RADON EXPOSURE AND LUNG CANCER RISK
- CZECH COHORT STUDY ON RESIDENTIAL RADON

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Epidemiological evidence of lung cancer risk from radon is based mainly on studies of men employed underground in mines where exposures are relatively high in comparison to indoor exposure. Nevertheless direct evidence of risk from residential radon is desirable. In 1990, a study was started comprising 12 000 inhabitants of an area with elevated radon concentrations. The mean level in the houses was higher than general mean of the country by factor of five. In the period 1961-95, a total of 173 lung cancers were observed. Comparing to nationally expected numbers (E), the observed number (O) of cases is elevated (O/E=1.11) - in contrast to generally low figures for cancers other than lung (O/E=0.85). Lung cancer risk related to cumulative exposures experienced in the past 5-24 or 5-35 years was both significant. In relation to standard radon progeny concentration 100 Bq/m³, the excess relative risk coefficient was 0.103 (95% CI: 0.039 – 0.168), the value somewhat lower than findings in other indoor studies.

Running head: Czech cohort study on residential radon and lung cancer

Key words: Residential radon, Lung cancer, Cohort study, Cumulative exposure, Relative risk

INTRODUCTION

Epidemiological evidence of lung cancer risk from radon is based mainly on studies of men employed underground in mines where exposures are relatively high in comparison to indoor exposure. One of first such studies was established by the late Josef Ševc. In 1971, the first results of this large epidemiological study were reported (Ševc et al, 1971). During the next 20 years, Ševc published a number of results based on extended follow-up of the original cohort and established two further cohorts of miners. The series of his papers on studies of miners ended in 1991 (Ševc et al, 1991).

The studies of Czech miners involve three cohorts (Table 1). The oldest cohort (S) comprises uranium miners at the Jáchymov region firstly exposed in 1948-59, miners of the second cohort (N) entered the Příbram U mines in 1968-74, and the third cohort (L) includes burnt-clay miners in the Rakovník district employed in 1960-80 (Tomášek et al, 1994, Plaček et al, 1997).

Results of follow-up by 1995, based on 908 cases of lung cancer that occurred among nearly 12 000 miners, confirmed linear relationship of relative risk and cumulative exposure. With the extended follow-up, factors that modify general linear model became more discernible, particularly the strong
dependence of the relative risk coefficient on time since exposure. The effect after 25 years dropped
to less than 10% when compared to the effect of the same exposure in time period 5-14 years.

Nevertheless direct evidence of risk from residential radon is desirable. In 1990, Ševec designed and
initiated a new large study among inhabitants exposed in homes. Unfortunately, his untimely death
in 1991 precluded his participation in this study.

DESCRIPTION OF STUDY AND METHODS OF ANALYSIS

The indoor study was designed as a prospective follow-up covering period since 1960. The study
area - Middle Bohemian Pluton - is mostly granitoid with considerable breaks. The levels of radon
progeny concentration in the selected area are considerably higher than in the rest of the country
(Fig1). The population in the area is characteristic by low migration. The study population include
inhabitants of the area (80 villages) who had resided there for at least 3 years (one of these years
after 1960), who were alive by the end 1960 or were born later. The collected data included date of
birth, past residences, smoking habits, occupation, and housing characteristics. Data on 12 010
subjects were collected by trained interviewers who also installed detectors. After revision of these
data, a total of 210 people were excluded from the present analyses for unsatisfactory personal data
to identify them in the national population registry or for large gaps in their residence histories or for
not permanent residence in the study area. Information on vital status and causes of death were
obtained mostly from local authorities and from the national population registry, the latter source
was applied to people that have moved from the study area.

Follow-up for each subject started at the latest of the following dates: three years after first year of
recorded residence in the study area or 1 January 1961. The follow-up ended at the earliest of date
of death, emigration, 85th birthday, or 1 January 1996. The condition of excluding person-years of
people older than 85 was used in order to eliminate the uncertainties in causes of death and also to
get clear of potential errors in the population registry.

The analyses are based on relative risk models in the form \( O \equiv cE(1+b(W-W_0)) \), where \( O \) denotes
the observed number of cases, \( E \) is the number expected from national mortality data, \( W \) is
cumulative exposure, \( W_0 \) is background cumulative exposure, \( b \) denotes coefficient of relative risk,
and \( c \) is an intercept term that allows the mortality rate for the 'unexposed' cohort to differ from that
in the general population. In the model, the cumulative exposure \( W \) is lagged by 5 years, which
corresponds to minimal latency period of lung cancer. As the effect from exposures among miners
before more than 25 years have little effect, the analyses of relative risk were related to exposures
received 5-24 years previously. For comparison the time window of 5-34 years was also used.
Person years corresponding to each year of follow-up and corresponding numbers of observed and
expected cases were therefore classified by cumulative exposure in the above time windows.
Parameters in the models were estimated by the maximum likelihood method in the Poisson
regression.

METHODS OF EXPOSURE ESTIMATION

The exposure assessment was based on measurements of equivalent equilibrium concentrations of
radon in most houses (\( N=2500 \)) of the study area. During the period 1991-92, usually two integral
detectors (Kodak LR115) were installed for one year in two mostly occupied rooms of the house. The distribution of concentration in terms of radon progeny is given in figure 2.

Exposure estimates in residences outside the area were derived from a large scale mapping of radon in the country (Hůlka et al, 1997) (Figure 1). The individual exposures in terms of kBq m\(^3\)a\(^-1\) were estimated by combining the radon equivalent equilibrium concentration (Bq m\(^-3\)) and duration of residence (a). For houses in the study area that were not available for measuring, the community means were used instead of missing values. Concentrations corresponding to residences outside the study area (21% of residence person-years) were estimated by (1) larger community means for inhabitants in the neighbouring four districts and by (2) district means for the residences in other districts, where concentrations were usually much lower (Table 2). The numbers in table 2 reflect relatively low migration in the study population.

The distribution of the cumulative exposure in the cohort was considerably asymmetrical, 79% of individual exposures were below 20 kBq m\(^-3\)a\(^-1\), the arithmetic mean was 14 kBq m\(^-3\)a\(^-1\) and maximum 647 kBq m\(^-3\)a\(^-1\) (Figure 3).

RESULTS OF FOLLOW-UP

By the end of 1995, 3616 subjects (30%) of the cohort have died, 395 of them after their 85th birthdays, and 17 subjects emigrated. A total of 173 lung cancers have been observed (Table 3). Although some causes of death have been missing, the present figures suggest slightly increased mortality from lung cancer (O/E=1.11) in comparison to generally low numbers corresponding to cancers other than lung (O/E=0.85). General cancer risk factors in the study environment can be assumed relatively sound. Somewhat lower mortality in the last five years might reflect potential loss of follow-up due to imperfections in the population registry in this period.

Lung cancer risk related to cumulative exposures in the past intervals 5-24 and 5-34 years was both significant (Table 4). Higher risk coefficients related to more recent time period (5-24) are in line with observations among miners, although the fit was better for time period 5-34 (deviance 2.41).

DISCUSSION

Direct estimation of risk from residential radon is more complex than in occupational studies. As the exposures in houses are by one order lower, such studies need larger numbers of cases. In addition, exposure estimates show higher uncertainty than in miners studies. Errors in exposure estimates are unavoidable. The concentrations of radon vary substantially in time and location. In most studies, recent exposures are estimated with higher accuracy than those in the past. Estimates of cumulative exposure in occupational studies are generally more precise; not only because the radon measurements in mines were conducted already in the past, but also because the duration of stay of workers in radon environment was recorded with higher precision. This might be one of the reasons why studies on residential radon have not clearly demonstrated the effect of radon to lung cancer risk in general population. In order to estimate risk of indoor radon, much larger studies are necessary. Sample size for case-control studies under realistic scenarios of measurement errors and population mobility are estimated to several thousands (Lubin et al, 1990). So far, the numbers of cases in separate studies are by one order lower (Table 5).
The cohort type of the present indoor study was selected mainly for two reasons. Firstly, radon concentrations in the Czech Lands belong to highest in Europe (mean concentration of radon gas is about 100 Bq m⁻³ and levels in the selected area are higher by factor of 5). Therefore it is technically easier to organize measurements and collection of personal data in a compact territory. Secondly, the access to records at the oncological registry is limited.

In the first report on the present indoor study (Kunz et al, 1996), the excess relative risk per 1kBq m⁻³a was estimated to 0.019 (95%CI: 0.006 - 0.032). These preliminary analyses were based on 134 cases observed by 1990. But the main reason for that different estimate in comparison to present results was the way how radon concentrations were estimated for houses not directly measured; the level was then uniformly set to 60 Bq m⁻³.

In most indoor studies, the risk of lung cancer is related to time weighted means of radon concentrations. The risk is related to some standard radon concentration, for example 100 Bq m⁻³. Another difference consists in the fact that risk is related to activity of radon gas and not to radon progeny, which was used in the present study. Although risk coefficients derived from separate studies show differences, a meta-analysis based on eight such studies (Lubin and Boice, 1997) and results from recent study in Devon and Cornwall (Darby et al, 1998) are consistent (Table 5). The estimated relative risk at 100 Bq m⁻³ in these studies was 1.09, the value that was also estimated from studies of miners (Lubin et al, 1997). In order to compare present results of the Czech indoor study, the risk was also expressed in terms of time weighted average of radon progeny concentrations. Graphical presentation of Czech results (Figure 4) shows a considerable agreement between the estimates of risk for different exposure windows (5-24 and 5-34 years). The risk derived from the Czech study is slightly lower than the risk estimated from existing indoor case-control studies. One reason for this difference might be relatively large proportion (35%) of estimated radon levels for unmeasured houses and possibly higher uncertainty of measurements (in terms of absolute error) at higher concentrations. To verify these assumptions, additional measurements in some houses were initiated.

CONCLUSION

Results of present follow-up by the end of 1995 demonstrated that increased incidence of lung cancer depends linearly on cumulative exposure experienced in the course of previous 5-24 or 5-34 years. The excess relative risk per standard radon progeny concentration 100Bq/m⁻³ was 0.103 (95% CI: 0.039 – 0.168). This value is somewhat lower than the risk coefficient derived from other indoor studies. Comparing to previous results of this study, the issue of correct exposure estimation seems to be crucial. Therefore further efforts are made to improve exposure estimates by measuring missing houses and also by estimating concentrations in the houses before substantial changes in houses (type of heating or insulation). In addition, more reliable estimates of risk coefficients are expected by extending the present follow-up.

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REFERENCES


Table 1: Czech cohorts of miners - status by 1995

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Since</th>
<th>Size</th>
<th>Cases</th>
<th>O/E(^a)</th>
<th>Died</th>
<th>Mean exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>S</td>
<td>1952</td>
<td>4320</td>
<td>788</td>
<td>4.76</td>
<td>66%</td>
<td>155 WLM(^b)</td>
</tr>
<tr>
<td>N</td>
<td>1969</td>
<td>5630</td>
<td>54</td>
<td>1.48</td>
<td>11%</td>
<td>7 WLM</td>
</tr>
<tr>
<td>L</td>
<td>1960</td>
<td>914</td>
<td>66</td>
<td>2.19</td>
<td>45%</td>
<td>28 WLM</td>
</tr>
</tbody>
</table>

\(^a\) O/E denotes proportion of observed cases to nationally expected numbers
\(^b\) The WLM is time-integrated exposure measure, i.e. the product of time in working months (170 hours) and working levels (1WLM=3.54 mJh m\(^{-3}\))

Table 2: Sources for estimation of radon progeny concentrations in the study

<table>
<thead>
<tr>
<th>Source</th>
<th>Person-years of Residence</th>
<th>%</th>
<th>Mean concentration (Bq/m(^3))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Own Measurements in the Study Area</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct Measurements</td>
<td>377 084</td>
<td>65</td>
<td>324</td>
</tr>
<tr>
<td>Municipality Means</td>
<td>84 277</td>
<td>14</td>
<td>312</td>
</tr>
<tr>
<td>Mapping</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Municipality Means in Neighbouring Districts</td>
<td>59 691</td>
<td>10</td>
<td>181</td>
</tr>
<tr>
<td>District Means</td>
<td>61 699</td>
<td>11</td>
<td>90</td>
</tr>
<tr>
<td>Total</td>
<td>582 751</td>
<td>100</td>
<td>282</td>
</tr>
</tbody>
</table>
Table 3: Cause and period specific mortality

<table>
<thead>
<tr>
<th>Period</th>
<th>PY c</th>
<th>LungCa O d O/E e</th>
<th>NlungCa a O O/E</th>
<th>Violent O O/E</th>
<th>OthCauses b O O/E</th>
<th>Unkn O O/E</th>
<th>All Deaths O O/E</th>
</tr>
</thead>
<tbody>
<tr>
<td>1961-70</td>
<td>69 186</td>
<td>30 0.82</td>
<td>121 0.84</td>
<td>35 0.61</td>
<td>570 1.04</td>
<td>11</td>
<td>767 0.98</td>
</tr>
<tr>
<td>1971-80</td>
<td>77 304</td>
<td>61 1.30</td>
<td>154 0.88</td>
<td>49 0.71</td>
<td>683 0.92</td>
<td>6</td>
<td>953 0.92</td>
</tr>
<tr>
<td>1981-90</td>
<td>81 038</td>
<td>63 1.30</td>
<td>155 0.87</td>
<td>51 0.76</td>
<td>801 1.05</td>
<td>8</td>
<td>1078 1.02</td>
</tr>
<tr>
<td>1991-95</td>
<td>40 991</td>
<td>19 0.80</td>
<td>70 0.78</td>
<td>22 0.62</td>
<td>306 0.99</td>
<td>6</td>
<td>423 0.93</td>
</tr>
<tr>
<td>Total</td>
<td>268 519</td>
<td>173 1.11</td>
<td>500 0.85</td>
<td>157 0.69</td>
<td>2360 1.00</td>
<td>31</td>
<td>3221 0.96</td>
</tr>
</tbody>
</table>

a Cancers other than lung cancer  
b Causes of death other than cancer or violent deaths  
c PY = person-years  
d O = number of observed cases  
e O/E = proportion of observed cases to expected numbers according to national data

Table 4: Estimates of excess relative risk per unit exposure of radon progeny in different time windows (background concentration - 50 Bq/m³)

<table>
<thead>
<tr>
<th>Time window</th>
<th>ERR/kBqm³ a</th>
<th>95%CI</th>
<th>Deviance b</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-24</td>
<td>0.052</td>
<td>0.019 - 0.084</td>
<td>8.19</td>
</tr>
<tr>
<td>5-34</td>
<td>0.034</td>
<td>0.012 - 0.056</td>
<td>2.95</td>
</tr>
</tbody>
</table>

a ERR/kBqm³ a = excess relative risk per unit exposure  
b measure of fit of the model to observed data
Table 5: Lung cancer risk from residential radon - case-control studies

<table>
<thead>
<tr>
<th>Publ.</th>
<th>Cases</th>
<th>$RR^a$ at 100 Bq m$^{-3}$$^b$</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Shenyang, China 1990</td>
<td>308</td>
<td>0.89</td>
</tr>
<tr>
<td>2</td>
<td>Finland 1991</td>
<td>238</td>
<td>1.19</td>
</tr>
<tr>
<td>3</td>
<td>New Jersey, USA 1992</td>
<td>433</td>
<td>1.50</td>
</tr>
<tr>
<td>4</td>
<td>Stockholm 1992</td>
<td>210</td>
<td>1.50</td>
</tr>
<tr>
<td>5</td>
<td>Missouri, USA 1994</td>
<td>538</td>
<td>1.08</td>
</tr>
<tr>
<td>6</td>
<td>Winnipeg, Canada 1994</td>
<td>733</td>
<td>0.97</td>
</tr>
<tr>
<td>7</td>
<td>Sweden 1994</td>
<td>1281</td>
<td>1.11</td>
</tr>
<tr>
<td>8</td>
<td>Finland 1996,8</td>
<td>517</td>
<td>1.11</td>
</tr>
<tr>
<td>1–8</td>
<td>Meta analysis $^c$ 1997</td>
<td>4263</td>
<td>1.09</td>
</tr>
<tr>
<td>9</td>
<td>England $^d$ 1998</td>
<td>982</td>
<td>1.08</td>
</tr>
<tr>
<td></td>
<td>Czech Cohort $^e$</td>
<td>173</td>
<td>1.06</td>
</tr>
</tbody>
</table>

$^aRR =$ relative risk $^b$ concentration of radon gas, $^c$ Lubin and Boice, 1997, $^d$ Darby et al, 1998 $^e$ Middle Bohemia Cohort Study (in terms of radon gas concentration)
Figure 1: Arithmetic means of radon progeny concentrations in Czech houses. The compact dark area in the middle of the western part of the country was selected as the study area, empty areas denote no measurement.
Figure 2: Radon progeny distribution in houses of the study area (3700 detectors)
Figure 3: Cumulated exposure distribution among cohort members (N = 11,800)
Figure 4: Relative risk by average concentration of radon progeny (c) in different time windows, O/E = ratio of observed to expected numbers of cases, \( \square \) = time windows 5-34 years and \( \bigcirc \) = time windows 5-24 years previously, vertical abscisae = 95%CI, solid line = fitted linear model \( RR=1+0.00103(c-50) \), dotted line = model derived from meta-analysis of 8 indoor studies.