Incidence of non-lung solid cancers in Czech uranium miners: a case-cohort study
ONLINE SUPPLEMENT

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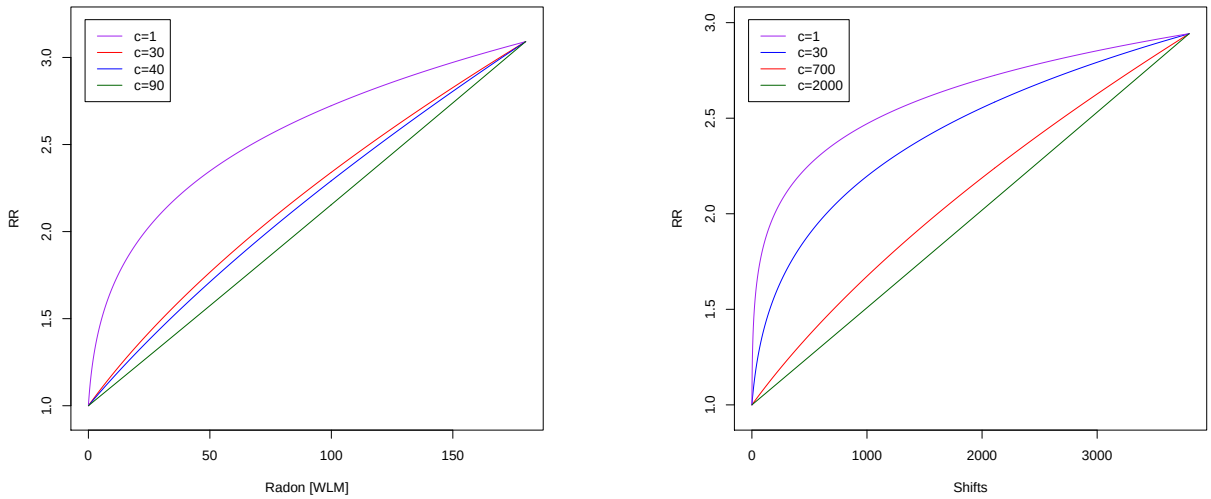
The Relative Risk Model

The primary analysis of non-lung solid cancers used the relative risk function of the form $\mathrm{RR}(y) = (c + y)^{\beta}$, where y was the cumulative exposure and c was an exposure-specific adjustment. This is a proportional hazards model with log-transformed shifted exposure, $\log(\mathrm{RR}) = \beta \log(c + y)$. Effects of smoking and calendar time are added to this model as additional terms.

The choice of the constant c determines the shape of the relative risk function. The relative risk function is monotone for all $c > 0$. If $\beta = 0$ (the null hypothesis of no exposure effect), the relative risk is 1 for all exposures, regardless of the choice of c. When $\beta > 0$ (a positive exposure effect), the relative risk is increasing with the exposure. For $0 < \beta < 1$, the relative risk function is concave (the slope is larger for small exposures then for large exposures), for $\beta > 1$, the relative risk function is convex (the slope is smaller for small exposures then for large exposures).

Figure 1: Relative risk functions induced by the model $\mathrm{RR}(y) = (c+y)^{\beta}$ for varying values of c and varying exposures. Left panel: y represents cumulative radon dose in WLM; right panel: y represents cumulative number of shifts worked underground.



The effect of the constant c on the relative risk function is illustrated in Figure 1. The left panel shows the relative risks for the effect of radon on malignant melanoma, the right panel shows melanoma risks associated with cumulative underground shifts. The exposure ranges in both panels run from 0 to the 90th percentile of the exposure estimated from the cohort of miners (180 WLM and 3800 shifts). The relative risk at the upper limit of the exposure range corresponds to the estimated risk at that exposure level for the malignant melanoma outcome.

The red lines show the relative risk functions that were actually fitted: they are only slightly curved. The constant $c = 30$ [WLM] for radon can be interpreted as an approximate lifetime radon exposure of a person living in a typical mean domestic radon concentration of 100 Bq/m^3 for 70 years. For cumulative shifts worked underground, we chose $c = 700$ [shifts]. This constant generates a relative risk function of approximately the same shape as that for radon. If we used the same value for c as in the radon analysis, the relative risk function for shifts would be much more severely curved. The usual choice for c in this type of a model is $c = 1$; however, this leads to quite unrealistic relative risk functions when exposures are measured on these scales.

Grouped exposure model for radon

The relative risks estimated from grouped exposure models are summarized in Table 1 located at the end of this supplement. This table is a counterpart to Table 2 from the main paper: there, naive descriptive estimates of similar relative risks were shown. In this table, the relative risks were estimated from proportional hazards models fitted to the case-cohort data, and were adjusted for the exact age, smoking status, and calendar time. The table also provides confidence intervals for the estimated risks and p-values for testing unity of all relative risks. The category > 200 WLM was merged with $100-200$ WLM because many of the outcomes had very small number of highly exposed cases.

Table 1: Relative risks estimated from grouped exposure models.

Outcome group	**Radon** [WLM]	RR	CI	p
All non-lung solid	< 10	1.00	—	0.032
	10 – 50	0.98	0.82 – 1.17	
	50 – 100	0.82	0.66 – 1.02	
	> 100	0.88	0.73 – 1.07	
Oral	< 10	1.00	—	< 0.001
	10 – 50	0.45	0.24 – 0.84	
	50 – 100	0.41	0.20 – 0.85	
	> 100	0.36	0.17 – 0.74	
All digestive	< 10	1.00	—	0.12
	10 – 50	1.07	0.84 – 1.37	
	50 – 100	0.92	0.69 – 1.23	
	> 100	0.91	0.70 – 1.19	
Stomach	< 10	1.00	—	0.063
	10 – 50	0.82	0.52 – 1.31	
	50 – 100	0.87	0.52 – 1.46	
	> 100	0.64	0.39 – 1.04	
Colon	< 10	1.00	—	0.24
	10 – 50	1.19	0.63 – 2.24	
	50 – 100	1.11	0.54 – 2.29	
	> 100	1.40	0.73 – 2.69	
Rectum	< 10	1.00	—	0.032
	10 – 50	1.30	0.80 – 2.13	
	50 – 100	0.78	0.43 – 1.41	
	> 100	0.98	0.58 – 1.65	
Liver	< 10	1.00	—	0.075
	10 – 50	2.36	0.89 – 6.25	
	50 – 100	1.66	0.55 – 4.96	
	> 100	1.84	0.66 – 5.12	
Gallbladder	< 10	1.00	—	0.086
	10 – 50	1.26	0.13 – 12.11	
	50 – 100	0.71	0.05 – 9.23	
	> 100	2.89	0.31 – 27.16	

RR: relative risk with respect to < 10 WLM

CI: 95% confidence interval

p: p-value for testing the unity of all RRs

Table 1: Relative risks estimated from grouped exposure models (continued).

Outcome group	**Radon** [WLM]	RR	CI	p
Pancreas	< 10	1.00	—	0.13
	10 – 50	0.69	0.36 – 1.33	
	50 – 100	0.55	0.24 – 1.25	
	> 100	0.70	0.34 – 1.47	
Larynx	< 10	1.00	—	0.30
	10 – 50	0.89	0.47 – 1.72	
	50 – 100	0.67	0.29 – 1.53	
	> 100	0.78	0.38 – 1.60	
Melanoma	< 10	1.00	—	0.0022
	10 – 50	2.16	0.67 – 6.90	
	50 – 100	5.55	1.83 – 16.86	
	> 100	3.38	0.82 – 13.94	
Genitourinary	< 10	1.00	—	0.0071
	10 – 50	0.93	0.64 – 1.37	
	50 – 100	0.54	0.33 – 0.89	
	> 100	0.86	0.58 – 1.26	
Prostate	< 10	1.00	—	0.042
	10 – 50	0.85	0.43 – 1.67	
	50 – 100	0.44	0.19 – 1.02	
	> 100	0.75	0.39 – 1.43	
Bladder	< 10	1.00	—	0.013
	10 – 50	1.18	0.58 – 2.41	
	50 – 100	0.42	0.16 – 1.12	
	> 100	0.88	0.42 – 1.85	
Kidney	< 10	1.00	—	0.31
	10 – 50	0.97	0.46 – 2.02	
	50 – 100	0.84	0.36 – 1.98	
	> 100	1.18	0.59 – 2.39	

RR: relative risk with respect to < 10 WLM

CI: 95% confidence interval

p: p-value for testing the unity of all RRs