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The German Uranium Miners Cohort Study: Feasibility and First Results

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In Germany, the largest single cohort study on uranium miners to date is being conducted. The cohort includes about 64,000 workers of the former Wismut company in eastern Germany. Inclusion criteria were: a date of employment between 1946 and 1989, a minimum period of employment of 180 days, and complete information on working history. Due to poor working conditions in the late 1940s and early 1950s, miners were exposed to high levels of radiation, while later radiation exposure was significantly reduced. The aim of the cohort study is to evaluate the risk of lung cancer and other cancers associated with several indicators of exposure to radon and its progeny, with particular attention to low levels of radiation. Radon exposure will be estimated by a detailed job–exposure matrix. Some information about smoking, dust and arsenic is already available. About 49,000 miners are defined as exposed (underground or processing), while the internal control group (surface only) consists of 15,000 workers. A total of 1,436 lung cancer deaths among cohort members have been reported. The first mortality follow-up will be finished early in 2002, and a total of about 3,000 lung cancer deaths are expected by then.

INTRODUCTION

In 1994, Lubin *et al.* (*1*) published a meta-analysis of 11 miner cohort studies conducted in the U.S., Canada, the Czech Republic, Sweden, France, Australia and China. The analysis included more than 60,000 miners and about 2,600 lung cancer deaths. The results demonstrated that underground miners are at an increased risk of lung cancer due to exposure to the radioactive gas radon (^{222}Rn) and its short-lived decay products. Based on the same pooled data set, Darby *et al.* (*2*) reported some evidence of risk associated with cancers other than lung cancer such as stomach cancer, liver cancer and leukemia. A causal relationship to radon exposure, however, is still questionable, since no exposure–response relationships were observed.

It is estimated that up to 500,000 persons may have worked at the German Wismut company between 1946 and 1989, most of them underground or in uranium ore processing facilities. Up to 1990, more than 5,000 of these workers had been compensated for radiation-induced lung cancers in the former GDR, and at least 200 to 300 registrations per year are expected in the next 10 years (*3*). The aim of the German uranium miners study, which includes about 64,000 former Wismut miners, is to further evaluate the lung cancer risk associated with radon and its progeny due to cumulative exposure, exposure rate, duration of exposure, time since last exposure, attained age, and the interactions with smoking and arsenic exposure. Moreover, particular attention will be given to the lung cancer risk associated with low levels of radiation and the risk of extrapulmonary cancers.

The cohort is now established and the mortality follow-up has been started. This paper presents the first characteristics of the study population and provides information about the feasibility of assessment of exposures to radon, smoking, dust and arsenic.

METHODS

The selection of cohort members was based on two personnel files of the Wismut company, which included 120,000 workers with information on gender, year of first employment, and—as proven later—arbitrary information on place of work (underground or milling/processing or surface) and area of the mining facility (Thuringia or Saxony). Due to financial restrictions, a random sample of about 64,000 persons was taken. The criterion for inclusion was the beginning of employment between 1946 and 1989. Since it was assumed that during the first years women had also worked at least some time underground and there is no other cohort of females, it was a unique opportunity to establish a female cohort. It was decided to select a random sample for both women and men stratified by place of work, area of mining, and date of first employment to reflect the different mining conditions at the Wismut company. These can be defined as follows: In the period 1946 to 1954, the so-called "wild years" (subcohort A), exposure to radiation and dust was at its peak due to dry drilling and the lack of artificial ventilation underground. No radon measurements were carried out. Between 1955 and 1970 (subcohort B), the working conditions of the miners improved. Dry drilling was replaced by wet drilling, radon measurements started, and due to a more efficient ventilation technique the concentrations decreased. After 1970 (subcohort C), international radiation protection standards were introduced, individual radon measurements were established, and the working conditions were stable with a high level of security. With the German reunification in 1990, mining was discontinued.

TABLE 1
Characteristics of the Study Population Stratified by Subcohorts

	Subcohorts			
	1946–1954 A	1955–1970 B	1971–1989 C	Total
Total numbers	24,423	20,244	19,108	63,775
Women	1,336	1,681	803	3,820
Men	23,087	18,563	18,305	59,955
Men only				
Exposure category (%)				
Underground[a]	73.5	62.1	77.0	71.0
Processing or milling[b]	7.5	8.2	7.3	7.7
Short-term exposure (<180 days)	1.3	2.6	2.7	2.1
Surface	17.6	27.1	12.9	19.1
Area of mines (%)				
Saxony (high levels of arsenic)	77.6	41.5	21.9	49.4
Thuringia (low levels of arsenic)	7.2	50.5	68.1	39.2
Saxony and Thuringia	15.1	8.0	10.0	11.3
Age at first employment (years)				
Mean ± SD	28.5 ± 9.7	25.5 ± 9.6	21.7 ± 6.4	25.5 ± 9.2
Duration of employment (years)				
Mean ± SD	16.2 ± 12.8	14.0 ± 11.9	8.3 ± 5.7	13.1 ± 11.2

[a] Underground for at least 6 months.
[b] Processing or milling for at least 6 months, but less than 6 months underground.

For the selected random sample, data were extracted from the original payrolls and medical records according to a fixed data catalogue and coding scheme and were entered into the computer. To ensure that the quality of the data was high, detailed plausibility checks were carried out and a subset of the data was extracted and entered twice. Working history for each employee is available arranged according to job periods, where a change in mining facility, type of job, or place of work results in a new period. This enables us to define an internal control group including employees who worked at the surface only. Exposed subjects were classified into three exposure categories: (1) underground (for at least 180 days), (2) milling or processing (for at least 180 days and less than 180 days underground), and (3) short-term exposed workers (less than 180 days underground or/and milling or processing). Subjects working less than 180 days at the Wismut company or with a date of first exposure after December 1989 were excluded.

Exposure to radon, its progeny, γ radiation and long-lived α-particle emitters will be estimated by using a job–exposure matrix, which was developed by the Miners' Occupational Compensation Board (BBG) in Gera. The job–exposure matrix provides the annual dose values for each calendar year of employment between 1946 and 1989, each place of work, and each type of job. More than 900 different jobs and several mining facilities have been evaluated. Radon measurements are available only after 1955. For the period 1946 to 1954, radon concentrations were estimated based on measurements from 1955, taking into account ventilation rate, vein space, uranium content and so on. In addition, since 1972, individual data on radon exposure are available for a subset of cohort members and will be used to validate the job–exposure matrix.

Miners working in Saxony are roughly categorized as highly exposed to arsenic and those working in Thuringia as having received low exposures. For the period from 1985 to 1990, individual information on arsenic exposure is available for a subset of cohort members. Information on dust exposure can be obtained for a subset of subjects for the period 1972–1989. Active smoking habits are derived from annual medical examination files, which are available since 1972.

The first mortality follow-up, which started early in 1999, will determine the vital status of cohort members as of December 31, 1998. Data are collected from registration offices, Registrar's offices, Public Health Administrations, and others. The feasibility of the mortality follow-up has been demonstrated in a pilot study with 485 cohort members. An incidence follow-up from 1961 to 1989 is planned by means of a record linkage with the data set of the former German Democratic Republic's National Cancer Registry.

RESULTS

The cohort presently includes a total of 63,775 subjects (59,955 men and 3,820 women). After their job histories were evaluated, it was discovered the 3,365 women had never been exposed (working at the surface only), while only a small number (167) had worked underground for some time, and 245 had been occupied in processing or milling facilities. Therefore, detailed characteristics stratified by subcohort are reported only for men (Table 1). There are slightly more miners in subcohort A (38%) than in subcohorts B and C (both 31%). Overall, 42,580 subjects worked underground and 4,601 in processing or milling facilities, and 1,287 were exposed for a short time. A total of 11,487 persons were not exposed. Miners of subcohort A were employed mainly in mines located in Saxony, which have high arsenic levels, whereas miners of subcohort C mostly worked in Thuringia, where levels of arsenic exposure were low. The mean age at first exposure was 25 years, with higher ages in subcohort A. On average, the study subjects were employed at the Wismut company for 13 years. The duration of employment, however, varies greatly between subcohorts (16 years in subcohort A compared to 8 years in subcohort C).

Table 2 lists the distribution of the vital status of the

TABLE 2
Information Presently Available on the Vital Status of the Cohort (Based on Data from the Social Insurance Pension Fund as of December 31, 1998)

	Subcohorts			
	1946–1954 A	1955–1970 B	1971–1989 C	Total
Total numbers	24,423	20,244	19,108	63,775
Vital status (%)				
Alive	44.4	65.8	85.0	63.3
Deceased	25.8	9.2	1.5	13.3
Unknown	29.9	25.0	13.5	23.4
Age of living subjects as of December 31, 1998 (mean ± SD)	71.7 ± 6.6	60.6 ± 8.2	40.6 ± 8.6	55.5 ± 15.2
Number of lung cancers among deceased subjects[a]	1,235	164	6	1,405

[a] Known from either occupational disease records or autopsy record of pathology files of the German Cancer Research Center (DKFZ).

whole cohort, based on data from the social insurance pension fund. The mean age of the subjects that were alive on December 31, 1998, in the three subcohorts A, B and C was 72, 61 and 41 years, respectively. More than 25% of the subjects of subcohort A are already known to be dead, in contrast to only 9% in subcohort B and 2% in subcohort C. Presently 17% (1,405) of all deceased subjects and 20% of those in subcohort A are known to have died of lung cancer. This information is derived from either occupational compensation agencies or the pathological files held at the German Cancer Research Center in Heidelberg.

DISCUSSION

The German cohort study is the largest single cohort study on uranium miners thus far. It provides a cohort of similar size as that used in the meta-analysis of Lubin *et al.* (*1*), yet it is more homogeneous with respect to data collection and the estimation of exposure. The wide range of exposure levels and the relatively long duration of employment at the Wismut company will contribute to improving present knowledge about the shape of the dose–response relationship for radon-induced cancer. Moreover, the combined effects of radon and smoking, dust and arsenic may be assessed. But beforehand, the validity of the data must be evaluated. Furthermore, a record linkage will be done with the pathology files at the German Cancer Research Center, where more than 28,000 diagnoses of autopsy files of former Wismut workers are kept. These files will be used to validate causes of death obtained from the mortality follow-up.

However, there are several potential limitations in this study. First, after the detailed working histories were evaluated, it turned out that, contrary to earlier assumptions, women had rarely worked underground. Thus women will be excluded from the cohort. Second, at present, information on smoking habits is available mainly for miners of subcohort C (67%), while overall this proportion is small (37%). Since smoking is a potential confounder of lung cancer risk, it will be necessary to look for other possible sources of information on smoking habits. A nested case–control study of lung cancer, in which information on the miners' smoking habits by their next of kin will be gathered, is in preparation.

The first mortality follow-up will be finished early in 2002, so that the first risk estimates will presumably be available by the end of 2002. The number of lung cancer deaths is estimated to be about 3,000. Subcohort C will be of particular interest, since risk estimates among workers exposed to low-level radiation may be applicable to the lung cancer risk arising from indoor radon exposure in houses. However, subcohort C is still relatively young, and the number of deaths in subcohort C will be small in the first follow-up. A further follow-up is planned.

In conclusion, the present knowledge about the health effects of exposure to radon and its progeny underground that was used for risk extrapolation to the indoor environment by the BEIR VI Committee (*4*) is based on cohorts including about 60,000 miners all together. This database will be doubled within the next few years by the study of the German Wismut miners.

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