ORIGINAL ARTICLE

Mortality and cancer incidence among underground uranium miners in the Czech Republic 1977–1992

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► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/oemed-2018-105562).

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Received 1 November 2018
Revised 3 May 2019
Accepted 6 May 2019

ABSTRACT

Objectives Uranium miners in Příbram, Czech Republic were exposed to low and moderate levels of radon gas and other hazards. It is unknown whether these hazards increase the risk of mortality or cancer incidence when compared with the general Czech population.

Methods A cohort of 16 434 male underground miners employed underground for at least 1 year between 1946 and 1976, and alive and residing in the Czech Republic in 1977, were followed for mortality and cancer incidence through 1992. We compared observed deaths and cancer incidence to expectation based on Czech rates. Standardised mortality ratios (SMRs), standardised incidence ratios (SIRs) and causal mortality ratios were calculated.

Results Underground workers in the Příbram mines had higher rates of death than expected due to all causes (SMR=1.23, 95% CI 1.20 to 1.27), all cancers (SMR=1.52, 95% CI 1.44 to 1.60), lung cancer (SMR=2.12, 95% CI 1.96 to 2.28) and extrathoracic cancer (SMR=1.41, 95% CI 1.15 to 1.77). Similar excess was observed in cancer incidence analyses, with the addition of stomach cancer (SIR=1.37, 95% CI 1.11 to 1.63), liver cancer (SIR=1.70, 95% CI 1.16 to 2.25) and rectal cancer (SIR=1.41, 95% CI 1.16 to 1.66). The SIR was elevated for all leukaemias (SIR=1.51, 95% CI 1.08 to 2.07) and for lymphatic and haematopoietic cancers combined (SIR=1.31, 95% CI 1.05 to 1.61), but results for specific subtypes were imprecise. Deaths due to hazardous mining conditions resulted in 0.33 person-years of life lost per miner.

Conclusions Occupational exposure to the Příbram mines resulted in excess cancers at several sites, including sites previously linked to radon and uranium exposure. Incidence analyses showed relative excess of several additional cancer subtypes.

Key messages

What is already known about this subject?

► Underground uranium miners are routinely exposed to several occupational hazards, including radon progeny, dust and gamma radiation. Excess morality among uranium miners has been observed in several cohorts, particularly lung cancer mortality.

What are the new findings?

► Compared with many studies of uranium miners, this study focuses on more recently employed miners with lower average radon exposures. We also investigate cancer incidence, which few studies of miners have examined.

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

► This study adds to the understanding of occupational hazards experienced by a large and historically significant uranium mining cohort routinely exposed to radon and its progeny and other occupational hazards.

INTRODUCTION

Between World War II and the Cold War, extensive uranium mining in the Příbram region was driven by demand from the former Soviet Union.[1] Czechoslovakia was the third largest supplier of uranium to the Soviet Union during this time, with a cumulative production through 1990 of 98 500 metric tons.[1] Příbram mine operations occurred between 1946 and 1991, during which over 46 000 workers were employed.

After the discovery of large uranium deposits in the region, Příbram became the largest mining operation in Czechoslovakia. By the 1960s, over 70% of all uranium production took place in Příbram.[2] However, extensive uranium mining operations occurred in other regions, notably the Jáchymov mines of Western Bohemia. Those mines operated through World War II, but production decreased in the mid-1960s. Jáchymov miners reportedly worked very strenuously with poor ventilation and few skilled explosives technicians.[2] Some workers from Jáchymov worked in Příbram after mining operations declined in Jáchymov.

Uranium miners experience several occupational hazards, including exposure to radiation, dust, accidents and vibration. They are routinely exposed to radiation as a result of inhalation of radon and its decay products and experience radiation exposure from long-lived radionuclides in uranium ore dust and external gamma radiation.[3] In Příbram, radon concentrations were highest at the start of the mining operations and decreased with improved ventilation. In 1975, an annual exposure limit of 3.4 working level months (WLM) of radon exposure was set. However, many miners continued to work in environments exceeding this limit.

Another occupational hazard of uranium mining is inhalation of total airborne dust and its components, including heavy metals and silica. Average area measurements of airborne dust in Příbram

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To cite: Kelly-Reif K, Sandler DP, Shore D, *et al*. *Occup Environ Med* Epub ahead of print: [please include Day Month Year]. doi:10.1136/oemed-2018-105562

were highest in the mid-1950s (10.5 mg/m^3 in 1956). With the introduction of a strong ventilation system in the 1970s, average concentrations fell steeply and remained around 1 mg/m^3 until the end of the mining operations. Heavy metals in samples of dust sediments were measured using ore from accessible mines. These contained higher levels of lead and lower levels of arsenic compared with the Jáchymov mines.[2] For instance, the arsenic levels averaged 144 mg/kg in Příbram and 789 mg/kg Jáchymov and lead levels averaged 1037 mg/kg in Příbram and 112 mg/kg in Jáchymov.[2] The mean concentration of free crystalline silica in dust from Příbram was estimated to be 15%, lower than many other hard-rock mines because dry drilling was not common. Unlike many other mining operations, Příbram miners were not occupationally exposed to diesel exhaust because all vehicles in the Příbram mines were electric.[2]

Hazards from uranium mining have been investigated in several large studies from the USA and Europe, which all report excess lung cancer risks, and in some instances excess stomach and digestive, haematopoietic, kidney and extrathoracic cancers.[4–8] In another cohort of Czech uranium miners, large excesses of lung cancer mortality, as well as excess of liver, gallbladder and extrahepatic bile duct cancers were observed among Jáchymov miners.[9] External comparisons of mortality and cancer incidence have not been described for the present cohort of Czech miners comprised solely of workers from Příbram, Central Bohemia. This cohort on average contains more recently employed workers and lower average radon, dust and diesel exposures than several other uranium miner cohorts. Our aim is to describe mortality and cancer incidence among a large cohort of uranium miners in Příbram relative to national rates. This study adds to the understanding of occupational hazards experienced by a large, historically significant uranium mining cohort routinely exposed to radon and its progeny and other occupational hazards.

MATERIALS AND METHODS

Study population

The Příbram cohort is based on information collected from employment records of the Příbram Uranium Industry (UI). Card records were kept for compensation purposes for each worker and subsequently computerised into an employment register containing 41 741 males and 6106 females. Records included personal identification numbers, dates of birth, dates of employment and location of employment within the mines (eg, underground, surface, sorting ore).[10 11]

A cohort of underground miners was selected from the registry UI employees. Male employees listed in the employment card registry who worked at least 12 months underground between 1946 and 1976 and were alive and residing in Czechoslovakia at the establishment of the Czech cancer registry (1 January 1977) qualified for inclusion in the cohort.[10 11] Workers who emigrated after the start of follow-up were censored at the date of emigration.

Outcome assessment

To identify workers who died or emigrated during the study period, personal identification numbers listed on employment records were used to obtain vital and emigration status from the Register of Inhabitants. Sources of information other than the Register of Inhabitants were used to obtain vital status for 8% of workers. Sources included regional death certificates, pensions, oncologic registers and UI records.[10 11] The date of last follow-up and vital status (dead, alive or emigrated) were coded. Workers who emigrated were censored at date of emigration. For deceased workers, copies of death certificates were obtained from district death registries, and cause of death was coded to the International Classification of Diseases, 9th Edition (ICD-9).[12]

Cancer diagnoses between 1977 and 1992 were obtained for eligible cohort members. Workers diagnosed with cancer were not allowed to work underground. Therefore, workers alive in 1977 and still working underground were assumed to be cancer free at the start of follow-up.[10 11] Cancers were identified by matching the cohort subjects with the Czech and Slovak national cancer registries using exact matches with individual government identification numbers, names and dates of birth, all listed in the employment registry. Reporting to the cancer registry was mandatory.[11] All cancers were coded according to ICD-9.[12] Cancer subtypes of interest include lung, stomach, liver, kidney, extrathoracic and haematopoietic cancers. Extrathoracic cancers are reported separately and as a group based on the International Commission on Radiological Protection (ICRP) dose calculations.[13] The extrathoracic group includes the nasal passages (ICD-9 160), larynx (161), pharynx (147–148), oropharynx (146) and mouth (141–145).

Statistical methods

All statistical analyses were conducted using SAS statistical software (SAS 9.4; SAS Institute, Cary, North Carolina, USA). SAS allows the calculation of person-time at risk contributed by each cohort member to tabulate time-dependent variables.[14] Miners contributed person-time from the start of follow-up (1/1/1977) until the earliest of the date of death among deceased miners, date of migration out of the Czech Republic or end of the study period (31/12/1992). No new hires after the start of follow-up were included in the cohort. For each person-year at risk, we calculated the expected numbers of deaths and cancer diagnoses by multiplying the cohort person-time at risk by annual Czech mortality and cancer incidence rates specific to 5 year age group and calendar period. Standardised mortality ratios (SMRs), standardised incidence ratios (SIRs) and associated Wald-type 95% CIs were estimated by fitting a lognormal Poisson model to calculate expected cases. The sum of observed cases is divided by the expected cases. This modelling approach was used to allow for flexible modelling for sensitivity analyses. Age-specific data at different calendar periods were employed to examine birth cohort effects, age effects and period effects based on variables in prior studies of uranium miners.[15] Duration of employment, time since exposure and age at exposure, birth cohort and hire cohort were examined.

Sensitivity analyses

Hazardous conditions may shorten the amount of person-time observed in a cohort. Standard SMRs, which use the observed person-time experienced by the cohort to calculate expected death rates, often lead to biased estimates in hazardous occupations such as mining.[16] To account for the reduction of person-time in the cohort, we calculated causal mortality ratios (CMRs). CMRs generate counterfactual failure times for members of the cohort in the absence of exposure based on external reference mortality rates.[16] CMRs are ratios of observed deaths to expected deaths, where expected deaths are the product of death rates in the standard population and cohort person-time based on the counterfactual failure times. The difference in observed person-time and expected person-time is the years of life lost in the cohort; this difference divided by the number of workers in the study is the average person-years of life lost per worker.

Table 1 Characteristics of the male Příbram Czech miners cohort 1977–1992

Variable	
Males in employment registry	41 741
Worked underground 12+ months	18 985
Deceased prior to 1977	1932
Emigrated prior to 1977	108
Vital Status Unconfirmed	511
Miners ineligible for inclusion in cohort	16 434
Follow-up period	1977–1992
Person-years	2 31 499
Employment characteristics, mean (range)	
Year of birth	1935 (1886–1957)
Year of hire	1963 (1946–1975)
Age at hire	28 (18–70)
Age at end of employment	35 (19–76)
Duration of employment, years	7 (1–38)
Time since first employment	29 (1.5–47)
Duration of follow-up	14 (0.1–16)
Age at end of follow-up	55 (22–102)
Age at death among deceased workers	62 (22–102)
Cumulative radon in WLM	53 (1.2–1121.9)
Vital status, n (%)	
Alive	12 209 (74.3)
Deceased	4212 (25.6)
Emigrated	12 (0.07)
Vital status unknown during follow-up	1 (0.01)
Availability of cause of death (among deceased workers)	3775 (89.6)
Year of birth n (%)	
1880–1909	543 (3.3)
1910–1919	1541 (9.4)
1920–1929	3810 (23.2)
1930–1939	3476 (21.2)
1940–1950+	7064 (43.0)
Year of hire n (%)	
1946–1952	1568 (9.5)
1953–1962	6397 (39.0)
1963–1976	8469 (51.5)

WLM, Working Level Months, n=number

Comparisons of SMR over calendar periods or other stratifying variables may be impacted by the changing covariate distribution in the cohort. Homogeneity of the rate ratio across covariates is a necessary condition for valid comparisons of SMRs. To assess if changes in population distribution over time affected comparisons of calendar period-specific SMRs, we fit a lognormal Poisson random effects model to test for heterogeneity of person-time distribution by age across calendar periods.[17] A random effect for age was included in standard SMR lognormal Poisson models to examine the influence of heterogeneity in age distribution across time. Heterogeneity is quantified by the variance of the random effect parameter, σ^2.

RESULTS

Eligibility for mortality and cancer incidence follow-up was met by 16 434 male underground uranium miners (table 1). The workers contributed 231 499 person-years and 25.6% of workers died during the 16-year follow-up period. Cause of death was available for 89.6% of deceased workers and 1788 incident cancers were identified. Mean duration of employment was 7 years.

There was a 23% increase in deaths from all causes compared with expected rates (SMR=1.23, 95% CI 1.20 to 1.27). A number of non-malignant causes of death were higher than expected. SMRs for all non-malignant causes of death are reported in table 2. Deaths due to tuberculosis and pneumoconiosis were two times higher than expected. Excess mortality from mental, psychoneurotic and personality disorders was observed (SMR=1.88, 95% CI 1.05 to 2.71). Mortality from diseases of the heart and other diseases of the circulatory system were near unity (SMR=0.93, 95% CI 0.89 to 0.98), however, SMRs of cardiovascular subgroups varied. Atherosclerosis mortality was in substantial excess (SMR=3.88, 95% CI 3.50 to 4.26), while acute myocardial infarction mortality was substantially lower than expected (SMR=0.38, 95% CI 0.33 to 0.42).

Deaths from several cancer types were elevated among the miners. There was a 52% increase in deaths from all malignant causes compared with expected rates (SMR=1.52, 95% CI 1.44 to 1.60). SMRs and SIRs for malignant causes of death of a priori interest or with three or more cases are reported in table 3. Lung cancer mortality was substantially elevated (SMR=2.12, 95% CI 1.96 to 2.28). Cancer mortality among several solid cancer subtypes was elevated, notably cancers of the stomach (SMR=1.27, 95% CI 1.02 to 1.51), rectum (SMR=1.33, 95% CI 1.04 to 1.62) and liver (SMR=1.63, 95% CI 1.17 to 2.10).

Cancer incidence was also elevated among the miners (table 3). Lung cancer incidence was substantially elevated (SIR=2.31, 95% CI 2.15 to 2.48). Stomach (SIR=1.37, 95% CI 1.11 to 1.63), rectal (SIR=1.41, 95% CI 1.16 to 1.66), liver (SIR=1.70, 95% CI 1.16 to 2.25) and extrathoracic cancer (SMR=1.41, 95% CI to 1.15 to 1.77) incidences were also in excess. There was a notable deficit in non-melanoma skin cancer incidence (SIR=0.68, 95% CI 0.56 to 0.80). Cancer incidence was elevated for all leukaemias, and lymphatic and haematopoietic cancers combined, and elevated but imprecise for Hodgkin's lymphoma, multiple myeloma, lymphoid leukaemia and myeloid leukaemia.

We examined all-cause mortality and lung cancer mortality by categories of duration of employment, time since hire, time since termination and age at hire (table 4). Lung cancer mortality increased with duration of employment and decreased with both longer time since hire and time since termination. Minimal differences were observed in lung cancer mortality by age at hire. All-cause mortality decreased with older age at hire and decreased substantially with both longer time since hire and time since termination. No substantial differences were observed for duration of employment.

Because variation in mortality may result from differences in age and duration of employment, we evaluated SMRs by birth cohort and period of hire for lung cancer and all-cause mortality (table 4). Excess lung cancer and all-cause mortality were observed among every birth cohort. The highest mortality occurred among miners born between 1920 and 1929 (all-cause SMR=1.35, 95% CI 1.29 to 1.42; lung cancer SMR=2.35, 95% CI 2.10 to 2.60). Earlier hiring period was associated with both an increase in all-cause and lung cancer mortality (1946–1952 hiring period all-cause SMR=1.38, 95% CI 1.28 to 1.47; lung cancer SMR=2.63, 95% CI 2.21 to 3.04). Mortality by hiring period was examined by categories of employment duration; no substantial differences by duration of employment were observed in the early hiring period. In the later hiring periods, cancer mortality decreases with longer duration of employment (table 3A).

Table 2 Non-malignant causes of death among Příbram uranium miners*

Major groups and select ICD-9 subgroups	Obs	Exp	SMR (95% CI)
(011–012) Respiratory tuberculosis	14	6.7	2.08 (0.99 to 3.18)
(250) Diabetes mellitus	34	45.3	0.75 (0.50 to 1.00)
(280–289) Diseases of the blood and blood forming organs	5	3.9	1.29 (0.15 to 2.42)
(290–319) Mental, psychoneurotic and personality disorders	20	10.6	1.88 (1.05 to 2.71)
(303) Alcohol dependence syndrome	7	9.1	0.77 (0.20 to 1.34)
(320–389) Disorders of the nervous system and sense organs	19	26.5	0.72 (0.39 to 1.04)
(390–459) Diseases of the heart and other diseases of the circulatory system	1536	1647.6	0.93 (0.89 to 0.98)
(410) Acute myocardial infarction (AMI)	230	613.0	0.38 (0.33 to 0.42)
(410–414) Ischaemic heart disease (including AMI)	737	933.0	0.79 (0.73 to 0.85)
(430–438) Cerebrovascular disease	148	424.2	0.35 (0.29 to 0.41)
(440) Atherosclerosis	403	103.8	3.88 (3.50 to 4.26)
(440–448) Diseases of the arteries, arterioles, capillaries and allied conditions (including atherosclerosis)	419	121.3	3.46 (3.12 to 3.79)
(460–519) Diseases of the respiratory system	166	187.6	0.89 (0.75 to 1.02)
(480–487) Pneumonia and influenza	37	51.6	0.72 (0.48 to 0.95)
(490–496) Chronic obstructive pulmonary disease and allied conditions	96	114.1	0.84 (0.67 to 1.01)
(500–505) Pneumoconiosis including silicosis and asbestosis	22	11.5	1.92 (1.11 to 2.72)
(520–579) Diseases of the digestive system	167	177.0	0.94 (0.80 to 1.09)
(530–537) Diseases of the stomach and duodenum	17	26.0	0.65 (0.34 to 0.97)
(571) Cirrhosis and other chronic liver disease	89	95.1	0.94 (0.74 to 1.13)
(577) Diseases of the pancreas	20	14.8	1.35 (0.76 to 1.94)
(580–629) Diseases of the genitourinary system	55	75.4	0.73 (0.54 to 0.92)
(580–589) Nephritis, nephrotic syndrome and nephrosis	26	27.8	0.94 (0.58 to 1.30)
(590) Infections of kidney	21	25.3	0.83 (0.47 to 1.19)
(591–608) Diseases of urinary system and male genital organs	8	22.3	0.36 (0.15 to 0.7)
(800–999) Injury and poisoning	101	277.5	0.36 (0.29 to 0.44)
(E800–E949) Transportation injuries, falls and accidents	95	163.8	0.58 (0.46 to 0.70)
(E950–E959) Suicide and self-inflicted injury	86	97.2	0.89 (0.70 to 1.07)
(E960–E969) Assault	4	3.3	1.20 (0.02 to 2.38)
(001–139) Other causes	19	15.3	1.25 (0.68 to 1.81)
(001–E999) All-cause mortality†	4211	3419.0	1.23 (1.20 to 1.27)

*Causes of death of a priori interest or with more than three observed deaths.
†Included in all-cause mortality are 437 miners with missing cause of death codes, and 12 with undetermined external causes of injury (ICD-9 E970- E999). One death with undetermined date of death was excluded.
Exp, Expected; Obs, Observed; SMR, standardised mortality ratio.

CMRs were slightly lower than SMRs for all cancer types examined and are reported for cancer subtypes of interest in table 5. Lower CMRs indicate that person-time in the cohort was lower than expected across several causes of mortality. Overall expected person-time was 2.3% higher than observed person time, averaging to 0.33 person-years of life lost per miner.

Random effects were used to assess changes in standardisation variables over time. SMRs from the random effects lognormal Poisson models are reported in 4-year calendar periods (see online supplementary appendix 1). The mortality ratios from the random effects model did not differ from the standard ratio estimates. All corresponding σ^2 estimates approached zero, indicating that the amount of heterogeneity in incidence ratios was minimal.

DISCUSSION

The mortality and cancer incidence experience among this group of uranium miners had not been previously described relative to an external population. We have estimated SMRs, SIRs and CMRs relative to a national reference. We examined trends over time, evaluated comparability in standard populations using random effects models and evaluated influences of healthy-worker hire effects by stratification of employment factors, evaluated workplace hazards using CMRs and examined cohort effects. Our results show that several cancer subtypes and non-malignant causes of death were elevated among miners. Elevated mortality rates of pneumoconiosis and tuberculosis were observed and are plausibly related to occupational exposure to dust and its components such as silica.[18]

Excess lung, haematopoietic, extrathoracic airway and stomach cancers were observed. While individual radiation exposures were not assessed in this study, the observed excesses are consistent with findings from dosimetric models and previous studies of uranium miners.[5 19–22] While we observed elevated cancer incidence and mortality of several non-lung subtypes, other studies of uranium miners have also identified elevated rates of stomach, haematopoietic, kidney and extrathoracic airway cancers.[4–8] When followed up through 1991, the miners from Western Bohemia had large excess lung cancer mortality (SMR=5.08, 95% CI 4.71 to 5.47) as well as an excess of liver cancer (SMR=1.67, 95% CI 1.04 to 2.52) and gallbladder and extrahepatic bile duct cancer mortality (SMR=2.26, 95% CI 1.16 to 3.94).[9] In a study of lung cancer with extended follow-up of Western and Central Bohemian miners, excess lung cancer mortality was again identified (SMR=3.47, 95% CI 3.27 to 3.68), and time since exposure was found to modify the association between radon and lung cancer.[23] The Ontario cohort is the only other uranium mining cohort which includes cancer incidence. Mean radon exposure and duration of employment are lower than in Příbram, and the only excess cancer reported was lung (SIR=1.30, 95% CI 1.23 to 1.37).[21]

Beyond findings that were expected for uranium miners based on known hazards, a few other hazards were implicated. Atherosclerosis mortality was almost four times higher than expected. Although radiation and other occupational exposures have been linked to cardiovascular disease, an excess of atherosclerosis is not generally associated with uranium mining activities. There are several explanations for this excess, namely, errors in cause of death reporting, coding errors or lack of adjustment for smoking. The excess of deaths due to atherosclerosis is counter-balanced by a decrease in deaths due to myocardial infarction, which suggests the possibility of misclassification of

Table 3 Cancer mortality and incidence for select ICD-9 groups

(ICD) Cancer subtype	Cancer mortality				Cancer incidence			
	Obs	Exp	SMR	95% CI	Obs	Exp	SIR	95% CI
(140) Malignant neoplasm of lip	0	–	–	–	6	8.6	0.70	0.14 to 1.26
(141) Malignant neoplasm of tongue	9	6.4	1.41	0.48 to 2.33	12	7.6	1.58	0.68 to 2.48
(146) Malignant neoplasm of oropharynx	3	4.5	0.66	0.00 to 1.41	6	7.7	0.78	0.15 to 1.40
(140–149) Lip, oral cavity and pharynx	25	21.8	1.14	0.75 to 1.65	41	42.1	0.98	0.71 to 1.31
(150) Malignant neoplasm of oesophagus	23	15.0	1.53	0.90 to 2.16	19	14.0	1.36	0.74 to 1.97
(151) Malignant neoplasm of stomach	102	80.6	1.27	1.02 to 1.51	108	78.9	1.37	1.11 to 1.63
(152) Malignant neoplasm of small intestine, including duodenum	6	2.1	2.91	0.57 to 5.25	7	2.1	3.26	0.83 to 5.69
(153) Malignant neoplasm colon	54	59.7	0.90	0.66 to 1.15	80	75.7	1.06	0.82 to 1.29
(154) Malignant neoplasm of rectum, rectosigmoid junction and anus	80	60.2	1.33	1.04 to 1.62	119	84.4	1.41	1.16 to 1.66
(155) Malignant neoplasm of liver and intrahepatic bile ducts	48	29.4	1.63	1.17 to 2.10	38	22.3	1.70	1.16 to 2.25
(156) Malignant neoplasm of gallbladder and extrahepatic bile ducts	13	14.7	0.88	0.40 to 1.37	9	14.8	0.61	0.21 to 1.00
(157) Malignant neoplasm of pancreas	53	44.6	1.19	0.87 to 1.51	54	41.3	1.31	0.96 to 1.66
(159) Malignant neoplasm of other and ill-defined sites	14	7.7	1.82	0.86 to 2.77	16	4.9	3.29	1.67 to 4.91
(140–148, 160, 161) Extrathoracic airway*	59	41.8	1.41	1.15 to 1.77	80	68.9	1.16	0.95 to 1.39
(150–159) Digestive organs and peritoneum	396	316.7	1.25	1.13 to 1.38	453	340.8	1.33	1.21 to 1.46
(161) Malignant neoplasm of larynx	33	19.8	1.67	1.10 to 2.24	45	33.6	1.34	0.95 to 1.73
(162) Malignant neoplasm of trachea, bronchus and lung	705	332.3	2.12	1.96 to 2.28	755	326.2	2.31	2.15 to 2.48
(163) Malignant neoplasm of pleura	5	2.4	2.06	0.25 to 3.87	5	2.5	1.97	0.24 to 3.71
(160–165) Respiratory and intrathoracic	749	358.5	2.09	1.95 to 2.25	808	367.0	2.20	2.05 to 2.36
(171) Malignant neoplasm of connective and other soft tissue	3	2.8	1.07	0.00 to 2.28	5	6.9	0.72	0.09 to 1.36
(172) Malignant melanoma of skin	14	11.9	1.18	0.56 to 1.80	18	23.3	0.77	0.41 to 1.13
(173) Other malignant neoplasm of skin	1	2.6	0.39	0.00 to 1.16	129	190.3	0.68	0.56 to 0.80
ICD 170–175: Bone, connective tissue, skin and breast	22	21.8	1.00	0.64 to 1.49	157	224.9	0.70	0.59 to 0.81
(185) Malignant neoplasm of prostate	30	45.1	0.67	0.43 to 0.90	57	65.9	0.86	0.64 to 1.09
(186) Malignant neoplasm of testis	4	3.8	1.05	0.02 to 2.09	10	11.7	0.85	0.32 to 1.38
(187) Malignant neoplasm of penis and other male genital organs	4	1.4	2.81	0.04 to 5.57	6	3.4	1.76	0.35 to 3.18
(188) Malignant neoplasm of bladder	29	27.7	1.05	0.67 to 1.43	54	50.8	1.06	0.78 to 1.35
(189) Malignant neoplasm of kidney and other and unspecified urinary organs	41	40.9	1.00	0.69 to 1.31	49	55.9	0.88	0.63 to 1.12
ICD 185–189: Genitourinary organs	108	118.9	0.91	0.75 to 1.09	176	187.8	0.94	0.81 to 1.08
(191) Malignant neoplasm of brain	13	17.0	0.76	0.35 to 1.18	13	15.6	0.83	0.38 to 1.29
(193) Malignant neoplasm of thyroid gland	2	2.2	0.91	0.00 to 2.19	5	4.3	1.17	0.14 to 2.20
(195) Malignant neoplasm of other and ill-defined sites	5	4.3	1.17	0.14 to 2.19	3	3.4	0.87	0.00 to 1.86
(197) Secondary malignant neoplasm of respiratory and digestive systems	8	0.1	71.70	21.81 to 121.60	7	5.4	1.29	0.33 to 2.25
(198) Secondary malignant neoplasm of other specified sites	6	0.1	52.86	10.39 to 95.33	13	4.5	2.86	1.30 to 4.42
(199) Malignant neoplasm without specification of site	14	13.8	1.02	0.48 to 1.55	19	8.0	2.36	1.30 to 3.43
(190–199) Other and unspecified sites	53	39.2	1.36	1.03 to 1.76	68	49.1	1.38	1.09 to 1.75
(200) Lymphosarcoma and reticulosarcoma	7	4.5	1.57	0.40 to 2.73	7	7.4	0.94	0.24 to 1.64
(201) Hodgkin's disease	8	6.8	1.18	0.36 to 2.00	15	9.5	1.57	0.77 to 2.37
(202) Other malignant neoplasms of lymphoid and histiocytic tissue	10	10.2	0.98	0.37 to 1.58	10	14.1	0.71	0.27 to 1.15
(203) Multiple myeloma and immunoproliferative neoplasms	8	7.5	1.07	0.33 to 1.82	16	9.2	1.75	0.89 to 2.61
(204) Lymphoid leukaemia	11	10.6	1.03	0.42 to 1.65	21	13.3	1.57	0.90 to 2.25
(205) Myeloid leukaemia	12	8.8	1.36	0.59 to 2.14	14	8.8	1.58	0.75 to 2.42

continued

Table 3 continued

(ICD) Cancer subtype	Cancer mortality				Cancer incidence			
	Obs	Exp	SMR	95% CI	Obs	Exp	SIR	95% CI
(204–208) All leukaemia†	25	24.0	1.05	0.69 to 1.52	37	24.0	1.51	1.08 to 2.07
(200–208) Lymphatic and haematopoietic	58	52.8	1.09	0.84 to 1.41	85	64.7	1.31	1.05 to 1.61
(140–232) All cancer types	1411	929.6	1.52	1.44 to 1.60	1788	1276.5	1.40	1.34 to 1.47

*Extrathoracic airway includes cancers of the oral cavity and pharynx (141–148), nasal cavities (160) and larynx (161).
†Lymphoid, myeloid, other and unspecified leukaemia.
Exp, expected, Obs, observed; SMR/SIR, standardised mortality/incidence ratio.

cardiovascular disease (CVD) deaths. Additionally, use of pneumatic drills can cause symptoms resembling atherosclerosis.[24]

There was a deficit of non-melanoma skin cancer incidence in this cohort. A substantial excess of skin cancer (SMR=5.7, 95% CI 4.1 to 7.8) has been reported among 3000 Jáchymov Czech uranium miners.[25 26] The difference in estimates may be because the Jáchymov cohort had a dermatology surveillance programme, while the Příbram study relies on ICD-9 codes.[26 27] There was also a deficit of prostate cancer mortality (SMR=0.67, 95% CI 0.43 to 0.90). Similar deficits were also reported among the German uranium miners (SMR=0.85, 95% CI 0.75 to 0.95); factors such as high physical activity and duration of underground work were identified.[28]

Prior studies of Příbram miners examined associations between radon exposure and incidence of some cancer subtypes. Two case-cohort studies of the Příbram miners using the same source population as the present study were conducted.[10 11] Incidence of leukaemia, lymphoma and multiple myeloma was investigated among a subcohort of 2393 workers; an elevated risk for all leukaemia combined (risk ratio (RR)=1.75, 95% CI 1.10 to 2.78) and for chronic lymphocytic leukemia (CLL) (RR=1.98, 95% CI 1.10 to 3.59) were observed when comparing high radon exposure (>110 WLM) to low radon exposure (<3 WLM). Suggestive associations between myeloid leukaemia and Hodgkin's lymphoma with radon exposure were reported.[11] In the present study, we found elevated risks for all leukaemia, Hodgkin's lymphoma, multiple myeloma, myeloid leukaemia and lymphoid leukaemia. We could not examine CLL alone due to unavailability of national rates for certain subtypes, but most lymphoid leukaemias in adults are CLL.[29] Rates of non-lung solid cancer incidence by WLM were examined among workers in the case-cohort study, but only excesses of malignant

Table 4 All-cause mortality and lung cancer mortality by duration of employment, time since hire, time since termination, age at hire, birth cohort and hiring period

	All-cause mortality			Lung cancer mortality		
	Obs	SMR	95% CI	Obs	SMR	95% CI
Duration of employment						
<2 years	1181	1.27	1.20 to 1.34	149	1.69	1.42 to 1.97
2 to <10 years	1579	1.30	1.24 to 1.37	247	2.15	1.88 to 2.42
≥10 years	1451	1.14	1.08 to 1.20	309	2.39	2.12 to 2.65
Time since hire						
<15 years	238	52.11	45.46 to 58.76	18	46.62	24.99 to 68.25
15 to <25 years	1096	2.39	2.24 to 2.53	187	5.09	4.36 to 5.83
25 to <35 years	2162	1.92	1.83 to 2.00	350	3.22	2.88 to 3.56
≥35 years	715	0.39	0.36 to 0.42	150	0.80	0.67 to 0.93
Time since termination						
<15 years	1124	3.30	3.11 to 3.49	189	5.68	4.86 to 6.49
15 to <25 years	1750	1.31	1.25 to 1.37	310	2.40	2.14 to 2.67
≥25 years	1337	0.77	0.73 to 0.81	206	1.21	1.05 to 1.38
Age at hire						
<25 years	825	1.24	1.15 to 1.32	134	2.04	1.70 to 2.39
25 to <35 years	1554	1.36	1.29 to 1.42	310	2.29	2.03 to 2.54
≥35 years	1832	1.14	1.09 to 1.19	261	1.99	1.75 to 2.23
Birth cohort						
1940–1950+	481	1.09	1.00 to 1.19	28	1.47	1.02 to 2.13
1930–1939	1049	1.16	1.09 to 1.23	141	2.01	1.68 to 2.35
1920–1929	1610	1.35	1.29 to 1.42	342	2.35	2.10 to 2.60
1910–1919	680	1.23	1.13 to 1.32	155	2.10	1.77 to 2.43
1890–1909	391	1.19	1.07 to 1.31	39	1.63	1.19 to 2.22
Hiring period						
1946–1952	821	1.38	1.28 to 1.47	154	2.63	2.21 to 3.04
1953–1962	2579	1.20	1.15 to 1.25	435	2.02	1.83 to 2.21
1963+	811	1.20	1.12 to 1.29	116	1.98	1.62 to 2.34

Obs, Observed, SMR=Standardised Mortality Ratio, CI=CI Interval

Table 5 Classical standardised mortality ratio calculations and causal mortality ratio calculations

		Classical SMR calculation		CMR calculation	
Outcome	**Observed**	**Expected**	**SMR**	**Expected**	**CMR**
All-cause mortality	4211	3419	1.23	3623	1.16
Lung cancer	705	332	2.12	351	2.01
Extrathoracic airway cancer	59	41.8	1.41	43.7	1.35
Kidney cancer	41	41	1.00	43	0.95
Liver cancer	48	29	1.63	31	1.54
Stomach cancer	102	81	1.27	85	1.20
Haematopoietic cancer	58	53	1.10	56	1.03

CMR, causal mortality ratio; SMR, standardised mortality ratio.

melanoma and gallbladder cancer were found.[10] The SIRs and SMRs in the present study are higher than expected for several non-lung solid cancers, namely, liver, stomach and extrathoracic airway cancers. Differences between this and prior studies are partially due to the different effect measures, comparison populations and follow-up periods. While prior case-cohort studies yielded many estimates close to unity, elevated SMRs and SIRs in this study indicate that many rates of cancers are higher in this uranium mining population compared with the national population.

Workers born between 1920 and 1929 had somewhat higher lung cancer mortality compared with other birth cohorts (table 4). This pattern may reflect cohort selection criteria, since cases in the earliest birth cohorts may have occurred prior to the start of follow-up. This pattern could reflect birth cohort trends across Europe, as smoking rates increased dramatically during and after World War II.[30] By the end of WWII, workers born 1920 to 1929 were ages 16–25. This birth cohort may have had a higher rate of smoking compared with other birth cohorts, which could account for the excess all-cause mortality and substantial excess lung cancer mortality.

Hazards in the Příbram mines gradually declined as ventilation practices and workplace protection improved.[10 11] Miners employed at earlier periods likely experienced hazards at higher exposure intensities than miners employed in later periods. This is reflected in table 4 where miners hired in the early period with the least ventilation and least workplace protections have the highest lung cancer mortality and highest all-cause mortality. Earlier hires may have been employed for longer, resulting in increased duration of exposure. However, table 4 shows that workers with shorter time since hire (notably, <15 years) and shorter time since termination have substantially higher lung and all-cause mortality. This may be due to cohort selection criteria requiring cohort members to be alive at the start of follow-up in 1977, which excludes older workers employed in earlier time periods and more susceptible workers whose risk was higher prior to the start of follow-up. Differences in mortality by time since hire and termination may also reflect healthy-worker bias. Further internal comparisons are needed to analyse differences in these factors.

Some limitations of the analyses should be considered. Results may be biased by the inclusion of only prevalent hires.[31] Additionally, mortality estimates are limited by missing cause of death for approximately 10% of decedents. This is likely due to incompleteness of the Czech death registry in early periods. Deaths prior to 1980 were not computerised and were found manually. Strong assumptions are required to impute missing outcome data, so no corrections were performed.

Another limitation is unknown employment status. An undetermined proportion of miners transferred from the Jáchymov mines to Příbram in the 1960s as production decreased in Jáchymov. While the other Czech cohort includes miners from the Jáchymov, overlap between cohorts has not been investigated.

This study is also limited by low numbers of some cancers, limited duration of follow-up and uncontrolled confounding. While follow-up ends in 1992, there is sufficient duration of follow-up to examine several outcomes of interest; on average almost 30 years elapsed since start of employment and the end of cancer follow-up. Internal analyses of cancer risks are needed to evaluate exposure-specific risks in this population. However, there are multiple exposures that occurred in this workplace such as dust, gases, traumatic injury; the overall SMRs and SIRs here serve to represent the total occupational hazards experienced in the cohort relative to the nation.

Smoking status is only available for a subcohort of miners (not analysed here). If smoking rates among workers differs from the national population, estimates may be biased. However, smoking rates appear to be high in both the cohort and national population. Among the subcohort, 66% of workers were listed as smokers on medical records, and the proportion of male smokers in Europe was about 60% in the 1960s.[30 32] No excess COPD was observed, indicating that smoking rates in the cohort were similar to Czechoslovakia.

This is a large, well enumerated cohort with cancer incidence and mortality data. In this relatively modern uranium mining cohort, which experienced occupational hazards of lower intensity compared with several other uranium mining cohorts, we were still able to demonstrate excess cancers compared with the general population from lung cancer, tuberculosis, pneumoconiosis, extrathoracic cancer, stomach and cancer and some haematopoietic cancer types. Our results support prior findings in this cohort and other uranium mining cohorts.[5 19–22]

Acknowledgements We thank the Regional Hospital in Příbram (Czech Republic) and the Uranium Industry Concern for their support of this project, providing exposure data and facilitating linkage to Czech registries. Vladimír Řeřicha, who made this work possible, died before this current analysis was undertaken. We also thank Radim J. Sram, Institute of Experimental Medicine, The Czech Academy of Sciences, Prague, CR for facilitating the initial collaboration leading to this work.

Contributor DPS and DS made substantial contributions to the conceptionof this work. KKR, DBR, DPS and DS led the initial design of this analysis. KKR led the data analysis and manuscript writing. All authors reviewed and made substantial contributions to the analysis plan and manuscript drafts. All authorsreviewed and approved the final version of the manuscript for publication.

Funding This work was funded in part by the Intramural Research Program of the NIH, National Institute of Environmental Health Sciences (Z01-ES049028). This work was also supported by the National Institute for Occupational Safety and Health, Centers for Disease Control and Prevention (T42-OH008673).

Disclaimer The findings and conclusions of this report are those of the authors and do not necessarily reflect those of the National Institute for Occupational Safety and Health.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study protocol was reviewed by the Institutional Review Boards (IRBs) at the NIEHS and UNC Chapel Hill and determined to be exempt from full IRB review, as it involved existing records and deidentified data.

Provenance and peer review Not commissioned; externally peer reviewed.

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