Recent Results from the Study of West Bohemian Uranium Miners Exposed to Radon and Its Progeny

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A brief description is given of the study of West Bohemian uranium miners, and recent and ongoing efforts to improve the quality of the data are summarized. Three recent analyses of the data from the cohort have led to rather different estimates of the excess relative risk of mortality from lung cancer per working-level month. The reasons for these different estimates are described, and it is concluded that estimates of lung cancer risk are strongly influenced by the quality of the exposure estimates, especially by the omission of some exposures accumulated during employment at other uranium mines, following the closure of most of the shafts at the original two mines. The most recent analysis has shown that, in common with other cohorts of radon-exposed miners, the excess relative risk of lung cancer per working-level month is modified by age and time since exposure. An inverse effect of exposure rate was also demonstrated, but it affected only men at very high concentrations and appears to be related to the time pattern of exposure. In addition, the risk was found to differ between the two main mines, possibly due to the influence of arsenic in the dust of the mines. — Environ Health Perspect 103(Suppl 2):55–57 (1996)

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Introduction

Studies of underground miners of uranium and other substances are at present the principal source of information on the effects of exposure to radon gas and its progeny. One of the largest such studies is that of uranium miners in west Bohemia. This study, sometimes referred to as the S cohort, was set up in 1970 by the late Josef Sevc. Recently, three analyses have been carried out that give rather different quantitative estimates of the lung cancer risk experienced by the men in the cohort (1–3). It is the purpose of this article to explain the reasons for these different estimates and to summarize the most recent results.

Methods

Study Population and Follow-Up

The study population was established by means of a search of the employment records of miners at the Jáchymov and Horní Slavkov mines. A man was included in the cohort if he commenced underground work in the period 1948 to 1959; if underground work lasted at least 4 years; and if details of his employment history were available, including the type of work he did and the specific mine shafts in which he worked, together with the relevant dates. A total of 4320 men satisfied these criteria and were included in the study.

During the decade up to 1990, follow-up of the cohort relied mainly on the national population registry at the Ministry of the Interior. However, at the end of 1991, a comparison of the numbers of deaths from causes other than lung cancer or accidents and violence by calendar period suggested that a substantial number of deaths had been missed, partly because of errors in the personal data of the cohort members and partly because of imperfections in the population registry. Therefore, during 1992 and 1993, a series of additional checks were conducted: in the files of the Czech and Slovak Pensions Offices, by local enquiries, and by direct correspondence. These additional efforts resulted in an increase of more than 10% in the number of men known to have died or emigrated. By the time the data were finalized for the most recent major series of analyses (3–5), it was established that, on the follow-up date of 1 January 1993, 2415 men (56%) had died, 314 (7%) had emigrated, 1548 (36%) were alive and living in Czechoslovakia, while only 43 (1%) were lost to follow-up. For the men who had died the cause of death was established for all but 41. Tomášek et al. (4) present further details of the recent method of follow-up.

Estimation of Exposures

An exceptional feature of this study is the large number of measurements of radon concentrations made in each mine shaft of the Czechoslovak uranium mines in almost every year, including the early period. In 1949 to 1960 the mean number of measurements per year and shaft was 223; in 1961 to 1969, it was 952. When the cohort was set up, manual calculations were carried out combining these data with the men’s employment details to estimate each man’s annual exposure to radon progeny in terms of working levels. A recent review of these exposure estimates revealed that there were errors in these manual estimates (3). In addition, some men also worked at other Czechoslovak uranium mines, and, for some of the men, this involved exposures that had not previously been taken into account. Therefore, in early 1993 a major revision of the exposure estimates was carried out estimating the exposure each man received during each month of his employment (3).

Recent Results

During the last year three, somewhat different, overall risk estimates have been reported for this study. First, in an analysis of data based on follow-up of the cohort to 1985, but excluding recent improvements in the
quality of the follow-up and revisions to the exposure estimates, a simple model in which the excess relative risk (ERR) increased linearly with cumulative exposure lagged by 5 years led to an estimated ERR/WLM per working level month (WLM) of 1.69% (95% confidence interval 1.51–1.87%) (1). Second, data including follow-up to 1990 based on the routine checks at the Ministry of the Interior, but before the improvements to the follow-up were carried out or the exposure estimates revised, were made available for a joint analysis of 11 underground miners studies (2). In this analysis, an apparently similar model led to an estimated ERR/WLM of 0.34% (95% confidence interval 0.2–0.66%) for the Czech cohort. Finally, in an analysis carried out after the follow-up had been improved and the exposure rates revised, a linear model with the same lag time led to an estimated ERR/WLM of 0.64% (95% confidence interval 0.39–1.07%) (3). The reasons for this wide range of risk estimates are partly methodological and partly due to differences in the data. The principal cause of the exceptionally high estimate given for the analysis of data up to the end of 1985 (1) is that it was assumed that, in the absence of exposure to radon, the age- and calendar-year-specific mortality rates from lung cancer for the men in the cohort would have been identical to those for men in Czechoslovakia as a whole. For example, if a similar assumption is made for the data used in the most recent analysis (3), the estimated ERR/WLM is 1.89% (95% confidence interval 1.72–2.08%), not very different from that obtained for the earlier data set; but if two additional parameters are included in the model, allowing for age-dependent departures in the baseline lung cancer rate from the national values, the estimated risk coefficient drops by a factor of three to the value of 0.64% given in (3) and referred to above.

In contrast, the difference between the risk estimate per unit exposure of 0.34% reported for the Czech cohort in the joint analysis (2) and the more recent value of 0.64% (3) was primarily due to the changes and improvements in the data that have become available during 1992 and 1993. Investigations show that revision of the exposure estimates had a larger influence than improvement of the follow-up. In fact, the methodology used to derive these two estimates was not quite identical: for the joint analysis, the national mortality rates for lung cancer were not used, and comparisons were made internally after stratification by calendar year and age. However, this methodologic difference had a negligible effect on the results. When the data supplied for the joint analysis were reanalyzed using the national lung cancer mortality rates but allowing for an age-dependent intercept, as in Tomášek et al. (3), the ERR/WLM remained virtually unchanged at 0.35%. However, when the more recent data were analysed omitting the national rates but stratifying on age, the resulting risk estimate was 0.66%, very similar to that reported in the same study (3).

Factors Influencing the Excess Relative Risk per Working-Level Month

The most recent analysis of the revised data included an extensive investigation of the factors affecting the estimated ERR/WLM (3). As would have been expected from the earlier analysis by the United States National Academy of Sciences of data from four cohorts of miners in North America and Sweden (6), attained age and time since exposure were strong modifiers of risk.

When the analysis was limited to men who had never worked in a shaft with exposure rate above 10 working levels (WL), age-specific excess relative risk was found to increase linearly with time-weighted cumulative exposure and did not depend on exposure rate or duration of exposure. Unexpectedly, it was also found that the ERR/WLM was substantially higher for men who spent more than 20% of their employment at Jachymov than for other men, who spent the majority of their underground employment at other mines, mainly Horni Slavkov. The reasons for this difference are unclear, but one possible explanation is that arsenic in the dust of the Jachymov mine may also be influencing lung cancer risk among the men who worked there. When the analysis also included men who worked in mine shafts where radon concentrations were very high, the relationship between excess relative risk and time-weighted cumulative exposure was nonlinear and depended on both exposure rate and duration of exposure in addition to the above factors. The nature of this dependence is still uncertain. However, some time ago it was suggested by Sevc, on the basis of data up to 1980, that the time pattern of the exposure rate might influence subsequent risk, with high exposure rates occurring after several years of underground employment causing relatively low subsequent risks, possibly through an effect of cell sterilization on cancers already induced during the initial few years (7).

The very high exposure rates that could influence the process occurred only in the first 5 years of employment. Later exposure rates were always below 4 WL. Therefore, men were subdivided into two groups on the basis of their exposure rate in years 3 to 5 of employment: those who in this period were exposed at a rate of no more than 8 WL were placed in group 1, even if they had experienced higher exposure rates in their first 2 years of employment, while men who had experienced exposure rates of 8 WL or above in years 3 to 5 of their employment were placed in group 2. As usual, men were entered into the analysis at the end of their fifth year after commence- ment of employment. The ratios of observed to expected deaths by categories of time-weighted exposure are given in Table 1. For group 1, the ratio of observed to expected deaths increases much more steeply with increasing time-weighted exposure than for group 2, in line with Sevc’s original observation. The age and time-since-exposure-specific ERR/WLM in group 2 was significantly lower than in group 1 (RR = 0.60; CI: 0.44–0.82).

Present Work

For the analysis reported by Tomášek et al. (3), full use was made for the first time of all the information held at the National

| Table I. Ratios of observed to expected deaths from lung cancer (0/E) by categories of time-weighted cumulative exposure (Wt(WLM)) in two groups of miners defined by time pattern of exposure rate. |
|---|---|---|---|---|
| | Group 1 | | Group 2 | |
| | Men with exposure rate < 8 WL in years 3–5 of employment | Men with exposure rate at least 8 WL during years 3–5 of employment |
| Wt(WLM) | 0 | 0/E | PY | 0 | 0/E | PY |
| 0–49 | 150 | 2.75 | 27,499 | 2 | 1.31 | 516 |
| 50–99 | 160 | 4.61 | 27,221 | 12 | 3.66 | 1,208 |
| 100–199 | 171 | 7.61 | 27,591 | 12 | 4.19 | 1,815 |
| 200–299 | 82 | 13.16 | 7,390 | 16 | 8.72 | 1,735 |
| 300+ | 53 | 21.45 | 3,233 | 40 | 12.77 | 4,313 |
| Total | 624 | 5.03 | 92,936 | 82 | 6.49 | 9,588 |

*Note: In calculating time-weighted cumulative exposure (Wt), exposures received 5–14, 15–24, 25–34, and 35+ years previously are given weights of 1.0, 0.4, 0.2, and 0.1, respectively.*
Institute of Public Health on the radon concentrations in the mines and on the employment histories of the men. As the impact of the exposure revision, and especially of the inclusion of additional periods of employment at other uranium mines after leaving Jachymov or Horni Slavkov, on the estimated ERR/WLM was so great, a systematic search is now being undertaken among all men who were below the retirement age for miners at the time they left Jachymov or Horni Slavkov. The aim is to ascertain whether any of them were subsequently employed at other uranium mines in Czechoslovakia. In addition, further efforts are being made to classify the new cases of lung cancer by histological type to enable type-specific analyses.

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