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Abstract

Objective To determine the risk of lung cancer associated with exposure at home to the radioactive disintegration products of naturally occurring radon gas

Design Collaborative analysis of individual data from 13 case-control studies of residential radon and lung cancer.

Setting Nine European countries.

Subjects 7148 cases of lung cancer and 14,208 controls.

Main outcome measures Relative risks of lung cancer and radon gas concentrations in homes inhabited during the previous 5-34 years measured in becquerels (radon disintegrations per second) per cubic metre (Bq/m³) of household air.

Results The mean measured radon concentration in homes of people in the control group was 97 Bq/m³, with 11% measuring >200 and 4% measuring >400 Bq/m³. For cases of lung cancer the mean concentration was 104 Bq/m³. The risk of lung cancer increased by 8.4% (95% confidence interval 3.0% to 15.8%) per 100 Bq/m³ increase in measured radon (P = 0.0007). This corresponds to an increase of 16% (5% to 31%) per 100 Bq/m³ increase in usual radon—that is, after correction for the dilution caused by random uncertainties in measuring radon concentrations. The dose-response relation seemed to be linear with no threshold and remained significant (P = 0.04) in analyses limited to individuals from homes with measured radon <200 Bq/m³. The proportionate excess risk did not differ significantly with study, age, sex, or smoking. In the absence of other causes of death, the absolute risks of lung cancer by age 75 years at usual radon concentrations of 0, 100, and 400 Bq/m³ would be about 0.4%, 0.5%, and 0.7%, respectively, for lifelong non-smokers, and about 25 times greater (10%, 12%, and 16%) for cigarette smokers.

Conclusions Collectively, though not separately, these studies show appreciable hazards from residential radon, particularly for smokers and recent ex-smokers, and indicate that it is responsible for about 2% of all deaths from cancer in Europe.

Introduction

In many countries exposure in the home to short lived radioactive disintegration products of the chemically inert gas radon-222 is responsible for about half of all non-medical exposure to ionising radiation. Radon-222 arises naturally from the decay of uranium-238, which is present throughout the earth's crust. It has a half life of four days, allowing it to diffuse through soil and into the air before decaying by emission of an α particle into a series of short lived radioactive progeny. Two of these, polonium-218 and polonium-214, also decay by emitting α particles. If inhaled, radon itself is mostly exhaled immediately. Its short lived progeny, however, which are solid, tend to be deposited on the bronchial epithelium, thus exposing cells to α irradiation.

Air pollution by radon is ubiquitous. Concentrations are low outdoors but can build up indoors, especially in homes, where most exposure of the general population occurs. The highest concentrations to which workers have been routinely exposed occur underground, particularly in uranium mines. Studies of exposed miners have consistently found associations between radon and lung cancer. Extrapolation from these studies suggests that in many countries residential radon, which involves lower exposure in much larger numbers of people, could cause a substantial minority of all lung cancers. This is of practical relevance because radon concentrations in existing buildings can usually be reduced at moderate cost—for example, by increasing underfloor ventilation—while low concentrations can usually be ensured at reasonable or low cost in new buildings—for example, by installing a radon proof barrier at ground level. These extrapolations, however, depend on uncertain assumptions because the levels of exposure in miners that produced evident risk were usually much higher, lasted only a few years, and took place under different particulate air and other conditions. Moreover, history on smoking is often lacking, or limited, in the studies of miners and some miners were also exposed to other lung carcinogens such as arsenic.

Studies to estimate directly the risk of lung cancer associated with residential radon exposure over several decades have been conducted in many European countries. Individually these studies have not been large enough to assess moderate risks reliably. Greater statistical power can be achieved by combining information from several studies, but this cannot be done satisfactorily from published information. Urban areas tend to have lower radon concentrations than rural ones as the underlying rock is usually sedimentary and more people live upstairs in apartments. Urban areas also usually have a higher prevalence of smoking. Hence, radon concentrations in homes tend to be negatively correlated with smoking, and a large dataset is needed to correct for this reliably. We therefore brought together and reanalysed individual data from all European studies of residential radon and lung cancer that satisfied certain criteria.
We assessed the association between radon and lung cancer in two ways. Firstly, a model was fitted in which the risk of lung cancer was the 30 years ending five years before the diagnosis of (or death from) lung cancer or, for those in the control group, before a corresponding index date. We excluded individuals for whom no radon measurements for this 30 year period were available or with unknown smoking status. The available radon measurements covered a mean of 23 years. For relevant homes where radon measurements could not be obtained (for example, because the house had been demolished), we estimated the concentration indirectly as the mean of all the radon measurements in the residences of control group members in the relevant study area. Finally, to obtain the “measured radon concentration” for each individual, we calculated a time weighted average of the radon concentrations in all the homes occupied over the past 5-34 years with weights proportional to the length of time the individual had lived in each.

Statistical methods

We assessed the association between radon and lung cancer in two ways. Firstly, a model was fitted in which the risk of lung cancer was proportional to \((1 + x^a)\) where \(x\) is measured radon concentration and \(a\) the proportionate increase in risk per unit increase in measured radon. Secondly, we subdivided cases and controls by categories of measured radon concentration and plotted relative risks across different categories against estimated mean exposure levels in those categories. In both types of analysis, confounding was controlled through stratification.

Radon measurements made in the same home but in different years show considerable random variability, indicating some uncertainty in the measured radon concentration for each individual. Further random uncertainty arises as radon concentrations in some homes could not be measured and were estimated indirectly. Both types of uncertainty lead to “regression dilution,” whereby the relation of risk to measured radon concentration is substantially weaker than the relation of risk to “usual” (that is, true long term average) concentration.4,8 We calculated dose-response relations both with and without correction for this and estimated a time weighted average usual radon concentration for each individual (see www.ctsu.ox.ac.uk/radonmethods for further details).

Results

Our analysis included 7148 people with lung cancer and 14,208 controls. For cases of lung cancer the mean measured radon concentration was 104 Bq/m³ while for controls the weighted average of the study specific means, with weights proportional to numbers of cases of lung cancer, was 97 Bq/m³ (table 1). Among controls, the percentage who were lifelong non-smokers increased as radon concentration increased (percentages were 39%, 40%, 41%, 46%, and 48% for measured radon < 100, 100-

### Table 1: European case-control studies of residential radon and lung cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Mean year of diagnosis</th>
<th>Mean measured radon concentration ((\text{Bq/m}^3))</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lung cancers</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Austria4</td>
<td>1983</td>
<td>267</td>
</tr>
<tr>
<td>Czech Republic5†</td>
<td>1981</td>
<td>528</td>
</tr>
<tr>
<td>Finland (nationwide)†</td>
<td>1989</td>
<td>104</td>
</tr>
<tr>
<td>Finland (south)5†</td>
<td>1982</td>
<td>221</td>
</tr>
<tr>
<td>France4</td>
<td>1985</td>
<td>138</td>
</tr>
<tr>
<td>Germany (eastern)6†</td>
<td>1985</td>
<td>76</td>
</tr>
<tr>
<td>Germany (western)6†</td>
<td>1983</td>
<td>49</td>
</tr>
<tr>
<td>Italy5</td>
<td>1985</td>
<td>113</td>
</tr>
<tr>
<td>Spain5</td>
<td>1985</td>
<td>123</td>
</tr>
<tr>
<td>Sweden (nationwide)5†</td>
<td>1982</td>
<td>99</td>
</tr>
<tr>
<td>Sweden (never smokers)5†</td>
<td>1990</td>
<td>79</td>
</tr>
<tr>
<td>Sweden (Stockholm)5†</td>
<td>1985</td>
<td>131</td>
</tr>
<tr>
<td>United Kingdom6†</td>
<td>1991</td>
<td>57</td>
</tr>
<tr>
<td>All studies</td>
<td>1990</td>
<td>104</td>
</tr>
</tbody>
</table>

†Estimate for each individual is time weighted average of measurements in different residences 5-34 years earlier.

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individuals with measured radon 100-199 Bq/m$^3$ (mean 136 Bq/m$^3$) versus those with measured radon < 100 Bq/m$^3$ (mean 52 Bq/m$^3$) the relative risk was 1.20 (95% confidence interval 1.05 to 1.30; $P = 0.01$). Models with no effect up to a “threshold” dose and then a linear effect did not fit significantly better than a linear effect with no threshold; in such models the upper 95% confidence limit for a possible threshold was 150 Bq/m$^3$ measured radon.

**Effect modification**

There was no good evidence that the proportionate increase in lung cancer risk per 100 Bq/m$^3$ was higher in homes where the mean measured radon differed by $\geq$ 400 Bq/m$^3$ (table 2). For current smokers of 15-24 cigarettes a day the risk of lung cancer was only 16% (5% to 31%) per 100 Bq/m$^3$ usual radon. The dose-response relation with usual radon was consistent with a linear model (fig 1). When we re-estimated the risk of lung cancer, correcting for random uncertainties in radon exposure, the increase in risk per 100 Bq/m$^3$ measured radon was only 678 Bq/m$^3$ (table 2). If the mean usual radon concentration in this highly exposed group is only about half the mean measured value, then the slope of the line of risk versus usual radon concentration becomes about twice as steep as that of the line of risk versus measured radon concentration. When we re-estimated the risk of lung cancer, correcting for random uncertainties in measuring radon concentrations, it increased to 16% (5% to 31%) per 100 Bq/m$^3$ usual radon. The dose-response relation with usual radon was consistent with a linear model (fig 1). Again there was no evidence that the risk per 100 Bq/m$^3$ differed according to age, sex, or smoking.

**Combined effect of smoking and radon on absolute risk of lung cancer**

For current smokers of 15-24 cigarettes a day the risk of lung cancer relative to that in lifelong non-smokers was 25.8 (21.3 to 31.2) for men in all 13 studies combined (after stratification by study, age, and region). Therefore, similarity of the relative risk between smokers and lifelong non-smokers would imply
substantial differences in absolute risk per 100 Bq/m³. If the risk of lung cancer increases by about 16% per 100 Bq/m³ usual radon, regardless of smoking status, then at usual radon levels of 0, 100, 400, and 800 Bq/m³, respectively, cumulative absolute risks of lung cancer by age 75 years would be 0.41%, 0.47%, 0.67%, and 0.93% in lifelong non-smokers and 10.1%, 11.6%, 16.0%, and 21.6% in cigarette smokers (fig 3).

Discussion
We were able to assess directly the risks from residential radon because our study involved large numbers of individuals with lung cancer and large numbers of unaffected individuals, all with detailed smoking histories. People with higher residential radon concentrations tended to smoke less, so that assessment of the magnitude of the risk associated with radon required detailed stratification for smoking history including amount smoked and age for current smokers, and years since stopping smoking and amount smoked for ex-smokers. Such detailed stratification has not previously been possible. Correction for the bias introduced by random uncertainties in the estimation of individual residential radon concentrations is also important.

After stratification for smoking there was strong evidence of an association between residential radon and lung cancer. The dose-response relation seemed linear with no evidence of a threshold, and a significant relation remained even among those whose measured radon concentrations were below 200 Bq/m³.
Correction for measurement error

After we corrected for random uncertainties in the assessment of radon concentrations, the dose-response relation in this study remained linear but nearly doubled in strength, to 16% (5% to 31%) per 100 Bq/m$^3$. The magnitude of the correction is approximate as data on the variability between repeated measurements made in the same dwelling in different years are limited, but substantial correction is certainly necessary. There are also random errors in the assessment of smoking, and, if it had been possible to adjust for them, we would expect this to increase further the estimated effect of radon as there is negative confounding between smoking and radon. Radon concentrations within a home vary from room to room and so the actual radon concentration relevant to an individual will also vary, depending on the amount of time spent in different rooms. This is an additional source of random uncertainty and, if it could be taken into account, the estimated effect of radon could increase still further.

Our study was based on measurements of radon gas made in the recent past. Any systematic increase in radon concentrations over recent decades due, say, to increased energy efficiency would be a further source of dilution in our present risk estimates. Techniques to estimate historical radon concentrations through measurements of accumulated radioactive damage to the surfaces of glass objects that have been in the home for many years are being developed and may help to overcome this, but the uncertainties and biases associated with these techniques, especially in the presence of environmental tobacco smoke, are not fully understood.

Comparison with other studies of radon

Before correction for random uncertainties, the increased risk of lung cancer of 8% (3% to 16%) per 100 Bq/m$^3$ in these European studies was consistent with that of 11% (0% to 28%) found in a recent combined analysis of North American studies. The European collaboration, however, has greater power and more extreme statistical significance because it involves twice as many cases of lung cancer and higher radon concentrations (10% of measured values were >200 Bq/m$^3$ versus 5% in the North American studies). Our results are also consistent with the pooled results of two Chinese studies and with a meta-analysis of the published results of 17 studies, which, however, found marked heterogeneity between the different publications. This heterogeneity disappeared in our analysis, in which data on each separate individual were collated centrally and analysed with uniform methods.

A comparison of miners exposed to concentrations below 0.5 “working levels” (approximately equivalent to 4600 Bq/m$^3$ radon gas in the home) suggested risks were 19-30% per 100 Bq/m$^3$, without correction for the effect of uncertainties in the assessment of radon exposures. These estimates are higher than, but compatible with, the present estimate of 16% (5% to 31%).

Absolute hazard of radon for smokers and non-smokers

If the proportionate increases in risk per unit exposure are approximately independent of smoking history then, as lung cancer is much commoner in cigarette smokers than in lifelong non-smokers, radon poses a much greater absolute hazard to cigarette smokers, and to recent ex-smokers, than to lifelong non-smokers.

We have shown that residential radon produces substantial hazards, particularly among smokers, even at concentrations below the action levels currently recommended in many countries of a few hundred Bq/m$^3$. The 2000 report from the United Nations Scientific Committee on the Effects of Atomic Radiation provided estimates of mean radon concentrations in dwellings for 29 European countries, with a population weighted average of 59 Bq/m$^3$. If this is approximately correct, and if the excess risk of lung cancer is about 16% per 100 Bq/m$^3$ throughout a wide range of exposure levels, then radon in homes currently accounts for about 9% of the deaths from lung cancer and hence 2% of all cancer deaths in Europe. In most countries residential radon concentrations vary widely, with levels in most homes well below the national average but levels in a minority of homes several times higher than the national average. High radon concentrations can be reduced in existing houses at moderate cost, and low concentrations can usually be achieved at reasonable or low cost when new buildings are constructed.
This paper is dedicated to the memory of Olav Axelson (1937-2004), who published the first study on radon in homes and lung cancer in the Scandianavian Journal of Work, Environment and Health in 1979. We thank the staff and participants in the collaborating studies, Richard Peto and Jon Miles provided helpful discussions during preparation of this paper, Gary Whitlock commented on a draft version, and Tom Fearn and David Cox provided helpful comments on the statistical methods.

Contributors: All authors were responsible for the design of this collaboration. The data for the component studies were the responsibilities of W, LK, ASR, MK, HEW (Austria); Czech Republic: LT (Czech Republic); AA, IM, MH (Finland nationwide); ER, IM, MH (Finland south); HB, MT (France); MK, ASR, IH, LK, HEW (Germany eastern); LK, MK, HEW (Germany western); FB, FF (Italy); GP, FL, RF (Sweden nationwide); FL, GP, RF (Sweden never smokers); GP (Sweden Stockholm); JMB-D, AR-R (Spain); SD, HD, DH, EW, RD (United Kingdom). CM coordinated the European Commission grant. DH, HD, EW, and SD collated the data for all studies in Oxford. The analysis was conducted and the report prepared by SD, DH, and RD with input from all other authors. SD, HD, and RD are guarantors.

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