Lung cancer risk among Czech tin and uranium miners – comparison of lifetime detriment*

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First epidemiological evidence of lung cancer risk from exposure to radon was based on studies of uranium miners. The risk in other mines was reported later. The cohort study among 2466 Czech tin miners was conducted in order to estimate the size of the risk and to compare it to that in uranium mines. Based on 205 lung cancers, the estimate of excess relative risk per unit exposure in the simple linear model 0.011 is compatible with findings from two cohort studies of Czech uranium miners. This similarity holds in more complex models that include modifying effects of age and time since exposure. In addition, an alternative description of the risk in terms of lifetime risk was used. This approach provides summarized characteristics, in which modifying effects of time and age are incorporated. The attributive risk derived from the lifetime relative risk is proportional to cumulated exposure observed in both tin and uranium miners. On the other hand, the expected life shortening of 19 years among radiation induced deaths is similar in these studies.

Key words: lung cancer, radon, tin miners, uranium miners, lifetime detriment

Exposure to radon and particularly to its radioactive decay products has been studied in relation to lung cancer risk since the 1960s [1, 2]. Studies were conducted mainly among uranium miners, however, there were also among some non-uranium mines, for instance fluorspar mines [3], iron mines [6, 13], or tin mines [4, 5, 20]. In the Czech Republic, a series of results on uranium miners were reported in the period 1971–91 by ŠEVC et al [15, 16].

A number of progressive measures in ventilation were introduced that resulted in the reduction of radon levels in most uranium mines during the 1950s. The hygienic supervision in Czech non-uranium mines started in the early 1960s [9, 14]. A lung cancer incidence study among Czech tin miners was reported in 1970 [10]. A pilot epidemiological study among 489 Czech tin miners was initiated in the late 1980s in order to compare observed and expected numbers of lung cancer in relation to cumulated exposure [21]. That study was extended to 1602 miners in the early 1990s [22] and the present study is a continuation of these efforts.

Methods

Study population and follow-up. The cohort involves men employed in the period 1953–1990 for at least 1 month in one of tin mines located in the Erz Mountains in north Bohemia. Individual information on miners were collected from the mines' personnel and pay files. These records included employment details going back to 1945. Before 1945, labour force in the mines was recruited from war prisoners. In the period 1931–39, the mines were not in operation.

Information on vital status and dates of death were obtained from the Czech population registry and data on causes of death from registries of deaths at local administrative offices. Follow-up for each subject started one month after entering employment or 1 January 1953, if later, and ended at the earliest of date of death, emigration, lost of follow-up, 85th birthday, or 31 December 1999. The condi-

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tion related to 85th birthday was used in order to eliminate potential losses of follow-up due to errors in the national population registry and misclassification in causes of death in older age categories. In comparison to national death rates, all 5 year age intervals are closed.

Results of the present study of tin miners are compared to two cohorts of Czech uranium miners described elsewhere [18, 19]. In brief, the S-cohort include 4339 miners who worked mainly in the Jáchymov uranium mines (west Bohemia) during 1948–1965 and the N cohort includes 5621 miners of the Příbram uranium mines (central Bohemia) who worked in the period 1968–1985.

Exposure estimation. Estimated exposure values in the study were derived from measurements of radon commencing since 1964. Radon concentrations before 1964 were assumed to be equal to those in 1964. Each man annual exposure to radon progeny was estimated by combining measurement data with his registered employment details, including duration of underground work and job category. Underground jobs were considered in two categories: full time (100%) and part time (50%) activities. Occupational exposures are given in working level months (WLM) integrating the concentration of radon progeny in air in terms of working levels (WL) and the duration of exposure in working months (170 hours). One WL corresponds to 130 000 MeV of potential alpha energy released by the short-lived progeny in equilibrium with radon in one litre of air (3.7 kBq/m^3).

Statistical methods. The analyses were based on the relative risk model. Generally, numbers of cases observed at given levels of exposure (W) and modifying variables (A,T) were supposed to have the Poisson distribution with a parameter iE (1 + f(W,A,T)), where "E" is the number of cases expected from national mortality data, parameter "i" is an intercept term that allows the background mortality rate for the hypothetically unexposed cohort to differ from that in the general population and "f(W,A,T)" represents the general dependence of excess relative risk on exposure and modifying variables. Specifically, the relative risk (RR) was assumed to depend on cumulated exposure (W) in forms according to models 1–4 specified below:

$$RR = 1 + b\,W \qquad \text{(model 1)}$$

$$RR = 1 + b_{5\text{-}19}\,W_{5\text{-}19} + b_{20\text{-}34}W_{20\text{-}34} + b_{35+}W_{35+} \qquad \text{(model 2)}$$

$$RR = 1 + b\,W \exp(c\,(A\text{-}50)/10) \qquad \text{(model 3)}$$

$$RR = 1 + (b_{5\text{-}19}W_{5\text{-}19} + b_{20\text{-}34}W_{20\text{-}34} + b_{35+}W_{35+}) \exp(c(A\text{-}50)/10) \qquad \text{(model 4)}$$

Parameters "b" in the models represent the excess relative risk per unit exposure (ERR/WLM). In models 2 and 4, subscripts denote periods before the manifestation of the risk. In models 3 and 4, the exponential term is used to modify the linear relationship by attained age (A). Parameter "c" in these models describes the relative change per decade of attained age. All parameters were estimated by the maximum likelihood method using software Epicure [11]. Stratification was based on age, calendar year, and birth year in 5 year groups. In all analyses, exposure is lagged by 5 years in order to allow for a minimal period between the exposure and the expression of the risk.

The relative risk model was supplemented by an alternative description of the risk, which is based on lifetable methodology using projections of the risk according to model 3. This included lifetime excess risk (LER), lifetime relative risk (LRR), years of lost life (YLL) and years of lost life among exposure induced deaths (YLL/EID). These characteristics, described elsewhere [17], are suitable for comparison of cohorts with different follow-up. In calculations of lifetime characteristics, we used baseline male mortality from lung cancer and from all causes according to the national data in the period 1995-99. The attributable risk (AR) among the exposed was calculated as AR=(LRR-1)/LRR.

Results

The study population involves a total of 2 466 miners who satisfied the selection criteria. A total of 2205 miners worked underground, mostly for short periods. For instance, 85% of miners worked for less than 10 years. Among exposed subjects who worked underground, the mean duration of exposure was 4.6 years and mean cumulated exposure was 54 WLM. A total of 261 miners (10.6%) who never worked underground were included in the cohort for a better estimation of background lung cancer rates. In this group, there were 8 cases of lung cancer corresponding to standardized mortality ratio O/E=1.09.

Among exposed miners, mean annual exposures varied in dependence of the proportion of job categories from 15–20 WLM before 1965 to about 1 WLM after 1977 reflecting improved ventilation in mines.

By the end of 1999, a total of 1294 (52.5%) miners had died, 32 of them in the age of 85 and more, 40 (1.6%) emigrated, and 181 (7.3%) miners were lost from follow-up, mainly because of incomplete personal data. These miners contributed to person-years and expected numbers till the date of loss, which was mostly the end of employment. Mortality figures by calendar periods and three main causes of deaths are shown in Table 1. The overall mortality was significantly elevated in comparison to nationally expected data (O/E=1.26, 95% CI: 1.19–1.33), mostly because of the elevated mortality from lung cancer (O/E=2.35, 95% CI: 2.04–2.69) and violent deaths (O/E=1.43, 95% CI: 1.19–1.70). Mortality from other diseases was increased, but not significantly (O/E=1.05, 95% CI: 0.99–1.13). However, the trend of this type of mortality with calendar period is significant (p=0.004) and reflects the healthy effect of work in early periods and the influence of hard work and lifestyle in later periods. The elevated mortality from external causes (violent deaths) reflects the social and life-style situa-

Table 1. Calendar period and cause specific mortality in the cohort of tin miners for age <85

Period	PY[a]	Lung cancer O[b]	Lung cancer O/E[c]	Violent deaths O[b]	Violent deaths O/E[c]	Other causes O[b]	Other causes O/E[c]	Unknown O[b]	All causes O[b]	All causes O/E[c]
1953–59	8,679	4	1.75	9	0.98	26	0.79	10	49	1.10
1960–69	15,801	25	2.38	26	1.34	87	0.84	7	145	1.08
1970–79	16,195	50	2.52	38	1.68	200	1.03	12	300	1.27
1980–89	14,573	63	2.28	31	1.52	290	1.14	17	401	1.32
1990–99	11,186	63	2.33	23	1.35	270	1.12	11	367	1.29
Total	66,418	205	2.35	127	1.43	873	1.05	57	1 262	1.26

[a]PY – person-years, [b]O – observed cases, [c]O/E – ratio of observed cases to nationally expected numbers.

Table 2. Age specific mortality from lung cancer in Czech studies of tin and uranium miners (S, N)

Age	Tin miners O[a]	Tin miners O/E[b]	S study O[a]	S study O/E[b]	N study O[a]	N study O/E[b]
–39	0	0.00	23	23.07	4	1.43
40–49	20	3.18	115	10.99	19	1.00
50–59	63	2.57	289	5.68	39	1.72
60–69	79	2.23	313	3.81	18	1.60
70–84	43	2.10	108	2.73	1	0.66
Total	205	2.35	848	4.61	81	1.42

[a]O – observed cases, [b]O/E – ratio of observed cases to nationally expected numbers.

Table 3. Distribution of person-years and observed lung cancers by cumulated exposure in the cohort of tin miners

WLM[a]	PY[b]	O[c]	O/E[d]	95% CI[e]
no exposure[f]	13 418	13	1.34	0.71–2.29
1–49	40 123	108	1.91	1.56–2.30
50–99	5 739	19	2.11	1.27–3.29
100–199	3 968	18	2.99	1.77–4.72
200–299	1 815	14	4.29	2.34–7.19
300–	1 352	33	12.33	8.48–17.3

[a]WLM – cumulated exposure lagged by five years, [b]PY – person-years, [c]O – observed cases, [d]O/E – ratio of observed cases to nationally expected numbers, [e]95% CI – 95% confidence interval for O/E, [f]no exposure category includes the contribution from miners who never worked underground and person-years within 5 years since the entry in the underground work corresponding to the 5 year lag.

tion in heavy industry. Unknown causes of deaths represent less than 5% of all deaths.

The age specific mortality from lung cancer (Tab. 2) and its trend from high excess in young age groups to lower excess in older age groups reflects two factors: 1) time since exposure and 2) age at exposure. These two factors were found as the most important modifying factors in studies of uranium miners [18]. In comparison, the S-study of uranium miners exhibits a stronger age dependence in contrast to the N study, where exposures were much lower. The mortality from lung cancer in the present study of tin miners reflects an intermediate exposure between the S- and N studies of uranium miners.

The dependence of the lung cancer risk on exposure is given in Table 3. Most of miners experienced cumulated exposure below 50 WLM. About 50% of all cases in the study experienced cumulated exposure in the range of 1–49 WLM. In this category, the risk in comparison to nationally expected numbers is significantly elevated. The risk from exposures over 300 WLM is more than 6 times higher and confirms the linear dependence on cumulated exposure. The estimated excess of relative risk per 1 WLM (ERR/WLM) related to the total cumulated exposure is given in Table 4 (model 1). In addition, when exposure is divided into three different time since exposure windows (Tab. 4, model 2), the fit between the observed data and the model is significantly better ($p=0.004$). Both models (1 and 2) can be improved by adding the modifying effect of attained age (models 3 and 4). The relative decrease of the risk is about 50% per decade of age.

A graphical presentation of the linear dependence and a comparison with uranium miners results are given in Figure 1. The linear trend in both cohorts is somewhat different, but the difference is not significant (Tab. 5, model 1). When modifying effect of age is included in the model, the difference is even smaller (Tab. 5, model 3).

The modifying effect of attained age for all three cohorts of miners is shown in Figure 2. Based on this model (model 3), further characteristics for each cohort were derived (Tab. 6). Both the lifetime excess risk (LER) and lifetime relative risk (LRR) reflects cumulated exposure in the cohorts. The attributable risks (AR) represents proportion of lung cancers related to exposure taking into account projected mortality in all cohorts. Although the follow-up in the present studies is different, the characteristics based on lifetime risk are directly comparable. Further characteristics given in Table 6 describes the total impact of exposure in terms of average number of years of life lost per exposure induced deaths (YLL/EID). The estimated 19 years of life lost (Tab. 6) is consistent in all present studies.

Table 4. Excess of relative risk per unit exposure, its temporal variations, and modifying effect of age in the cohort of tin miners

Model	Time since exposure	ERR/WLM[a]	90% CI	RC/10y[b]	90% CI	Comparison of models	
1	all years	0.011	0.007–0.015				
	5–19	0.022	0.014–0.035				
2	20–34	0.006	0.002–0.012			2 vs 1	p=0.004
	35–	0.002	–.004–0.009				
3	all years	0.025[c]	0.015–0.042	0.43	0.26–0.72	3 vs 1	p=0.001
	5–19	0.034[c]	0.020–0.060	0.55	0.33–0.91		
4	20–34	0.013[c]	0.004–0.026			4 vs 3	p=0.074
	35–	0.007[c]	–.007–0.023				

[a]excess relative risk per 1WLM, [b]relative change per decade of attained age, [c]modifying effect of age, ERR/WLM corresponding to age 50.

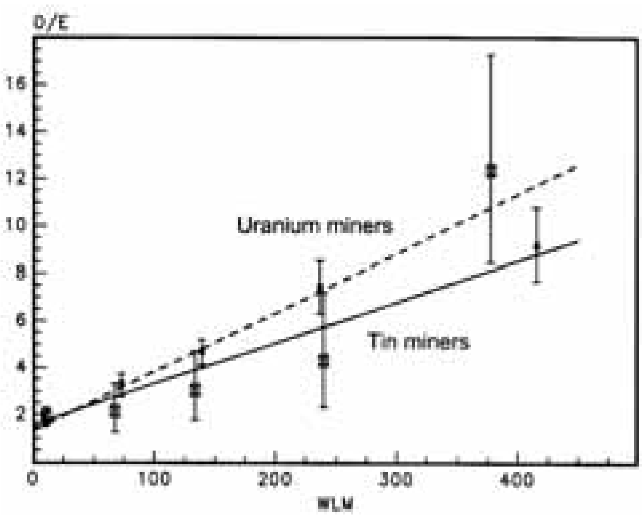

Figure 1. Lung cancer relative risk (O/E) in dependence to cumulated exposure to radon progeny (WLM) in the cohort of tin miners (—), comparison to uranium miners (- - -).

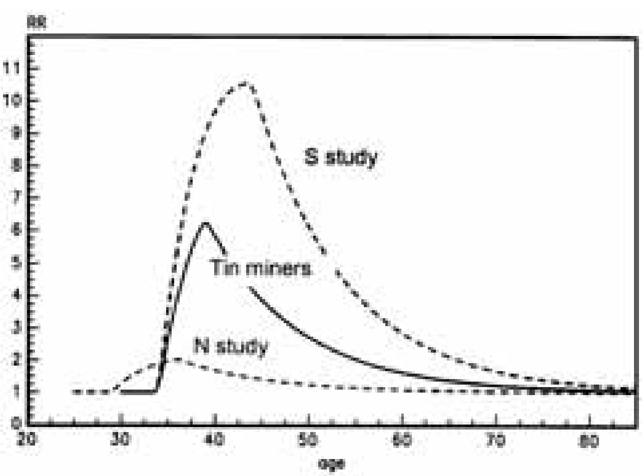

Figure 2. Relative risk of lung cancer in dependence on age – comparison of cohorts.

Table 5. Comparison of risk models between tin and uranium miners

Cohort	Model	ERR/WLM	90% CI	Test of differences[a]
Tin	1	0.011	0.007–0.015	p=0.099
S+N	1	0.018	0.013–0.025	
Tin	3[b]	0.029[c]	0.018–0.045	p=0.357
S+N	3[b]	0.039[c]	0.027–0.056	

[a]test of differences between tin and uranium miners, [b]equal modifying effect of attained age in all cohorts, [c]ERR/WLM corresponding to age 50

Table 6. Lifetime risk of lung cancer and years of life lost -- comparison of cohorts

	WLM	LER[a]	LRR[b]	AR[c]	YLL/EID[d]
Tin miners	54	3.7%	1.42	29%	19.3
S study	152	10.4%	2.18	54%	19.2
N study	7	0.5%	1.06	6%	19.4

[a]LER lifetime excess risk, [b]LRR lifetime relative risk, [c]AR attributable risk among exposed, [d]YLL/EID years of life lost among exposure induced deaths.

Discussion

The quality of all epidemiological studies depends both on the quality of follow-up and exposure assessment. The proportion of miners lost from the follow-up in the present cohort is about 7%. These men contributed to person-years up to the date of loss. If lost miners were completely excluded from the cohort, expected numbers in the beginning of follow-up would be underestimated. Individual exposures in the cohort were derived from records of the mining company and from measurement of radon since 1964. Concentrations before that year could be only approximately estimated. This drawback is common in most studies of miners [7, 8]. Lower precision of exposure estimates in early years can partly explain lower values of risk coefficients (ERR/WLM) corresponding to the distant past. The departure from the linear relationship in the highest category of exposure (Fig. 1) reflects probably lower precision in exposure estimates.

Results from studies of tin miners were reported in England (Cornwall) and China [4, 5, 20]. Mean annual exposure levels in Czech, Cornwall, and China tin mines were comparable. For instance, in the China mines, the levels decreased from about 2.2 WL before 1970 to 0.9 WL in the 1980s [20] and in the Cornwall mines [5] the levels were in the range of 1–2 WL. Mean concentrations in the Czech tin mines decreased from about 3.5 WL in 1964 to 0.04 WL in 1983. All these figures are related to full time jobs. Comparisons in terms of lung cancer mortality data are possible only for the Cornwall study (O/E=1.58) [5], which is comparable to our results and corresponds to somewhat higher concentrations in the Czech study. In the China study, lung cancer mortality in relation to nationally expected numbers was not reported [20]. The ERR/WLM in this study was lower (0.0062) in comparison to our study. In the Cornwall study the risk in terms of ERR/WLM was not reported. The present model with modifying effect of age and time since exposure (model 4) is very close to the model suggested by the BEIR IV committee [7]. For instance, exposure to 100 WLM in age 35–45 results in ERR=3.0 according to BEIR IV, our estimate is ERR=2.5 for model 3 and 3.4 for model 4.

Smoking is an obvious issue in studies of lung cancer. When the present cohort was established, most miners had already left the mining company. Therefore smoking information could not been collected. This is the usual problem in cohorts that are established retrospectively. However, in the absence of individual smoking data, estimates of relative risk and related characteristics in the cohort can be adjusted for by using stratified estimates (by age and birth cohort). The appropriateness of this approach can be supported by results of a case-control study nested in the Czech study of uranium miners [19] where smoking information was additionally collected. When smoking was adjusted for, the ERR/WLM was 0.024 and when smoking information was ignored, the stratified estimate of ERR/WLM was 0.026, therefore virtually equal estimates.

The description of mortality and particularly the dependence of relative risk on age leads to alternative characteristics of the risk. This approach based on lifetime risk is increasingly used in studies with relatively long follow-up, e.g. in a recent analyses of atomic bomb survivors [12]. In contrast to the description in terms of standardized mortality ratio (O/E) that reflects the situation in the cohorts at the end of follow-up, the measure of lifetime relative risk takes into account background rates estimated in the cohorts and the projections of the risk that cover the entire life span. In calculating years of life lost, this characteristic is usually related to radiation induced deaths (corresponding to the lifetime excess risk) and it reflects years of life lost due to exposure among cases. Generally, this values depend little on exposure [12]. The value of 19 years of life lost was similar in all studies presented here. It reflects the increased relative risk of lung cancer observed in age 40–50 in the present studies (Fig. 2) and the mean age of about 65 among lung cancers in the general population.

In conclusion, results from the follow-up of tin miners are in line with findings of uranium miners. The size of the risk corresponds to cumulated exposure in the cohorts. On the other hand, the estimated years of life lost do not show any dependence on cumulated exposure.

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