n* (%) | | | | |
| Compulsory or less | 236,638 (22.0) | 323 (11.7) | 197,239 (21.8) | 251 (15.2) |
| Upper secondary | 543,197 (50.4) | 1532 (55.6) | 447,047 (49.4) | 848 (51.5) |
| Tertiary | 260,692 (24.2) | 864 (31.3) | 226,132 (25.0) | 535 (32.5) |
| Unknown | 36,960 (3.4) | 38 (1.4) | 33,716 (3.7) | 13 (0.8) |
| Canton, *n* (%) | | | | |
| Fribourg/ Freiburg | 127,028 (11.8) | 199 (7.2) | 127,027 (14.1) | 138 (8.4) |
| Ticino | 173,427 (16.1) | 362 (13.1) | NA | 699 (42.4) |
| Vaud | 336,869 (31.3) | 1009 (36.6) | 336,902 (37.3) | 237 (14.4) |
| Valais/Wallis | 141,533 (13.1) | 373 (13.5) | 141,540 (15.7) | 102 (6.2) |
| Neuchâtel | 87,686 (8.1) | 238 (8.6) | 87,696 (9.7) | 471 (28.6) |
| Genève | 210,944 (19.6) | 576 (20.9) | 210,969 (23.3) | 176 (10.7) |
| Swiss-SEP | | | | |
| Mean (SD) | 60.0 (10.6) | 62.4 (10.5) | 60.4 (10.8) | 63.8 (10.7) |
| Range | 5.9–97.3 | 25.5–90.7 | 10.8–97.3 | 23.9–93.5 |
| 25th–75th percentile | 52.8–67.3 | 55.3–70.0 | 53.0–68.2 | 56.1–71.8 |
| IQR | 14.5 | 14.7 | 15.2 | 15.7 |
| Residential radon, Bq/$m^3$ | | | | |
| Mean (SD) | 75.4 (39.9) | 75.4 (44.9) | 67.1 (35.3) | 66.2 (31.4) |
| Range | 25.6–1154.1 | 27.0–1032.7 | 25.6–1154.1 | 28.0–440.3 |
| 25th–75th percentile | 49.7–92.3 | 50.3–90.1 | 47.0–78.3 | 45.9–79.3 |
| IQR | 42.6 | 39.8 | 31.3 | 33.4 |
| Ambient residential UV, mW/$m^2$ | | | | |
| Mean (SD) | 20.3 (0.8) | 20.3 (0.7) | 20.3 (0.8) | 20.3 (0.7) |
| Range | 18.2–29.1 | 18.5–24.7 | 18.2–29.1 | 18.5–26.3 |
| 25th–75th percentile | 20.0–20.5 | 20.0–20.5 | 19.8–20.5 | 20.1–20.5 |
| IQR | 0.5 | 0.5 | 0.7 | 0.4 |
| Ambient residential $PM_{2.5}$, μg/$m^3$ | | | | |
| Mean (SD) | 20.7 (3.7) | 21.1 (3.5) | 20.7 (3.5) | 20.9 (3.4) |
| Range | 3.5–35.4 | 4.9–33.0 | 3.5–29.0 | 7.7–28.9 |
| 25th–75th percentile | 18.9–23.2 | 19.1–23.3 | 19.1–23.4 | 19.4–23.5 |
| IQR | 4.3 | 4.2 | 4.3 | 4.1 |

Melanoma cases: Primary invasive cutaneous melanomas (ICD-O-3: C43, 8720–8790). Squamous cell carcinoma (SCC) cases: Primary squamous cell carcinoma (ICD-O-3: C44, 8050–8084, 8560–8574). No in situ cases.
Note: SD, standard deviation; (*n*), number, SEP, socio-economic position; SD, standard deviation; IQR, interquartile range; UV, ultra-violet PM, particulate matter.

**Table 2**
Association between occupational exposures and melanoma incidence, conservative exposure assessment.

| Occupational exposures | Method 1 | |
|---|---|---|
| | Exposed (cases), *n* | HR (95 % CIs) |
| UVR | 37,383 (111) | 1.23 (1.02, 1.50) |
| Ionizing radiation | 6579 (21) | 1.06 (0.69, 1.63) |
| RF & MW | 12,144 (27) | 0.84 (0.57, 1.23) |
| Benzene | 24,847 (69) | 1.18 (0.93, 1.51) |
| MAH | 51,774 (126) | 1.05 (0.88, 1.26) |
| PAH | 63,583 (165) | 1.00 (0.85, 1.18) |
| Chromium VI | 16,800 (47) | 1.14 (0.85, 1.52) |
| Nickel | 28,422 (80) | 1.12 (0.90, 1.41) |
| Coal tar | 5979 (22) | 1.40 (0.92, 2.13) |
| Soot | 15,832 (36) | 0.91 (0.65, 1.26) |
| Black carbon | 12,146 (46) | 1.59 (1.18, 2.13) |
| Ozone | 30,967 (106) | 1.14 (0.94, 1.39) |
| $NO_X$ | 36,549 (86) | 0.97 (0.78, 1.21) |

Study population includes 1,077,487 individuals with 2757 incident melanoma cases observed during follow up.
Models adjusted for age as time scale, age category, sex, Swiss-SEP, residential UV exposure, residential radon exposure, residential PM2.5 exposure, canton and mother tongue. Education level and marital status were included in the model as strata variables to allow for different baseline hazards.
HR, hazard ratio; CIs, confidence intervals; UVR, ultra-violet radiation; RF & MW, radio frequency and microwaves; MAH, monocyclic aromatic hydrocarbons; PAH, polycyclic aromatic hydrocarbons; $NO_X$, nitrogen oxides.
Method 1 is a conservative approach of exposure assessment and stands for "likely exposure".

in studies including lentigo maligna melanoma (LMM), a type of melanoma occurring in frequently sun exposed body sites (Diepgen and Drexler, 2020). Though we could not distinguish subtypes of skin melanoma, LMM cases were included in our analysis, except in situ cases. Another review with 14 studies, however, concluded no increased risk of melanoma for those with outdoor vs. indoor occupations (Maduka et al., 2023). It was previously argued that intermittent and intense exposures to UVR are more related to melanoma, especially earlier in life, while

**Table 3**
Association between occupational exposures and melanoma incidence stratified by age groups, conservative exposure assessment.

| Occupational exposure | 20–34 y | | 35–49 y | | 50–65 y | |
|---|---|---|---|---|---|---|
| | Exposed (cases), *n* | HR (95 % CIs) | Exposed (cases), *n* | HR (95 % CIs) | Exposed (cases), *n* | HR (95 % CIs) |
| UVR | 13,677 (18) | 0.73 (0.46, 1.78) | 14,778 (55) | 1.48 (1.13, 1.95) | 8928 (38) | 1.33 (0.96, 1.84) |
| Ionizing radiation | 1829 (1) | 0.24 (0.03, 1.72) | 2905 (14) | 1.61 (0.95, 2.73) | 1845 (6) | 0.86 (0.38, 1.92) |
| RF & MW | 3294 (3) | 0.45 (0.15, 1.41) | 5343 (13) | 0.92 (0.53, 1.60) | 3477 (11) | 0.97 (0.53, 1.75) |
| Benzene | 8798 (12) | 0.78 (0.44, 1.39) | 10,175 (32) | 1.28 (0.90, 1.82) | 5874 (25) | 1.39 (0.93, 2.07) |
| MAH | 17,674 (20) | 0.65 (0.42, 1.02) | 21,339 (59) | 1.15 (0.88, 1.50) | 12,761 (47) | 1.23 (0.92, 1.66) |
| PAH | 20,650 (33) | 0.82 (0.60, 1.17) | 26,685 (73) | 1.03 (0.81, 1.31) | 16,248 (59) | 1.09 (0.84, 1.43) |
| Chromium VI | 5585 (7) | 0.71 (0.34, 1.50) | 6845 (25) | 1.44 (0.97, 2.14) | 4370 (15) | 1.06 (0.63, 1.76) |
| Nickel | 10,567 (12) | 0.62 (0.35, 1.10) | 10,980 (44) | 1.53 (1.13, 2.07) | 6875 (24) | 1.03 (0.69, 1.55) |
| Coal tar | 1777 (0) | NA | 2652 (15) | 2.08 (1.25, 3.47) | 1550 (7) | 1.38 (0.65, 2.90) |
| Soot | 4945 (8) | 0.90 (0.45, 1.80) | 6753 (18) | 1.04 (0.65, 1.66) | 4134 (10) | 0.74 (0.40, 1.39) |
| Black carbon | 4485 (18) | 2.30 (1.44, 3.68) | 4717 (12) | 1.00 (0.57, 1.77) | 2944 (16) | 1.74 (1.06, 2.85) |
| Ozone | 9436 (25) | 1.28 (0.86, 1.91) | 13,225 (49) | 1.19 (0.89, 1.58) | 8306 (32) | 1.00 (0.70, 1.42) |
| $NO_X$ | 11,784 (10) | 0.47 (0.25, 0.88) | 15,368 (44) | 1.16 (0.85, 1.57) | 9397 (32) | 1.09 (0.76, 1.55) |

Study population include 1,077,487 individuals with 2757 observed melanoma cases.
Models adjusted for age as time scale, age category, sex, Swiss-SEP, residential UV exposure, residential radon exposure, residential PM2.5 exposure, canton and mother tongue. Education level and marital status were included in the model as strata variables to allow for different baseline hazards.
An interaction term between occupational exposure and age category was introduced into each model.
HR, hazard ratio; CIs, confidence intervals; UVR, ultra-violet radiation; RF & MW, radio frequency and microwaves; MAH, monocyclic aromatic hydrocarbons; PAH, polycyclic aromatic hydrocarbons; $NO_X$, nitrogen oxides; NA, not applicable.
Method 1 is a conservative approach of exposure assessment and stands for "likely exposure" and used in this analysis.

**Table 4**
Association between occupational exposures and squamous cell carcinoma incidence (secondary analysis), conservative exposure assessment.

| Occupational exposure | Method 1 | |
|---|---|---|
| | Exposed (cases), n | HRs (95 % CIs) |
| UVR | 31,959 (61) | 1.08 (0.84, 1.40) |
| Ionizing radiation | 5593 (14) | 1.14 (0.68, 1.94) |
| RF & MW | 21,628 (42) | 0.93 (0.60, 1.45) |
| Benzene | 10,398 (20) | 1.14 (0.84, 1.56) |
| MAH | 45,067 (82) | 1.07 (0.85, 1.34) |
| PAH | 54,929 (104) | 0.99 (0.81, 1.21) |
| Chromium VI | 14,522 (26) | 0.96 (0.65, 1.41) |
| Nickel | 24,397 (46) | 1.03 (0.77, 1.39) |
| Coal tar | 5436 (12) | 1.19 (0.68, 2.10) |
| Soot | 13,649 (24) | 0.91 (0.61, 1.36) |
| Black carbon | 10,315 (13) | 0.71 (0.41, 1.22) |
| Ozone | 26,756 (54) | 0.94 (0.72, 1.23) |
| NOX | 31,793 (60) | 1.04 (0.80, 1.34) |

Study population includes 904,134 individuals with 1647 cases observed during follow up (SCC was not available for cancer registry of canton Ticino).
Models adjusted for age as time scale, age category, sex, Swiss-SEP, residential UV exposure, residential radon exposure, residential PM2.5 exposure, canton and mother tongue. Education level and marital status were included in the model as strata variables to allow for different baseline hazards.
HR, hazard ratio; CIs, confidence intervals; UVR, ultra-violet radiation; RF & MW, radio frequency and microwaves; MAH, monocyclic aromatic hydrocarbons; PAH, polycyclic aromatic hydrocarbons; NOx, nitrogen oxides.
Method 1 is a conservative approach of exposure assessment and stands for "likely exposure".

cumulative and regular exposure is more relevant for SCC (Diepgen and Drexler, 2020). We assigned exposures at baseline and the duration of the employment was unknown. This method does not allow us to directly quantify cumulative exposure. Instead, it provides a proxy measure for exposure status during a participant's job at baseline, which may correlate with cumulative exposure under the assumption of occupational stability over time. Thus, the assessment likely reflects cumulative exposure, rather than intermittent and intense exposures. Newer evidence supports a dual pathway to melanoma, with a distinct nevus prone pathway initiated by early intermittent exposure and a chronic exposure pathway in sun sensitive individuals (Armstrong and Cust, 2017). Our results could not provide any evidence supporting the importance of intermittent and intense UVR exposure, but may offer limited support for the role of long term cumulative exposure in melanoma risk, similar to a multicentre European case-control study showing higher associations among workers exposed to UVR for more than 5 years (Trakatelli et al., 2016). Our secondary analysis on SCC incidence, however, showed a lack of evidence for an association with occupational UVR exposure, which was not in line with previous studies (Diepgen and Drexler, 2020; Schmitt et al., 2011; Diepgen et al., 2012). The reason for this observation could relate to incomplete capture of SCC in the registry data, since skin cancer registration was not mandatory until January 2020. We also did not include basal cell carcinoma in the study, as such data were not available for half of the included cantons.

Certain air pollutants are known to have detrimental effects on skin, including aging pressure by oxidative stress, and dysregulation of immune system, hyperpigmentation, and carcinogenesis (Kim et al., 2016). We observed associations among workers exposed to BC and ozone in one of the two exposure assessment methods. Increased standardized incidence ratios of melanoma were reported for occupational exposure to BC among dockyard workers in Genova, Italy (Puntoni et al., 2004). However, the study included few cases and the role of BC could not be isolated from that of sun exposure. Co-exposure of ozone and UVR has been shown to induce additive damage in human skin explants (Ferrara et al., 2021). In line with this evidence, we tested and found elevated melanoma incidence among workers co-exposed to UVR and ozone (HR = 1.26; 95 % CI: 0.93–1.71, 13,551 workers co-exposed, 42 cases observed). Industrial sources of ozone form when oxygen is exposed to UVR near electrical sources, thus a non-negligible percentage of the workers including welders and high voltage equipment operators/maintenance workers may be co-exposed. This may explain why we only found an association for ozone when using exposure assessment method 2 (inclusive approach) and not in the conservative definition in method 1. Our exposure assessment captured both indoor and outdoor ozone exposures, for jobs ranging from workers in textile bleaching to truck drivers. We did not, however, observe increased risk for nitrogen oxides, an important marker for traffic related air pollution. This might be simply because such relationship does not exist or nitric oxide can be both tumour promoting and suppressing depending on duration, concentration and mode of exposure (Jimenez et al., 2023).

Regarding ionizing radiation, we did not find an association when using the conservative approach (method 1), but observed a weak association using the inclusive approach (method 2). The overall evidence linking ionizing radiation to melanoma remains limited and inconsistent. A recent semi-systematic review (1990–2023) concluded there is no robust epidemiologic evidence that IR causes malignant melanoma, while increased risks are well documented for BCC at higher doses (Caramenti et al., 2024). Studies on occupational exposure to ionizing radiation and melanoma incidence focused on specific industries or workers, such as pilots and cabin crew (Miura et al., 2019), radiologist (Wakeford, 2009) and other medical workers, and nuclear facility workers (Azizova et al., 2021). A recent meta-analysis showed increased risk for melanoma among cabin crews and pilots that was higher than in the general population (Miura et al., 2019). The authors noted this may partially be explained by increased exposure to UVR from recreational activities in the destination locations or disrupted circadian rhythm by long haul routes. Difference in lifestyle and the frequency of travelling to locations that have higher ambient UVR could mask the relationship between occupational exposure to ionizing radiation and melanoma risk (Rafnsson et al., 2003). These are also skilled workers likely meaning higher socio-economic status, which could obscure the associations because higher socio-economic status is related to melanoma risk. Generally, our results provide little evidence for the association between occupational ionizing radiation exposure and melanoma incidence.

Several associations were only apparent in the age-stratified analysis and thus may be chance findings in the absence of an overall association. Higher melanoma incidence was observed among the small number of 35–49 years old workers exposed to coal tar. Occupational dermal absorption of coal tar is linked to several skin diseases including irritation, allergic dermatitis, hyperpigmentation, and cancer (Moustafa et al., 2015). A study among tar refinery workers noted a lower age of diagnosis for keratoacanthomas and differences in the incidence of skin tumours in the areas generally not exposed to sun but affected by coal tar, such as upper arms and nostrils compared to general population (Voelter-Mahlknecht et al., 2007). We found increased melanoma incidence among 35–49 years old workers with nickel exposures and a borderline increase with hexavalent chromium. Hexavalent chromium exposure is higher in some occupations such as in welders, with one study reporting an association with respiratory cancers (Seidler et al., 2013). A case-control study with 58 melanoma cases found an association with copper, but not chromium and other heavy metals, with exposure determined in toenail clippings (Vinceti et al., 2005). The importance of co-exposure to UVR and chromium VI was emphasized based on genomic evidence (Berwick et al., 2016). Evidence also suggested that inhalation and ingestion of trace elements is more important to cancer induction than dermal absorption (Davidson et al., 2004; Matthews et al., 2019). However, our JEM-based exposure assessment did not include the information on the mode of contact. Despite previous evidence showing a relationship between petroleum chemicals and solvents in the workplace and melanoma risk (Jameson, 2019), we found no associations with benzene, PAHs, and MAHs. We also found no association between occupational exposure to RF and MW and melanoma incidence, in line with earlier research (Atzmon et al., 2016).

The main strengths of this study include the use of cantonal cancer registry data in combination with the national census in a large prospective cohort study, and that registration of skin cancer is considered complete for the cancer registries (by outcome) included in this study.

Regarding limitations, our analysis could not account for several potentially important confounding factors including skin phenotype, family history of melanoma and SCC, nevus count and medications that may predispose individuals to melanoma and/or SCC (Nardone et al., 2018; Carr et al., 2020). We also had no information about other risk factors, such as skin's ability to tan and history of sunburn. Additionally, we had no data to account for behaviour patterns that influence UVR exposure in leisure time. The absence of these risk factors may have resulted in residual confounding of unpredictable direction and magnitude. For example, the proportion of people with skin that tans easily, thus with a skin pigmentation which results in lower risk of skin malignancies, is higher in occupations that involve outdoor activities which may make UVR exposure appear protective (World Health Organization, 2021). Also people working in high stress jobs could have higher use of medicines that make them susceptible to skin cancer thus might appear to be at high risk, even though their actual job exposure is not directly associated with skin cancer. We could, however, adjust for ambient UVR at the residence along with residential $PM_{2.5}$ and residential radon levels, as biological plausibility and epidemiological evidence support that residential exposure to air pollution (Kim et al., 2016; Abolhasani et al., 2021) and residential radon (Vienneau et al., 2017; Boz et al., 2022) might also be relevant for melanoma. It should also be noted that we used marital status rather than partnership status which is likely more relevant for skin cancer detection. Single persons could be in a partnership and cohabiting, and this is not accurately captured with the available data from census.

One of the major limitations of the study is that participants' profession was only available at the baseline and was missing for 25 % of the workers. As we have no other temporal information on occupation, job duration could not be determined. Additionally, we had no way of knowing all jobs that participants previously held during their career and the associated exposures. Swiss Labour Force Survey data indicated a median job tenure of ~6–7 years (men) and ~3.5–5.2 years (women) in 1991–2008 (Weber and Luzzi, 2014) and a net turnover rate of 10.4 in 2023 (Federal Statistical Office (FSO), 2024), suggesting that a substantial fraction of workers remain with the same employer over time spans comparable to our follow-up. Nonetheless, occupational mobility may lead to non-differential exposure misclassification and bias towards the null. Although relying on a single occupational entry does not allow for lifetime cumulative exposure assessment, it still provides a valuable proxy for participants' occupational exposures in this large administrative cohort. Similarly for residential coordinates, we lack address histories for the cohort, any residential mobility during follow-up is expected to be largely non-differential with respect to outcome and would therefore bias associations towards the null. Moreover, although JEMs are useful for estimating workplace exposures, they represent an average exposure. It is expected that misclassification of exposure due to these issues would be non-differential with respect to skin cancer incidence (Peters, 2020). Another issue is that CANJEM is mainly related to the jobs defined in Canada (Siemiatycki and Lavoué, 2018), estimated to cover 90 % of the working population. However, it has previously been used and considered applicable to populations in other developed countries with similar well-established industrial processes and employment practices including several European countries, New Zealand and United States (Xu et al., 2024; Amari et al., 2024). We think it is reasonable to assume CANJEM is also applicable to Switzerland. Thus, we utilized CANJEM as a single and compatible source for exposure assessment across the range of exposures investigated in this explorative study. The alternative, to use multiple JEMs from different studies, would have introduced additional unmeasurable complexity caused by heterogeneity between different JEMs. A recent European initiative, Exposure Project for Health and Occupational Research (EPHOR), aims to provide tools for harmonized exposure assessment including EuroJEM that will be beneficial to studies similar to ours (Pronk et al., 2022). Another limitation is the loss of information in translating the occupational coding systems to enable linkage between CANJEM and the SNC. Such loss of information using crosswalks was found to be comparable to manual coding (Koeman et al., 2013), and would create non-differential exposure misclassification. Among the two exposure assessment approaches, the conservative approach (method 1) likely reduced the proportion of false positives at the cost of increasing type 2 error; while the inclusive approach (method 2) likely resulted in a larger proportion of workers considered exposed than they truly were, thus leading to bias towards the null. For rare exposure prevalence, as is the case here, sensitivity is less critical than specificity. A low specificity would result in dilution of the small exposed group and result in substantial underestimation. Thus, preference was given to method 1 compared to method 2. We have no statistical way of measuring the sensitivity nor directly comparing the two methods. Finally, the study period spans from 2001 to 2012 depending on the canton (Fig. S1). This may limit the relevance of our findings to current occupational practices, as exposure levels, safety regulations, and workplace conditions have changed over the past decades. However, the underlying biological relationships between occupational exposures and melanoma risk remain relevant for understanding disease aetiology.

We included 6 of the 26 cantons in Switzerland, represented by 6 of 13 cancer registries that were initiated at different points in time between 1969 and 2019 (National Agency for Cancer Registration, 2021), and previously linked to the SNC (Feller et al., 2017, 2018). While the registration of melanoma and SCC in cantonal registries was considered systematic during the study period, it did not become mandatory until 2020 with the implementation of the Cancer Registration Act (KRG [Krebsregistrierungsgesetz], RS 818.33). The Ticino cancer registry also lacked data on SCC, thus we treated SCC as a secondary outcome. We also saw slightly higher Swiss-SEP in the SCC cases compared to the study population (Table 1); given the link between SES and many of these occupational exposures, it could be that the null findings for SCC incidence is related to under-registration. Future studies that utilize all cantonal cancer registries would be beneficial to elaborate the relationship between workplace exposures and skin cancer.

We censored individuals at the retirement age (64 for women and 65 for men) to ensure comparability of exposures assigned only at baseline. According to a European study that included 11 countries with 123,360 invasive melanoma cases the average age of diagnosis was 54 years (Sacchetto et al., 2021). The average age of diagnosis when not censoring at retirement in our study was 62 years, leading to a small to moderate loss in the number of cases. Although melanoma can occur many years after exposure, for some cancer may develop fast or not at all. Thus, retaining retired individuals and considering them exposed, without knowing more about their exposure history, could increase the exposure misclassification and potentially bias the hazard ratios. Furthermore, after the occupational exposure ceased to exist, its associated risks may not decrease at the same rate for all exposures. This can introduce complex latency effects that we cannot account for uniformly across all exposures. Additionally, most of the time, retirement leads to changes in lifestyle and behaviours (e.g., changes outdoor recreational activities). This could introduce unforeseen biases specific to each type of exposure. The results of our sensitivity analysis where we did not censor at retirement age were similar to the main findings.

## 5. Conclusion

We investigated the association between a number of occupational risk factors and skin cancer incidence, finding associations primarily with UVR and black carbon in relation to melanoma. Limited evidence was found for the associations of nickel and coal tar. Our data suggest that occupational exposures other than UVR might be relevant; however, considering the limitations in the occupational exposure assessment and exploratory nature of this study, the results should be interpreted with caution. Future occupational skin cancer research should focus on personal exposure histories and include established confounders such as skin phenotype and family history to strengthen causal inference. Despite the weak evidence from this study, we tentatively suggest that occupational health policies should continue to prioritize improved UVR protection programs for outdoor workers and workers exposed to UVR from artificial sources, and consider surveillance of workers exposed to black carbon and other potential carcinogens. Maintaining and improving exposure monitoring systems, enhancing risk communication to workers, and developing exposure and industry specific prevention guidelines would be beneficial to reduce risks among exposed workers.

Declaration of Generative AI and AI-assisted technologies in the writing process

During the preparation of this work S. Boz used Chat GPT to translate concepts formulated in their native language and to improve their English writing. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

## CRediT authorship contribution statement

**Seçkin Boz:** Writing – review & editing, Writing – original draft, Validation, Methodology, Investigation, Formal analysis, Data curation. **Marek Kwiatkowski:** Writing – review & editing, Supervision, Methodology, Conceptualization. **Murielle Bochud:** Writing – review & editing, Resources, Investigation. **Jean-Luc Bulliard:** Writing – review & editing, Resources, Data curation. **Marcel Zwahlen:** Writing – review & editing, Resources. **Isabelle Konzelmann:** Writing – review & editing, Resources. **Yvan Bergeron:** Writing – review & editing, Resources. **Bernadette W.A. van der Linden:** Writing – review & editing, Resources. **Elisabetta Rapiti:** Writing – review & editing, Resources. **Manuela Maspoli Conconi:** Writing – review & editing, Resources. **Andrea Bordoni:** Writing – review & editing, Resources. **Martin Röösli:** Writing – review & editing, Supervision, Resources, Methodology. **Danielle Vienneau:** Writing – review & editing, Validation, Supervision, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.scitotenv.2025.180938.

## Data availability

The SNC data cannot be shared by the authors. The data are the responsibility of the Federal Statistical Office, and may be ordered here: https://www.bfs.admin.ch/bfs/en/home/statistics/population/surveys/snc.html.

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