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Average uranium bedrock concentration in Swedish municipalities predicts male lung cancer incidence rate when adjusted for smoking prevalence: Indication of a cumulative radon induced detriment

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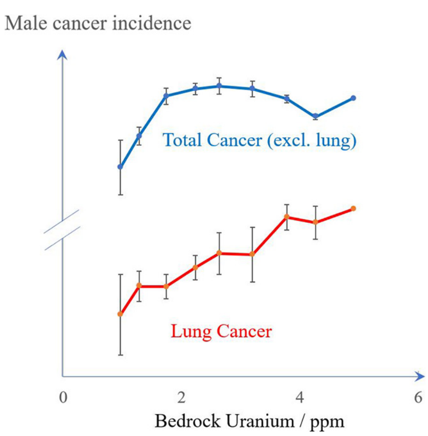
HIGHLIGHTS

- Lung cancer incidence correlates with local uranium bedrock concentration.
- Crude non-lung cancer incidence correlates with local uranium bedrock concentration.
- Only the lung cancer correlation remained after adjustment by smoking prevalence.
- Local bedrock uranium concentration is a tentative proxy for indoor radon exposure.

GRAPHICAL ABSTRACT



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ABSTRACT

Bedrock U has been used as a proxy for local indoor radon exposure. A preliminary assessment of cancer incidence rate in a cohort of 809,939 adult males living in 9 different Swedish counties in 1986 has been used to correlate the cumulative lung cancer and total cancer (excluding lung) incidence rates between 1986 and 2020, respectively with the municipality average value of bedrock U concentration obtained from Swedish geological Survey (SGU). To control for regional difference in tobacco smoking, data on county average smoking prevalence, obtained from a survey conducted by the Public Health Agency of Sweden from 2001 to 2004, was used. Regression analysis shows that there is a significant positive correlation between smoking prevalence adjusted lung cancer incidence rate in males and the municipality bedrock U concentration ($R^2 = 0.273$ with a slope $5.0 \pm 0.87 \cdot 10^{-3}$ ppm^{-1}). The correlation is even more significant ($R^2 = 0.759$ with a slope $= 4.8 \pm 0.25 \cdot 10^{-3}$ ppm^{-1}) when assessed on population weighted cancer incidence data binned in nine intervals of municipality average bedrock U concentration (ranging from 0.97 to 4.9 ppm). When assessing the corresponding correlations for total cancer incidence rate (excluding cancer of the lung) with adjustment for smoking prevalence, there appears to be no or little correlation with bedrock U concentration ($R^2 = 0.031$). We conclude that an expanded future study needs age-standardized cancer incidence data to obtain a more consistent exposure-response model. Such model could be used to predict future lung cancer cases based on

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geological survey maps of bedrock U as an alternative to laborious indoor radon measurements, and to discern what future lung cancer rates can be expected for a population nearing zero smoking prevalence, with and without radon prevention.

1. Introduction

Radon (^{222}Rn) is a ^{238}U progeny and occurs as a noble gas in the indoor air emitted from soil, bedrock and building material or from radon enriched water used in the household from drilled wells (ICRP, 2010). Radon is a prominent source of radiation exposure to the general public and in some cases also in certain occupations e.g. miners (ICRP, 2010). Known health effects of radon exposure consist mainly of increased risk for developing lung cancer, particularly among smokers living in houses with high radon concentration, and according to WHO (2009) radon is the second most common cause of lung cancer. In a recent update of national radon exposures for 66 countries (Gaskin et al., 2018), the highest geometric mean radiation levels were found in Poland (133 Bq m^{-3}), followed by Armenia (101 Bq m^{-3}), Czech republic (94 Bq m^{-3}) and Finland (84 Bq m^{-3}). Sweden, with a corresponding value of 67 Bq m^{-3}, is above the median value of the listed country data. Radon-attributable lung cancer deaths for all these 66 countries were estimated to about 226 thousand in 2012, representing a median of 3.0 % of total cancer deaths.

According to Statistics Sweden, SCB (2022a) about 50 % of the Swedish residential buildings consist of small houses (detached and semidetached one or two storey buildings) representing 60 % of all households. Most of these buildings are wooden houses. The remaining residential buildings consist of multistorey buildings, often with concrete or stone walls. A survey made by Radonova (2022) in Sweden shows that elevated indoor radon concentration (>200 Bq m^{-3}) is more often found in small houses (>30 % for buildings constructed before 1979), but as much as 17.4 % of older multistorey residential buildings also exhibit elevated indoor radon concentration.

The specific challenge for radon and lung cancer epidemiology is to attain a reliable long-term exposure history. Darby et al. (2005) concluded that for every 100 Bq m^{-3} increase in indoor radon concentration, the likelihood of lung cancer is increased with 16 %. An illustration of this challenge is the high variability of indoor radon concentration for a given local ^{238}U bedrock concentration (expressed as elemental uranium concentration in ppm). However, Olsthoorn et al. (2022) found a relatively weak, but statistically significant, positive correlation between indoor radon concentration and local bedrock concentration of ^{238}U, with Spearmans *r* ranging between 0.19 and 0.34 depending on type of housing. Hence, a large variability in cumulative indoor radon exposure can be expected based on local ^{238}U bedrock concentration.

Based on years of aerial measurement using fix winged aircrafts equipped with low-resolution gamma spectrometry, Swedish Geological Survey (SGU) has created a digital database presented in a map of bedrock ^{238}U concentration in Sweden (expressed in terms of ppm natural uranium) (SGU, 2022a). For a more extensive description of the methods used by SGU to derive these maps, we refer to e.g. SGU (2022b). According to this dataset, the U concentration in the Swedish bedrock ranges from 0.9 to 5.1 ppm. In spite of the relatively weak correlation between indoor radon and bedrock U found by Olsthoorn et al. (2022), it is nevertheless, due to the cost effectiveness, interesting to investigate whether a similar correlation exists between the local cumulative lung cancer incidence rate and the U bedrock concentration. In this communication the authors have taken advantage of having access to a subset of the Swedish male population (809,939 adult men living in 9 counties of Sweden in 1986) to conduct and present a preliminary assessment of such a correlation, with the aim of discussing the prerequisites for a continued in-depth analysis of the whole Swedish population.

2. Material and methods

Since several years we are working with a closed cohort of all individuals living in the 9 most northern counties of Sweden after the Chernobyl fallout in 1986. An inclusion criterium was that the individuals were free of cancer prior to the Chernobyl Nuclear Power Plant accident, and this could be obtained by removing cancer diagnoses registered in the national cancer registry 1958 to 1985. The cancer incidence rate in adult males, a sub-cohort of the full cohort, has recently been analyzed in relation to colon absorbed dose (Tondel et al., 2022). Hence, for the present study we could take advantage of this cohort with information on cancer incidence rate on municipality level up to 2020. Instead of using ^{137}Cs to calculate the colon absorbed dose we decided to use the bedrock concentration of ^{238}U at municipality level to investigate the relationship with lung cancer incidence and other cancer sites, respectively. Annual numbers of primary cancer cases in each of the 92 municipalities were retrieved from the National Board of Health and Welfare (NBHW) in Sweden and classified according to the International Classification of Diseases, version 7. Of this cohort, the adult male population (age > 20 y) consisted of 809,939 individuals living in 92 different municipalities (with an average land surface of 3050 km^2). The corresponding average value for the 9 counties is 32,300 km^2. The cumulative incidence rate of lung cancer and remaining cancers for a given municipality, $I_{Crude,i}$ was obtained by summing the annual cases 1986 to 2020 and then dividing by the number of males older than 20 years ($P_{Coh,i}$) in each municipality in 1986 (Eq. (1)).

$$I_{Crude,i} = \text{Number of primary cancer cases reported between 1986 and } 2020/\left(P_{Coh,i}\right) \tag{1}$$

Municipality average values of U bedrock concentration for the 92 studied municipalities, $U_{Bedrock,I}$, were retrieved by taking the average of all U bedrock concentration within a given municipality (excluding water surfaces such as lakes, rivers or coastal waters) using a grid of 200 m by 200 m in the digitized SGU map (SGU, 2022a). Natural uranium contains 99.3 % of the radon-generating ^{238}U and was used as an indirect generic proxy for indoor radon exposure to the population in each municipality. Hence, combining the data sets, a preliminary correlation was calculated between $I_{Crude,i}$ for primary lung cancer and total cancer (excluding lung cancer), respectively with $U_{Bedrock,i}$ (ppm).

Since tobacco smoking is a well-known lung carcinogen, any attempt of estimating the potential correlation between lung cancer and any other factor must then in some way be adjusted for smoking prevalence. Health and lifestyle surveys in Sweden have regularly been performed by the Public Health Agency of Sweden (PHAS). Data on self-reported county specific smoking prevalence, S_{County} (%·10^{-2}), could therefore be retrieved from the publicly available database from PHAS (2022). The data on S_{County} (summed over both reported current and past smoking prevalence) was therefore used to adjust $I_{Crude,i}$ for both lung cancer and non-lung cancer cumulative incidence rate in the cohort to compensate for regional differences in smoking prevalence. The S_{County} values of ever smokers from the survey done in year 2001 to 2004 were judged the most representative for the cumulative historic smoking prevalence of the cohort, before 1986 and up to 2020. Hence, the adjusted cancer incidence rate, $I_{adj,i}$, is given by $I_{Crude,i}$ divided by the county specific smoking prevalence, S_{County}(Eq. (2)).

$$I_{Adj,i} = I_{Crude,i}/S_{County} \tag{2}$$

Three initial approaches of regression analysis have been made:

1. Municipality average $U_{Bedrock}$ as a proxy for cancer caused from either radon and/or external terrestrial radiation: regression of crude, I_{Crude}, and adjusted cancer incidence rate, I_{adj}, normalized to the county average ever smoking fraction (%·10^{-2}) vs. municipality average of bedrock U concentration (Eq. (1)). This was done for i) lung cancer and ii) total cancer (excl. lung cancer).
2. County average $U_{Bedrock}$ as a proxy for cancer: $I_{Crude,i}$ and $I_{Adj,i}$ were binned and pooled into 9 county averages of cancer incidence and plotted vs the corresponding county average U bedrock concentration. The latter was a weighted average of the population in the municipalities belonging to each county. A linear regression was then carried out between $I_{Crude,County}$ and $I_{Adj,County}$ vs population weighted average $U_{Bedrock,County}$ for lung and total cancer (excl. lung), respectively.
3. Stratified $U_{Bedrock}$ data as a proxy for cancer: Municipalities were binned in intervals of $U_{Bedrock}$ according to Table 1. For each of these bins, the municipality averages of I_{Crude} and I_{adj} were pooled into categories of average $U_{Bedrock}$. A population weighted regression were used due to the variable cohort size in the binned intervals, $P_{Coh,int}$, between the different bins of $U_{Bedrock}$. Weighting factors proportional to $P_{Coh,int}$ in 1986 in each bin of $U_{Bedrock}$ values were used as listed in Table 1. This weighted regression procedure was done for lung and total cancer (excl. lung cancer) separately.

The ongoing study was approved by the Ethics Review Authority in 2020 (Dnr2020-06609), and with the current extension of correlating data with U bedrock in 2022 (Dnr 2022-02791-02).

3. Results

Cumulative cancer incidence rate by municipality in males between 1986 and 2020, I_{Crude} and I_{Adj}, vs municipality average bedrock uranium concentration is presented in Fig. 1. I_{Crude} and I_{Adj} for lung cancer (Fig. 1a) and total cancer (except lung cancer; Fig. 1b) are plotted. Pearsons R^2 for $I_{Crude,i}$ is higher for lung cancer than for remaining cancers (0.388 vs. 0.225). The corresponding values for $I_{adj,i}$ vs $U_{Bedrcok,i}$ regressions are 0.273 (slope $= 5.0 \pm 0.87 \cdot 10^{-3}$ ppm^{-1}) and 0.028 with a non-significant slope ($p > 0.10$), respectively, showing clearly that the correlation between lung cancer and bedrock U is significantly higher than for the total of remaining cancers.

When using county average of I_{Crude}, I_{adj} and $U_{bedrock}$, a significant correlation between lung cancer and bedrock U appears even after adjusting for smoking prevalence by county ($R^2 = 0.505$ with a significant slope $= 4.29 \pm 1.7 \cdot 10^{-3}$ ppm^{-1}; Fig. 1c). The corresponding value for total cancer incidence rate, (excluding lung cancer) is close to zero ($R^2 = 0.002$ with a non-significant slope ($p > 0.8$); Fig. 1d) indicating once again a non-existing correlation between total cancer and bedrock U in this cohort.

Finally, using the approach with binned municipality data for the regression analysis (Table 1), it can be deduced that both the population weighted I_{Crude} and I_{Adj} are significantly correlated with municipality average bedrock U (Pearsons $R^2 = 0.919$ vs. 0.759 (slope $= 4.8 \pm 0.25 \cdot 10^{-3}$ ppm^{-1}); Fig. 1e). Interestingly, for the remaining cancer sites there is a relatively strong correlation between I_{Crude} and $U_{Bedrock}$, but when adjusting for smoking prevalence there is no apparent correlation ($R^2 = 0.031$ with a close-to-zero slope of $5.8 \pm 3.0 \cdot 10^{-3}$ ppm^{-1} ($p = 0.06$); Fig. 1f).

Table 1
Bins of $U_{Bedrock}$ intervals, cohort population > 20 years of age in 1986 in the respective bins and corresponding weighting factors in population weighted linear regression of cumulative cancer incidence rate. Weighting factors applied both for regression on I_{Crude} and I_{Adj}, respectively.

$U_{Bedrock}$ interval (Bin)	Interval average $U_{Bedrock}$	Interval Cohort size $P_{Coh,int}$	Weighting factor
(ppm)			
<1	0.966	6727	1
1.0–1.5	1.28	64,139	9.5
1.5–2.0	1.74	160,514	24
2.0–2.5	2.23	161,548	24
2.5–3.0	2.63	161,068	24
3.0–3.5	3.20	86,546	13
3.5–4.0	3.78	99,773	15
4.0–4.5	4.27	60,270	9.0
>4.5	4.90	9254	1.4

4. Discussion

Cumulative male lung cancer incidence rate in the 9 studied Swedish counties appears to correlate significantly with the municipality average bedrock U concentration, even after adjusting for smoking prevalence. A positive correlation with bedrock U concentration is also found for cancer incidence rate in general, but when adjusting for smoking prevalence there appears to be no correlation between total cancer incidence rate and bedrock U concentration. Hence, the authors believe that an expanded study, including the whole national population, is warranted to investigate the relationship between bedrock U, smoking prevalence and likelihood of lung cancer in Swedish populations. Such a study should be designed so that cancer incidence data can be age-standardized to obtain more consistent exposure-response models, that can be compared with existing predictions based on indoor radon concentration studies (e.g. Darby et al., 2005), and ultimately to predict what future lung cancer incidence can be expected for a population with zero smoking prevalence in Sweden and elsewhere. Such study can also better disentangle the indoor radon exposure from the contribution of ground gamma-radiation from uranium. A special group of interest is children in high $U_{bedrock}$ areas growing up in non-smoking households, since there is an uncertainty whether the age dependence in the life-time likelihood of lung cancer from cumulative indoor radon exposures follows that of external radiation (e.g. Kendall and Smith, 2005).

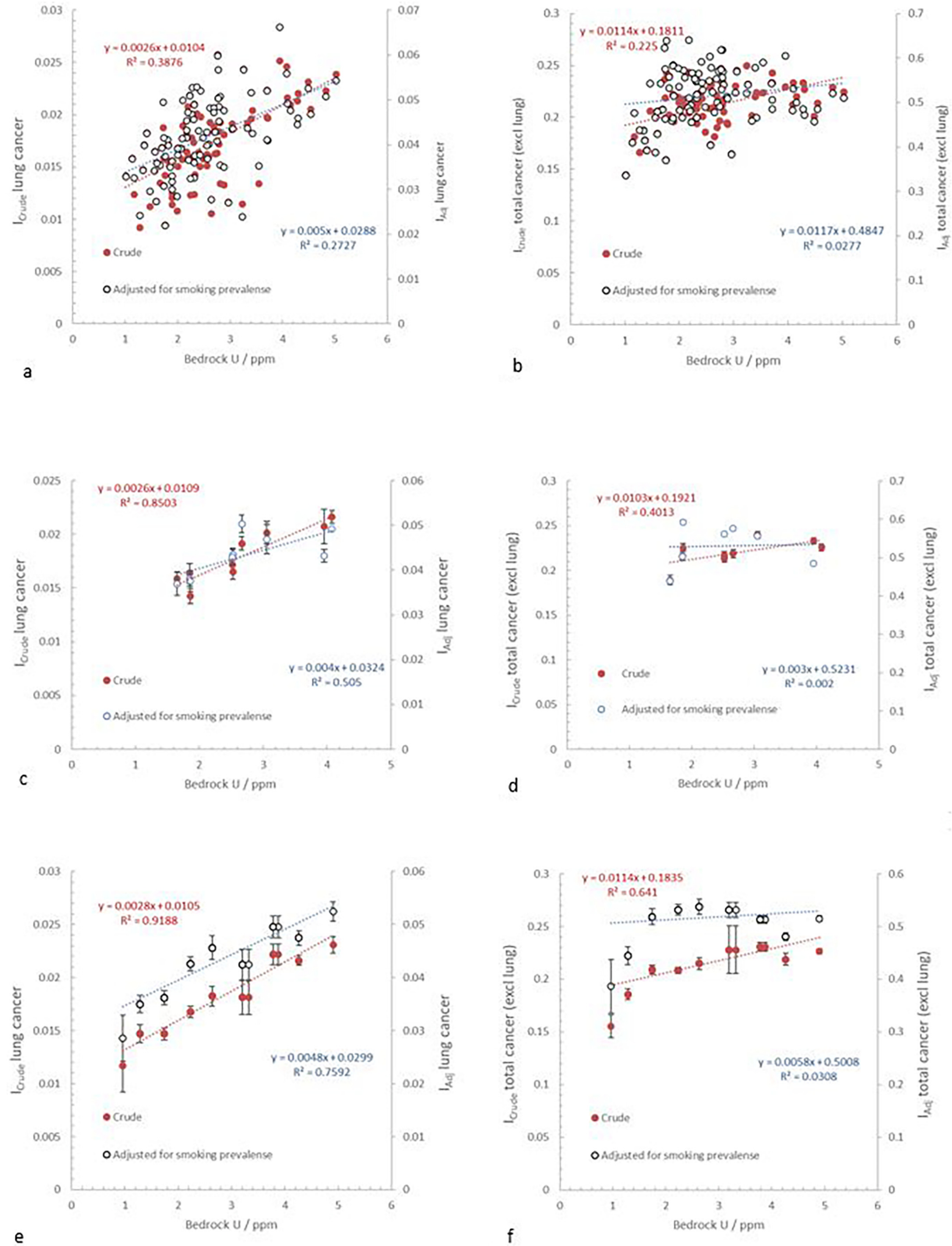
To reproduce this type of study in other countries, a study design as described here would require; i) access to cancer diagnoses in a large cohort that is spread over ii) areas with a large contrast in local average U bedrock concentration within the survey area and iii) surveys of district specific smoking prevalence. These prerequisites should be especially explored in the countries mentioned in the introduction (Poland, Armenia, Czech republic and Finland).

Since we have not yet been able to age-standardize the data, the parameter values for the slope and intercepts of the linear regressions shown in Fig. 1 cannot be directly compared with other studies.

5. Limitations and strengths of the study

Register studies are often of cohort design comparing disease rate in an exposed group with an unexposed group used as a reference category. An ecological study uses information on exposure and disease on a group level, often defined by geographical areas. The advantage of an ecological study is that data is more easily accessible in open sources and enables quick analysis for testing a hypothesis. The disadvantage is possible misclassification of exposure on the individual level making these studies less sensitive to detect small increased risks associated with that exposure (e.g. Lagarde and Pershagen, 1999; Yoon et al., 2016).

The misclassification of radon progeny exposure using municipality average concentration, $U_{Bedrock}$, can be substantial since there are significant variations in the local U bedrock concentration within a given municipality. The dispersion of local bedrock U concentration taken from the SGU map within any of the 92 studied municipalities is, on average, 46 % (1 SD) of the municipality mean value. It is expected, however, that the systematic geographical misclassification on a municipality cohort level will be somewhat less. An additional source of bias in the correlation analysis stems from the misclassification during the follow-up period from 1986 to 2020, due to inter-municipality migration. Although annual mobility of Swedish citizens is high, it involves almost 60 % movements within the home municipality and 80 % within the home county (SCB, 2022b), and hence the migration effect should be relatively limited in this study. Furthermore, regarding misclassification of smoking prevalence it is expected that


y = 0.0026x + 0.0104
R² = 0.3876
y = 0.005x + 0.0288
R² = 0.2727
Crude
Adjusted for smoking prevalense
I_Crude lung cancer
I_Adj lung cancer
Bedrock U / ppm
a
y = 0.0114x + 0.1811
R² = 0.225
y = 0.0117x + 0.4847
R² = 0.0277
Crude
Adjusted for smoking prevalense
I_Crude total cancer (excl lung)
I_Adj total cancer (excl lung)
Bedrock U / ppm
b
y = 0.0026x + 0.0109
R² = 0.8503
y = 0.004x + 0.0324
R² = 0.505
Crude
Adjusted for smoking prevalense
I_Crude lung cancer
I_Adj lung cancer
Bedrock U / ppm
c
y = 0.0103x + 0.1921
R² = 0.4013
y = 0.003x + 0.5231
R² = 0.002
Crude
Adjusted for smoking prevalense
I_Crude total cancer (excl lung)
I_Adj total cancer (excl lung)
Bedrock U / ppm
d
y = 0.0028x + 0.0105
R² = 0.9188
y = 0.0048x + 0.0299
R² = 0.7592
Crude
Adjusted for smoking prevalense
I_Crude lung cancer
I_Adj lung cancer
Bedrock U / ppm
e
y = 0.0114x + 0.1835
R² = 0.641
y = 0.0058x + 0.5008
R² = 0.0308
Crude
Adjusted for smoking prevalense
I_Crude total cancer (excl lung)
I_Adj total cancer (excl lung)
Bedrock U / ppm
f

average smoking prevalence among males in a municipality will not significantly deviate from county average estimates reported by the PHAS (2022).

Regardless of the magnitude of these misclassifications as a potential bias in the correlation analysis between I_{Crude} and $U_{Bedrock}$, they will also influence corresponding results for total cancer incidence rate in the same cohort, using identical adjustment for smoking. Therefore, since all three approaches used in the linear regression analysis consistently point to a higher correlation between smoking prevalence adjusted cumulative lung cancer incidence rate and municipality U bedrock concentration compared with that for total cancers, the results indicate that on a municipality level, the U bedrock concentration will to some extent predict lung cancers caused by cumulative indoor radon exposures among males in Sweden, rather than gamma-radiation exposure from uranium in the ground. However, since the historic smoking prevalence among women in Sweden differs from men (PHAS, 2022), a more thorough investigation is needed to obtain a method to adjust cancer incidence rate data that can be evaluated in a comparable way between sexes.

6. Preliminary conclusions

The results of this study suggest that average U bedrock concentration over an administrative area covering, on average, 3000 km^2, can be used as a proxy for indoor radon induced lung cancer in ecological studies. The prerequisite for further studies includes exhaustive cancer registry, access to regional data on smoking prevalence and high contrast in detailed U bedrock concentration.

CRediT authorship contribution statement

Christopher L. Rääf: Conceptualization, Methodology, Validation, Investigation, Resources, Software, Writing – original draft, Writing – review & editing, Visualization, Supervision, Project administration. **Martin Tondel:** Conceptualization, Methodology, Software, Validation, Investigation, Resources, Writing – review & editing. **Mats Isaksson:** Conceptualization, Methodology, Validation, Investigation, Resources, Writing – review & editing. **Robert Wålinder:** Conceptualization, Methodology, Validation, Resources, Writing – review & editing.

Data availability

Data will be made available on request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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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.2022.158899.

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Fig. 1. Filled circles represent crude cumulative cancer incidence rate and open circles represent cumulative cancer incidence rate adjusted for smoking prevalence 1986–2020. Top: I_{Crude} and I_{Adj} vs municipality average U bedrock conc (ppm) for cumulative lung cancer (a) and total cancer (excl. lung) incidence rate (b). Middle: County average I_{Crude} and I_{Adj} vs. population weighted county average U bedrock concentration for lung cancer (c) and total ca (excl. lung) (d). Bottom: Binned population weighted I_{Crude} and I_{Adj} vs U bedrock (ppm) for cumulative lung cancer (e) and total cancer (excl. lung; right) (f). Uncertainty bars in panels c-f refer to standard deviation of the mean estimate of I_{Crude} and I_{adj}.