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Residential radon and lung cancer—detailed results of a collaborative analysis of individual data on 7148 persons with lung cancer and 14 208 persons without lung cancer from 13 epidemiologic studies in Europe

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This report is dedicated to the memory of Olav Axelson (1937–2004), who, following the observation that decreased ventilation as a result of energy-saving measures had been leading to increased residential radon concentrations in Sweden, published the first study specifically designed to examine the effect of residential radon concentrations on the risk of lung cancer

(Axelson O, Edling C, Kling H. Lung cancer and residency—a case-referent study on the possible impact of exposure to radon and its daughters in dwellings. Scand J Work Environ Health 1979;5:10–5.)

Abstract

Darby S, Hill D, Deo H, Auvinen A, Miguel Barros-Dios J, Baysson H, Bochicchio F, Falk R, Farchi S, Figueiras A, Hakama M, Heid I, Hunter N, Kreienbrock L, Kreuzer M, Lagarde F, Mäkeläinen I, Muirhead C, Oberaigner W, Pershagen G, Ruosteenoja E, Schaffrath Rosario A, Tirmarche M, Tomášek L, Whitley E, Wichmann H-E, Doll R. Residential radon and lung cancer—detailed results of a collaborative analysis of individual data on 7148 persons with lung cancer and 14 208 persons without lung cancer from 13 epidemiologic studies in Europe. *Scand J Work Environ Health* 2006;32 suppl 1:1–84.

Objectives Studies seeking direct estimates of the lung cancer risk associated with residential radon exposure lasting several decades have been conducted in many European countries. Individually these studies have not been large enough to assess moderate risks reliably. Therefore data from all 13 European studies of residential radon and lung cancer satisfying certain prespecified criteria have been brought together and analyzed.

Methods Data were available for 7148 persons with lung cancer and 14 208 controls, all with individual smoking histories and residential radon histories determined by long-term radon gas measurements.

Results The excess relative risk of lung cancer per 100 Bq/m^3 increase in the observed radon concentration was 0.08 [95% confidence interval (95% CI) 0.03–0.16; P=0.0007] after control for confounding. The dose-response relationship was linear with no evidence of a threshold, and it remained significant when only persons with observed radon concentrations of <200 Bq/m^3 were included. There was no evidence that the excess relative risk varied with age, sex, or smoking history. Removing the bias induced by random uncertainties related to radon exposure assessment increased the excess relative risk of lung cancer to 0.16 (95% CI 0.05–0.31) per 100 Bq/m^3. With this correction, estimated risks at 0, 100, and 400 Bq/m^3, relative to lifelong nonsmokers with no radon exposure, were 1.0, 1.2, and 1.6 for lifelong nonsmokers and 25.8, 29.9, and 42.3 for continuing smokers of 15-24 cigarettes/day.

Conclusions These data provide firm evidence that residential radon acts as a cause of lung cancer in the general population. They provide a solid basis for the formulation of policies with which to manage risk from radon and reduce deaths from the most common fatal cancer in Europe.

Executive summary

Background

The radioactive gas radon is the most important natural source of human exposure to ionizing radiation. In most countries, the majority of the exposure is received indoors, especially in houses and other dwellings. Radon is known to be a human carcinogen and studies of underground miners exposed occupationally, and usually at very high concentrations, have consistently demonstrated an increased risk of lung cancer for both smokers and nonsmokers. However, there is little direct information on the risk of lung cancer that is associated with exposure to residential radon, for which concentrations are usually much lower than those of miners and the conditions of exposure are different.

Material and methods

Thirteen studies of residential radon and lung cancer that satisfy certain prespecified criteria have been carried out in Europe. The studies were performed in Austria, the Czech Republic, Finland (2 studies), France, Germany (2 studies), Italy, Spain, Sweden (3 studies), and the United Kingdom. Individual data from all of these studies have been assembled in a uniform manner. Data on smoking history and also on radon exposure history, based on long-term measurements of radon gas concentrations, were available for a total of 7148 persons with lung cancer and 14 208 controls. Among the people with lung cancer, the mean time-weighted observed average residential radon concentration during the 30-year period ending 5 years prior to diagnosis was 104 Bq/m^3. The ratio of the number of controls to the number of cases differed between the different studies, and the weighted mean observed residential radon concentration for the controls, with weights proportional to the study-specific numbers of cases, was 97 Bq/m^3. The difference between the mean for the cases and the weighted mean for the controls differed highly significantly from zero (P=0.0002). The association between the risk of developing lung cancer and residential radon concentrations in these data was studied using linear models for the relative risk, with stratification for study, age, sex, region of residence within each study, and detailed smoking history. Analyses were carried out first in relation to the observed radon concentration without making any adjustment for the effect of random uncertainties in the assessment. The major analyses were then repeated with an approximate adjustment to take these uncertainties into account.

Results

There was clear evidence (P=0.0007) of an association between the residential radon concentration during the previous 35 years and the risk of lung cancer. The dose–response relationship was linear, and the estimated excess relative risk of lung cancer was 0.08 [95% confidence interval (95% CI) 0.03–0.16] for a 100 Bq/m^3 increase in the time-weighted average observed radon concentration. When the analysis was repeated for only people with observed radon concentrations of <200 Bq/m^3, the dose–response relationship remained significant (P=0.04), and the estimated excess relative risk per 100 Bq/m^3 was similar to that based on the entire dataset. Models that allowed for a possible threshold concentration did not provide a significant improvement in fit when compared with a model in which risk was proportional to the radon concentration, even for very low concentrations (P=0.44), and the upper 95% confidence limit for a possible threshold was 150 Bq/m^3.

There was no evidence that the dose–response relationship varied between the different studies (P=0.94), nor were the results dominated by any individual study. In addition, there was no significant evidence that the dose–response relationship depended on the detailed aspects of the study design or on the characteristics of the radon measurements or by age, sex, or smoking status. When lifelong nonsmokers were considered separately, the estimated excess relative risk of lung cancer was 0.11 (95% CI 0.00–0.28, P=0.04) per 100 Bq/m^3 observed radon concentration.

When small-cell lung cancers and lung cancers of other histological types were examined separately, there was evidence (P=0.03) that the dose–response relationship was steeper for small-cell lung cancer than for other histological types. The estimated excess relative risk for small-cell lung cancer was 0.31 (95% CI 0.13–0.61) per 100 Bq/m^3 observed radon concentration. For adenocarcinoma the estimated excess relative risk per 100 Bq/m^3 observed radon concentration was 0.06 (95% CI <-0.03–0.20), and, for squamous-cell and other histologically confirmed types, the estimates were -0.01 (95% CI <-0.03–0.09) and 0.04 (95% CI <-0.03–0.24), respectively. For all of the confirmed histologies other than small-cell lung cancer, the estimated excess relative risk was 0.03 (95% CI <-0.03–0.10) per 100 Bq/m^3 observed radon concentration.

After an approximate adjustment was made for the effects of random uncertainties in the assessment of radon concentrations, the dose–response relationship remained linear, and the estimated excess relative risk per 100 Bq/m^3 increased to 0.16 (95% CI 0.05–0.31). This risk is slightly lower, but compatible with, the risk that has been postulated on the basis of studies of radon-exposed underground miners.

There was no evidence that the excess relative risk per unit increase in the observed radon concentration varied with the smoking status of the person (P=0.92). Therefore, in analyses of the joint effects of smoking and radon exposure, the effect of radon on relative risk was assumed to be the same, regardless of smoking status. For lifelong nonsmokers, the risks of lung cancer at corrected radon concentrations of 100 and 400 Bq/m^3 were estimated to be 1.2 and 1.6, respectively, relative to the risk for lifelong nonsmokers at 0 Bq/m^3. Combining the excess relative risk for radon with the relative risks for different categories of smoking status determined for the men in these data suggests that the risks to smokers of 15–24 cigarettes per day, relative to lifelong nonsmokers exposed at 0 Bq/m^3, are 25.8 at 0 Bq/m^3 and 29.9 and 42.3 at corrected radon concentrations of 100 and 400 Bq/m^3, respectively, while the risks for ex-smokers of <10 years' duration are 20.8, 24.2, and 34.2 at 0, 100, and 400 Bq/m^3, respectively.

When the data from these European case–control studies were combined with external data on the absolute risk of death from lung cancer, the cumulative risks of death from lung cancer by the age of 75 years in the absence of radon exposure were estimated to be 0.41% and 10.11% for lifelong nonsmokers and continuing smokers of 15–24 cigarettes per day, respectively. These cumulative risks increased with increasing radon concentration, reaching 0.47% for lifelong nonsmokers and 11.63% for continuing cigarette smokers at a corrected radon concentration of 100 Bq/m^3, 0.67% for lifelong nonsmokers, and 16.03% for continuing cigarette smokers at 400 Bq/m^3. For those who gave up smoking, the cumulative risks in the first 10 years would be about 80% of those for continuing smokers. Thereafter they would be lower, but they cannot be estimated precisely from the data in the present study.

Conclusions

These data provide firm evidence that residential radon acts as a cause of lung cancer in the general population. The results are crucial to the development and refinement of policies to manage exposure to this form of natural radiation so as to reduce the annual number of deaths from the most common type of fatal cancer in Europe.

A short report summarizing the main findings of this study has been published elsewhere (Darby S, Hill D, Auvinen A, Barros-Dios JM, Baysson H, Bochicchio F et al. Radon in homes and lung cancer risk: a collaborative analysis of individual data from 13 European case-control studies. BMJ 2005;330:223–7).

Introduction

Radon-222 is a chemically inert radioactive gas that has a half-life of 3.8 days and gives rise to a series of short-lived radioactive decay products. Radon arises naturally from the decay chain of uranium-238, which is present throughout the earth's crust, and it seeps out of rocks and soil before decaying, by emission of an alpha particle, into a series of short-lived radioactive progeny. Two of these, polonium-218 and polonium-214, also decay by emitting alpha particles. If inhaled, radon itself is mostly exhaled immediately. However, its short-lived progeny, which are solid, tend to be deposited on the bronchial epithelium and, as a result, sensitive cells may be exposed to alpha radiation.

Radon concentrations are usually very low in outdoor air, but concentrations can build up in situations in which it is unable to disperse readily. Some of the highest radon concentrations occur in underground mines of uranium and other igneous rocks, but concentrations in dwellings and other buildings are also often appreciably higher than those in outdoor air. Worldwide it is estimated that the average annual effective dose from radon and its decay products is 1.15 mSv and that it is responsible for almost 50% of the total effective dose from all sources of natural radiation (1). In most countries, the majority of the exposure is received indoors, especially in houses and other dwellings, where the principal source is usually the subsoil under the building, although, under some circumstances, appreciable exposure may occur from building materials or from radon dissolved in water. Residential radon concentrations vary greatly, depending on local conditions, and, in many countries, the concentrations normally observed vary over two orders of magnitude or more.

Studies of underground miners exposed to high concentrations of radon have consistently shown an increased risk of lung cancer for both smokers and nonsmokers (2). Similar observations have been made in experimental studies on rats and dogs, and radon has been classified as a human carcinogen by the International Agency for Research on Cancer (3, 4). On the basis of estimates of the risk of lung cancer derived from studies of underground miners, it has been suggested that, in many countries, residential radon may be the cause of a considerable proportion of lung cancers. This possibility has potential public health relevance, as it is possible both to reduce indoor radon levels in most existing buildings at moderate cost and to ensure that radon concentrations are negligible in new buildings for a reasonable or low cost. Calculations of the probable numbers of lung cancers caused by residential radon depend, however, on several assumptions. One of these assumptions concerns the extent to which estimates of the lung cancer risk derived from studies of underground miners are applicable to residential situations. The information on the concentrations of radon gas and its decay products to which the miners were exposed is crude and subject to sizeable errors. Conditions of exposure are very different in mines and homes, and the differences affect the typical radiation dose to the lung cells for a given concentration of radon gas. The studies of miners, moreover, provide information only about the effects of radon exposure to adult males, most of whom were exposed for only a few years and at much higher concentrations than usually occur in dwellings. Some of the miners were also exposed to other carcinogens, such as arsenic or silica, and, although many of them are thought to have been cigarette smokers, little or no information is available about their smoking habits. All of these factors mean that there is considerable uncertainty over the extent to which the estimates of the lung cancer risk derived from studies of underground miners are applicable to exposure to residential radon.

A direct estimate of the risk of lung cancer associated with residential radon would avoid many of these uncertainties, and, in several countries, studies have been carried out that have sought to provide such an estimate. However, the studies have had limited power to detect the effects of residential radon, and none has provided a sufficiently precise estimate of the risk. Greater precision can be obtained by combining information from several studies, but it is impossible to combine the data in a satisfactory manner on the basis of only the published information from the various studies. This difficulty is partly because exposure to radon decay products has been categorized somewhat differently in the various publications and partly because confounding with smoking is dealt with in different ways by the different studies. Urban areas tend to have lower radon concentrations than rural ones, as the underlying rock is usually sedimentary and urban residents live upstairs in apartments more often than rural residents. Urban areas also usually have a high smoking prevalence. Hence radon levels in homes tend to be negatively correlated with smoking, and a large dataset, with detailed information on smoking in a uniform format for all persons, is needed if this correlation is to be corrected for reliably. In the Collaborative Analysis of Individual Data on 7148 Persons with Lung Cancer and 14208 Persons without Lung Cancer from 13 Epidemiologic Studies in Europe, we have therefore brought together individual data from all of the studies of residential radon and lung cancer that have been carried out in Europe and satisfy certain criteria laid down in advance, with the objectives of investigating the consistency of the different studies and of estimating more precisely the change in lung cancer risk associated with increasing residential radon concentration and the extent to which it is modified by factors such as age, sex, and smoking history. A short report summarizing the main findings of this study has been published elsewhere (5).

Materials and methods

Criteria for inclusion in the Collaborative Analysis

European studies of the relationship between residential radon and lung cancer were selected for inclusion in the Collaborative Analysis provided that they satisfied the following criteria: clear rules had been used in the selection of persons with lung cancer (to be referred to as lung cancer cases); controls had been selected in such a way as to be representative of the population from which the lung cancer cases had been drawn; detailed residential histories going back at least 15 years had been compiled in a similar way both for the lung cancer cases and the controls; long-term (minimum 2 months) measurements of radon gas concentrations that were likely to be representative of the levels experienced by the study subjects during the time they were living there had been made for most of the residences; data on smoking habits and other variables were available for each subject, collected either from the subject in person or from the subject's next of kin; information on the design of the study was available and on its completeness in relation to the target populations of cases and controls; the study included at least 150 lung cancer cases and 150 controls. A total of 13 studies satisfied these criteria, carried out in Austria, the Czech Republic, Finland (2 studies), France, Germany (2 studies), Italy, Spain, Sweden (3 studies), and the United Kingdom (table 1). All of these studies were included in the Collaborative Analysis.

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

Study	Years of diagnosis for the lung cancer cases
Austria: Oberaigner et al, 2002 (6)	1970–1992
Czech Republic: Tomášek et al, 2001 (7)	1960–1999
Finland nationwide: Auvinen et al, 1996 (8)	1986–1992
Finland southern: Ruosteenoja et al, 1996 (9)	1979–1985
France: Baysson et al, 2004 (10)	1990–1999
Germany eastern: Wichmann et al, 1999 (11); Kreuzer et al, 2003 (12); Wichmann et al (13)	1991–1997
Germany western: Wichmann et al, 2005 (13); Wichmann et al, 1998 (14); Kreienbrock et al 2001, (15)	1990–1995
Italy: Bochicchio et al, 2005 (16)	1993–1996
Spain: Barros-Dios et al, 2002 (17)	1992–1994
Sweden nationwide: Pershagen et al, 1994 (18); Lagarde et al, 1997 (19)	1980–1984
Sweden never-smokers: Lagarde et al, 2001 (20)	1978–1995
Sweden Stockholm: Pershagen et al, 1992 (21)	1983–1987
United Kingdom: Darby et al, 1998 (22)	1988–1995

Design of the studies included in the Collaborative Analysis

Twelve of the thirteen studies had been designed as case–control studies, while in the Czech study, which was originally a cohort study, all of the lung cancer cases were included in the Collaborative Analysis, together with four controls per case, chosen from the original cohort according to a nested case–control design. Seven of the studies had enrolled recently diagnosed cases of lung cancer prospectively (France, Germany eastern, Germany western, Italy, Spain, Sweden Stockholm, United Kingdom), while the remainder (Austria, Czech Republic, Finland nationwide, Finland southern, Sweden nationwide, Sweden never-smokers) had identified some or all of the lung cancer cases retrospectively using high-quality cancer registries or death indices. For most of the studies, the years of diagnosis for which the lung cancer cases were included lay in the 1980s and 1990s, but the use of retrospective data sources enabled the inclusion of cases from the 1970s or, in some, even the 1960s (Austria, Czech Republic, Finland southern, Sweden never-smokers) to be included (see table 1).

In most of the studies, information on the diagnosis of lung cancer was taken from hospital records or cancer registries, and all of the persons whose final diagnosis was lung cancer were included in the study irrespective of whether or not microscopic information had been obtained. However, in the German studies, only microscopically confirmed cases of lung cancer were included, while in the Austria and Czech Republic studies diagnoses were based on death certificates only. Three studies (France, Italy, and United Kingdom) included only persons who were long-term residents of the defined study area, and one study (Finland nationwide) included only persons who had lived in the same single family house for at least 19 years. Most of the studies included both men and women, but the Finland southern study included only men and the Sweden Stockholm study included only women. In five studies (France, Germany eastern, Germany western, Sweden nationwide, United Kingdom) people were included in the study only if they were under 75 years of age, while, in the remaining studies, there was no upper age limit.

Most of the studies included only population-based controls, but three (Sweden never-smokers, Sweden Stockholm, and United Kingdom) included both hospital and population controls, and two (France and Italy) included only hospital controls. In most of the studies, the controls were matched to lung cancer cases by sex and age or year of birth, while, the Sweden nationwide study, was matched for age but not sex, and in the Spain and Sweden Stockholm studies no age matching was carried out. In six studies (France, Germany eastern, Germany western, Spain, Sweden never-smokers, United Kingdom) the control group was matched to the lung cancer cases for geographic region of current residence, while, for the remaining studies, no geographic matching was carried out within the area selected for study.

Additional selection criteria were used for the controls in some studies. In three studies (France, Italy, and United Kingdom) hospital controls were selected from people whose current hospital admission was for a disease not strongly related to smoking. In the Sweden never-smokers study, all of the members of the control group were also lifelong nonsmokers. In the Austria study, where all the lung cancer cases had died, the controls were chosen from those who had also died and whose cause of death was not strongly related to smoking. The controls in the Austria study were also matched to lung cancer cases by year of death. In the Swedish nationwide study, one of the two control groups was matched to the lung cancer cases by vital status.

In the Finland southern study, an initial screening questionnaire was used to determine the smoking status of potential members of the control group; among those who replied, all of the current smokers were selected for the study, as were random samples of approximately 10% each of ex-smokers and lifelong nonsmokers. Before the main collaborative analysis, preliminary analyses were carried out on the data from the Finland southern study and the Swedish nationwide study to ascertain whether it was necessary to account specifically for these aspects of study design in the analysis. It was concluded that no special adjustment was necessary.

In six of the studies (France, Germany eastern, Germany western, Italy, Sweden Stockholm, United Kingdom), people were not included unless they were in a position to provide information personally, while, in the Austria study, all of the information was supplied by surrogates, as all of the people in that study had already died, and, for the remaining studies, information was accepted from both the study subjects themselves and their surrogates. Most of the studies collected data from the study subjects or their surrogates in person, but the primary method of data collection was by mail in the nationwide studies in Finland and Sweden, and also in a part of the Swedish study of never-smokers. Additional details of the method used for selecting the cases and controls are given in appendix A (table A1).

Period of interest for exposure to radon

In the Collaborative Analysis, it was assumed that the period of residential radon exposure that is relevant to the risk of lung cancer at a particular point in time is the 30-year period ending 5 years prior to the index date. This period was chosen on the basis of the studies of underground miners in which exposure within the previous 5 years and exposure more than 35 years previously were found to have little or no effect on the risk of the disease (2). In order to determine the 30-year period of interest, an index year was determined for each subject. For the lung cancer cases, the index year was usually the year of diagnosis of, or the year of death from, lung cancer, while, for the controls, a suitable date was chosen depending on the study design. [See appendix A (table A1) for further details.]

Radon measurement procedures in the participating studies

In the Czech Republic study the aim was to measure the radon concentration in all of the dwellings occupied by the subjects within the 30-year period of interest, while nine studies (Austria, Finland southern, France, Germany western, Italy, Sweden nationwide, Sweden never-smokers, Sweden Stockholm, and United Kingdom) restricted attention to dwellings that had been occupied for at least 1 or 2 years during the period of interest. In four studies, only one dwelling was considered (the most recent home occupied for at least 2 years in the Austria study, the current dwelling in the Germany eastern and Spain studies, and the dwelling occupied in 1985 in the Finland nationwide study). Eleven of the studies used closed alpha-track detectors, whereas two studies (Czech Republic, France) used open alpha-track detectors, and, in one study (Sweden Stockholm), the measurements from the alpha-track detectors were supplemented by measurements made with thermoluminescence detectors for dwellings in which no alpha-track measurement was possible. In nine of the studies, two detectors were placed either in the bedroom and living room or in the two most occupied rooms of the dwelling, while, in one study (Italy), two pairs of detectors were placed, one pair in the bedroom and one pair in the living room, and in three studies (Finland nationwide, Finland southern, Spain) one detector only was placed, either in the bedroom or in the living room. When more than one measurement had been made, an appropriately weighted average was calculated to give a single representative value for each dwelling. In five studies (Czech Republic, Finland nationwide, Germany eastern, Germany western, Sweden Stockholm) the detectors were left in place for a full year, in the Austria study they were mostly left in place for a full year, but for shorter periods and with seasonal corrections, in dwellings with high concentrations, and in the Italy study the detectors were in place for two consecutive 6-month periods. In the remaining studies the measurement period was less than a year (range 2–6 months), and seasonal adjustments were applied when necessary. Additional details of the radon measurement procedures in the various studies are given in appendix A (table A2).

Data on individual persons in the study

For each person included in the study, information was compiled on all the variables necessary for the Collaborative Analysis according to a common data format. [See appendix A (table A3).] The variables included case-control status, interview type and method, sex, index year, age and region of residence during the index year, histological type of cancer (for lung cancer cases), diagnosis (for hospital controls), detailed smoking history, social status, occupational exposure to radon, asbestos or another established occupational lung carcinogen (23), average duration of occupancy of the home during the 30-year period of interest, proportion of 30-year period of interest spent living in an urban area, usual position of the bedroom window at night, number of years spent working outdoors, and exposure to environmental tobacco smoke (for lifelong nonsmokers). As far as was possible, uniform definitions were used across all of the studies even though it was necessary to use study-specific definitions for social status, based either on occupation or on education, depending on the information available within each study. The subjects were included in the analysis only if there was a radon measurement corresponding to at least one dwelling that they had occupied during the 30-year period of interest ending 5 years prior to the index date; their smoking history was available; and, for the lung cancer cases, the final diagnosis was primary cancer of the trachea, bronchus, or lung [International Classification of Diseases (ICD), 9th revision, code 162 (24), but excluding carcinoid tumors]. Details of the numbers of persons included in the Collaborative Analysis, both in relation to the original study publication and to the total number of persons initially selected for the study are given in appendix A (table A4).

For each person, information was also sought on the measured radon gas concentration for each dwelling during the 30-year period of interest and on the geographic area of residence (or, for the Sweden Stockholm study, the type of dwelling) where the person had been living. Proxy measurements made in dwellings close to the subject's own dwelling were used only in the Italy and Sweden Stockholm studies. For the Italy study, proxy measurements were used only for apartments above ground level, in the same building and, generally, on the same floor as the target dwelling, whereas, in the Sweden Stockholm study, proxy measurements were only used for apartments in the same building and on the same floor as the target dwelling. For years in which no measurement of the person's dwelling was available, estimates were made. Ideally, such estimates would be based on the distribution of radon concentrations in the whole population. In these case–control studies, the controls should, to a close approximation, reflect the distribution in the population as a whole. Therefore, the estimates in each study were based on the measurements made for the controls in the same study. These estimates were either the overall arithmetic mean for all the controls or else area-specific control means. For each study, the effect of using area-specific means as compared with the overall mean was evaluated by considering all of the available measurements in each study and calculating the mean squared error of prediction using the overall and area-specific estimates. In four studies (Austria, Czech Republic, Italy, United Kingdom), the use of area-specific estimates improved the mean squared error of prediction by >10%, and area-specific estimates were used throughout the analysis. For the remaining studies, the reduction in the mean squared error of prediction was <10% and the estimates for missing values were based on the overall mean of the measurements made for the controls. Further details are given in appendix C (table C1).

Statistical methods

Main analyses

The association between radon and lung cancer risk was studied by considering the relationship between the odds of developing lung cancer and various measures of radon exposure using the following linear odds model:

$$\frac{\pi}{1-\pi} = e^{\alpha}(1+\beta x), \qquad \text{equation 1}$$

where π is the probability of developing lung cancer, x is a continuous variable summarizing the radon exposure of each subject, e^{α} is the odds of developing lung cancer when $x = 0$, and β describes the linear relationship between the odds of developing lung cancer and radon exposure. This model was used, rather than the usual logistic regression model, because radiobiological theory suggests that it is more appropriate to quantify the risk on a linear scale than on an exponential one. In addition, results expressed on a linear scale are more easily applied in the context of radiological protection.

For many analyses x was the time-weighted average (TWA) observed radon concentration for a subject, and it was calculated as $x = \sum_j w_j x_j$, where x_j are the observed radon concentrations, either measured or estimated, corresponding to the dwellings occupied by the person during the 30-year period of interest, and w_j are weights representing the proportion of the 30-year period interest corresponding to each dwelling.

As the probability of developing lung cancer is small, $\pi / (1-\pi) \approx \pi$ in equation 1, and $1 + \beta x$ is, to a good approximation, the relative risk of lung cancer when radon exposure takes value x compared with no radon exposure or, equivalently, β is, to a good approximation, the excess relative risk of lung cancer per unit increase in the radon exposure.

Allowance was made for potential confounders either through stratification (ie, by allowing each stratum to have its own α in equation 1) or by including covariates in the model through the addition of categorical terms in the linear part of equation 1:

$$\frac{\pi}{1-\pi} = \exp(\alpha)\left(\Sigma\gamma_j z_j + \beta x\right), \qquad \text{equation 2}$$

where the z_j are indicator variables representing different levels of the covariates and γ_j are their associated regression coefficients.

Within each stratum, the number of lung cancer cases was assumed to have a binomial distribution with parameters n and π, where n is the total number of persons in the stratum. Models were fitted using conditional maximum likelihood, along the lines usually used in conditional logistic regression using the software packages Epicure (25) and Stata (26). When linear odds models of the form given in equation 1 were used, confidence intervals for β were based on the conditional likelihood, and, as the log likelihood was asymmetric, they usually differed appreciably from those based on standard errors. For linear odds models in which more than one parameter was fitted, such as those of the form given in equation 2, confidence intervals were based on the profile of the conditional likelihood. For some analyses the lower limit of the confidence interval, and occasionally also the estimated value of β, could not be evaluated precisely as they were less than $-1/x_{max}$, where x_{max} was the largest value of x, and thus corresponded to negative fitted values for the odds. In such cases, all that could be presented was the fact that the values were less than $-1/x_{max}$.

In analyses exploring the potential heterogeneity of β with various categorical attributes of the subjects, the single term βx was replaced by separate terms $\beta_1 x$, $\beta_2 x$, $\beta_3 x$, and so forth, corresponding to categories of the attribute under consideration or, if there was an ordering to the categories involved, by $(\beta + \theta c)x$, where c took values 1, 2, 3, ... and represented the categories, while θ represented the trend across the ordered categories. If the categorical attribute was not already included in the stratification, appropriate additional categorical covariates were included in the model, as in equation 2.

Tests of $\beta = 0$ and other hypotheses were carried out using the likelihood ratio and were two-sided where appropriate. However, when the heterogeneity of β with respect to cell type was considered, where all the controls were included in each estimate, the likelihood ratio test could not be computed easily. In this case the approximate test statistic $\sum_{i=1}^{n} w_i (b_i - \bar{b})^2$ was used, where n was the number of cell types involved, b_i were the estimates of β for the individual cell types, $\bar{b}$ was the average of b_i, and w_i were the inverses of the estimated variances of b_i. The test statistic was evaluated by comparison with the χ^2 distribution on $n - 1$ degrees of freedom.

In order to examine the goodness of fit of different models, some analyses were repeated with both linear and quadratic terms in radon, that is, using the equation: $\pi / (1-\pi) = \exp(\alpha)(1 + \beta_1 x + \beta_2 x^2)$, rather than equation 1, and some analyses were repeated with a logistic model, that is, one with a log-linear rather than a linear term for radon: $\pi / (1-\pi) = \exp(\alpha + \beta x)$.

Analyses that considered categorical, rather than continuous, measures of radon were based on the following log-linear model:

$$\frac{\pi}{1-\pi} = \exp(\alpha)\exp(1 + \beta_1 x_1 + \beta_2 x_2 + \beta_3 x_3 + \beta_4 x_4 + \ldots), \qquad \text{equation 3}$$

where x_1, x_2, x_3, x_4, ..., denote indicator variables corresponding to the categories of radon. A further goodness- of-fit test was carried out by testing whether the inclusion of terms representing the categories of radon, as in equation 3, gave any improvement in fit over the model given in equation 1.

For the analyses in which log-linear models were fitted (including those based on categorical measures of radon), confidence intervals were based on asymptotic standard errors. For the analyses based on categorical measures of radon, when confidence intervals were calculated for β_i, it seemed undesirable to regard one category as a fixed baseline and present confidence intervals for the other categories relative to it, as it would have meant that the confidence intervals for the other pairs of categories could not be easily interpreted because they would not be independent but would both be substantially influenced by the variability in the baseline category. Therefore, floated variances were calculated for each of the β_i (27). This procedure provided confidence intervals for each category that were all approximately independent of each other and so could be more easily interpreted.

For the analyses that considered radon as a continuous variable, the relative risk was set to 1 at zero radon exposure. For estimates of risk based on categorical measures of radon, it seemed desirable to choose the arbitrary constant in the relative risk in such a way as to make the categorical analysis compatible with the corresponding continuous analysis. To achieve this goal, for each categorical analysis, the arbitrary constant was chosen to minimize the sum of the weighted squared distances of the categorical estimates from the regression line for the corresponding analysis using radon as a continuous variable, with weights set equal to the inverse of the approximate variances of the relative risks. These approximate variances were calculated from the floated variances of the β_i using a Taylor series expansion.

An upper confidence limit on any possible threshold was computed using the method used previously in analyses of atomic bomb survivors (28). For a postulated threshold exposure, t, the radon exposure, x, was transformed to x_t, where $x_t = 0$ for $x < t$ and $x_t = x - t$ for $x \geq t$. The model in equation 1 was then fitted with x replaced by x_t. This procedure was repeated for $t = 10, 20, 30, \ldots$ Bq/m^3, and the confidence interval was derived from the profile of the resulting conditional likelihoods.

If the effects of radon and smoking combined in an additive fashion, their joint effect on the odds of lung cancer could be represented by: $\pi / (1 - \pi) = e^{\alpha} (1 + \beta x + \gamma z)$, where α, β, and x are as in equation 1, z represents a person's smoking history, and γ decribes the effect of smoking on the odds of lung cancer. If smoking is considered as a categorical variable, this model can be rewritten as: $\pi / (1 - \pi) = e^{\alpha} (1 + \beta x + \delta_i)$, where δ_i represents the effect of smoking in the different categories (lifelong nonsmokers, current smokers of <15, 15–24, and ≥25 cigarettes per day, and ex-smokers of <10 and ≥10 years' duration, separately for each sex). If, however, the different smoking categories all corresponded to different strata, then this model is equivalent to the following model: $\pi / (1 - \pi) = e^{\alpha_i^*} (1 + \beta_i x)$, where β_i varies across the different smoking categories according to the relation $\beta_i = \beta / (1 + \delta_i)$, and $(1 + \delta_i)$ is the relative risk of lung cancer for persons in smoking category i compared with lifelong nonsmokers and α_i^* differs from α in that it takes this relation into account. Therefore, in order to test whether the data were compatible with an additive effect of smoking, the following model was fitted to the data: $\pi / (1 - \pi) = e^{\alpha_i^*} [1 + \beta x / (1 + \delta_i)]$, where δ_i is the proportionate increase in risk for persons in smoking category i compared with lifelong nonsmokers of the same sex and, as before, i indicates categories of smoking for each sex. The values of δ_i were assumed to be known and were taken from the analysis of the effects of smoking in these data. The fit of this model was then compared with the fit of a model in which β_i was allowed to vary freely across the different smoking categories.

Combined effect of smoking history and radon exposure on lung cancer risk

The variation in the excess relative risk of lung cancer per unit increase in radon exposure in the groups of persons with different smoking habits was studied using the methods described in the preceding section. However, it was desirable also to provide some estimates of the combined risks of smoking and radon. It was to be expected that the major determinant of the absolute value of the lung cancer risk for most of the persons in the study would be their smoking history. It was also to be expected that, for persons with identical radon exposure histories who were also current or ex-smokers, lung cancer risks would vary substantially depending on the details of their smoking histories, including the age at which they started to smoke, the amount of each product smoked at each age, and, for ex-smokers, the time since they had given up the habit. Within any population the risks associated with smoking take many decades to mature (29). Cigarette smoking became popular at different times in the different countries in which the component studies of the Collaborative Analysis were carried out, and it also became popular among men and women at different times within most of the countries involved (30). Therefore, joint modeling of the effects of smoking and radon for the data in the Collaborative Analysis would have had to allow for the fact that smoking risks differ from country to country (31), and between men and women within any country. Such joint modeling would have required very complex models and would have led only to imprecisely estimated risks for persons with any particular smoking history. This situation did not seem desirable. Instead, estimates of the joint effect of radon and smoking were calculated for broad categories of smokers by assuming that, for any radon concentration, the relative risk of lung cancer for the persons in each broad smoking category was known precisely and was equal to the relative risk that was seen for all men in that smoking category compared with all male lifelong nonsmokers. Relative risks of the effect of smoking on women were not used, as, in the present studies, many of the women who were current smokers did not start smoking until well into adult life. More recently, most of the female smokers in these European countries have tended to start smoking at a much earlier age and to smoke a similar number of cigarettes per day as men. Studies have shown that women are as susceptible to lung cancer as men, given similar cigarette smoking histories (32). Therefore, the observed relative risks associated with smoking for women in these studies are likely to underestimate substantially the risks of smoking that will result from the present smoking patterns of women (29).

The cumulative risk of death from lung cancer at various ages was calculated by assuming that the age-specific death rate from lung cancer for lifelong nonsmokers exposed to the mean residential radon concentration observed in the United States (46 Bq/m^3) was equal to that observed for men in a prospective study of one million people carried out by the American Cancer Society during the 1980s (33). [See appendix A, table A5.] Calculations were based on the rates for men only, as the rates for men and women were virtually identical. The American rates were used in preference to those based on European data, as they are based on a much larger sample than any European data, including 316 deaths, and they are consistent with the findings of the two main European studies that provide data on the death rate from lung cancer among lifelong nonsmokers {Swedish longitudinal smoking study: 26 deaths observed [95% confidence interval (95% CI) 17.0–38.1] (34) and 20.7 expected based on the rates in table A5 in appendix A; British doctors' study: 18 deaths observed (95% CI 10.7–28.4) and 19.9 expected based on the rates in table A5 in appendix A (35)}. From the rates in table A5 in appendix A, the hypothetical death rate at each age for lifelong nonsmokers with zero radon exposure was calculated on the assumption of a linear relationship between radon exposure and mortality from lung cancer. The death rates at each age for lifelong nonsmokers with no radon exposure were then combined with the relative risk for current smokers for all of the studies combined and with the relative risks at various levels of radon exposure, to provide estimates of the absolute death rate for each age group of people with various smoking histories and with various radon exposures. The cumulative death rates up to the ages of 75, 80, and 85 years were calculated by summing the relevant age-specific death rates, and these were converted into the percentage cumulative risks using the formula $100 \times [1 - \exp(-c)]$, where c is the relevant cumulative death rate.

Method of adjustment for random uncertainties in the assessment of residential radon exposures

Measurements of radon gas made in the same dwelling in different years have shown considerable variability, indicating that, when the radon concentration in a dwelling is assessed from measurements taken during a single year, there is appreciable random uncertainty in the assessment of the long-term average concentration of residential radon in a dwelling over a period of several years. [See, for example, Bochicchio et al, personal communication, Hunter et al (36), Lomas & Green (37).] The sources of this variation include uncertainties in the measurement process itself and also variation in the true radon concentration in the dwelling due, for example, to year-to-year variation in the weather, variation in the lifestyle of those living in the dwelling, and alterations to the dwelling itself. Regression coefficients calculated using measurements that are subject to appreciable random variability of this type (usually referred to as classical or measurement error in the statistical literature) are known to suffer from bias unless special methods of analysis are used that take them into account (19, 22, 38, 39). In the present data, in addition to the uncertainty of the measured radon concentrations, there are also uncertainties for the TWA observed radon concentrations due to the fact that, for many persons, radon measurements were not available for some of the dwellings occupied during the 30-year period of interest, and uncertainties of this type (usually referred to as Berkson error in the statistical literature) also cause some bias in the present situation, for which the response variable is binary (38). To correct for the biases caused by both types of uncertainty, the main analyses were repeated with them taken explicitly into account.

Measurements of residential radon concentrations from representative samples of dwellings in a given geographic district have been shown on many occasions to be approximately log-normally distributed. In addition, analyses of repeated radon measurements in the same dwelling have shown that the size of the variability associated with repeated measurements made in different years tends to increase as the radon concentration increases but that, after logarithmic transformation, the variability is approximately independent of the radon concentration (38, 40, 41). Therefore, in the analyses that adjusted for uncertainties, it was assumed that, within each geographic district, the true (ie, long-term average) radon concentrations had a log-normal distribution, and it was also assumed that, on a log scale, the variability associated with repeated measurements in the same dwelling was normally distributed about the true radon concentration for that dwelling.

According to the preceding information, if Z_t and Z_m denote the logarithms of the true and the measured radon concentrations in a dwelling, respectively, and ε_m denotes the difference between the logarithm of the true and the logarithm of the measured radon concentration, then $Z_m = Z_t + \varepsilon_m$, and $Z_t \sim N(\mu, V_t)$, where μ is the mean of the logarithms of the true long-term average radon concentrations in the district, and $\varepsilon_m \sim N(0, V_m)$. It therefore follows from Bayes' theorem that, for dwellings for which a radon measurement was available, the logarithm of the true radon concentration given the measured value would have the following distribution:

$$Z_t | Z_m \sim N\left[\frac{(\mu/V_t + Z_m/V_m)}{(1/V_t + 1/V_m)}, \frac{1}{(1/V_t + 1/V_m)}\right], \quad \text{equation 4}$$

while, for dwellings for which no radon measurement was available, the true long-term radon concentration would have the following distribution:

$$Z_t \sim N[\mu, V_t]. \quad \text{equation 5}$$

No information on V_m was provided by the data collected in the studies contributing to the Collaborative Analysis. Therefore, all of the information available from other sources on the variability of repeated measurements made in the same house in different years was assembled and used to indicate appropriate values for V_m for each study. Each study was considered to be a separate geographic district and, within each study, the sample mean and variance of the logarithms of the measurements made on the dwellings for controls were used to derive estimates of μ and $(V_t + V_m)$. For the four studies in which area-specific estimates had been used to estimate the radon concentrations for dwellings that could not be measured (Austria, Czech Republic, Italy, United Kingdom), separate estimates of μ and $(V_t + V_m)$ were constructed for each area when sufficient data were available to allow such estimates to be constructed.

Maximum likelihood estimates of β, taking into account the error structure described in the previous paragraph, were derived by integrating the likelihood over the unknown true radon measurement. These estimates were calculated using simulation. For each person in the Collaborative Analysis, a value of the true radon concentration for each dwelling occupied during the 30-year period of interest was generated, using the distribution in equation 4, where it had been possible to measure the radon concentration of the dwelling, or equation 5, where the radon concentration had been estimated indirectly rather than measured. The TWA radon concentration corresponding to these simulated true radon values was then calculated using the same weights as previously, and the conditional likelihood corresponding to equation 1 was evaluated for a range of values of β. This procedure was repeated several times for the same set of values of β. The average of the simulated likelihoods was then determined, and its maximum was considered to be the estimated value of β, and likelihood-based confidence intervals were derived. This method was used, rather than the averaging of the maximum values of the individual simulated likelihoods, as such a procedure leads to biased estimates of β (T Fearn, personal communication). An investigation showed that stable estimates of β were derived when the number of simulations was set at 2000, and therefore this number was used throughout. The methods that had been developed previously to take uncertainties in the assessment of radon exposure into account in the analysis of the United Kingdom study (38) were not used in the present analysis because it was desirable, in the present analysis, to use the linear odds model given in equation 1, rather than a linear logistic model, and it was also desirable to fit models conditional on the total number of persons in each stratum. Neither of these aspects can be easily accommodated using the previous methodology.

In addition to the analyses in which the uncertainties in the assessment of radon concentrations were taken into account by the method of integrated likelihood, additional analyses were carried out in which a TWA corrected radon concentration was calculated for each person in the Collaborative Analysis. These TWA corrected radon concentrations were derived by assuming that every measured or estimated radon concentration was equal to the expected value of the corresponding distribution of the true radon concentrations given the observed value, using the distribution for the true log radon concentration given in either equation 4 or equation 5. These corrected values were used to derive the mean corrected radon concentrations for groups of persons. The main analyses were then repeated using a regression calibration method in which the standard methods used in the previous section were applied, but with the corrected radon concentrations in place of the observed ones. The regression calibration technique has been shown to provide reasonable adjusted-point estimates in nonlinear dose-effect relationships (42), but it may not fully take into account all of the variability induced by the uncertainties in the assessment of radon concentrations.

Results

Persons included in the Collaborative Analysis

Overall, 7148 lung cancer cases were included in the Collaborative Analysis. The contributions from the individual studies varied between 1323 lung cancer cases in the Germany western study and 156 lung cancer cases in the Spain study (table 2). Altogether there were 14 208 controls included in the analysis, and the number of controls exceeded the number of lung cancer cases in every study. Of the lung cancer cases, 5521 (77%) were men, and in 11 of the studies the number of men with lung cancer exceeded the number of women with lung cancer, in some cases by a factor of 10. The remaining two studies were the Sweden never-smokers study, in which there were 114 men with lung cancer and 144 women with lung cancer, and the Sweden Stockholm study, which included only women.

Of the men with lung cancer, 268 (5%) were lifelong nonsmokers, while 2832 (51%) were current smokers of cigarettes at the time their illness developed, 2209 (40%) were ex-smokers, and 212 (4%) were either occasional smokers or else smoked only a pipe, cigars, or cigarillos. Among the women with lung cancer, 616 (38%) were lifelong nonsmokers, 743 (46%) were current cigarette smokers, and 256 (16%) were ex-smokers (table 3). As would be expected, the distribution of the controls by smoking status differed substantially from that of the lung cancer cases. Among the male controls, 2888 (28%), 2692 (26%), 4309 (41%), and 499 (5%) were lifelong nonsmokers, current cigarette smokers, ex-smokers, and occasional cigarette smokers or smokers of a pipe but not of cigarettes, respectively, whereas 2530 (66%), 630 (16%), and 621 (16%) of the female controls were lifelong nonsmokers, current cigarette smokers, and ex-smokers, respectively. After stratification

Table 2. Numbers of persons in the European case–control studies by sex.

Study	Cases (N)			Controls (N)		
	Men	Women	Total	Men	Women	Total
Austria	161	22	183	164	24	188
Czech Republic	159	12	171	657	56	713
Finland nationwide	798	83	881	1 277	158	1 435
Finland southern	160	.	160	328	.	328
France	509	62	571	1 080	129	1 209
Germany eastern	833	112	945	1 322	194	1 516
Germany western	1117	206	1323	1 741	405	2 146
Italy	325	59	384	296	109	405
Spain	145	11	156	213	22	235
Sweden nationwide	546	414	960	1 017	1028	2 045
Sweden never-smokers	114	144	258	220	267	487
Sweden Stockholm	.	196	196	.	375	375
United Kingdom	654	306	960	2 073	1053	3 126
Total	5521	1627	7148	10 388	3820	14 208

Table 3. Distribution of the cases and controls by smoking status and sex and the risk of lung cancer relative to that of lifelong nonsmokers. (95% CI = 95% confidence interval)

Smoking status	Men				Women			
	Cases (N)	Controls (N)	Relative risk[a]	95% CI	Cases (N)	Controls (N)	Relative risk[a]	95% CI
Lifelong nonsmoker	268	2 888	1.0	.	616	2530	1.0	.
Current cigarette smoker								
<15 per day	690	1 075	13.2	10.9–16.1	311	360	5.8	4.7–7.2
15–24 per day	1361	1 144	25.8	21.3–31.2	323	220	11.4	9.0–14.5
≥25 per day	781	473	39.5	31.9–48.9	109	50	17.4	11.7–26.0
Ex-smoker								
<10 years	1279	1 176	20.8	17.2–25.2	176	219	5.5	4.3–7.1
≥10 years	930	3 133	5.0	4.2–6.0	80	402	1.3	1.0–1.8
Other[b]	212	499	8.3	6.5–10.5	12	39	1.5	0.8–3.1
Total	5521	10 388			1627	3820		

[a] Risks estimated after stratification by study, age, sex, and region of residence.
[b] Occasional cigarette smokers and current smokers of a pipe, cigars or cigarillos, but not of cigarettes.

by study, age in 5-year age groups, sex, and region of residence within study, the risks of lung cancer among the men currently smoking cigarettes relative to lifelong nonsmokers were, for all of the studies combined, 13.2 (95% CI 10.9–16.1), 25.8 (95% CI 21.3–31.2), and 39.5 (95% CI 31.9–48.9) for those smoking <15, 15–24, and ≥25 cigarettes per day, respectively, while, for the men who had stopped smoking <10 and ≥10 years previously, the corresponding risks were 20.8 (95% CI 17.2–25.2) and 5.0 (95% CI 4.2–6.0), respectively. For the women, the corresponding relative risks for lung cancer among the current cigarette smokers were 5.8 (95% CI 4.7–7.2), 11.4 (95% CI 9.0–14.5), and 17.4 (95% CI 11.7–26.0) for those smoking <15, 15–24, and ≥25 cigarettes per day, respectively, and for the female ex-smokers of <10 and ≥10 years' duration the corresponding values were 5.5 (95% CI 4.3–7.1) and 1.3 (95% CI 1.0–1.8), respectively. These relative risks were consistent with the relative risks of lung cancer for people with different smoking habits that have previously been observed in these countries. Additional tables of the distribution of the persons studied according to demographic and other characteristics are given in appendix B, tables B1-B17.

The mean number of addresses reported per person during the 30-year period ending 5 years prior to the index date was 2.7 (range 1 to 15), and the mean number of addresses at which the radon concentration was measured per person was 1.6 (range 1 to 12) (table 4). The mean number of years during the 30-year period of interest for which measurements were available was 23 (77%),

Table 4. Numbers of residential addresses reported and measured per person during the 30-year period ending 5 years before the index date and numbers of years for which measurements were available in each study.

Study	Addresses reported (N)		Addresses measured (N)		Years for which measurements available (N)	
	Mean	Range	Mean	Range	Mean	Range
Austria	1.5	1–3	1.0	1–1	23	1–30
Czech Republic	1.4	1–5	1.2	1–3	27	1–30
Finland nationwide	1.5	1–3	1.0	1–1	27	1–30
Finland southern	3.0	1–10	1.3	1–4	22	1–30
France	2.4	1–10	1.5	1–5	24	1–30
Germany eastern	2.3	1–10	1.0	1–1	20	1–30
Germany western	2.7	1–12	1.0	1–4	19	1–30
Italy	2.9	1–9	2.2	1–7	27	1–30
Spain	2.0	2–2	1.0	1–1	20	7–25
Sweden nationwide	3.6	1–12	2.2	1–8	23	1–30
Sweden never-smokers	2.8	1–9	2.1	1–7	25	1–30
Sweden Stockholm	3.8	1–10	2.4	1–6	23	1–30
United Kingdom	3.2	1–15	2.3	1–12	26	1–30
Total	2.7	1–15	1.6	1–12	23	1–30

and it ranged from 19 (63%) in the Germany western study to 27 (90%) in the Czech Republic, Finland nationwide, and Italy studies. The mean observed TWA residential radon concentration for the persons included in the Collaborative Analysis varied from 50 Bq/m^3 in the Germany western study to 500 Bq/m^3 in the Czech study, and in every study the mean value exceeded the median value, reflecting the skewed distribution of the residential radon concentrations (table 5). The standard deviation of the measurements tended to be higher in the studies with the higher mean values, but every study included persons with observed values of <100 Bq/m^3 and >500 Bq/m^3. When all of the studies were considered together, the overall mean TWA observed residential radon concentration was 105 Bq/m^3, the median value was 63 Bq/m^3, and the range was 1-4606 Bq/m^3. When the lung cancer cases and controls were considered separately, the distributions of the TWA observed residential radon concentrations remained highly skewed in each group. For the lung cancer cases, the mean value was 104 Bq/m^3 (table 6). In all but three of the studies (Germany western, Spain, and Sweden Stockholm), the mean radon concentration of the lung cancer cases exceeded that of the controls (appendix C, table C5). The ratio of the number of cases of lung cancer to the number of controls differed from study to study. Therefore, rather than calculating the overall mean observed radon concentration for the controls, a weighted mean was calculated, with weights proportional to the study-specific numbers of cases, and it took the value 97 Bq/m^3 (table 6). The estimated common difference between the TWA observed radon concentration for the lung cancer cases and the controls was 6.8 Bq/m^3, with a standard error of 1.8 (P=0.0002).

The completeness of the radon measurements was similar for the lung cancer cases and the controls, at 77% and 78% of the 30-year period of interest, respectively (table 7). As would be expected, coverage was higher in the more recent past than in the more distant past, with measurements for 92%, 80%, and 59%, respectively, of the 10-year periods ending 5, 15, and 25 years prior to the index date for the lung cancer cases. For the controls the values were 92%, 81%, and 62%, respectively (table 7). For the lung cancer cases, the mean TWA observed radon concentrations in these three periods were similar, at 103, 104, and 104 Bq/m^3. For the controls, the corresponding weighted means were 96, 97, and 98 Bq/m^3. For all three periods the mean after adjustment for study was significantly greater for the lung cancer cases than for the controls (P=0.0005, 0.0001, and 0.006 for 5–14, 15–24, and 25–34 years prior to the index date, respectively (table 7). Additional information about the TWA observed radon concentrations of the cases and controls is given in appendix C, figure C1 and tables C2-C7.

Table 5. Distribution of the time-weighted average observed residential radon concentrations during the 30-year period of interest by study, based on measured values and estimates when no measurement could be obtained. (SD = standard deviation)

Study	Time-weighted average observed residential radon (Bq/m³)								
	Arithmetic mean	Arithmetic SD	Geometric mean	Geometric SD	Minimum	Quartile			Maximum
						1st	2nd	3rd	
Austria	198	353	120	1.90	18	78	105	146	2649
Czech Republic	500	273	441	1.28	81	309	437	614	2209
Finland nationwide	103	125	80	1.48	19	52	74	110	3244
Finland southern	215	198	175	1.43	24	125	176	232	2823
France	133	186	94	1.83	6	60	91	138	4606
Germany eastern	76	83	65	1.27	14	51	64	76	2867
Germany western	50	35	45	1.19	9	37	45	52	818
Italy	108	69	93	1.30	28	65	88	125	529
Spain	131	132	100	1.56	30	63	90	133	955
Sweden nationwide	96	112	72	1.69	1	48	75	105	2253
Sweden never-smokers	74	65	58	1.64	2	37	58	90	596
Sweden Stockholm	134	77	119	1.25	22	92	118	151	636
United Kingdom	55	78	36	2.03	1	21	33	60	1700
All studies	105	153	68	2.35	1	41	63	106	4606

Table 6. Overall distribution of the observed time-weighted average residential radon concentration for the lung cancer cases and the controls, based on measured values and estimates for which no measurement could be obtained.

Observed radon concentration	Cases		Controls	
	N	%	N	%
<25 Bq/m³	566	7.9	1 474	10.4
25–49 Bq/m³	1 999	28.0	3 905	27.5
50–99 Bq/m³	2 618	36.6	5 033	35.4
100–199 Bq/m³	1 296	18.1	2 247	15.8
200–399 Bq/m³	434	6.1	936	6.6
400–799 Bq/m³	169	2.4	498	3.5
800–1599 Bq/m³	53	0.7	104	0.7
≥1600 Bq/m³	13	0.2	11	0.1
Total	7 148	100.0	14 208	100.0
Mean [a]	104		97 [b]	

[a] The estimated common difference between the cases and controls was 6.8 Bq/m³ with a standard error of 1.8 Bq/m³ (P=0.0002).
[b] Weighted mean for the controls, with weights proportional to study-specific numbers of cases.

Table 7. Completeness of the residential radon measurements and the mean observed radon concentrations by time period.

Time period prior to index date	Cases		Controls	
	Years with measurement (%)	Mean radon concentration (Bq/m³)	Years with measurement (%)	Mean radon concentration (Bq/m³)
5–14 years	92	103	92	96 [a]
15–24 years	80	104	81	97 [a]
25–34 years	59	104	62	98 [a]
All years	77	104	78	97 [a]

[a] Weighted means for the controls, with weights proportional to study-specific numbers of cases. Estimated common difference between the cases and controls: 5–14 years: 7.3 Bq/m³ (standard error 2.1); 15–24 years: 7.8 Bq/m³ (standard error 2.0); 25–34 years: 5.2 Bq/m³ (standard error 1.9); all years: 6.8 Bq/m³ (standard error 1.8).

Correlation between radon and smoking

It was to be expected that the observed radon concentrations would be correlated with smoking history in the populations in which these studies had been conducted, and this correlation was examined using the information on the controls. After stratification for study, sex, age, and current region of residence within the study, the percentage of the population that had never smoked increased as the radon concentration increased (estimated percentages 39, 40, 41, 46 and 48 for observed radon concentrations of <100, 100–199, 200–399, 400–799, and ≥800 Bq/m³, respectively; P for trend 0.001). The odds ratio of being a current cigarette smoker correspondingly decreased with the increasing observed radon concentration (P=0.01), while, for ex-smokers, there was no clear trend (table 8).

Effect of confounding factors on the estimated risk associated with radon

Without any allowance for confounding factors, β, the excess relative risk of lung cancer per 100 Bq/m³ increase in the TWA observed radon concentration was estimated to be slightly, but not significantly, negative

Table 8. Percentage of controls estimated to be lifelong nonsmokers (or ex-smokers or current cigarette smokers) by observed radon concentration.

Observed radon concentration (Bq/m^3)	Lifelong nonsmoker[a] (%)	Ex-smoker[a] (%)	Current cigarette smoker[a] (%)
<100	39	22	39
100–199	40	22	37
200–399	41	23	35
400–799	46	23	31
≥800	48	17	34
P for trend[b]	0.001	0.24	0.01

[a] Calculation performed separately for each category of smoking status by considering controls in that smoking category versus controls in all other smoking categories combined. The percentages were then derived by first estimating odds ratios using logistic regression with stratification for study, sex, age, and current region of residence within the study and then setting the percentage of controls with an observed radon concentration of <100 Bq/m^3 equal to that observed.

[b] Significance of trends calculated using a likelihood ratio test, based on individual values of the observed radon concentration.

at −0.005 (X^2 = 0.36. P=0.55, see table 9, stratification 1). The five factors "study", "age", "sex", "region of current residence within each study", and "smoking history" were considered a priori to be likely confounders of the relationship between radon concentration and lung cancer and, when these factors were taken into account through stratification, the estimate of β changed to +0.052 and was significantly positive (X^2 = 6.82, P=0.009, see table 9, stratification 2).

To evaluate whether any of the variables included in this initial stratification could be omitted, the analysis was repeated omitting each of them in turn. Only when sex was omitted from the stratification did the estimate of β remain essentially unchanged, while, when age was omitted, the estimated value of β increased by 13%. For the variables "study", "region", and "smoking", their removal from the stratification resulted in a change in the value of β of at least 50%, indicating the presence of substantial confounding (table 9, stratification 3).

In addition to the variables included in the a priori stratification, information was available on social status, occupational risk, home occupancy, and urban–rural status. To assess whether any of them had a confounding effect on the relationship between radon and lung cancer, each of them was added in turn to the a priori stratification. The estimated value of β did not change at all when home occupancy was included, but it changed by 5% when urban–rural status was included (table 9, stratification 4). These variables were therefore not considered further as potential confounders. The inclusion of social status decreased the estimate of β by 9%, and the inclusion of employment in an occupation with an established lung cancer risk decreased it by 11%. These two variables were considered again, after a more-detailed examination of the effect of stratification for smoking, and additional details of this examination are described in subsequent paragraphs.

To determine whether it was better to account for the confounding from the a priori stratification variables by including them in the model rather than by stratification, the analysis was repeated omitting each variable from the stratification in turn and including categorical covariates representing its main effect in the model. Once again, only for sex did the estimate of β remain essentially unchanged, while, when each of the variables "study", "age", "region", and "smoking" was omitted in turn, the estimate of β changed appreciably, increasing by 49%, 7%, 40%, and 12%, respectively (table 9, stratification 5). In none of these models did the inclusion of the variable as a main effect in the model rather than by stratification result in an appreciable reduction in the standard error of β. These results indicate that, in order to take the confounding effects of these variables adequately into account by including them in the model, it would not only be necessary to include the main effects, but also a considerable number of interaction terms. In addition, there was no material loss of information about the relationship between radon and lung cancer risk when the variables were included as stratifying variables rather than directly as main effects in the model, as measured by the standard error of β. It was therefore considered preferable to use stratification rather than explicit modeling to take into account these variables.

In the a priori stratification, the following seven categories of smoking were considered: never-smokers, current cigarette smokers of <15, 15–24, and ≥25 cigarettes per day, ex-smokers of <10 years and ≥10 years duration, and other (ie, occasional smokers and current smokers of cigars or a pipe only). Additional analyses were carried out to determine whether confounding by smoking status could be adequately controlled with fewer categories for the current and ex-smokers or, alternatively, whether additional categories were needed. First, the number of smoking categories was reduced either by combining all of the current cigarette smokers into one group or by combining all of the ex-smokers into one group. These changes caused the estimated value of β to change by 10% and 18%, respectively (table 9, stratification 6a); this finding indicates that subdivision according to these attributes was desirable. Second, the number of smoking categories was increased either by increasing the number of amount-smoked categories among current smokers from 4 to 7 or by increasing the number of categories of duration since stopping among ex-smokers from 2 to 6. Both of these changes had a negligible effect on the estimate of β, indicating that additional subdivision of these particular aspects of smoking history was unnecessary (table 9, stratification 6b).

Table 9. Derivation of the stratification scheme used in the analysis. (SE = standard error, 95% CI = 95% confidence interval, β = the excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average observed radon concentration)

Stratification	Estimate of β	Ratio of β to β for a priori stratification	SE of β	95% CI for β	Likelihood ratio chi-squared for test of β=0 (1 df)
1. None	-0.005	–	0.009	-0.017–0.013	0.36
2. Strata selected a priori (study, age (5-year groups), sex, region, smoking [7 groups: never-smokers, current cigarette smokers (<15, 15–24, ≥25 per day), ex-smokers (<10, ≥10years), others])	0.052	1.00	0.026	0.011–0.107	6.82
3. Omitting each variable in turn from the a priori stratification					
Study	-0.014	-0.28	0.009	-0.021– -0.001	3.16
Age	0.059	1.13	0.024	0.018–0.111	9.51
Sex	0.052	1.00	0.025	0.011–0.106	6.97
Region	0.080	1.55	0.026	0.036–0.136	17.28
Smoking	0.023	0.45	0.017	-0.005–0.061	0.64
4. Adding extra variables to the a priori stratification					
Social status (3 groups)	0.047	0.91	0.026	0.006–0.104	5.45
Occupational risk (3 groups)	0.046	0.89	0.025	0.006–0.102	5.34
Home occupancy (2 groups)	0.052	1.00	0.027	0.009–0.110	6.21
Urban–rural status (2 groups)	0.054	1.05	0.027	0.011–0.114	6.77
5. Removing each variable in turn from the a priori stratification and including its main effect as a categorical covariate in the model					
Study	0.077	1.49	0.025	0.035–0.130	17.73
Age	0.055	1.07	0.024	0.015–0.107	8.52
Sex	0.050	0.97	0.025	0.010–0.105	6.64
Region	0.072	1.40	0.025	0.030–0.127	14.56
Smoking	0.058	1.12	0.024	0.018–0.110	5.83
6. Sensitivity analysis of different aspects of smoking history					
a. Reducing the number of smoking categories in the stratification					
5 groups: (never–current–ex × 2–other)	0.057	1.10	0.025	0.016–0.112	8.51
6 groups: (never–current × 3–ex–other)	0.042	0.82	0.024	0.004–0.094	4.98
b. Increasing the number of smoking categories in the stratification [a]					
(i) Current cigarette smokers: 7 amount-smoked groups (<8, 8–12, 13–17, 18–22, 23–27, 28–31, ≥32 per day)	0.052	1.00	0.026	0.010–0.109	6.56
(ii) Ex-smokers: 6 groups (<5, 5–9, 10–14, 15–19, 20–24, ≥25 years since stopping)	0.051	0.99	0.027	0.009–0.109	6.21
c. Considering age at start of smoking for current and ex-smokers and amount smoked for ex-smokers [a]					
(i) Current cigarette smokers: 12 groups (<15, 15–17, 18–20, ≥21 years of age when started within each amount-smoked group)	0.058	1.12	0.028	0.013–0.119	7.33
(ii) Ex-smokers: 8 groups (<15, 15–17, 18–20, ≥21 years of age when started within each group of ex-smokers)	0.053	1.02	0.027	0.010–0.111	6.41
(iii) Ex-smokers: 6 groups (<15, 15–24, ≥25 cigarette per day for each group of ex-smokers)	0.070	1.35	0.029	0.022–0.134	9.90
d. Varying number of groups when stratifying for age when started smoking for current smokers and amount smoked for ex-smokers [a]					
Age started: 6 groups	0.055	1.06	0.027	0.012–0.114	7.00
Age started: 12 groups, as in 6c above	0.058	1.12	0.028	0.013–0.119	7.33
Age started: 18 groups	0.050	0.96	0.027	0.007–0.109	5.64
Amount smoked: 4 groups	0.062	1.19	0.028	0.017–0.121	8.81
Amount smoked: 6 groups, as in 6c above	0.070	1.35	0.029	0.022–0.134	9.90
Amount smoked: 14 groups	0.070	1.36	0.030	0.022–0.136	9.77
e. Effect of including age started among current smokers and amount smoked among ex-smokers as effects in the model rather than as additional strata [a]					
(i) Current smokers: 12 age-started groups, 4 within each cigarettes/day group	0.052	0.61 [b]	0.026	0.011–0.107	6.78
(ii) Ex-smokers: 6 amount-smoked groups, 3 within each years since stopped group	0.055	0.64 [b]	0.026	0.012–0.112	7.21
(i) and (ii) simultaneously	0.054	0.64 [b]	0.026	0.012–0.112	6.11
7. Final stratification: as strata selected a priori and given above, but sub-dividing current smokers by age started (<15, 15–17, 18–20, ≥21 years) separately for smokers of <15, 15-24, and ≥25 cigarettes/day, and sub-dividing ex-smokers by amount smoked (<15, 15–24, ≥25 cigarettes/day) separately for smokers of <10 and ≥10 years' duration	0.084	1.63	0.033	0.030–0.158	11.57

[a] Any persons for whom the additional information needed for this stratification was unavailable were allocated to separate groups within each of their original number-per-day or years-since-stopped categories.
[b] Ratio of β to β for final stratification in stratification 7.

The effect of the age when a person started to smoke was then considered. First, among the current cigarette smokers, each of the three categories of current smokers was subdivided by age at the time smoking was started into four categories. This change increased the estimate of β by 12%, indicating that subdivision by age at the start of smoking was appropriate for current smokers (table 9, stratification 6c). In contrast, when each of the two duration-since-stopping categories was subdivided into four categories according to age when smoking was started, the estimate of β changed by only 2%, indicating that it was unnecessary to take age at the start of smoking into account for ex-smokers. However, when each of the two duration-since-stopping categories was subdivided into three categories according to the average number of cigarettes smoked per day, the estimated value of β increased by 35%, indicating that it was desirable to take this aspect of smoking history into account for the ex-smokers.

Further investigation of the confounding effects of age at the start of smoking among the current smokers and of the amount smoked among ex-smokers was carried out in the form of a sensitivity analysis of the number of groups necessary when these two aspects of smoking history were both considered and also by including them as main effects in the model, rather than as additional strata. The results of this analysis indicated that there was little to be gained by increasing the number of groups (table 9, stratification 6d) and also that considerable confounding remained if fewer groups were included in the stratification for these attributes (table 9, stratification 6d) or if they were included as main effects in the model, rather than through stratification (table 9, stratification 6e).

The results of the smoking sensitivity analysis suggested that it is appropriate to control for smoking history by stratification into 20 main groups: never-smokers, current cigarette smokers in 12 groups (ie, subdivided according to whether the subjects smoked <15, 15–24, or ≥25 cigarettes per day and according to whether they started to smoke when aged <15, 15–17, 18–20 or ≥21 years within each amount-smoked-per-day group), ex-smokers in six groups (ie, subdivided according to whether the subjects stopped <10 or ≥10 years prior to the index date and according to whether they smoked <15, 15–24, or ≥25 cigarettes per day when they were smokers within each years-since-stopped group), and others (ie, occasional smokers and smokers of a pipe, cigars or cigarillos only but not of cigarettes). The few current smokers for whom age at the start of smoking was unknown (appendix B, table B9) were allocated to additional groups within the three amount-smoked-per-day groups, and the few ex-smokers for whom the number of cigarettes per day was unknown (appendix B, table B11) were allocated to additional groups within each of the two years-since-stopping groups.

To see whether the inclusion of social status or employment in an occupation with an established lung cancer risk made any appreciable difference with the finer stratification for smoking, the analysis was repeated with additional stratification on each of these variables in turn. The addition of social status did not change the estimate of β, while the addition of occupational risk reduced it by only 2%.

It was therefore concluded that it was appropriate to control for the effects of confounding by stratification for study, age in 5-year groups, sex, region of current residence, and smoking history in 20 main groups, as described earlier. With the stratification carried out in this way, it was estimated that β, the excess relative risk per 100 Bq/m^3 TWA observed residential radon concentration was 0.084 (95% CI 0.030–0.158) (see table 9, stratification 7). This value differed highly significantly from zero [X^2 on 1 degree of freedom (df)=11.57, P=0.0007]. All of the subsequent analyses were based on this stratification unless otherwise indicated.

Homogeneity of studies, influence of each study and effect of the study design

The estimated value of β inevitably varied somewhat between the individual studies (table 10), but there was no evidence that the effect of radon differed between the studies (X^2 on 12 df=5.48, P=0.94). Furthermore, the overall result was not strongly influenced by any individual study. When the analysis was repeated omitting each study in turn, the estimated value of β changed by <10% for 11 of the 13 studies. Two studies caused the estimate of β to change by >10% when they were omitted. These were the Germany eastern study, whose omission decreased the estimated value of β by 11%, and the Finland nationwide study, whose omission increased the estimated value of β by 21% (table 11).

Although all of the studies had broadly the same design, detailed aspects of the design differed somewhat between the studies. Therefore, a series of analyses was carried out to see if the estimated effect of radon differed according to study design (table 12). There were no significant differences in the estimated effect of radon according to whether clinical information was used in the ascertainment of the lung cancer cases when compared with studies in which ascertainment was made using death certificates only (X^2=0.79, 1 df, P=0.37) or according to whether the study included hospital controls (X^2=0.04, 1 df, P=0.84). Similarly, there were no significant differences in the estimated effect of radon according to whether or not surrogate interviews were accepted (X^2=0.01, 1 df, P=0.93) or whether the radon

Table 10. Estimated linear relationship between the relative risk of lung cancer and the observed residential radon concentration for each study and for all studies combined. (95% CI = 95% confidence interval, β = the excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history)

Study	Estimate of β	95% CI for β
Austria	0.464	<- 0.046[a]–>5.000[b]
Czech Republic	0.187	- 0.003–2.073
Finland nationwide	0.032	<-0.031[a]–0.173
Finland southern	0.064	- 0.079–1.578
France	0.106	- 0.006–0.411
Germany eastern	0.178	- 0.002–0.563
Germany western	-0.025	<- 0.122[a]–0.393
Italy	0.099	- 0.178–1.397
Spain	<-0.106[b]	<- 0.106[a]–0.587
Sweden nationwide	0.114	- 0.043–0.460
Sweden never-smokers	0.237	- 0.075–0.946
Sweden Stockholm	0.121	- 0.135–1.413
United Kingdom	0.044	- 0.045–0.223
All studies [c]	0.084	0.030–0.158

[a] Values below these limits, but cannot be ascertained, as lower values of β lead to negative fitted values for the probability of lung cancer.
[b] The upper 95% confidence limit is greater than 5.00.
[c] Chi-squared for heterogeneity = 5.48, 12 df; P=0.94.

Table 11. Influence analysis showing the estimated linear relationship between the relative risk of lung cancer and the observed residential radon concentration when each study was omitted in turn. (β = increase in the relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history)

Study omitted	Estimate of β	95% CI for β
Austria	0.083	0.029–0.157
Czech Republic	0.077	0.020–0.153
Finland nationwide	0.102	0.036–0.194
Finland southern	0.085	0.029–0.160
France	0.081	0.022–0.160
Germany eastern	0.075	0.020–0.151
Germany western	0.089	0.032–0.166
Italy	0.084	0.029–0.159
Spain	0.088	0.032–0.163
Sweden nationwide	0.082	0.026–0.159
Sweden never-smokers	0.080	0.026–0.153
Sweden Stockholm	0.084	0.029–0.158
United Kingdom	0.093	0.032–0.180
All studies included	0.084	0.030–0.158

Table 12. Effect of study design on the estimate of β. (95% CI = 95% confidence interval; β = excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; df = degrees of freedom)

Study design	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test for heterogeneity of β		
					Chi-squared	df	P-value
Ascertainment of cases							
Clinical information used	6794	13 307	0.075	0.019–0.151	0.79	1	0.37
Death certificates only	354	901	0.214	0.004–2.757			
Ascertainment of controls							
Hospital controls used	2111	5115	0.076	- 0.001–0.206	0.04	1	0.84
Population controls only	5037	9093	0.090	0.022–0.188			
Method of interview							
Surrogates accepted	2769	5431	0.082	0.009–0.193	0.01	1	0.93
No surrogates used	4379	8777	0.087	0.014–0.197			
Type of detector							
Closed	6406	12286	0.071	0.010–0.153	0.52	1	0.47
Open	742	1922	0.131	0.018–0.393			
Coverage by study of target population							
≥80%	1025	2071	0.133	0.008–0.378	0.39	1	0.53
72–79%	1131	3839	0.084	- 0.004–0.245			
56–71%	1660	3013	0.075	- 0.041–0.308			
<56%	3332	5285	0.066	- 0.009–0.187			

detectors used were open or closed (X^2=0.52, 1 df, P=0.47). Finally, there were no significant differences in the estimated effect of radon according to the extent to which the studies had managed to cover their target populations (X^2=0.39, 1 df, P=0.53).

Effect modification according to the characteristics of the radon measurements

Both the mean and the standard deviation of the measured radon concentrations varied substantially between the different geographic regions in which the cases and controls lived. However, when the cases and controls were subdivided into five groups according to the mean radon concentration typical of their region, as determined by the mean measured radon concentration for the residences of controls in that region, there was no evidence of heterogeneity in the relationship between the observed residential radon concentration and lung cancer risk (X^2=0.90, 4 df, P=0.93) (table 13). Similarly, when the cases and controls were grouped according to the standard deviation of the measured radon concentration for the residences of the controls in their region, there was no evidence of heterogeneity in the effect of radon (X^2=3.06, 4 df, P=0.55).

The cases and controls included in the Collaborative Analysis also varied substantially according to the number of residences in which radon measurements had been made and the number of years during the 30-year period of interest for which radon measurements were available. However, when they were subdivided into four or five groups according to either of these characteristics alone or according to a combination of these characteristics, there was no evidence of any heterogeneity in the effect of radon (X^2=3.49, 3 df, P=0.32; X^2=3.23, 4 df, P=0.52; X^2=1.30, 3 df, P=0.73) (table 13). In view of these results, subsequent analyses did not subdivide the cases and controls according to any of these characteristics.

Effect of different measures of the observed radon concentration and of different models for the relationship between radon concentration and lung cancer

In the results presented in the preceding section, a person's radon exposure was taken to be the average observed radon concentration in the 30-year period ending 5 years prior to the index date with the contribution from each year weighted equally (ie, the contribution from each address weighted according to the length of time that the person lived there during the 30-year period). When only the 10-year period ending 5 years prior to the index date was considered, the estimated value of β was 0.075 (95% CI 0.027–0.138) (table 14), and,

Table 13. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to characteristics of the radon measurements. (β = excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval; df = degrees of freedom)

Characteristic of the radon measurements	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test for heterogeneity of β		
					Chi-squared	df	P-value
Regional radon concentration, as determined by mean measurements for controls							
<50 Bq/m^3	1363	3494	0.026	<-0.101–0.340	0.90	4	0.93
50–74 Bq/m^3	2123	3678	0.140	0.003–0.372			
75–99 Bq/m^3	1045	2126	0.112	-0.021–0.350			
100–119 Bq/m^3	1437	2327	0.063	-0.025–0.215			
≥120 Bq/m^3	1180	2583	0.075	0.003–0.212			
Variation in regional radon concentration, as determined by standard deviation of measurements for controls (Bq/m^3)							
<45 Bq/m^3	1748	2955	0.286	0.022–0.748	3.06	4	0.55
45–54 Bq/m^3	892	2867	0.031	<-0.101–0.338			
55–84 Bq/m^3	1438	2317	0.154	0.002–0.430			
85–119 Bq/m^3	1272	2425	0.059	-0.036–0.245			
≥120 Bq/m^3	1798	3644	0.063	0.005–0.157			
Number of residences with radon measurements							
1	4981	9239	0.070	0.015–0.147	3.49	3	0.32
2	1109	2554	0.208	0.060–0.447			
3	625	1350	0.027	<-0.082–0.266			
≥4	433	1065	0.038	<-0.085–0.515			
Number of years with radon measurements							
<15 years	1260	2284	-0.051	-0.126–0.143	3.23	4	0.52
15–19 years	745	1454	0.170	-0.056–0.669			
20–24 years	1023	1956	0.136	-0.010–0.409			
25–29 years	1383	2697	0.072	-0.015–0.216			
30 years	2737	5817	0.080	0.019–0.169			
Number of residences measured x number of years measured							
<3 residences, <20 years	1869	3422	0.019	<-0.069–0.238	1.30	3	0.73
<3 residences, ≥20 years	4221	8371	0.094	0.034–0.175			
≥3 residences, <20 years	136	316	0.013	-0.300–1.041			
≥3 residences, ≥20 years	922	2099	0.021	<-0.082–0.229			

Table 14. Effect of different measures of observed residential radon concentration on the estimate of β. (95% CI = 95% confidence interval; β = excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; df = degrees of freedom)

Measure of observed residential radon concentration	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test for $\beta = 0$		
					Chi-squared	df	P-value
Time-weighted average							
5–34 years [a]	7148	14 208	0.084	0.030–0.158	11.57	1	0.0007
Only 5–14 years (ie, recent past)	7148	14 208	0.075	0.027–0.138	11.54	1	0.0007
Only 15–24 years	7148	14 208	0.076	0.027–0.140	11.64	1	0.0006
Only 25–34 years (ie, distant past)	7148	14 208	0.066	0.016–0.135	7.84	1	0.005
BEIR VI weighting [b]	7148	14 208	0.084	0.030–0.156	11.89	1	0.0006

[a] Observed radon concentration for each address in 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there, with each year receiving equal weight.
[b] Periods 5–14, 15–25, 25–34 years before the index date weighted in proportions 1.0 : 0.75 : 0.50.

Table 15. Comparison of different models for the relationship between the time-weighted average observed radon concentration and the risk of lung cancer. (RR = relative risk, df = degrees of freedom)

Model for radon	Deviance at maximum likelihood estimate	Fitted parameters (N)	Likelihood ratio chi-squared for test of $\beta = 0$	Estimated risk versus 0 Bq/m³ at:			
				100 Bq/m³	200 Bq/m³	500 Bq/m³	1000 Bq/m³
1. Linear: $RR=1+\beta x$	12 562.27	1	11.57[a]	1.084	1.169	1.422	1.844
2. Linear-quadratic: $RR=1+\beta_1 x+\beta_2 x^2$	12 561.81	2	12.03[b]	1.065	1.134	1.375	1.879
3. Log-linear: $RR=\exp(\beta x)$	12 561.55	1	12.28[a]	1.064	1.132	1.364	1.861

[a] Test of $\beta = 0$ (1 df).
[b] Test of $\beta_1 = 0$ and $\beta_2 = 0$ (2 df).

when only the 10-year periods ending 15 and 25 years prior to the index date were considered, the estimated values of β were 0.076 (95% CI 0.027–0.140) and 0.066 (95% CI 0.016–0.135), respectively. If radon exposures throughout the 30-year period were considered, but the contributions from periods 5–14, 15–24, and 25–34 years before the index date weighted in the proportions 1.0 : 0.75 : 0.50, as in the BEIR VI Committee's preferred models of the effect of occupational exposure to radon among underground miners, the estimated value of β was 0.084, identical to the value obtained when all three periods were given equal weight.

The results presented in the preceding section all assumed that the relative risk (RR) of lung cancer increases linearly with radon concentration, taking the form $RR=1+\beta x$. When this model was extended to allow a quadratic relationship (ie, to take the form $RR=1+\beta_1 x+\beta_2 x^2$), there was no significant improvement in the fit, with deviance taking the value of 12 561.81 in comparison with 12 562.27 (corresponding to $X^2=0.46$, 1 df, $P=0.50$) (table 15). When a log-linear relationship between lung cancer and radon concentration was assumed [ie, $RR=\exp(\beta x)$], the fit was also very similar, with deviance=12 561.55. In addition to providing equally good fits to the data, the predicted RR values corresponding to these three models were also very close throughout the range of 0 to 1000 Bq/m³ (table 15 and figure 1), with the maximum absolute difference occurring at

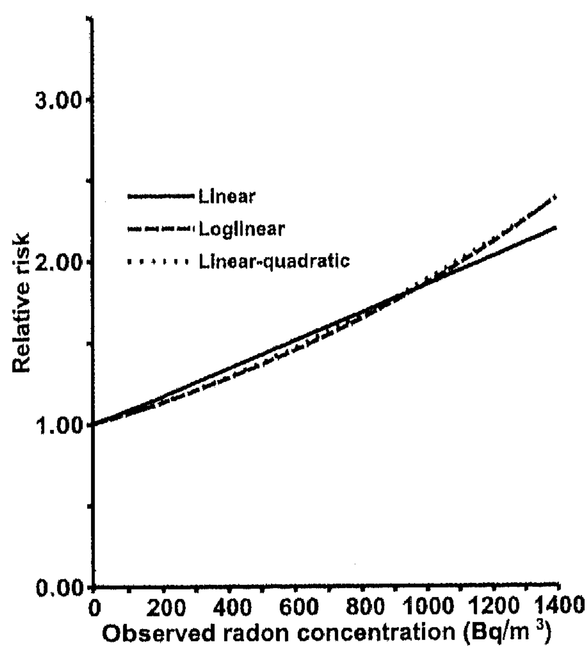

Figure 1. Comparison of different models for the relationship between the observed radon concentration and the risk of lung cancer. The equations for the fitted models are: linear $RR = 1 + 0.000844\ X$, log-linear: $RR = \exp(0.000621\ X)$, and linear-quadratic: $RR = 1 + 0.000622\ X + 0.000000258\ X^2$.

495 Bq/m³, where the fitted value from the log-linear model was 1.360, compared with 1.418 for the linear model. Estimated values of β for the individual studies, based on a log-linear relationship between lung cancer and radon concentration, and an influence analysis, showing the effect of omitting each study in turn, assuming a log-linear relationship, are given in appendix D, tables D3 and D4. All of the other presented results that used a continuous measure of radon exposure were based on the linear model.

Table 16. Relative risk of lung cancer according to the categories of the time-weighted average observed residential radon concentration. (95% CI = 95% confidence interval)

Observed radon concentration[a]	Cases (N)	Controls (N)	Mean observed radon concentration	Relative risk[b]	95% CI[c]
<25 Bq/m³	566	1 474	17	1.00	0.87–1.15
25–49 Bq/m³	1999	3 905	39	1.06	0.98–1.15
50–99 Bq/m³	2618	5 033	71	1.03	0.96–1.10
100–199 Bq/m³	1296	2 247	136	1.20	1.08–1.32
200–399 Bq/m³	434	936	273	1.18	0.99–1.42
400–799 Bq/m³	169	498	542	1.43	1.06–1.92
≥800 Bq/m³	66	115	1204	2.02	1.24–3.31
Total	7148	14 208			

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Relative risks calculated after stratification by study, age, sex, region of residence, and smoking history. Risks scaled so that relative risk is 1.00 at 0 Bq/m³ on the assumption of a linear relationship, see the Statistical Methods section for details.
[c] Confidence intervals calculated using the method of floated variances.

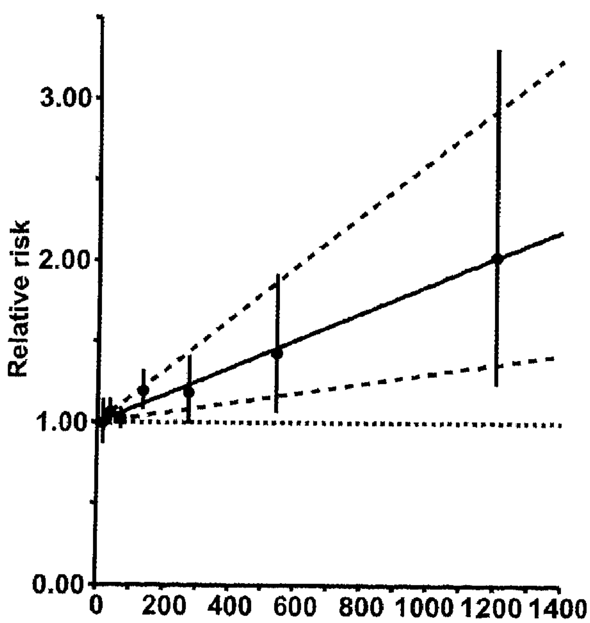

Figure 2. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration after stratification by study, age, sex, region of residence, and smoking habits. The relative risks and 95% confidence intervals are shown for the categories <25, 25–49, 50–99, 100–199, 200–399, 400–799 and ≥800 Bq/m³, as is the estimated linear relationship RR=1 + 0.00084 X (solid line), with 95% confidence limits (dashed lines). The relative risk is equal to 1 at 0 Bq/m³.

Relative risk of lung cancer according to categories of observed residential radon concentration, a further test of linearity, the significance of the dose–response relationship excluding high radon concentrations, and a confidence interval for a possible threshold radon concentration

When the cases and controls were subdivided according to categories of TWA observed radon concentration, the relative risk compared with 0 Bq/m³ in categories <25, 25–49, 50–99, 100–199, 200–399, 400–799, and ≥800 Bq/m³ were 1.00 (95% CI 0.87–1.15), 1.06 (95% CI 0.98–1.15), 1.03 (95% CI 0.96–1.10), 1.20 (95% CI 1.08–1.32), 1.18 (95% CI 0.99–1.42), 1.43 (95% CI 1.06–1.92), and 2.02 (95% CI 1.24–3.31), respectively (table 16). These estimated risks are consistent with the results of the analysis to that considered radon concentration as a continuous variable (figure 2). An analysis based on an alternative set of categories was requested at the outset of the study by the German collaborators, and the results are given in appendix D, table D10 and figure D2. The analysis given in figure 2, but for each individual study, is presented in figure D1.

As a further test of the evidence for any nonlinearity in the dose–response relationship, the fit of the linear model RR=1+βx was compared with the fit of a model that also included categorical terms in the radon concentration for the categories listed in table 16. These additional terms provided no significant improvement in fit (X^2=4.00, 6 df, P=0.68).

To examine the extent to which the evidence in favor of a dose–response relationship between radon and lung cancer was dependent on the cases and controls with high TWA observed radon concentrations, the model RR=1+βx was fitted after the exclusion of cases and controls with observed radon concentrations of ≥800 Bq/m³, ≥400 Bq/m³, ≥200 Bq/m³, ≥150 Bq/m³, ≥100 Bq/m³, and ≥50 Bq/m³ in turn. There were statistically significant dose–response relationships when the radon concentrations in the ranges of 0–800 Bq/m³, 0–400 Bq/m³, and 0–200 Bq/m³ were considered (P=0.02, P=0.04, and P=0.04, respectively), with estimated values of 0.078 (95% CI 0.012–0.164), 0.095 (95% CI 0.005–0.206), and 0.140 (95% CI 0.004–0.309), respectively, for β (table 17). Models that allowed for a possible threshold concentration did not

Table 17. Estimated linear relationship between the relative risk of lung cancer and the observed residential radon for persons with observed radon concentrations in specific ranges. (β = excess of the relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval; df = degrees of freedom)

Range of the observed radon concentrations	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test of β=0		
					Chi-squared	df	P-value
<800 Bq/m³ only	7082	14 093	0.078	0.012–0.164	5.59	1	0.02
<400 Bq/m³ only	6913	13 595	0.095	0.005–0.206	4.34	1	0.04
<200 Bq/m³ only	6479	12 659	0.140	0.004–0.309	4.12	1	0.04
<100 Bq/m³ only	5183	10 412	0.025	- 0.192–0.306	0.04	1	0.84
All values	7148	14 208	0.084	0.030–0.158	11.57	1	0.0007

Table 18. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to characteristics of the cases and controls. (β = excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval; df = degrees of freedom)

Characteristic [a]	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test for heterogeneity or trend [a]		
					Chi-squared	df	P-value
Age							
<45 years	222	588	-0.111	<- 0.157–0.350	0.001	1	0.98
45–54 years	878	1994	-0.015	<- 0.070–0.439			
55–64 years	2506	4818	0.136	0.030–0.311			
65–74 years	3051	5889	0.085	0.013–0.189			
≥75 years	491	919	-0.002	<- 0.078–0.278			
Sex							
Male	5521	10388	0.112	0.041–0.212	1.69	1	0.19
Female	1627	3820	0.025	- 0.038–0.144			
Smoking status							
Current cigarette smoker	3575	3322	0.070	- 0.014–0.217	0.17	3	0.98
Ex-smoker	2465	4930	0.082	0.003–0.211			
Lifelong nonsmoker	884	5418	0.106	0.003–0.280			
Other	224	538	0.077	- 0.029–0.562			
Social status							
Higher	943	2687	0.167	- 0.003–0.461	0.10	1	0.75
Intermediate	1783	4130	0.054	- 0.039–0.209			
Lower	3147	4968	0.093	0.011–0.225			
Unknown	1275	2423	0.077	- 0.002–0.216			
Employment in an occupation known to be associated with an increased risk of lung cancer							
None	5106	10511	0.080	0.019–0.165	0.15	1	0.70
Some	1675	2609	0.051	- 0.034–0.224			
Unknown	367	1088	0.167	0.001–0.864			
Proportion of time spent at home							
<50%	1087	1804	0.010	<- 0.031–0.188	0.64	1	0.42
50–74%	4052	7567	0.073	0.005–0.180			
≥75%	951	2471	0.093	- 0.005–0.263			
Unknown	1058	2366	0.162	0.021–0.464			
Residence in urban or rural area							
All rural	4153	8711	0.127	0.050–0.236	6.76	1	0.01
Some urban	2114	4062	-0.070	<-0.070–0.060			
Unknown	881	1435	0.032	<-0.031–0.174			
Position of bedroom window at night							
Open	2247	3519	0.010	- 0.032–0.130	4.64	1	0.03
Closed	1825	3427	0.304	0.100–0.641			
Unknown	3076	7262	0.072	0.010–0.162			

[a] For each characteristic, persons with unknown values for that characteristic were omitted from the likelihood ratio test.

provide a significant improvement in fit when compared with a model in which the risk was proportional to the concentration, even for very low concentrations (P=0.44), and the estimated upper 95% confidence limit for a possible threshold was 150 Bq/m³.

Table 19. Relative risk of lung cancer according to categories of observed residential radon concentration calculated separately for current cigarette smokers, ex-smokers, and lifelong nonsmokers. (95% CI = 95% confidence interval)

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration (Bq/m³)	Relative risk [b]	95% CI [c]
Current cigarette smokers					
<25 Bq/m³	281	335	17	0.92	0.72–1.19
25–49 Bq/m³	975	808	39	1.00	0.86–1.17
50–99 Bq/m³	1304	1071	72	1.05	0.93–1.19
100–199 Bq/m³	654	595	136	1.24	1.03–1.51
200–399 Bq/m³	234	294	275	1.19	0.86–1.64
≥400 Bq/m³	127	219	652	1.48	0.92–2.35
Total	3575	3322	115	–	–
Ex-smokers					
<25 Bq/m³	198	621	18	0.94	0.75–1.18
25–49 Bq/m³	750	1515	38	1.10	0.97–1.24
50–99 Bq/m³	898	1734	70	1.03	0.92–1.15
100–199 Bq/m³	431	680	135	1.18	0.99–1.41
200–399 Bq/m³	127	251	266	1.08	0.78–1.49
≥400 Bq/m³	61	129	689	1.45	0.86–2.42
Total	2465	4930	90	–	–
Lifelong nonsmokers					
<25 Bq/m³	56	467	17	1.06	0.78–1.45
25–49 Bq/m³	222	1443	38	1.07	0.90–1.26
50–99 Bq/m³	332	2023	71	1.02	0.90–1.16
100–199 Bq/m³	170	866	135	1.23	1.02–1.48
200–399 Bq/m³	63	362	278	1.37	1.00–1.90
≥400 Bq/m³	41	257	711	1.72	1.04–2.88
Total	884	5418	113	–	–

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Relative risks estimated separately within each smoking category after stratification by study, age, sex, region of residence, and, for current and ex-smokers, detailed smoking history. The baseline within each smoking category was 0 Bq/m³ on the assumption of a linear relationship.
[c] Estimated using the method of floated variances.

Effect modification according to the characteristics of the cases and controls

There was no evidence that the effect of the observed residential radon concentration on lung cancer risk differed according to attained age (X^2=0.001, 1 df, P=0.98), sex (X^2=1.69, 1 df, P=0.19), or smoking status (X^2=0.17, 3 df, P=0.98) (table 18 on page 27). When the relative risk of lung cancer according to categories of residential radon concentration was examined separately for current cigarette smokers, ex-smokers, and lifelong nonsmokers, a similar pattern was found for each of the three groups, and, within each of the three groups, the pattern was consistent with that seen for all of the cases and controls combined (table 19 and figure 3). When the effect of smoking was considered separately for six smoking categories for the men (lifelong nonsmokers, current smokers of <15, 15–24, and ≥25 cigarettes per day, and ex-smokers of <10 and ≥10 years' duration) and also for the same six smoking categories for the women, an additive interaction between smoking and radon was rejected (X^2=19.89, 11 df, P=0.05).

When the cases and controls were subdivided according to social status, employment in an occupation known to be associated with an increased risk of lung cancer, or proportion of time spent at home, there was no evidence of any variation in the effect of residential radon on lung cancer risk (X^2=0.10, 1 df, P=0.75; X^2=0.15, 1 df, P=0.70; and X^2=0.64, 1 df; P=0.42, respectively) (table 18). When the men and women were considered separately, there was still no evidence of variation in the effect of radon with the proportion of time spent at home (men: X^2=2.18, 1 df, P=0.14; women: X^2=0.17, 1 df, P=0.68). In contrast, there was some

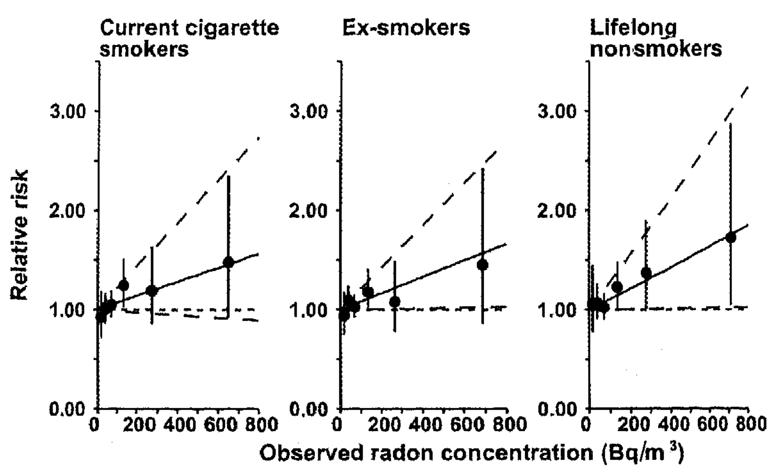

Figure 3. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration by smoking status. The relative risks and 95% floated confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) and 95% confidence intervals (dashed lines). The risks were calculated after stratification by study, age, sex, region of residence and, for current and ex-smokers, detailed smoking history. The relative risks are equal to 1 at 0 Bq/m³.

evidence that the effect of radon concentration on lung cancer risk differed according to whether the cases and controls had lived in an urban area for part of the 30-year period of interest (X^2=6.76, 1 df, P=0.01), with clear evidence of a positive effect among the cases and controls who had lived in a rural area for all 30 years (estimate of β = 0.127, 95% CI 0.050–0.236), while, for those who had lived for some of the 30-year period in an urban area, the estimated effect was negative (estimate of β = -0.070, 95% CI <0.070–0.060). There was also evidence that the effect of radon concentration on lung cancer risk differed according to the position of the bedroom window at night (X^2=4.64, 1 df, P=0.03), with a greater effect for those who slept with their bedroom window closed (estimate of β = 0.304, 95% CI 0.100–0.641) than for those who slept with it open (estimate of β =0.010, 95% CI -0.032–0.130). The position of the bedroom window at night was first suggested as an effect modifier of residential radon by the Sweden nationwide study (18), and, when the analysis was repeated excluding this study, it was no longer a significant effect modifier (X^2=1.47, 1 df, P=0.23) although the estimated effect of radon on lung cancer risk remained higher for those who slept with the window closed than for those who slept with it open (table 20). When the analyses of residence in an urban or a rural area and of the position of the bedroom window at night were repeated with only the cases and controls for whom both characteristics were known, the results were similar to those shown in table 18 (table 20). However, when both characteristics were considered simultaneously, the modifying effect of residence in an urban or a rural area remained significant (X^2=5.46, 1 df, P=0.02), while the effect of the position of the bedroom window at night was no longer so (X^2=0.73, 1 df, P=0.39) (table 20). When the analysis of the modifying effect of residence in an urban or a rural area on the effect of residential radon was repeated separately for each study, no consistent effect was found. The effect was positive in six studies (France, Germany eastern, Germany western, Italy, Spain, Sweden never-smokers), while it was negative in four studies (Czech Republic, Sweden nationwide, Sweden Stockholm, United Kingdom) and could not be estimated in the remaining studies, either because data were not available or because it could not be distinguished from the stratification variables. Among the 10 studies in which an effect could be estimated, there was evidence of heterogeneity (X^2=23.77, 10 df, P=0.008). The cases and controls known to have lived in a rural area for all 30 years of interest had spent similar proportions of time at home when compared with those who had lived for some time in an urban area (all rural: 54% of the persons spent 50–74% and 17% spent >75% of the time at home; some urban: 56% of the persons spent 50–74% and 18% spent >75% of the time at home). The mean number of residences with radon measurements and the mean number of years with radon measurements were similar in the two groups (all rural: 1.6 residences, 23.6 years; some urban: 1.8 residences, 21.7 years). However, those who

Table 20. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to residence in an urban or rural area and the position of the bedroom window at night. (β = the excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval; df = degrees of freedom)

Characteristic	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Likelihood ratio test for difference [a]		
					Chi-squared	df	P-value
1. Position of bedroom window at night—omitting data from Sweden nationwide study							
Open	1988	2922	0.055	- 0.027–0.248	1.47	1	0.23
Closed	1245	2221	0.281	0.057–0.701			
Unknown	2956	7020	–	–			
2. Characteristics fitted separately, but including only persons for whom both characteristics known							
Residence in urban or rural area							
All rural	2742	4788	0.207	0.071–0.423	9.97	1	0.00
Some urban	1330	2158	-0.071	< -0.071– -0.013			
Position of bedroom window at night							
Open	2247	3519	0.032	-0.029–0.183	4.64	1	0.03
Closed	1825	3427	0.292	0.091–0.632			
At least one characteristic unknown	3076	7262	–	–			
3. Characteristics fitted simultaneously, but including only persons for whom both characteristics known							
Residence all rural and window open	1402	2219	0.147	– [b]			
Change in β for some urban residence	845 [c]	1300 [c]	-0.234	– [b]	5.46	1	0.02
Change in β for window closed	1340 [d]	2569 [d]	0.067	– [b]	0.73	1	0.39

[a] For each test, persons with unknown values for that characteristic were omitted from the model.
[b] Numerical difficulties were experienced in the computation of the 95% confidence intervals.
[c] Numbers of persons with some urban residence and window open.
[d] Numbers of persons with all rural residence and window closed (485 cases and 858 controls had some urban residence and slept with the window closed).

had lived in a rural area for the whole of the 30-year period of interest had considerably higher radon concentrations than those who had lived for part of the time in an urban area (the mean TWA observed radon concentration being 123 Bq/m^3 for all rural and 67 Bq/m^3 for some urban).

Effect modification among lifelong nonsmokers according to the characteristics of the cases and controls

There was a significant association between the observed residential radon concentration and lung cancer risk when lifelong nonsmokers were considered separately (estimate of $\beta = 0.106$, 95% CI 0.003–0.280; X^2=4.15, 1 df; P=0.04) (table 18 and figure 3). When the cases and controls who were lifelong nonsmokers were subdivided according to age, sex, the smoking status of spouse, social status, proportion of time spent at home, whether or not they had spent some of the 30-year period of interest living in an urban area, or the position of the bedroom window at night, there was no evidence of any variation in the effect of residential radon on lung cancer risk (table 21). In contrast, when lifelong nonsmokers were subdivided according to whether or not they had been employed in an occupation known to be associated with an increased risk of lung

Table 21. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to characteristics of the cases and controls among the lifelong nonsmokers. (β = the excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex and region of residence; 95% CI = 95% confidence interval; df = degrees of freedom)

Characteristic	Lifelong nonmokers				Likelihood ratio test for heterogeneity or trend [a]		
	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Chi-squared	df	P-value
Age							
<45 years	34	209	-0.329	<- 0.329–1.557	0.46	1	0.50
45–54 years	101	735	-0.008	<- 0.131–0.903			
55–64 years	262	1811	0.093	<- 0.031–0.458			
65–74 years	348	2189	0.155	<- 0.045–0.482			
≥75 years	139	474	0.071	<- 0.078–0.890			
Sex							
Male	268	2888	0.320	0.014–1.118	1.74	1	0.19
Female	616	2530	0.060	- 0.028–0.232			
Smoker as spouse							
Yes	389	1928	0.194	0.014–0.556	1.81	1	0.18
No	442	3225	0.044	- 0.036–0.209			
Unknown	53	265	>5.000	0.031–>5.000			
Social status							
Higher	179	1133	0.025	<- 0.101–0.477	2.54	1	0.11
Intermediate	260	1675	-0.014	- 0.072–0.200			
Lower	297	1567	0.369	0.067–1.037			
Unknown	148	1043	0.105	<- 0.031–0.580			
Employment in an occupation known to be associated with an increased risk of lung cancer							
None	769	4353	0.032	<- 0.031–0.180	7.26	1	0.01
Some	51	589	2.859	0.272–>5.000			
Unknown	64	476	0.957	0.007–>5.000			
Proportion of time spent at home							
<50%	51	589	-0.009	<- 0.031–0.752	0.95	1	0.33
50–75%	345	2461	0.012	<- 0.046–0.235			
≥75%	144	1154	0.134	- 0.022–0.557			
Unknown	344	1214	0.313	0.029–0.953			
Residence in urban or rural area							
All rural	528	3394	0.121	0.004–0.336	0.99	1	0.32
Some urban	268	1364	0.382	- 0.022–1.526			
Unknown	88	660	-0.031	<- 0.031–0.247			
Position of bedroom window at night							
Open	167	1151	-0.085	<- 0.085–0.118	2.74	1	0.10
Closed	234	1396	0.216	- 0.011–0.767			
Unknown	483	2871	0.145	0.000–0.439			

[a] For each characteristic, persons with unknown values for that characteristic were omitted from the likelihood ratio test.

cancer, there was evidence of a difference in the effect of residential radon on lung cancer (X^2=7.26, 1 df, P=0.01), with a larger increase in the relative risk per unit radon concentration for the cases and controls who had been exposed to an occupational risk than for those who had not (estimates of β were 2.859, 95% CI 0.272–>5.000, for those with occupational exposure and 0.032, 95% CI <-0.031–0.180, for those without). When the analysis of the modifying effect of occupational exposure was repeated separately for the men and women, the estimated effect of residential radon was greater for those with some occupational exposure among both the men and women, although only 12 women with lung cancer and 35 female controls were known to have had occupational exposure (table 22). When the analysis was repeated separately for occupational exposure to asbestos, radon, and other established risk factors, the modifying effect of asbestos and of other established risk factors was similar in size, although only 18 cases and 357 controls had occupational exposure to asbestos. Only 2 cases and 5 controls had occupational exposure to radon (table 22).

To gain further insight into the possible role of employment in an occupation known to be associated with an increased risk of lung cancer as an effect modifier of radon among the lifelong nonsmokers in this data set, the effect of such an occupation directly on lung cancer risk (ie, without radon being considered) was examined. It was found that lung cancer risks were, in fact, very similar for the cases and controls with and without employment in such an occupation (relative risk = 1.219, 95% CI 0.844–1.759; X^2=1.10, 1 df, P=0.30) (table 23). When the numbers of persons who were lifelong nonsmokers were tabulated by case–control status, the observed residential radon concentration and whether or not the persons had been employed in an occupation known to be associated with an increased risk of lung cancer, it was found that the modifying effect of employment was not primarily due to more cases than controls with occupational exposure to an established lung cancer risk having high observed radon concentrations, but rather due to a deficit of cases with low radon concentrations having such exposure. Among all of the lifelong nonsmokers, 51 cases and 589 controls had some employment in an occupation known to be associated with an increased risk of lung cancer. However, among the people with a TWA observed radon concentration of <25 Bq/m³, there was only 1 case compared with 45 controls.

Table 22. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to sex and whether or not the person had been employed in an occupation known to be associated with an increased risk of lung cancer among the lifelong nonsmokers. (β = the excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, and region of residence; 95% CI = 95% confidence interval; df = degrees of freedom)

Characteristic	Lifelong nonsmokers				Likelihood ratio test for heterogeneity of β [a]		
	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Chi-squared	df	P-value
1. Employment in an occupation known to be associated with an increased risk of lung cancer							
Males							
None	213	2095	0.067	<-0.031–0.624	3.83	1	0.05
Some	39	554	2.714	<-0.126–>5.000			
Unknown	16	239	>5.000	> 5.000 [b]			
Females							
None	556	2258	0.028	<-0.046–0.190	2.86	1	0.09
Some	12	35	10.940	<-0.083–>5.000			
Unknown	48	237	0.239	<-0.045–>5.000			
2. Employment in an occupation with exposure to specific risks							
Asbestos							
None	802	4585	0.062	-0.028–0.224	3.33	1	0.07
Some	18	357	>5.000	0.003–>5.000			
Unknown	64	476	0.960	0.007–>5.000			
Radon							
None	818	4937	-				
Some	2	5	-				
Unknown	64	476	-				
Other							
None	783	4689	0.040	<-0.031–0.196	3.92	1	0.05
Some	37	253	1.697	<-0.083–>5.000			
Unknown	64	476	0.96	0.0071–>5.000			

[a] For each characteristic, persons with unknown values for that characteristic were omitted from the likelihood ratio test.
[b] Upper 95% confidence limit: numerical difficulties were experienced in the computation of the lower 95% confidence limit.

Table 23. Employment in an occupation known to be associated with an increased risk of lung cancer among the lifelong nonsmokers. (95% CI = 95% confidence interval, df = degrees of freedom)

Characteristic	Lifelong nonsmokers				Likelihood ratio test for difference		
	Cases (N)	Controls (N)	Relative risk[a]	95% CI for relative risk	Chi-squared	df	P-value
None	769	4353	1.000	–	1.10	1	0.30
Some	51	589	1.219	0.844–1.759			
Unknown	64	476	–[b]				

[a] Relative risks stratified by study, region of residence, age, sex, and smoking history.
[b] Estimate could not be obtained for persons with unknown values, as it could not be distinguished from the stratification variables.

Table 24. Relationship between the relative risk of lung cancer and the observed residential radon concentration according to histological type. (β = the excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval; df = degrees of freedom)

Histological type	Cases (N)	Controls (N)	Estimate of β	95% CI for β	Test for heterogeneity of β		
					Chi-squared	df	P-value
1. Availability of microscopic confirmation in studies seeking clinical information regarding the diagnosis of lung cancer							
Microscopically confirmed lung cancer	6310	13 307	0.075	0.019–0.151	0.24	1	0.63
No microsopic evidence	484	13 307	0.039	<-0.022–0.220			
2. Small-cell compared with other microscopically confirmed histological type							
Small-cell	1379	13 307	0.312	0.128–0.606	4.84	1	0.03
Other microscopically confirmed	4931	13 307	0.026	<-0.031–0.102			
3. Histological type							
Small-cell	1379	13 307	0.312	0.128–0.606	7.07	3	0.07
Squamous-cell	2479	13 307	–0.014	<-0.031–0.086			
Adenocarcinoma	1698	13 307	0.063	<-0.031–0.202			
Other confirmed type	754	13 307	0.035	<-0.031–0.235			

Differences in the effect of residential radon on different histological types of lung cancer

In the 11 studies that sought clinical information regarding the diagnosis of lung cancer, microscopic information confirming the diagnosis was available for all but 484 cases. The estimated value of β for those for whom no microscopic confirmation was available was somewhat lower than for the those for whom it was available (estimates 0.039 with 95% CI <-0.022–0.220 and 0.075 with 95% CI 0.019–0.151, respectively), but the difference was not statistically significant (X^2=0.24 on 1 df, P=0.63). (See table 24.)

A steeper dose–response relationship for small-cell lung cancer than for other types has previously been reported among underground miners occupationally exposed to radon and, when the lung cancer cases for whom microscopic information was available were subdivided according to whether they had small-cell lung cancer or another histological type, the dose–response relationship in the two groups differed significantly (X^2=4.84 on 1 df, P=0.03). The estimated value of β for small-cell lung cancer was substantially higher than for other histological types (estimates of β were 0.312, 95% CI 0.128–0.606, for small-cell lung cancer and 0.026, 95% CI <-0.031–0.102, for other histological types) (table 24). For squamous cell carcinoma the estimated value of β was slightly negative, while for adenocarcinoma and for other confirmed histological types it was positive. However, in all these three groups the 95% confidence interval for β included zero (table 24). When the analysis by histological type was repeated separately for the men and women and for current cigarette smokers, ex-smokers and lifelong nonsmokers, the dose–response relationship for small-cell lung cancer was steeper than for other confirmed types in all five groups (table 25). Overall 21.8% (1379 of 6310) of the microscopically confirmed lung cancers were of the small-cell type (table 26). All 11 studies in which clinical information was sought on the diagnosis of lung cancer had persons with observed radon concentrations of <50 Bq/m^3, and, in this group, the proportion of microscopically confirmed lung cancers that were of the small-cell type was similar to the overall value, at 21.4% (508 of 2376). In contrast, among the cases and controls with observed radon of >800 Bq/m^3, 55.0% (11 of 20) of the microscopically confirmed lung cancers were of the small-cell type, and all five of those with observed radon concentrations of >1600 Bq/m³ were small-cell lung cancers. The 11 persons with small-cell lung cancer who had observed residential radon concentrations of >800 Bq/m³ came from seven different studies (Finland nationwide, Finland southern, France, Germany eastern, Spain, Sweden nationwide, and United Kingdom); 9 were male and 2 were female, while 4 were current cigarette smokers, 5 were ex-smokers, 1 was a lifelong nonsmoker, and 1 was an occasional smoker; their ages were 58, 61, 63, 66 (2 persons) 68, 69, 70, 71 (2 persons), and 80 years, respectively.

When the effect of residential radon on small-cell lung cancer was examined by categories of observed residential radon concentration, the relative risks compared with 0 Bq/m³ in the categories <25, 25–49, 50–99, 100–199, 200–399, and ≥400 Bq/m³ were 1.17 (95% CI 0.93–1.50), 1.15 (95% CI 1.00–1.31), 1.22 (95% CI 1.09–1.38), 1.27 (95% CI 1.06–1.53), 1.91 (95% CI 1.40–2.64), and 2.74 (95% CI 1.51–5.09), respectively (table 27 and figure 4). These values differed appreciably from those seen for other histological types of lung cancer, for which the relative risks compared with 0 Bq/m³ in the same categories were 0.95 (95% CI 0.80–1.12), 1.03 (95% CI 0.94–1.13), 0.99 (95% CI 0.91–1.07), 1.17 (95% CI 1.04–1.32), 1.00 (95% CI 0.79–1.26), and 1.23 (95% CI 0.84–1.81), respectively.

Combined effect of smoking and radon exposure

The estimates of β for current cigarette smokers, ex-smokers, and lifelong nonsmokers were similar, at 0.070, 0.082 and 0.106, respectively, with no evidence of heterogeneity (table 18). It is therefore appropriate to assume that the overall estimate of β, at 0.084 (95% CI 0.030–0.158) is appropriate regardless of smoking status. Among the men, the risk of lung cancer for those smoking 15–24 cigarettes per day, relative to lifelong nonsmokers, was 25.8 for all of the studies

Table 25. Relationship between the risk of lung cancer and the observed residential radon concentration according to histological type, calculated separately for the men and women and for current cigarette smokers, ex-smokers, and lifelong nonsmokers. (95% CI = 95% confidence interval)

Histological type	Cases (N)	Estimate of β[a, b]	95% CI for β[a, b]
Men[c]			
Small-cell	1051	0.313	0.117–0.642
All other microscopically confirmed	3771	0.045	<-0.031–0.154
Squamous-cell	2134	0.003	<-0.031–0.124
Adenocarcinoma	1127	0.046	<-0.031–0.252
Other type	510	0.184	-0.014–0.561
Women[c]			
Small-cell	328	0.304	<-0.045–1.382
All other microscopically confirmed	1160	-0.002	-0.062–0.117
Squamous-cell	345	-0.069	<-0.045–0.138
Adenocarcinoma	571	0.079	-0.036–0.308
Other type	244	-0.069	<-0.045–0.048
Current cigarette smokers[d]			
Small-cell	829	0.150	<-0.045–0.512
All other microscopically confirmed	2308	0.046	<-0.066–0.235
Squamous-cell	1253	-0.028	<-0.066–0.163
Adenocarcinoma	718	0.129	<-0.066–0.636
Other type	337	0.278	<-0.066–1.094
Ex-smokers[d]			
Small-cell	416	0.344	0.078–0.876
All other microscopically confirmed	1758	0.013	<-0.082–0.146
Squamous-cell	997	0.018	<-0.082–0.201
Adenocarcinoma	508	-0.029	<-0.082–0.189
Other type	253	0.015	<-0.082–0.351
Lifelong nonsmokers[d]			
Small-cell	84	1.402	<-0.031–>5.000
All other microscopically confirmed	704	0.042	<-0.031–0.203
Squamous-cell	137	-0.031	<-0.031–0.279
Adenocarcinoma	438	0.108	<-0.031–0.359
Other type	129	-0.069	<-0.031–0.239

[a] β for the men and women was the excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, region of residence, and smoking history.
[b] β for current smokers, ex-smokers, and lifelong nonsmokers was the excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and, for current and ex-smokers, detailed smoking history.
[c] Numbers of controls are 10 388 men and 3820 women.
[d] Numbers of controls are 3322 current cigarette smokers, 4930 ex-smokers, and 5418 lifelong nonsmokers.

Table 26. Numbers of persons with small-cell lung cancer and other microscopically confirmed types of lung cancer, by the time-weighted average observed radon concentration.

Type of lung cancer	Observed radon concentration (Bq/m³)								Total number of persons
	<25	25–	50–	100–	200–	400–	800–	≥1600	
Small-cell lung cancer	123	385	518	235	94	13	6	5	1379
Other microscopically confirmed lung cancer	389	1479	1863	894	235	62	9	–	4931
Total	512	1864	2381	1129	329	75	15	5	6310

Table 27. Relative risk of lung cancer according to categories of observed residential radon concentration by histological type of lung cancer. (95% CI = 95% confidence interval)

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration (Bq/m³)	Relative risk [b]	95% CI [c]
Small-cell lung cancer					
<25 Bq/m³	123	1474	17	1.17	0.93–1.50
25–49 Bq/m³	385	3905	38	1.15	1.00–1.31
50–99 Bq/m³	518	5033	71	1.22	1.09–1.38
100–199 Bq/m³	235	2247	135	1.27	1.06–1.53
200–399 Bq/m³	94	936	275	1.91	1.40–2.64
≥400 Bq/m³	24	613	668	2.74	1.51–5.09
Total (Bq/m³)	1379	14 208	105	–	–
Other microscopically confirmed					
<25 Bq/m³	389	1474	17	0.95	0.80–1.12
25–49 Bq/m³	1479	3905	39	1.03	0.94–1.13
50–99 Bq/m³	1863	5033	71	0.99	0.91–1.07
100–199 Bq/m³	894	2247	136	1.17	1.04–1.32
200–399 Bq/m³	235	936	273	1.00	0.79–1.26
≥400 Bq/m³	71	613	651	1.23	0.84–1.81
Total (Bq/m³)	4931	14 208	100	–	–

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Relative risks estimated after stratification by study, age, sex, region of residence, and, for current and ex-smokers, detailed smoking history. Risks scaled so that the relative risk was 1.00 at 0 Bq/m³ on the assumption of a linear relationship, see the Statistical Methods section for details.
[c] Confidence intervals calculated using the method of floated variances

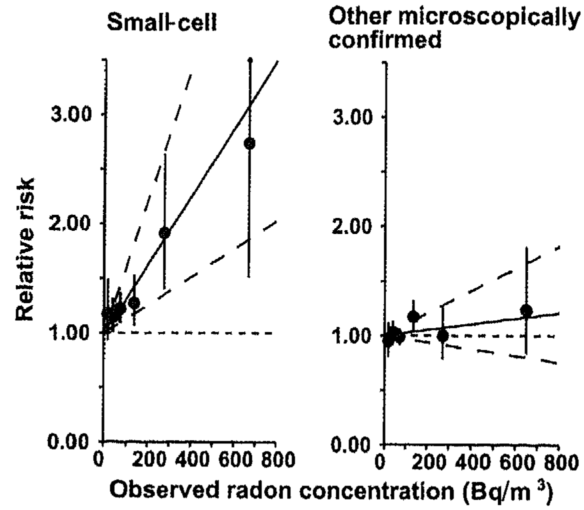

Figure 4. Risk of lung cancer according to the time-weighted average observed residential radon concentration by histological type. The risks were calculated after stratification by study, age, sex, region of residence, and, for current and ex-smokers, detailed smoking history. The relative risks and 95% confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) and 95% confidence intervals (dashed lines). The relative risks are equal to 1 at 0 Bq/m³. The lower confidence interval of the linear relationship for the "other microscopically confirmed" group was lower than that shown, but it could not be determined precisely.

combined, while for ex-smokers of <10 and ≥10 years' duration the risks relative to that of lifelong nonsmokers were 20.8 and 5.0, respectively (table 3). When these smoking-related risks are combined with the overall estimate of β, the result suggests that current smokers of 15–24 cigarettes per day have risks, relative to that of lifelong nonsmokers, varying from 25.8 to 43.1, as their observed radon concentration increases from 0 to 800 Bq/m³, while ex-smokers of <10 years' duration have risks varying from 20.8 to 34.8, as their observed radon concentration increases from 0 to 800 Bq/m³, and ex-smokers of ≥10 years' duration have risks increasing from 5.0 to 8.3, as their observed radon concentration increases from 0 to 800 Bq/m³ (table 28 and figure 5).

For lifelong nonsmokers with an observed radon concentration of 0 Bq/m³, the cumulative risk of death from lung cancer was estimated to be 0.42% by the age of 75 years, increasing to 0.81% by the age of 85 years. For lifelong nonsmokers with observed radon concentrations of >0 Bq/m³, the cumulative risks of death were somewhat greater, but, even at an observed radon concentration of 800 Bq/m³, the risk increased only to 0.71% (95% CI 0.43–0.95) by the age of 75 years and to 1.35% (95% CI 0.83–1.82) by the age of 85 years (table 29 and figure 6). For continuing smokers of 15–24 cigarettes per day, not only was the cumulative risk of death from lung cancer at an observed radon concentration of 0 Bq/m³ much higher, at 10.43% by the age of 75 years and increasing to 19.06% by the age of 85 years, but the increase in the cumulative risk with an increasing observed radon concentration was also substantially higher—by the age of 75 years the cumulative risks associated with observed radon concentrations of 100, 200, 400, and 800 Bq/m³ were 11.25% (95% CI 10.45–11.97), 12.07% (95% CI 10.48–13.49), 13.68% (95% CI 10.54–16.45), and 16.81% (95% CI 10.66–22.06), respectively. By the age of 85 years, these risks had risen substantially further, to 20.48% (95% CI 19.11–21.72), 21.88% (95% CI 19.16–24.29), 24.61% (95% CI 19.61–29.18), and 29.78% (95% CI 19.47–38.04), respectively. For those who gave up smoking, the relative risks during the first 10 years were about 80% of those of the continuing smokers (table 28). Hence the cumulative risks for ex-smokers would also be about 80% of those of continuing smokers. Thereafter they would be lower, but there were not enough persons in the present study who were ex-smokers of 10–19, 20–29, and so forth years' duration to calculate specific estimates of cumulative risk.

Table 28. Risk of lung cancer relative that of to lifelong nonsmokers with no radon exposure by observed radon concentration for various smoking categories. (95% CI = 95% confidence interval)

Observed radon concentration [a]	Relative risk [b]	95% CI
Current cigarette smokers (15–24 per day)		
0 Bq/m³	25.8	–
100 Bq/m³	27.9	26.5–29.8
200 Bq/m³	30.1	27.3–33.9
400 Bq/m³	34.4	28.9–42.1
800 Bq/m³	43.1	32.0–58.3
Ex-smokers (<10 years)		
0 Bq/m³	20.8	–
100 Bq/m³	22.6	21.5–24.1
200 Bq/m³	24.3	22.1–27.4
400 Bq/m³	27.8	23.3–34.0
800 Bq/m³	34.8	25.8–47.2
Ex-smokers (≥10 years)		
0 Bq/m³	5.0	–
100 Bq/m³	5.4	5.1–5.8
200 Bq/m³	5.8	5.3–6.6
400 Bq/m³	6.7	5.6–8.1
800 Bq/m³	8.3	6.2–11.3
Lifelong nonsmokers		
0 Bq/m³	1.0	–
100 Bq/m³	1.1	1.0–1.2
200 Bq/m³	1.2	1.1–1.3
400 Bq/m³	1.3	1.1–1.6
800 Bq/m³	1.7	1.2–2.3

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Risk of lung cancer relative to lifelong nonsmokers with 0 Bq/m³ radon concentration. Risks for smokers of 15–24 cigarettes per day, ex-smokers of <10, and ex-smokers of ≥10 years' duration relative to that of lifelong nonsmokers, assumed to be 25.8, 20.8 and 5.0, respectively (see table 3), regardless of the radon concentration. Relative risks of lung cancer assumed to increase by 0.084 (95% CI 0.033–0.158) per 100 Bq/m³ regardless of smoking status.

Table 29. Cumulative risk of death from lung cancer by age for the lifelong nonsmokers and continuing smokers of 15–24 cigarettes per day at various levels of observed radon concentration.[a] (95% CI = 95% confindence interval)

Age	Lifelong nonsmokers		Continuing smokers of 15–24 cigarettes per day	
	Cumulative risk (%)	95% CI	Cumulative risk (%)	95% CI
Observed radon concentration of 0 Bq/m³				
75 years	0.42	–	10.43	–
80 years	0.59	–	14.26	–
85 years	0.81	–	19.06	–
Observed radon concentration of 100 Bq/m³				
75 years	0.46	0.42–0.49	11.25	10.45–11.97
80 years	0.64	0.59–0.68	15.36	14.30–16.32
85 years	0.88	0.81–0.94	20.48	19.11–21.72
Observed radon concentration of 200 Bq/m³				
75 years	0.49	0.43–0.56	12.07	10.48–13.49
80 years	0.69	0.59–0.78	16.45	14.34–18.33
85 years	0.95	0.81–1.06	21.88	19.16–24.29
Observed radon concentration of 400 Bq/m³				
75 years	0.56	0.43–0.69	13.68	10.54–16.45
80 years	0.79	0.60–0.96	18.58	14.42–22.21
85 years	1.08	0.82–1.32	24.61	19.26–29.18
Observed radon concentration of 800 Bq/m³				
75 years	0.71	0.43–0.95	16.81	10.66–22.06
80 years	0.98	0.60–1.33	22.69	14.58–29.42
85 years	1.35	0.83–1.82	29.78	19.47–38.04

[a] Absolute risk of lung cancer for the lifelong nonsmokers taken from a prospective study of the American Cancer Society. The relative risk of lung cancer for continuing smokers of 15–24 cigarettes per day was assumed to be equal to the overall estimates in the present study (see table 3). The relative risk of lung cancer was assumed to increase by 0.084 (95% CI 0.030–0.158) per 100 Bq/m³ increase in the time-weighted average observed radon concentration (see table 9).

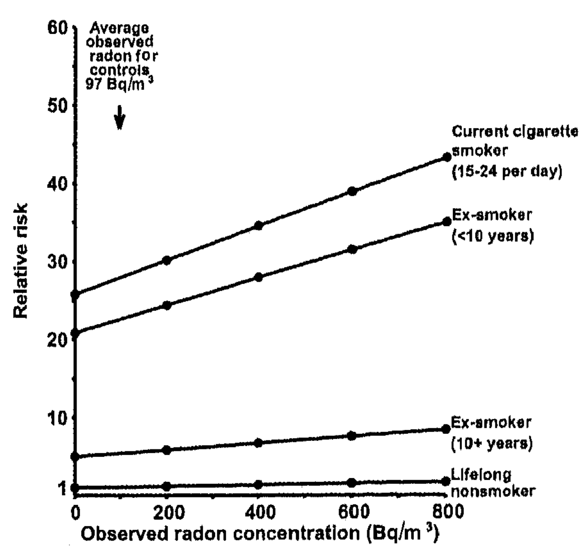

Figure 5. Risk of lung cancer relative to that of lifelong nonsmokers with no radon exposure by the observed radon concentration. See table 28 for the methodological details.

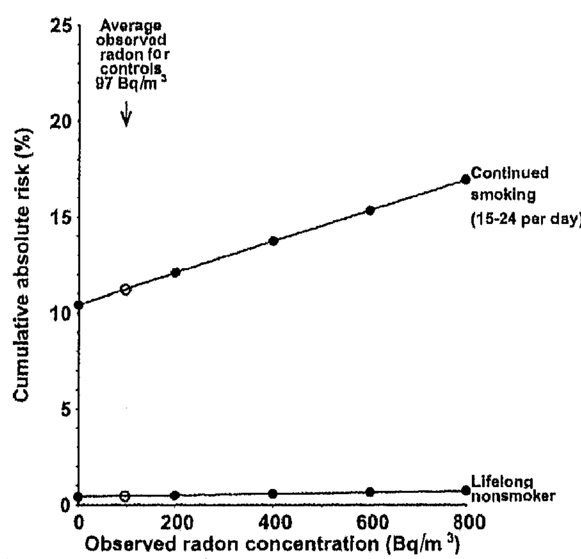

Figure 6. Cumulative risk of death from lung cancer by 75 years of age for various smoking histories by the observed radon concentration. (see table 29 for the methodological details.)

Analyses adjusted for the effect of random uncertainties in the assessment of radon concentration

The extent to which random uncertainties in the assessment of radon concentrations have affected the results presented in the previous sections is determined primarily by the variability of the repeated measurements of radon gas in the same dwelling in different years. No information about this variability is provided in the data presented in the preceding paragraphs. Therefore the laboratories that had performed the radon measurements for the 13 studies were contacted and requested to provide any information that they had available on the variability of repeated measurements of radon gas taken in the same dwelling on different occasions, in the same areas as the study and under approximately the same conditions as in the study. All of the information that could be obtained is summarized in table 30. There were substantial differences between the different countries in the amount of variation observed, from a variance on the log scale of 0.029 in Italy to one of 0.33 in Finland.

In table 30, in one of the two sets of data from Finland, the dwellings had specifically been selected to have small variability between repeated measurements, and the data from eastern Germany had been obtained

Table 30. Summary of the available information on the variability of repeated measurements of radon gas taken in the same dwelling on different occasions.

Location	Description of information	Type of dwelling	Typical duration of measurement period in each year	Occupier or building changes	Measurements always in same room	Main source of radon	Geometric mean (Bq/m³)	Variance on logarithmic scale	Coefficient of variation on linear scale
Czech Republic [a]	1920 measurements made in 960 dwellings in 1992 and repeat-in 1993 (J Hulka & L Tomášek, personal communication)	Mainly single family houses	1 year	None	Yes	Subsoil under dwelling	327	0.12	0.36
Finland	301 dwellings in Finland southern who had requested more than one measurement and who responded to a questionnaire (I Mäkeläinen, personal communication)	Mostly single family houses	Mostly 2 months during winter, but some 1 year	Same occupier; buildings with radon mitigation excluded	Not necessarily	Subsoil under dwelling	319	0.33	0.62
Finland [b]	337 measurements made in 80 dwellings in 18 different years; dwellings were selected to have small variability (I Mäkeläinen, personal communication)	Mostly single family houses	Mostly 1 year, but some 2 months during winter with seasonal correction	No occupier changes; building changes in 7 dwellings	Not necessarily	Subsoil under dwelling	196	0.12	0.36
Germany eastern [b]	110 measurements made in 11 dwellings in 5 different years [Heid et al (41)]	Mainly cellars of single family houses or laboratories	1 year	None	Yes	Subsoil under dwelling	~20 000	0.30	0.59
Italy	363 measurements made in 80 different dwellings in 3–5 consecutive years; each measurement is average of living and bedroom detectors [Bochicchio et al, personal communication]	Nine single family houses, remainder apartments	1 year (2 x 6 months consecutively)	Occupier changes in 1 dwelling; building changes in 1 dwelling	Yes	Probably both building material and subsoil	97	0.029[c]	0.17[c]
Sweden	860 measurements made in 44 dwellings in 13 different years (R Falk, personal communication)	Mostly single family houses[d]	3 months in winter	None	Yes	Subsoil under dwelling	178	0.14	0.39
United Kingdom	436 measurements made in 218 dwellings with time intervals of up to 10 years; each measurement is average of living and bedroom detectors [Darby et al (22), Lomas & Green (37)]	Mostly single family houses	Either 1 year (2 x 6 months consecutively) or 3 months with seasonal correction	Occupier changes in 148 dwellings; dwellings with radon mitigation omitted, but other building changes not ruled out	Not necessarily	Subsoil under dwelling	107	0.23	0.51
United Kingdom	576 measurements made in 96 dwellings in 6 different years; each measurement is average of living and bedroom detectors [Hunter et al (36)]	Mostly single family houses	3 months with seasonal correction	None	Not necessarily	Subsoil under dwelling	96	0.18	0.44

[a] Open detectors used in the Czech Republic and closed detectors used everywhere else.
[b] The data from Finland in which dwellings had been specifically selected to have small variability and the data from the Germany eastern study in which the dwellings considered had very high radon concentrations were not used in determining the values for the variation of repeated measurements made in the same dwelling on different occasions.
[c] All of the detectors were from same batch of material; therefore batch-to-batch variation was excluded.
[d] The variance estimate increases if the calculation is repeated after restriction to the three above-ground apartments.

from buildings with much higher radon concentrations than the dwellings included in the German epidemiologic studies. Therefore these two datasets were not used in determining the parameter values for the Collaborative Analysis. For the remaining datasets summarized in table 30, the estimated variances on the logarithmic scale were used to estimate the corresponding country-specific variances in the Collaborative Analysis, and for the United Kingdom the average of the two estimates given in table 30 was used. For studies carried out in countries in which there were no data available on the variability of repeated measurements, the median of the estimated values for the other countries was used (ie, 0.14). Additional details for the values of the parameters used in the analyses correcting for uncertainties in the assessment of radon concentrations are given in table D5 in appendix D.

When uncertainties in the assessment of the radon concentrations were taken into account using the method of integrated likelihood, the excess relative risk of lung cancer per 100 Bq/m^3 (ie, β) was estimated to be 0.16 (95% CI 0.05–0.31). As the variability of repeated measurements in the same dwellings on different occasions was not known precisely, this analysis was repeated using both higher and lower values (table 31). When the variability estimates were all decreased by 30%, the estimated value of β was 0.14 (95% CI 0.05–0.27), and, when the variability estimates were all increased by 30%, the estimated value of β was 0.19 (95% CI 0.06–0.41). All of the subsequent results presented in this report were calculated using the central estimates of the variability of the repeated measurements.

A TWA radon concentration correcting for uncertainties in the assessment of radon concentrations was calculated for each person. For the lung cancer cases, the mean value of the corrected radon concentrations was 90 Bq/m^3, somewhat lower than the mean of the observed values, which was 104 Bq/m^3. For the controls the weighted mean after correction was 86 Bq/m^3, compared with 97 Bq/m^3 before the correction. The estimated common difference between the corrected TWA radon concentration for the lung cancer cases and the controls was 3.4, with a standard error of 1.0 (P=0.0007) (table 32). Summaries of the distributions of the corrected radon concentrations in the individual studies are given in table D6 of appendix D.

For those with high values for their observed TWA radon concentration, the value after correction for uncertainties tended to be substantially lower. For example, for the 181 persons (66 lung cancer cases and 115 controls) with observed radon concentrations of >800 Bq/m^3, the mean observed radon concentration was 1204 Bq/m^3, while the mean corrected radon concentration was 678 Bq/m^3 (table 33). For those with low TWA observed radon concentrations, the corrected values tended to be somewhat increased—for the 2040 persons (566 lung cancer cases and 1474 controls) with observed radon concentrations of <25 Bq/m^3, the mean observed value was 17 Bq/m^3, while the mean corrected value was 21 Bq/m^3.

The linear relationship between the relative risk of lung cancer and TWA-corrected radon concentration, for which the estimated value of β was 0.16 per 100 Bq/m^3, is shown on the right in figure 7. Also shown on the right in figure 7 are the relative risks for the original categorical analysis (ie, for persons with *observed* radon concentrations in categories <25, 25–49, 50–99, 100–199, 200–399, 400–799, and ≥800 Bq/m^3), but these relative risks are now plotted against the mean *corrected* radon concentration for the

Table 31. Estimated linear relationship between the relative risk of lung cancer and the residential radon concentration correcting for uncertainties in the assessment of radon concentrations. (β = the excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history and correcting for uncertainties in the assessment of radon concentrations; 95% CI = 95% confidence interval)

Method of correction for uncertainties	Estimate of variability of repeated measurements in the same dwelling on different occasions	Estimate of β	95% CI for β
1. Integrated likelihood	Central estimate [a]	0.16	0.05–0.31
2. Integrated likelihood	Central estimate x 0.7	0.14	0.05–0.27
3. Integrated likelihood	Central estimate x 1.3	0.19	0.06–0.41
4. Regression calibration	Central estimate	0.16	0.05–0.3

[a] The central estimate uses the values of V_m given in table D5 in appendix D.

Table 32. Overall distribution of the time-weighted average of the residential radon concentration for the cases and controls after correction for uncertainties in the assessment of residential radon.[a]

Radon concentration	Cases		Controls	
	N	%	N	%
<25 Bq/m^3	403	5.6	1168	8.2
25–49 Bq/m^3	1985	27.8	4033	28.4
50–99 Bq/m^3	3096	43.3	5788	40.7
100–199 Bq/m^3	1207	16.9	2036	14.3
200–399 Bq/m^3	286	4.0	650	4.6
400–799 Bq/m^3	159	2.2	519	3.7
800–1599 Bq/m^3	11	0.2	14	0.1
≥1600 Bq/m^3	1	0.0	-	0.0
Total	7148	100.0	14 208	100.0

[a] The mean for the persons with lung cancer was 90 Bq/m^3. The estimated difference between the cases and controls was 3.4 Bq/m^3 (standard error 1.0 Bq/m^3), based on a linear model with separate effects for each study and a common difference between the cases and controls. The mean for the controls was 86 Bq/m^3 [weighted mean for the controls, with weights proportional to the study-specific numbers of cases].

Table 33. Mean observed and corrected radon concentrations by categories of observed radon concentration for the cases and controls.

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration [a] (Bq/m³)	Mean corrected radon concentration [b] (Bq/m³)
<25 Bq/m³	566	1 474	17	21
25–49 Bq/m³	1999	3 905	39	42
50–99 Bq/m³	2618	5 033	71	69
100–199 Bq/m³	1296	2 247	136	119
200–399 Bq/m³	434	936	273	236
400–799 Bq/m³	169	498	542	433
≥800 Bq/m³	66	115	1204	678
Total	7148	14 208	–	–

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Corrected radon concentration after uncertainties in the assessment of the radon concentrations were taken into account.

persons in each category. The original analysis, based entirely on observed radon concentrations, and for which the estimated value of β was 0.084 per 100 Bq/m³, is shown on the left in figure 7 for comparison.

An additional analysis was carried out in which it was assumed that each person's TWA radon concentration was known precisely and was equal to his or her corrected value (ie, using the method of regression calibration). With this method, the estimated value of β was also 0.16 (95% CI 0.05–0.30), a value very similar to the estimated value of β using the method of integrated likelihood (table 31). Estimated values of β in the individual studies using the method of regression calibration are given in table D7 of appendix D. The analysis shown in table D7 was repeated omitting each study in turn, and the estimated value of β changed by <10% for 10 of the 13 studies. However, omitting either the Czech Republic or the Germany eastern study reduced the estimate of β by 11%, while omitting the United Kingdom study increased the estimate of β by 34%. Study-specific estimates based on a log-linear rather than a linear model are shown in table D8 of appendix D.

The analyses correcting for uncertainties in the assessment of radon concentrations were repeated separately for the cases and controls in different age groups, for the men and women, and for current cigarette smokers, ex-smokers, and lifelong nonsmokers (table 34). The estimates of β calculated using the method of regression calibration were similar to those calculated using the method of integrated likelihood throughout. As with the analysis based on the observed radon concentrations, there was no evidence of a trend in β with the age of the person, nor was there any evidence of differences in β between the men and women, or of heterogeneity in β between the three main categories of

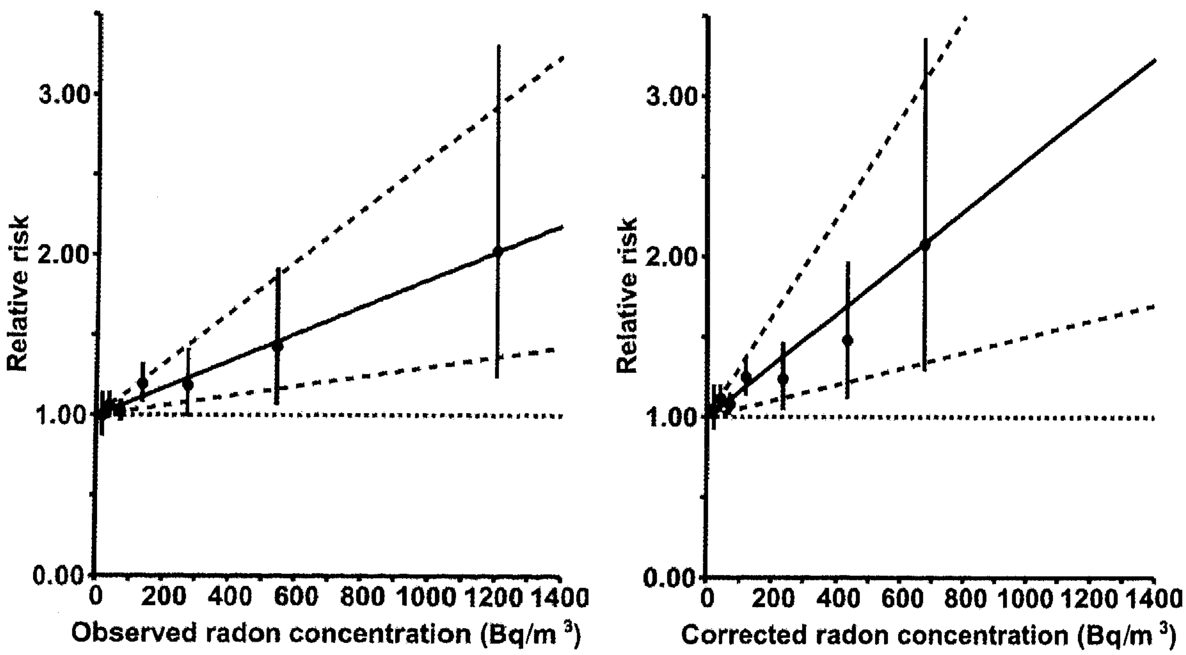

Figure 7. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration (on the left) and the time-weighted average corrected residential radon concentration (on the right). The relative risks and 95% confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) with 95% confidence intervals (dashed lines). The risks were calculated after stratification by study, age, sex, region of residence, and smoking history. On the right, the estimated linear relationship was calculated using the method of integrated likelihood, and the relative risks from the categorical analysis based on categories of observed radon were plotted against the mean corrected radon concentration in each of these categories. In both figures, the relative risks are equal to 1 at 0 Bq/m³.

Table 34. Relationship between the relative risk of lung cancer and the radon concentration according to age, sex, smoking status, and histological type, based on the observed radon concentration and also after correction for uncertainties in the assessment of the residential radon concentrations. (b = the excess relative risk of lung cancer per 100 Bq/m^3 increase in the time-weighted average radon concentration, estimated after stratification by study, age, sex, region of residence, and detailed smoking history; 95% CI = 95% confidence interval)

	Cases (N)	Controls (N)	Based on observed radon concentration		After correction for uncertainties in the assessment of radon concentration			
					Integrated likelihood method		Regression calibration method	
			Estimate of β	95% CI for β	Estimate of β	95% CI for β	Estimate of β	95% CI for β
Age								
<45 years	222	588	0.11	<-0.16–0.35	-0.15	<-0.08–0.69	-0.12	<-0.17–0.73
45–54 years	878	1994	-0.02	<-0.07–0.44	0.12	<-0.03–0.95	0.13	<-0.14–0.97
55–64 years	2506	4818	0.14	0.03–0.31	0.17	0.01–0.45	0.16	<-0.04–0.46
65–74 years	3051	5889	0.08	0.01–0.19	0.16	0.03–0.37	0.16	0.03–0.36
≥75 years	491	919	0.00	<-0.08–0.28	0.77	<-0.04–>5.00	0.57	<-0.14–4.54
P for trend			0.98		0.26		0.28	
Sex								
Men	5521	10388	0.11	0.04–0.21	0.25	0.09–0.49	0.25	0.09–0.48
Women	1627	3820	0.03	-0.04–0.14	0.04	<-0.03–0.23	0.04	-0.06–0.22
P for difference			0.19		0.26		0.08	
Smoking status								
Current cigarette smoker	3575	3322	0.07	-0.01–0.22	0.10	<-0.03–0.38	0.09	<-0.08–0.37
Ex-smoker	2465	4930	0.08	0.00–0.21	0.22	0.02–0.57	0.18	0.02–0.47
Lifelong nonsmoker	884	5418	0.11	0.00–0.28	0.20	0.02–0.52	0.20	0.02–0.53
P for heterogeneity			0.92		0.86		0.78	
Histological type of lung cancer								
Small-cell	1379	13 307	0.31	0.13–0.61	0.51	0.18–1.09	0.49	0.17–1.07
Other microscopically confirmed	4931	13 307	0.03	<-0.03–0.10	0.06	<-0.02–0.21	0.06	-0.04–0.21
P for difference			0.03		0.05		0.08	
All persons	7148	14 208	0.08	0.03–0.16	0.16	0.05–0.31	0.16	0.05–0.30
P for test of β=0			0.0007		0: 0.006		0: 0.0008	

smokers (table 34). With the method of integrated likelihood, the estimated value of β was 0.10 (95% CI -0.06–0.38) for current cigarette smokers, 0.22 (95% CI 0.02–0.57) for ex-smokers, and 0.20 (95% CI 0.02–0.52) for lifelong nonsmokers, and there was no evidence of heterogeneity (P=0.86). For persons with high observed radon concentrations, the corrected radon concentrations tended to be substantially lower, while, for people with low observed radon concentrations, the corrected values tended to be somewhat higher in all three smoking categories (table 35). The outcome of the analysis correcting for uncertainties in the three main smoking categories is summarized in the bottom half of figure 8, and the original analysis, based on the observed radon concentrations, is shown in the top half of the figure for comparison.

The correction for uncertainties had a proportionately greater effect on the estimated excess relative risks of the ex-smokers and lifelong nonsmokers than of the current smokers. To see whether this finding could be explained by the differing estimates of the variability between repeated measurements of radon gas in the different studies, the regression calibration analysis described in the previous paragraph was repeated on the assumption that, on the logarithmic scale, the variance between repeated radon measurements was the same in all of the studies and equal to 0.12. When this procedure was carried out, the differences between the three main smoking groups were smaller, and the estimated excess relative risks per 100 Bq/m^3 had values of 0.09 (95% CI -0.04–0.32), 0.14 (95% CI 0.01–0.35), and 0.16 (95% CI 0.00–0.42) for current cigarette smokers, ex-smokers, and lifelong nonsmokers, respectively.

The analyses correcting for uncertainty were also repeated considering only the persons with microscopically confirmed small-cell lung cancer, together with all of the controls, and considering only the persons with microscopically confirmed lung cancers of other types, together with all of the controls. For small-cell lung cancer, the estimated value of β using the method of integrated likelihood was 0.51 (95% CI 0.18–1.09), while for other microscopically confirmed lung cancers the estimated value of β was 0.06 (95% CI -0.04–0.21). Estimates derived using the method of regression calibration

Table 35. Mean observed and corrected radon concentrations by categories of observed radon concentration and smoking status.

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration [a] (Bq/m³)	Mean corrected radon concentration [b] (Bq/m³)
Current cigarette smokers				
<25 Bq/m³	281	335	17	21
25–49 Bq/m³	975	808	39	42
50–99 Bq/m³	1304	1071	72	70
100–199 Bq/m³	654	595	136	123
200–399 Bq/m³	234	294	275	253
≥400 Bq/m³	127	219	652	478
All concentrations	3575	3322	..	..
Ex-smokers				
<25 Bq/m³	198	621	18	21
25–49 Bq/m³	750	1515	38	42
50–99 Bq/m³	898	1734	70	67
100–199 Bq/m³	431	680	135	116
200–399 Bq/m³	127	251	266	212
≥400 Bq/m³	61	129	689	469
All concentrations	2465	4930	..	..

(continued)

Table 35. Continued.

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration [a] (Bq/m³)	Mean corrected radon concentration [b] (Bq/m³)
Lifelong nonsmokers				
<25 Bq/m³	56	467	17	21
25–49 Bq/m³	222	1443	38	42
50–99 Bq/m³	332	2023	71	69
100–199 Bq/m³	170	866	135	119
200–399 Bq/m³	63	362	278	237
≥400 Bq/m³	41	257	711	505
All concentrations	884	5418	..	..

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Corrected radon concentration, after uncertainties in the assessment of radon concentrations were taken into account.

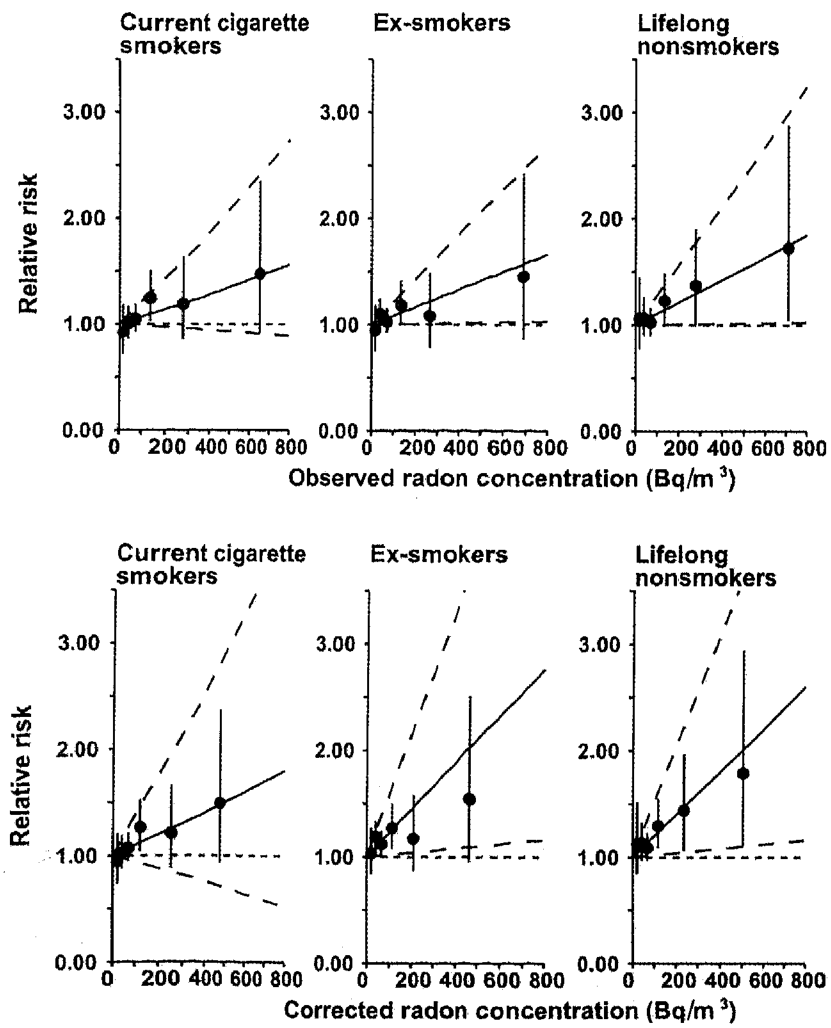

Figure 8. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration (top) and the time-weighted average corrected residential radon concentration (bottom) by smoking status. The relative risks and 95% floated confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) and 95% confidence intervals (dashed lines). (See figure 7 for additional methodological details.)

were, once again, very similar to those calculated using the integrated likelihood method (table 34). As with the analyses already described, the corrected radon concentrations tended to be substantially lower than the observed ones for the persons with high observed concentrations, while, for persons with low observed concentrations, the corrected values were somewhat higher in both analyses (table 36). The outcome of the analyses correcting for uncertainties considering only the persons with small-cell lung cancer and considering only the persons with microscopically confirmed lung cancers of other types are summarized in the lower half of figure 9, and the original analyses, based on observed radon concentrations, are shown in the upper half of the figure for comparison.

As with the analyses based on the observed radon concentrations, there was no evidence of heterogeneity between the estimates of β in the three main smoking categories (table 34). The overall estimate of β obtained using the method of integrated likelihood (ie, 0.16, 95% CI 0.05–0.31) was therefore considered together with the risks of lung cancer relative to that of the lifelong nonsmokers for men, as given in table 3. This procedure suggested that, for lifelong nonsmokers, the risk of lung cancer increases by a factor of 2.3 (95% CI 1.4–3.5) as the corrected radon increases from 0 to 800 Bq/m³. For current smokers of 15–24 cigarettes per day, the risks relative to that of lifelong nonsmokers were much higher, varying from 25.8 to 58.8, as the corrected radon concentration increased from 0 to 800 Bq/m³, while, for ex-smokers of <10 years' duration, the risks varied from 20.8 to 47.5 as the corrected radon concentration increased from 0 to 800 Bq/m³, and, for ex-smokers of ≥10 years' duration, the risks increased from 5.0 to 11.4 as the corrected radon concentration increased from 0 to 800 Bq/m³ (table 37 and figure 10).

Using the methods described in "Combined Effect of Smoking History and Radon Exposure on Lung Cancer Risk" in the Statistical Methods section, the cumulative risk of death from lung cancer for lifelong nonsmokers with a corrected radon concentration of 0 Bq/m³

Table 36. Mean observed and corrected radon concentrations by categories of observed radon concentration and histological type of lung cancer.

Observed radon concentration [a]	Cases (N)	Controls (N)	Mean observed radon concentration [a] (Bq/m³)	Mean corrected radon concentration [b] (Bq/m³)
Small-cell lung cancer				
<25 Bq/m³	123	1 474	17	21
25–49 Bq/m³	385	3 905	38	41
50–99 Bq/m³	518	5 033	71	68
100–199 Bq/m³	235	2 247	135	119
200–399 Bq/m³	94	936	275	240
≥400 Bq/m³	24	613	668	487
All concentrations	1 379	14 208	..	..
Other microscopically confirmed				
<25 Bq/m³	389	1 474	17	21
25–49 Bq/m³	1 479	3 905	39	42
50–99 Bq/m³	1 863	5 033	71	68
100–199 Bq/m³	894	2 247	136	119
200–399 Bq/m³	235	936	273	235
≥400 Bq/m³	71	613	651	473
All concentrations	4 931	14 208	..	..

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.
[b] Corrected radon concentration after uncertainties in the assessment of radon concentrations were taken into account.

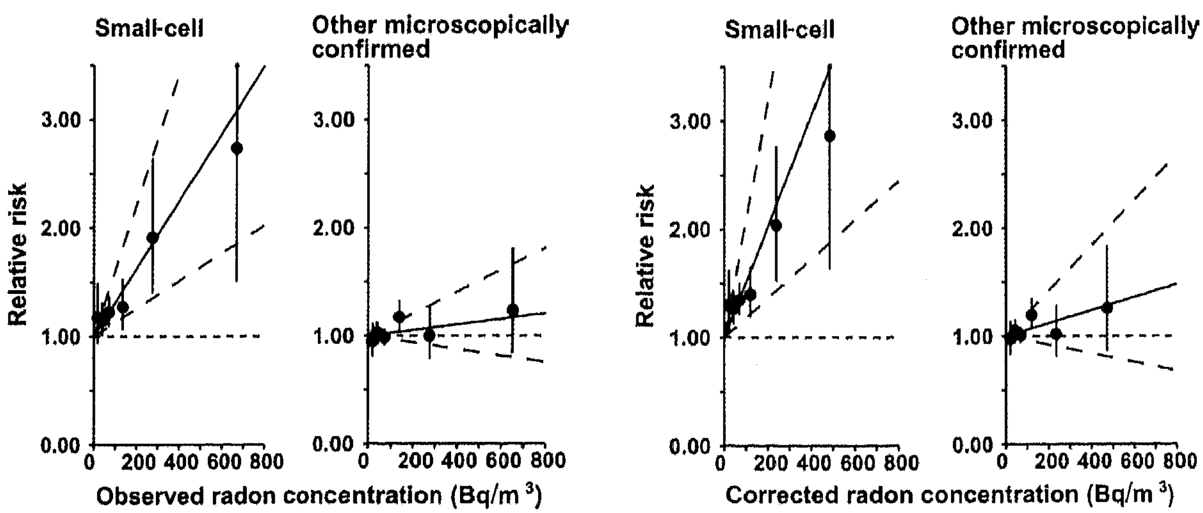

Figure 9. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration (top) and the time-weighted average corrected residential radon concentration (bottom) by histological type. The relative risks and 95% floated confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) and 95% confidence intervals (dashed lines). (See figure 7 for additional methodological details.)

Table 37. Risk of lung cancer relative to lifelong nonsmokers with no radon exposure by corrected radon concentration for various smoking categories. (95% CI = 95% confidence interval)

Corrected radon concentration [a]	Relative risk[b]	95% CI
Current cigarette smokers (15–24 per day)		
0 Bq/m³	25.8	..
100 Bq/m³	29.9	27.1–33.8
200 Bq/m³	34.0	28.3–41.7
400 Bq/m³	42.3	30.9–39.3
800 Bq/m³	58.8	36.1–89.7
Ex-smokers (<10 years)		
0 Bq/m³	20.8	..
100 Bq/m³	24.2	21.9–27.3
200 Bq/m³	27.5	22.9–33.8
400 Bq/m³	34.2	25.0–46.7
800 Bq/m³	47.5	29.2–72.5
Ex-smokers (≥10 years)		
0 Bq/m³	5.0	..
100 Bq/m³	5.8	5.2–6.5
200 Bq/m³	6.6	5.5–8.1
400 Bq/m³	8.2	6.0–11.2
800 Bq/m³	11.4	7.0–17.4
Lifelong nonsmokers		
0 Bq/m³	1.0	..
100 Bq/m³	1.2	1.1–1.3
200 Bq/m³	1.3	1.1–1.6
400 Bq/m³	1.6	1.2–2.2
800 Bq/m³	2.3	1.4–3.5

[a] Radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there and corrected for uncertainties in the assessment of radon concentrations.

[b] Risk of lung cancer relative to that of lifelong nonsmokers with a 0 Bq/m³ radon concentration. Risks for smokers of 15–24 cigarettes per day, ex-smokers of <10 and ≥10 years' duration relative to that of lifelong nonsmokers assumed to be 25.8, 20.8, and 5.0, respectively (see table 3), regardless of the radon concentration. Relative risks of lung cancer assumed to increase by 0.16 (95% CI 0.05–0.30) per 100 Bq/m³ regardless of smoking status.

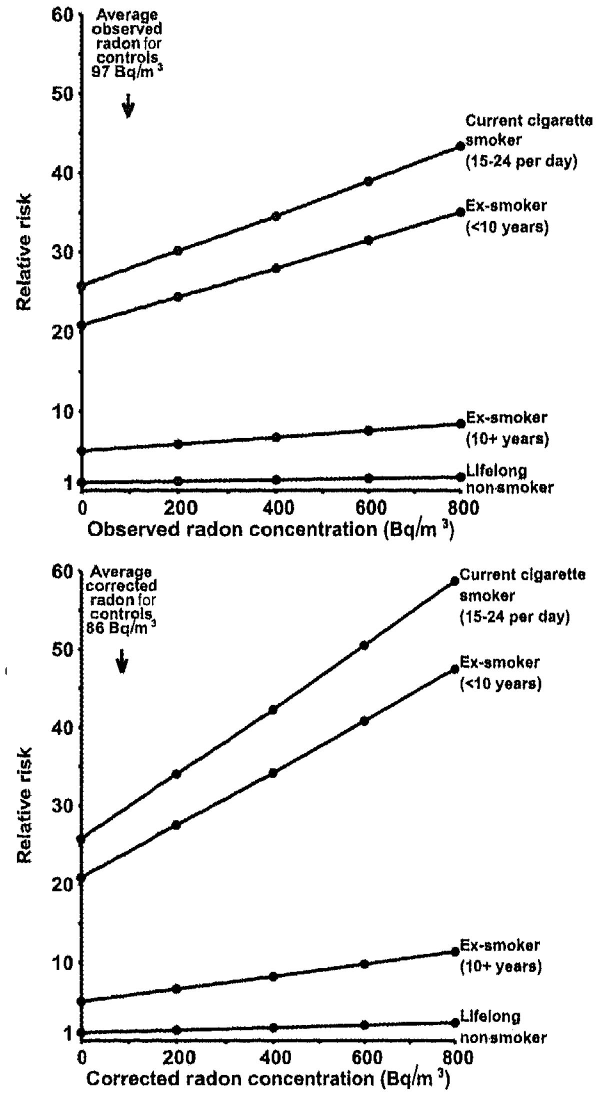

Figure 10. Risk of lung cancer relative to that of lifelong nonsmokers with no radon exposure by the observed radon concentration (top) and the corrected radon concentration (bottom).(See tables 28 and 37 for the methodological details.)

was estimated to be 0.41% by the age of 75 years, increasing to 0.78% by the age of 85 years. For lifelong nonsmokers with corrected radon concentrations of >0 Bq/m³, the cumulative risks of death were somewhat greater, but even at a corrected radon concentration of 800 Bq/m³, the risk rose only to 0.93% (95% CI 0.57–1.42) by the age of 75 years and to 1.78% (95% CI 1.10–2.70) by the age of 85 years (table 38 and figure 11). For continuing smokers of 15–24 cigarettes per day, not only was the cumulative risk of death from lung cancer at a corrected radon concentration of 0 Bq/m³ much higher, at 10.11% by the age of 75 years and increasing to 18.51% by the age of 85 years, but the increase in the cumulative risk with an increasing corrected radon concentration was also substantially higher—by the age of 75 years, the cumulative risks associated with corrected radon concentrations of 100, 200, 400, and 800 Bq/m³ were 11.63% (95% CI 10.59–13.03), 13.12% (95% CI 11.06–15.85), 16.03% (95% CI 12.00–21.23%), and 21.57% (95% CI 13.86–30.98), respectively. By the age of 85 years these values had risen substantially further, to 21.13% (95% CI 19.34–23.52), 23.67% (95% CI 20.16–28.22), 28.51% (95% CI 21.77–36.77), and 37.29% (95% CI 24.91–50.94), respectively. As with the analyses based on the observed radon concentration, for those who gave up smoking, the relative risks in the first 10 years were about 80% of those for continuing smokers (table 37). Therefore, the cumulative risks for the ex-smokers would also be about 80% of those for continuing smokers during the first 10 years after having stopped smoking. Beyond this time, they would be lower than the proportion of risks for

Table 38. Cumulative risk (%) of death from lung cancer by age for lifelong nonsmokers and continuing smokers of 15–24 cigarettes per day at various levels of radon concentration after correction for uncertainties in the assessment of radon concentrations.[a] (95% CI = 95% confidence interval)

Age	Lifelong nonsmokers		Continuing smokers of 15–24 cigarettes per day	
	Cumulative risk	95% CI	Cumulative risk	95% CI
No radon exposure				
75 years	0.41	..	10.11	..
80 years	0.57	..	13.84	..
85 years	0.78	..	18.51	..
Corrected radon concentration of 100 Bq/m³				
75 years	0.47	0.43–0.54	11.63	10.59–13.03
80 years	0.66	0.60–0.75	15.87	14.48–17.73
85 years	0.91	0.82–1.03	21.13	19.34–23.52
Corrected radon concentration of 200 Bq/m³				
75 years	0.54	0.45–0.66	13.12	11.06–15.85
80 years	0.75	0.63–0.92	17.85	15.11–21.44
85 years	1.03	0.86–1.27	23.67	20.16–28.22
Corrected radon concentration of 400 Bq/m³				
75 years	0.67	0.49–0.91	16.03	12.00–21.23
80 years	0.94	0.69–1.27	21.67	16.37–28.37
85 years	1.28	0.94–1.75	28.51	21.77–36.77
Corrected radon concentration of 800 Bq/m³				
75 years	0.93	0.57–1.42	21.57	13.86–30.98
80 years	1.30	0.80–1.97	28.79	18.82–40.45
85 years	1.78	1.10–2.70	37.29	24.91–50.94

[a] Absolute risk of lung cancer for lifelong nonsmokers taken from the prospective study of the American Cancer Society. Relative risk of lung cancer for continuing smokers of 15-24 cigarettes per day assumed equal to the overall estimates in the present study (see table 3). Relative risk of lung cancer assumed to increase by 0.16 (95% CI 0.05–0.31) per 100 Bq/m³ increase in the time-weighted average observed radon concentration (see table 31).

continuing smokers, but there were insufficient persons in the present study who were ex-smokers of 10–19, 20–29, and so forth years' duration to calculate specific estimates of cumulative risk.

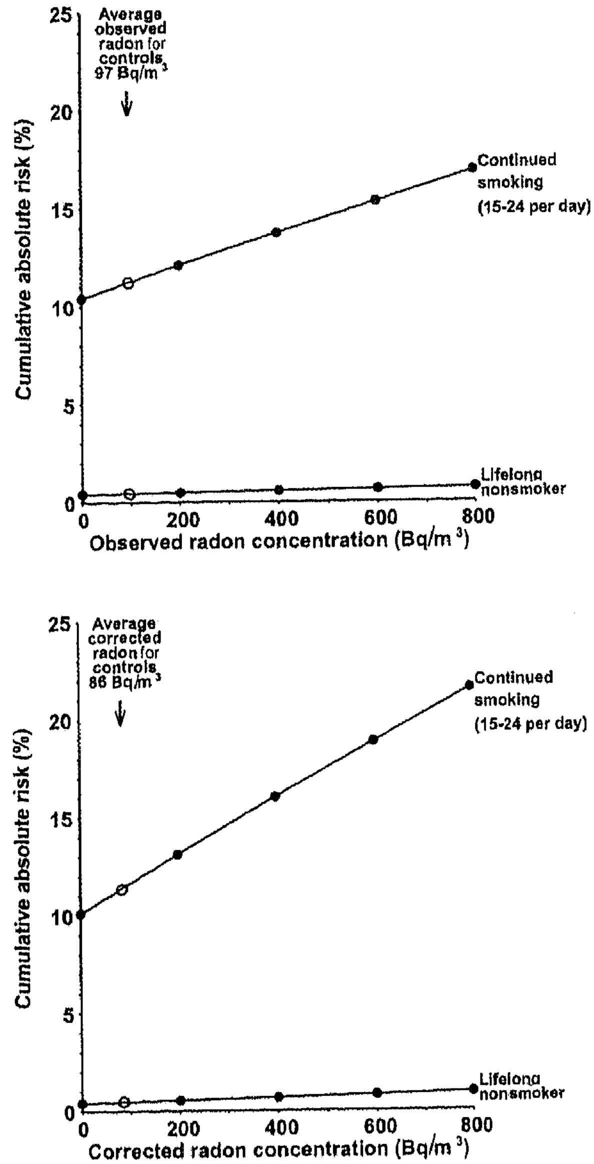

Figure 11. Cumulative risk of death from lung cancer by 75 years of age for various smoking histories by the observed radon concentration (on the left) and the corrected radon concentration (on the right). (See tables 29 and 38 for the methodological details.)

Discussion

Overall results and comparison with other studies of residential radon and lung cancer

This analysis combined data from the 13 European studies of residential radon and lung cancer that have included at least 150 lung cancer cases selected according to clear rules, together with controls representative of the populations from which the lung cancer cases had been drawn, and in which individual information on both smoking history and radon exposure history, based on long-term measurements of radon gas concentrations, was available in the detail that was agreed upon when collaboration began. Other European studies of residential radon and lung cancer that do not meet these criteria have been reported by Axelson et al (43), Axelson et al (44), Edling et al (45), Damber & Larsson (46), Svensson et al (47), Axelson et al (48), Poffijn et al (49), Deri et al (50), Zaridze & Zemlyanaya (51), Magnus et al (52), Pressyanov et al (53), Pisa et al (54) and Conrady et al (55). The data presented here provide, for the first time, very strong evidence (P=0.0007), based on individual data, of an association between residential radon concentration during the previous 35 years and the risk of lung cancer after adjustment for smoking history. There was no evidence of heterogeneity between the different studies in this relationship (P=0.94), nor were the results dominated by any individual study. In addition, there was no evidence that the estimated dose–response relationship depended on detailed aspects of the study design (table 12) or the characteristics of the radon measurements (table 13).

The estimated excess relative risk of lung cancer of 0.084 (95% CI 0.030–0.158) per 100 Bq/m^3 increase in the TWA observed radon concentration is statistically consistent with the estimate of 0.11 (95% CI 0.00–0.28) found in a recent collaborative analysis of seven North American studies of residential radon and lung cancer (56). Compared with the North American collaborative analysis, data from larger numbers of persons were available for analysis in the European study (7148 lung cancer cases and 14 208 controls, against 3662 lung cancer cases and 4966 controls), and the TWA observed radon concentrations tended to be higher (10.4% of the persons with >200 Bq/m^3, compared with 4.9% in the North American collaborative analysis), and these differences are likely to account for the greater precision of the estimate in the European study. The results of the present European study are also consistent with those of a recent study carried out in Gansu, China (57), which found an excess relative risk of 0.19 (95% CI 0.05–0.47) per 100 Bq/m^3 observed radon concentration on the basis of 768 lung cancer cases and 1659 controls, although they differed substantially from the findings of an earlier Chinese study carried out in Shenyang, which reported a negative dose–response relationship [the excess relative risk at 100 Bq/m^3 being -0.16 (95% CI -0.2–-0.1) on the basis of 308 lung cancer cases and 356 controls (58, 59)]. One possible explanation for this discrepancy may be differences in the etiology of lung cancer between Europe and China and within China, as indoor air pollution is known to play a substantial role in causing lung cancer in some areas of China, including Shenyang (60). Another possible explanation may be the fact that the Shenyang study included two controls whose radon measurements were more than 50% greater than the next largest value in that study. When included, these two persons are highly influential, but when they are omitted the results from the Shenyang and Gansu studies do not differ significantly (61).

Prior to this study, meta-analyses based on published reports of studies of residential radon and lung cancer have reported statistically significant associations between radon and lung cancer (2, 59, 62, 63). In all of these analyses, however, there was strong evidence of heterogeneity in the dose–response relationships observed in the different studies. The main explanation for this finding is likely to be that the degree to which the individual studies corrected for confounding by smoking differed between the different studies, and none had sufficient data to be able to correct in as much detail as in the present study. Other explanations for the heterogeneity in the meta-analyses based on published data may include differences in the statistical methods used and, possibly, also the inclusion of the Shenyang study. One other meta-analysis of published data (64) did not test for heterogeneity, but reported that there was some evidence of a U-shaped dose–response relationship, with a lower risk of lung cancer at 25–50 and 50–75 Bq/m^3. However, there was no suggestion of such an effect in the Collaborative Analysis of individual data.

Shape of the dose–response, evidence at <200 Bq/m^3 and the effect of exposure at different times in the past

In the analyses presented in this report, the relationship between the odds of developing lung cancer and the

TWA observed radon concentration has been modeled. The results given are based on linear models, although both linear and log-linear models provided equally good fits to the data (table 15). Reasons for preferring the linear to the log-linear model include the fact that the weight of scientific evidence suggests that a linear non-threshold model is the most plausible dose–response relationship for ionizing radiation (65). In addition, linear rather than log-linear models have been used in other analyses of the effects of exposure to radon, including an analysis of 11 cohort studies of miners of uranium and other igneous rocks who were occupationally exposed (2, 66), albeit at radon concentrations that were usually much higher than those normally found in dwellings. The ability of the linear model to summarize the data was not improved by the addition of a quadratic term (table 15), nor by the inclusion of additional categorical terms for radon, and no departure from linearity was found when the data were subdivided into categories of radon (figure 2). In particular, there was no evidence of any departure from linearity that could be attributed to the existence of radio-sensitive subpopulations, adaptive responses, or bystander effects (2, 67–69); neither was there any evidence of a protective effect of exposure to radon at low concentrations, which has sometimes been postulated (70), nor of a threshold, and, indeed, postulated thresholds of >150 Bq/m^3 lie outside the upper 95% confidence limit.

The evidence in favor of an association between residential radon and lung cancer risk did not rely on the persons with unusually high radon concentrations, and, when the linear model was fitted to the data from only the persons with TWA observed radon concentrations below a certain value, the association remained statistically significant even when only the persons with radon concentrations of <200 Bq/m^3 were considered. The estimated excess relative risk of lung cancer per 100 Bq/m^3 when only the persons with observed radon concentrations of <200 Bq/m^3 were considered was 0.140 (95% CI 0.004–0.309), in good agreement with the estimate based on the entire data set (excess RR 0.084, 95% CI 0.030–0.158).

The distribution of the residential radon concentrations is usually highly skewed and, in this analysis, the distribution of the radon concentrations in the component studies and in the overall data had long upper tails (figure C1 in appendix C). Estimates of linear trend are known to be sensitive to outlying observations and, consequently, in some of the component studies, a very small number of persons with very high radon concentrations had a disproportionate influence on the estimated excess relative risk of lung cancer per 100 Bq/m^3. [See table D1 in appendix D, Heid et al (71), and Schaffrath Rosario et al (72) for further discussion of this issue.] For the Collaborative Analysis, however, the amount of data available was sufficient to overcome this problem.

Analyses of studies of underground miners have suggested that radon exposures in the relatively recent past have substantially greater influence on lung cancer risk than exposure in the more distant past, with periods 5–14, 15–24, and 25–34 years previously having influences approximately in proportions of 1.00 : 0.75 : 0.50, respectively (2, 66). In the present data set, an estimate of the excess relative risk per 100 Bq/m^3 weighting these three periods in proportions of 1.00 : 0.75 : 0.50 is identical to the estimate derived by giving equal weights to every year in the 30-year period ending 5 years previously, and separate estimates, each considering only exposures in the three periods 5–14, 15–24, and 25–34 years previously, were also all very similar (table 14). This difference is not surprising, for the exposures of the miners would often have varied substantially from year to year as mine ventilation was introduced, and the overall length of employment of the men in a job involving radon exposure was usually relatively short (average 5.7 years). In this study, in contrast, the radon exposures varied little from year to year because the people moved their residence only seldom, an average of only 2.7 addresses being reported during the entire 30-year period of interest. In consequence, the TWA observed radon concentrations during the three time periods were highly correlated (correlations between exposures in periods 5–14 & 15–24 years: 0.94; 5–14 & 25–34 years: 0.85; and 15–24 & 25–34 years: 0.88). Consequently, with these data, distinguishing between the effects of exposures received in different periods of the past is impossible. An analysis estimating separately the effects of exposures received during the periods 5–19 and 20–34 years previously has recently been carried out in the Czech Republic cohort study from which the Czech Republic case–control data included in this Collaborative Analysis have been derived (73). The estimated effect of the exposures received in the distant past was lower than that for exposures received more recently. However, the confidence intervals associated with both estimates were very wide [estimated excess relative risks per 1000 Bq/m^3 a: 0.045 (90% CI 0.000–0.153) and 0.013 (90% CI 0.000–0.123), respectively].

Confounding

Residential radon concentrations vary geographically, and it was to be expected that there would be substantial confounding by study, as the studies were carried out in different geographic areas and with different case–control ratios. The overall mean TWA observed radon concentrations for all of the lung cancer cases in the study was 104 Bq/m^3, slightly lower than the corresponding value for the controls, which was 105 Bq/m^3, and this finding is reflected in the slight negative trend in the risk of lung cancer with increasing radon concentration when no confounding factors were taken into account (table 9, stratification 1). However, when the mean TWA observed radon concentrations was calculated separately for each study, it was larger for the lung cancer cases than for the controls, in some cases by considerable amounts, for 10 of the 13 studies (Austria, Czech Republic, Finland southern, Finland nationwide, France, Germany eastern, Italy, Sweden nationwide, Sweden never-smokers, United Kingdom). Only in three studies (Germany western, Spain, Sweden Stockholm) was the mean observed radon concentration lower for the lung cancer cases than for the controls. [See table C4 in appendix C for details.] When a weighted mean observed TWA radon concentration was calculated for the controls, with weights proportional to the numbers of lung cancer cases in each study, its value was 97 Bq/m^3; and a highly significant difference between the two groups of persons was revealed (P=0.0002) (table 6).

Most of the studies were matched for age and sex and, therefore, ensured that there was little confounding with these factors, and several studies were matched for region of residence. However, the ratio of cases to controls varied between the different studies, and the change from the crude excess relative risk of lung cancer per 100 Bq/m^3 of -0.005 (95% CI -0.017–0.13) to 0.023 (95% CI -0.005–0.061) when study, age, sex, and region were taken into account (table 9 stratifications 1 and 3) is primarily the effect of this correction.

In addition, there was also substantial negative confounding by smoking, and, after stratification by smoking habits, the preceding estimate of 0.023 increased substantially, to 0.084. This topic is discussed further in the section Radon and Smoking, on page 49.

Effect modification according to characteristics of the cases and controls

Overall there was little evidence of any modification of the effect of exposure to the TWA observed residential radon concentration on the relative risk of lung cancer according to the characteristics of the cases and controls. The estimated excess relative risk per 100 Bq/m^3 observed radon concentration was larger for the men than for the women (table 18), but the position was reversed in the North American studies of residential radon and lung cancer, with the excess relative risk being greater for the women than for the men (56, 74). In neither study was the difference between the men and women significant statistically, and it seems likely that, in both studies, the difference between the two sexes is due to chance. There was little evidence that the effect of residential radon varied with age, nor was there evidence of such variation in the North American data. This finding is in marked contrast to the results of the analysis of the entire group of occupationally exposed miners, among whom there was a statistically significant trend in the excess relative risk per unit radon concentration, with estimated values at ages <55, 55–64, 65–74, and ≥75 years in the proportions 1.00 : 0.57 : 0.34 : 0.28, respectively (2, 59, 63). In the miners' studies, persons who reached the older age groups during the period of follow-up were likely to have started smoking later in life than those who were younger at the end of the follow-up. Thus, as no adjustment for confounding by smoking was carried out in the main analyses of the miners' studies, there is scope for differential confounding with the effect of smoking in the different age groups in the miners' studies. An alternative explanation might be differences in the accuracy of the exposure assessment in the different age groups. In the miners' studies, persons who reached the older age groups during the period of follow-up were likely to have started their exposure earlier in calendar time than the younger persons. In most mines, the accuracy of exposure assessment was lowest for the earliest calendar periods. Radon concentrations would also have been highest during the earliest calendar periods, and it is noteworthy that, when the analysis of radon-exposed miners was restricted to those exposed at low radon concentrations, there was no trend with age (excess relative risk per unit radon concentration, with estimated values at ages <55, 55–64, ≥65 years, respectively, in the proportions 1.00 : 0.92 : 1.43) (75). In contrast, in the present study, there was a tendency for older people to spend a greater proportion of their time indoors at home, and, among those for whom this variable was known, the percentages spending >75% of their time at home were 11.1%, 15.6%, and 24.6% for those aged <55, 55–64, and ≥65 years, respectively. As a consequence, the observed radon concentrations may be a somewhat poorer reflection of the bronchial dose due to radon and its decay products for older persons than for younger ones in the miners' studies and a somewhat better reflection of it in the residential studies.

In the present study the estimated excess relative risk of lung cancer per 100 Bq/m^3 observed radon concentration was slightly higher for the ex-smokers than for the current smokers [excess RR 0.082 (95% CI 0.003–0.211) versus excess RR 0.070 (95% CI -0.014–0.217] (table 18) and slightly higher again among the lifelong nonsmokers [excess RR 0.106 (95% CI 0.003–0.280)], although the heterogeneity between these estimates was not statistically significant. Similarly, there was no significant difference in the effect of radon exposure by smoking status in the North American data. Further discussion of this issue is given in the section Radon and Smoking, on page 49.

There was evidence that the excess relative risk per 100 Bq/m^3 observed radon concentration was higher among those who had lived in a rural area for the entire 30-year period of interest than among those who had lived in an urban area for part of the time (P=0.01) (table 18). Residence in an urban, as opposed to a rural, area has not been suggested as an effect modifier of radon by any previous study. Furthermore, the effect was not consistent across all of the studies. The significance level of the effect was not extreme, and, therefore, it may be a chance finding. Alternatively, it could reflect some, as yet, unidentified difference in behavior between people living in urban and rural areas. The persons living in rural areas tended to be exposed to higher radon concentrations than those living in urban areas, and they had moved their residence less often than those living in urban areas, but no other specific difference could be identified.

There was also some evidence that the excess relative risk per 100 Bq/m^3 observed radon concentration was higher among those who usually slept with the bedroom window closed rather than open (P for difference 0.03) (table 18). The apparently modifying effect of sleeping with the bedroom window open was discussed in the Sweden nationwide study (18). As a rule, the radon concentration decreases when a window is kept open, sometimes by 50% to 70%. In the Sweden nationwide study, most of the cases and controls had slept with their bedroom window closed. All of the lung cancer cases and half the controls in the present study had died by the time the radon measurements were obtained, and, although no information on window position was obtained when the measurements were made, it is likely that most of the measurements were made with the windows closed. Therefore a greater degree of exposure misclassification would be expected for the persons who slept with their window open. The weaker association for those who slept with an open window might also be explained by greater residual negative confounding. It is likely that there is some residual confounding (eg, with cigarette smoking or other lifestyle factors) in these data, and it is possible that the confounding is stronger for those who slept with an open window. The position of the bedroom window at night as a possible effect modifier was first suggested by the data from the Sweden nationwide study, and, when this study is excluded, the effect is no longer significant statistically. Neither does it remain significant when fitted simultaneously with residence in an urban or a rural area (table 20). Thus the evidence suggesting that it is an effect modifier is not strong.

When lifelong nonsmokers were considered separately, there was no evidence that the effect of exposure differed according to whether or not the person had been married to a smoker (table 21). Neither was there any evidence that the effect of residential radon differed according to most of the other characteristics that were examined. The one exception was employment in an occupation known to be associated with lung cancer in other studies, with a larger excess relative risk of lung cancer for those who had been employed in such an occupation. However, there was no evidence in these data that such employment per se increased lung cancer risk (table 23), nor that it modified the effect of residential radon concentration when all of the data in the Collaborative Analysis were considered together after stratification for smoking history (table 18). Furthermore, the significance of the effect was primarily due to a deficit of persons with low radon concentrations having such employment. Overall, therefore, the evidence that employment in an occupation known to be associated with a risk of lung cancer is an effect modifier is not strong.

Histological type of lung cancer

The present study provides evidence of a stronger association between exposure to residential radon and small-cell lung cancer than between radon and other histological types of the disease. Although a central pathological review was carried out in only three studies (Germany eastern, Germany western, and United Kingdom), several studies contributed to the finding, and it is therefore unlikely to be an artifact of variations in the pathological classification. The result is in line with early clinical and autopsy reports on highly exposed miners in the Schneeberg region (76), where an excess of intrathoracic neoplasms was identified and the tumors were classified as lymphosarcomas, with the implication that they were mostly small-cell lung cancers. In addition, autopsy studies from highly exposed uranium miners in Jáchymov and Schneeberg in the early part of the 20th century suggested a preponderance of small-cell lung cancers (77, 78). More recently, histological studies of radon-exposed uranium miners who died of lung cancer in the Czech Republic (79, 80), the United States (81), and China (82) have also found that radon-induced lung cancers are more likely to be of the small-cell type than of other histological types.

In the United States study (81), a comparison was made of the localization of tumors within the lung between radon-exposed miners and nonminers, and it was found that the proportion of lung tumors and, especially, small-cell lung tumors in the central zone was greater for the miners than for the nonminers. Thus the explanation for the preponderance of small-cell lung cancers may be the fact that radon and its decay products deliver the highest radiation dose to the central zone of the lung (2). Other factors may also play a role, however, as histological studies of lung cancers in survivors of the atomic bombings of Hiroshima and Nagasaki who were exposed to uniform whole-body radiation, predominantly from gamma rays (83), have also suggested that radiation-induced lung cancers are more likely to be of the small-cell type than of other histological types. For the atomic bomb survivors, the reason for the greater risk of small-cell tumors has not yet been resolved.

Although it had been expected a priori that small-cell lung cancers would be more closely associated with radon than other cell types, the lack of any appreciable association between radon exposure and other types of lung cancer observed in the present study was not expected. In studies of occupationally exposed miners, increased risks of both squamous-cell carcinomas (81) and adenocarcinomas (82) have been found to be associated with radon exposure. Most recently, in a large study of miners in eastern Germany (84), the data suggested that all cell types were associated with radon exposure, but that high radon exposure tended to increase the proportion of both small-cell and squamous-cell cancers. A recent review has also pointed out that the histological type of lung cancer has not proved to be a definitive indicator of radon progeny as a cause of the lung cancer in radon-exposed underground miners (2).

Effects of uncertainties in the assessment of radon concentrations

Correction for the effects of random uncertainties in the assessment of radon concentrations had a major impact, with the estimated increase in relative risk per 100 Bq/m^3 nearly doubling, from 0.084 to 0.16, and the width of the associated 95% confidence interval also increasing, from 0.030–0.158 to 0.05–0.31. Data on the degree of variability between repeat measurements of radon gas taken in the same dwelling on different occasions in the same areas as the study and under approximately the same conditions as in the study were sought from the laboratories that had performed the radon measurements for the 13 studies (table 30). Data were not available for all the countries in which the studies had been carried out. Nevertheless, they provide strong evidence that there is an appreciable degree of variability between repeated measurements in the same dwelling, and they give an approximate estimate of its size.

Analyses of data from Germany (41), Sweden (R Falk, personal communication), and the United Kingdom (38) have all shown that there is greater variability between repeated measurements in dwellings with high radon concentrations than in dwellings with low radon concentrations, but that, after logarithmic transformation, the variability is approximately independent of the radon concentration. Therefore, estimates of variability were made after logarithmic transformation, and, in the statistical model used for the analysis, it was assumed that the variability was multiplicative rather than additive. The size of the variability of the repeated measurements differed from one dataset to the other, and, in particular, a much lower variability was observed in the Italian dataset than elsewhere (table 30). The Italian data are likely to be highly representative of the random measurement uncertainties in the Italy case–control study, because they were obtained in a sample of dwellings from the same area as the case–control study, and using the same radon measurement technique and protocol, the same measurement laboratory and personnel, and the same detector batch. The other datasets were also likely to be reasonably representative of the random uncertainties of the case–control studies in the countries in which they were carried out. One possible difference between the Italian dataset and the other datasets included in table 30 is that both the building material and the subsoil under the building may have contributed to the residential radon concentration in the region where the Italy study was conducted (85), whereas elsewhere the primary source was predominantly the subsoil. This difference should be present also in the corresponding case–control studies.

Although the estimates of the variability of repeat measurements were subject to considerable uncertainty, the estimated increase in the relative risk per 100 Bq/m^3 was relatively insensitive to the precise values used, decreasing only from 0.16 to 0.14 when the estimates of variability were decreased by 30% and increasing only to 0.19 when they were increased by 30% (table 31). The value of the corrected estimate obtained using the regression calibration method was virtually identical to those obtained using the more rigorous integrated likelihood method.

As was expected, correction for random uncertainties in the assessment of radon concentrations increased the residential radon concentrations among the persons with low observed concentrations and decreased them among those with high observed concentrations. As a consequence of the assumption that the uncertainties were multiplicative, the amount by which the high radon concentrations were reduced was much greater than the amount by which the low radon concentrations were increased (table 33). However, the dose–response relationship remained approximately linear after correction for uncertainties (figure 7). The effect of making separate corrections for current cigarette smokers, ex-smokers, and lifelong nonsmokers is discussed in the section Radon and Smoking, on page 49. When separate corrections were made for small-cell and other microscopically confirmed lung cancers, the estimated increase in relative risk per 100 Bq/m^3 rose to 0.51 (95% CI 0.18–1.09) for small-cell lung cancers, and the dose–response relationship remained approximately linear (figure 9), while the estimated risk increase remained much smaller and not significantly different from zero for other microscopically confirmed tumors.

The preceding corrections take into account the random uncertainties present in the assessment of residential concentrations in the case–control studies but, as the assessment of the residential radon concentrations was based on measurements of radon gas made in the recent past, it was not possible to take into account systematic factors such as the tendency for radon concentrations to have increased by around 30% between the 1950s and the 1990s, as is thought to have taken place in Sweden (86) and may also have occurred in some other countries, particularly those experiencing severe winters. It was not possible to take this factor into account in the present analysis, as there was too little information available on the amount by which the radon concentrations were likely to have increased in individual dwellings. However, if it had been possible to take this factor into account, then it would have tended to increase the estimated excess relative risk per unit radon concentration. Recent research has led to the development of methods to estimate the historical average radon concentrations to which people have been exposed, through measurements of the surface activity on a glass object that has been in a person's dwellings during the entire period of interest (87–89). Several epidemiologic studies using this technology are currently underway, and, to date, the results of two have been published (90, 91). Although the uncertainties associated with this method are not yet fully understood (92, 93), both of these studies have provided larger estimates of the excess relative risk associated with residential radon than corresponding estimates using recent measurements of radon gas concentrations.

An additional issue is the fact that, in the Collaborative Analysis, risk was considered in relation to the residential radon concentration rather than in relation to the person's bronchial dose from residential radon. For a fixed residential radon concentration, defined as a weighted average of living room and bedroom values, as in the Collaborative Analysis, individual persons experience a range of bronchial doses depending on the variation in the radon concentrations within the home, the amount of time the person spends in the different parts of the home, the amount of time the person spends away from the home, and the radon concentrations in the places outside the home where time is spent. If taken into account, it seems likely that this variation would also tend to increase the estimated excess relative risk per unit radon concentration (94).

Radon and smoking

As is well known, the risk of lung cancer from smoking, and especially from smoking cigarettes, is substantial. In the present study, there was negative confounding between residential radon and smoking. The estimated increase in the relative risk of lung cancer per 100 Bq/m^3 was 0.023 when study, region, age, and sex, but not smoking, were included in the stratification. This value increased to 0.052 after stratification for smoking in seven categories (never-smokers, current cigarette smokers of <15, 15–24, and ≥25 cigarettes per day, ex-smokers of <10 years and ≥10 years' duration, and others), and increased further, to 0.084, when current smokers were further stratified by age at starting to smoke and ex-smokers were stratified by amount smoked (table 9).

When the analysis based on the observed radon concentrations was repeated separately for broad categories of smokers, the estimated excess relative risk of lung cancer per 100 Bq/m^3 observed radon concentration was slightly higher for the ex-smokers than for the current smokers (excess RR 0.082, 95% CI 0.003–0.211, versus excess RR 0.070, 95% CI −0.014–0.217) (table 18), and higher still for lifelong nonsmokers (excess RR 0.106, 95% CI 0.003–0.280). When corrections were made for the effects of random uncertainties in the assessment of radon concentrations, the estimated effect of radon increased in all three smoking groups, and the corrected values were 0.10 (95% CI −0.06–0.38) for current smokers, 0.22 (95% CI 0.02–0.57) for ex-smokers, and 0.20 (95% CI 0.02–0.52) for lifelong nonsmokers (table 34). Thus the size of the correction for uncertainties was greater for the ex-smokers and lifelong nonsmokers than for the current cigarette smokers. This result was due to the fact that the variability between the repeated measurements of radon gas differed between the different studies, as did the distribution of smoking histories (table B7 in appendix B). Although the estimates of the effect of radon on the relative risk of lung cancer differed appreciably between the three main smoking categories, the confidence intervals were so wide that there was no formal evidence of heterogeneity between the categories, and the data are compatible with the relative risks when the same value is used for all three smoking categories.

The presence of random uncertainties in the assessment of residential radon concentrations means that risk estimates based on measured radon concentrations inevitably underestimate the true magnitude of the risks.

In the present study it was possible to make an approximate adjustment for the effects of random uncertainties, and this adjustment increased the estimated effects of residential radon substantially. It seems certain that there were also random errors in the assessment of smoking habits. As there was negative confounding between smoking and radon in these data, a correction adjusting for such uncertainties would be likely to increase the estimated effect of exposure to radon still further, particularly among current smokers, and, in principle, it would be desirable to make such an adjustment (41). However, there is little quantitative information available on the nature and extent of random errors in the reporting of smoking histories in the context of studies such as this. In addition, making such adjustments in the context of a complex analysis would present considerable technical challenges. Therefore such adjustments were not attempted, nor were such adjustments made in any of the other major studies of the joint effects of radiation and smoking.

The effect of radon exposure among persons with different smoking histories has also been examined among miners occupationally exposed to radon (2, 66). For 7 of the 11 studies for which data were available, there was some, although usually very limited, information on smoking status. When those reported to be lifelong nonsmokers (among whom there were 64 deaths from lung cancer) and others were considered separately, the estimated excess relative risk per unit radon concentration was 3.03 times higher than the corresponding ratio for those who were nonsmokers. Despite the large size of this ratio, these estimates had wide confidence intervals, and the difference between them was not statistically significant.

The effect of exposure to ionizing radiation on persons with different smoking histories has recently been examined in the life-span study of the survivors of the atomic bombings of Hiroshima and Nagasaki (95), where the exposures were predominantly to gamma radiation. In this population there was strong evidence that the excess relative risk per sievert varied within the categories of smoking level ($P<0.01$). There was a tendency for the risks relative to those of unexposed persons with the same smoking level to decrease with an increasing amount smoked, and, in the age group of 60–70 years, the estimated excess relative risk per sievert was 0.64 [standard error (SE) 0.45] for the nonsmokers and 1.02 (SE 0.66), 0.10 (SE 0.14), and 0.00 (SE 0.14) for the smokers of 1–15, 16–25 and ≥26 cigarettes per day, respectively. The ex-smokers were omitted from this analysis. When radiation exposure and smoking were considered simultaneously for the survivors of the atomic bombings, a multiplicative model was rejected, but the data were consistent with an additive model (ie, one in which the increase in the absolute risk of lung cancer per sievert was the same, regardless of smoking history).

In all of the three studies referred to in the previous paragraph, the excess relative risk per unit exposure was lower for continuing smokers than for nonsmokers, although, in the present dataset and in the studies of radon-exposed miners, the difference did not reach statistical significance. The consistency of the finding may suggest that the effect of radon is, in fact, proportionately somewhat greater for nonsmokers than for smokers. In the present study, however, there was negative confounding with smoking and, although it had been taken into account as far as is possible, it seems likely that some residual confounding with smoking remained, particularly for current smokers, due to random errors in the reporting of smoking histories. Thus, in the present study, the observed differences between continuing smokers and lifelong nonsmokers in the excess relative risks per unit radon concentration may also be simply a reflection of an inadequate allowance for confounding. Therefore, in the analyses of the joint effects of smoking and radon presented in this publication, we have assumed that the excess relative risk per 100 Bq/m^3 is the same, regardless of smoking status.

When the implications of the risks of exposure to residential radon, especially in the context of public health, are considered, it is desirable to consider jointly the effects of radon and the likely risks of lung cancer from smoking. In the present analysis, the relative risks of current and ex-smokers relative to that of lifelong nonsmokers (table 3) were similar to those found in other studies carried out with these populations (31). In the present analysis the joint effect of smoking and radon has been estimated by assuming that the relative risk for persons in each broad smoking category was known precisely and was equal to the relative risk that was found for all men in that smoking category when they were compared with lifelong nonsmokers (tables 37 and 38, and figures 10 and 11). [A discussion of why this was done is given under "Joint Effect of Smoking History and Radon Exposure on Lung Cancer Risk" in the Statistical Methods section.]

For the persons in the collaborative analysis, the mean time-weighted corrected radon concentration during the period of interest was 90 Bq/m^3 for the lung cancer cases and 86 Bq/m^3 for the controls (table 32) and only 7.7% of them had TWA corrected radon concentrations of >200 Bq/m^3. Thus, for the vast majority of the persons included in this analysis, the risk of lung cancer was determined predominantly by their smoking history rather than by their radon exposure (figures 10 and 11). The component studies of the Collaborative Analysis were, on the whole, carried out in high radon areas of the countries concerned, and several studies included only persons with low residential mobility.

Summaries of the results of the surveys of the indoor radon concentrations that have been carried out for the general population in different countries are given in the reports of the United Nations Scientific Committee on the Effects of Atomic Radiation (1). According to these surveys, the population-weighted average indoor radon concentration for Europe as a whole is around 60 Bq/m^3, while the worldwide average is 39 Bq/m^3. Thus with respect to the general population, both in Europe and worldwide, most people have residential radon concentrations that are <200 Bq/m^3. At these concentrations, for those who smoke cigarettes, a far greater reduction in the cumulative risk of lung cancer would likely be attained if they gave up smoking than if they reduced the level of their radon exposure.

Quantitative comparison of the risks observed in the present study with those observed for underground miners occupationally exposed to radon

In a collaborative analysis of 11 cohorts of underground miners of uranium and other igneous rocks who were occupationally exposed to radon, there were substantial inverse dose-rate effects (2, 66). This finding may be due, at least in part, to the effects of random errors in the assessment of radon exposures among the miners, although several other mechanisms have been postulated (2, 96). In the Collaborative Analysis of the 11 miner cohorts, the average exposure received by the miners was 158 working level months (WLM),[19] received over an average of 5.7 years (2, 66). In contrast, the mean residential radon concentration experienced by the populations represented in the studies included in the Collaborative Analysis was 86 Bq/m^3 after correction for uncertainties in the assessment of the radon concentration. Living in a home with a radon concentration at this level for 30 years results in an exposure of approximately 10 WLM,[20] less than one tenth the average cumulative exposure of the miners.

The generally higher exposures and also the existence of inverse dose-rate effects in the miners' data complicate the quantitative comparison of the risks of lung cancer between the present study and that of the occupationally exposed miners. The most relevant comparison is with an analysis of a subset of the data from the 11 studies of miners that was limited to total exposures of <50 WLM (2, 75). The bronchial dose received by such an exposure would be approximately equal to that incurred by living in a home with a concentration of 427 Bq/m^3 for 30 years. Within this group, the estimated excess relative risk for those exposed at concentrations below 0.5 WL was 0.0251 per WLM, which is equivalent to an increase in the relative risk of 0.30 per 100 Bq/m^3 when residential exposure over the previous 30 years is taken into consideration, while removing the restriction to total exposures below 50 WLM suggested an increase of 0.19 in the relative risk per 100 Bq/m^3. In a more recent follow-up of one of the miner cohorts in which the average cumulative exposure was only 36.5 WLM, the estimated excess relative risk per WLM for those exposed only to concentrations lower than 1 WL was similar to that for the miners with total exposures of less than 50 WLM, at 0.024 per WLM (97).

The increase in the relative risk per unit exposure seen in the collaborative analysis of data from the 11 miner cohorts with total exposures below 50 WLM is compatible with, although somewhat higher than, the estimated value of 0.16 (95% CI 0.05–0.31) per 100 Bq/m^3 after correction for uncertainties in the assessment of the radon concentrations that was obtained in the present Collaborative Analysis. When the two results are compared, the uncertainties in them both should be borne in mind. The uncertainties in the estimate from the present Collaborative Analysis have already been discussed. However, there are also substantial uncertainties for the estimated excess relative risk from the miners' studies. Confidence intervals have not been published for the estimates based on the 11 cohorts of miners cited in the previous paragraph. In addition, there was substantial heterogeneity between the effects of radon in the different

19 The working level (WL) is defined as any combination of the short-lived radon progeny in one liter of air that results in the ultimate release of 1.3×10^5 MeV of potential α-particle energy. Exposure to this concentration for a "working month" of 170 hours (or twice this concentration for half as long, and so forth) is defined as a working level month (WLM).

20 This follows if it is assumed that 1 Bq/m^3 at equilibrium is equivalent to 0.00027 WL, that the equilibrium factor (see below) in dwellings is 0.40, that people spend 70% of the time at home, that there are $365.25 \times 24 / 170 = 51.6$ "working months" (see footnote 19) in 1 year, and that the ratio of the dose to lung cells for exposures in homes to that for similar exposures in mines (sometimes referred to as the K-factor) is unity. Under these assumptions, living in a home with 86 Bq/m^3 for 30 years will result in $86 \times 0.00027 \times 0.40 \times 0.70 \times 51.6 \times 1 \times 30 = 10.1$ WLM. (The equilibrium factor is defined as the ratio of the equilibrium equivalent concentration of radon to the actual radon concentration, for which the equilibrium equivalent concentration is the activity concentration of radon in equilibrium with its short-lived progeny that has the same potential alpha energy concentration as the actual nonequilibrium mixture.)

miners' studies (2, 66). It should also be borne in mind that the effect of uncertainties in the assessment of radon exposures has not been taken into account in the main analyses of the miners' studies. In the study of a single cohort of miners in which it was taken into account, it was found that the estimated excess relative risk was increased by around 60% for high dose-rate exposures, but was little changed for low dose-rate (0–15 WL) exposures (98).

Concluding remarks

The Collaborative Analysis of data from 13 European studies of the effects of residential radon on the risk of lung cancer presents, for the first time, strong evidence of an association between residential radon and the risk of lung cancer after adjustment for smoking history. The dose–response relationship was linear with no evidence of a threshold; it remained statistically significant even when the analysis was limited to observed radon concentrations of <200 Bq/m^3; and there was no evidence that the excess relative risk per unit increase in the radon concentration varied with smoking history. When based on the observed radon concentration, the estimated excess relative risk per 100 Bq/m^3 was 0.084 (95% CI 0.03–0.158). However, this estimate is likely to underestimate the true risk, as it does not take into account the uncertainties present in the assessment of residential radon concentrations. When an approximate correction for the effect of such uncertainties was included, the estimated excess relative risk per 100 Bq/m^3 was 0.16 (95% CI 0.05–0.31). These results are crucial to the development and refinement of policies for managing exposure to this form of natural radiation, so as to help reduce the annual number of deaths from the most common type of fatal cancer in Europe.

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References

1. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). Sources and effects of ionizing radiation. New York (NY): United Nations; 2000. UNSCEAR 2000 report to the General Assembly, with scientific annexes, vol I: sources.
2. National Research Council. Health effects of exposure to radon. Washington (DC): Committee on Health Risks of Exposure to Radon: BEIR VI, National Academy Press; 1999.
3. International Agency for Research on Cancer (IARC). Man-made mineral fibres and radon. Lyon: IARC; 1988. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol 43.
4. International Agency for Research on Cancer (IARC). Ionizing radiation, part 2: some internally deposited radionuclides. Lyon: IARC; 2001. IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, vol 78.
5. Darby S, Hill D, Auvinen A, Barros-Dios JM, Baysson H, Bochicchio F, et al. Radon in homes and lung cancer risk: a collaborative analysis of individual data from 13 European case-control studies. BMJ. 2005;330:223–7.
6. Oberaigner W, Kreienbrock L, Schaffrath Rosario A, Kreuzer M, Wellmann J, Keller G, et al. Radon und Lungenkrebs im Bezirk Imst/Österreich [Radon and lung cancer in the district of Imst, Austria]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 2002. Fortschritte in der Umweltmedizin
7. Tomášek L, Müller T, Kunz E, Heribanová A, Matzner J,

Plaček V, et al. Study of lung cancer and residential radon in the Czech Republic. Cent Eur J Public Health 2001;9:150–3.
8. Auvinen A, Mäkeläinen I, Hakama M, Castrén O, Pukkala E, Reisbacka H, et al. Indoor radon exposure and risk of lung cancer: a nested case–control study in Finland. J Natl Cancer Inst 1996;88:966–72. Erratum in J Natl Cancer Inst 1998; 90:401–2.
9. Ruosteenoja E, Mäkeläinen I, Rytömaa T, Hakulinen T, Hakama M. Radon and lung cancer in Finland. Health Phys 1996; 71:185–9.
10. Baysson H, Tirmarche M, Tymen G, Gouva S, Caillaud D, Artus JC, et al. Case–control study on indoor radon and lung cancer in France. Epidemiology 2004;15:709–16.
11. Wichmann HE, Gerken M, Wellmann J, Kreuzer M, Kreienbrock L, Keller G, et al. Lungenkrebsrisiko durch Radon in der Bundesrepublik Deutschland (Ost)—Thüringen und Sachsen [Lung cancer risk due to radon in the Federal Republic of Germany (East)—Thuringia and Saxony]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 1999. Fortschritte in der Umweltmedizin.
12. Kreuzer M, Heinrich J, Wölke G, Schaffrath Rosario A, Gerken M, Wellmann J, et al. Residential radon and risk of lung cancer in eastern Germany. Epidemiol 2003;14:559–68.
13. Wichmann HE, Rosario AS, Heid IM, Kreuzer M, Heinrich J, Kreienbrock L. Increased lung cancer risk due to residential radon in a pooled and extended analysis of studies in Germany. Health Phys. 2005;88:71–9.
14. Wichmann HE, Kreienbrock L, Kreuzer M, Gerken M, Dingerkus G, Wellmann J, Keller G. Lungenkrebsrisiko durch radon in der Bundesrepublik Deutschland (West) [Lung cancer risk due to radon in the Federal Republic of Germany (West)]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 1998. Fortschritte in der Umweltmedizin.
15. Kreienbrock L, Kreuzer M, Gerken M, Dingerkus G, Wellmann J, Keller G, et al. Case–control study on lung cancer and residential radon in western Germany. Am J Epidemiol 2001;153:42–52.
16. Bochicchio F, Forastiere F, Farchi S, Quarto M, Sera F, Axelson O. Residential radon exposure, diet and lung cancer: a case–control study in a Mediterranean region. Int J Cancer. 2005;114:983–91.
17. Barros-Dios JM, Barreiro MA, Ruano-Ravina A, Figueiras A. Exposure to residential radon and lung cancer in Spain: a population-based case–control study. Am J Epidemiol 2002;156:548–55.
18. Pershagen G, Åkerblom G, Axelson O, Clavensjö B, Damber L, Desai G, et al. Residential radon exposure and lung cancer in Sweden. N Engl J Med 1994;330:159–64.
19. Lagarde F, Pershagen G, Åkerblom G, Axelson O, Bäverstam U, Damber L, et al. Residential radon and lung cancer in Sweden: risk analysis accounting for random error in the exposure assessment. Health Phys 1997;72:269–76.
20. Lagarde F, Axelsson G, Damber L, Mellander H, Nyberg F, Pershagen G. Residential radon and lung cancer among never-smokers in Sweden. Epidemiology 2001;12:396–404.
21. Pershagen G, Liang Z-H, Hrubec Z, Svensson C, Boice Jr JD. Residential radon exposure and lung cancer in Swedish Women. Health Phys 1992;63:179–86.
22. Darby S, Whitley E, Silcocks P, Thakrar B, Green M, Lomas P, et al. Risk of lung cancer associated with residential radon exposure in south-west England: a case–control study. Br J Cancer 1998;78:394–408.
23. Ahrens W, Merletti F. A standard tool for the analysis of occupational lung cancer in epidemiologic studies. Int J Occup Environ Health 1998;4:236–40.
24. World Health Organisation (WHO). Manual of the International Statistical Classification of Diseases, Injuries and Causes of Death, 9th revision. Geneva: WHO; 1975.
25. Preston DL, Lubin JH, Pierce DA, McConney ME. Epicure: release 2.10. Seattle (WA): HiroSoft International Corporation; 1998.
26. StataCorp. Stata Statistical Software: release 6.0. College Station (TX): Stata Corporation; 1999.
27. Plummer M. Improved estimates of floating absolute risk. Stat Med 2004;23:93–104.
28. Pierce DA, Preston DL. Radiation-related cancer risks at low doses among atomic bomb survivors. Radiat Res 2000;154:178–86.
29. Peto R, Darby SC, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case–control studies. BMJ 2000;321:323–9.
30. Nicolaides-Bouman A, Wald N, Forey B, Lee P, editors. International smoking statistics: a collection of historical data from 22 economically developed countries. London: Oxford University Press; 1993.
31. Simonato L, Agudo A, Ahrens W, Benhamou E, Benhamou S, Boffetta P, et al. Lung cancer and cigarette smoking in Europe: an update of risk estimates and an assessment of inter-country heterogeneity. Int J Cancer 2001;91:876–87.
32. Bain C, Feskanich D, Speizer FE, Thun M, Hertzmark E, Rosner BA, Colditz G. Lung cancer rates in men and women with comparable histories of smoking. J Natl Cancer Inst 2004;96:826–34.
33. Peto R, Lopez A, Boreham J, Thun M, Heath C. Mortality from tobacco in developed countries: indirect estimation from national vital statistics. Lancet 1992;339:1268–78.
34. Cederlöf R, Friberg L, Hrubec Z, Lorich U. The relationship of smoking and some social convariables to mortality and cancer morbidity: a ten year follow-up in a probability sample of 55 000 Swedish subjects age 18 to 69. Stockholm: The Karolinska Institute; 1975.
35. Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. BMJ 2004;328:1519–28.
36. Hunter N, Howarth CB, Miles JCH, Muirhead CR. Year-to-year variations in radon levels in a sample of UK houses with the same occupants. In: McLaughlin JP, Simopoulos ES, Steinhäusler F, editors. The natural radiation environment VII. Oxford (UK): Elsevier; 2005. p 438–47.
37. Lomas PR, Green BMR. Temporal variations of radon levels in dwellings. Radiat Prot Dosim 1994;56:323–5.
38. Reeves GK, Cox DR, Darby SC, Whitley E. Some aspects of measurement error in explanatory variables for continuous and binary regression models. Stat Med 1998;17:2157–77.
39. Heid IM, Küchenhoff H, Miles J, Kreienbrock L, Wichmann HE. Two dimensions of measurement error: classical and Berkson error in residential radon exposure assessment. J Expo Anal Environ Epidemiol 2004;14:365–77.
40. Bäverstam U, Swedjemark GA. Where are the errors when we estimate radon exposure in retrospect? Radiat Prot Dosim 1991;36:107–12.
41. Heid IM, Rosario AS, Kreienbrock L, Küchenhoff H, Wichmann HE. The impact of measurement error on studies on lung cancer and residential radon exposure in Germany. J Toxic Environ Health. In press.
42. Carroll RJ, Ruppert D, Stefanski LA. Measurement error in nonlinear models. London: Chapman and Hall; 1995.

43. Axelson O, Edling C, Kling H. Lung cancer and residency—a case-referent study on the possible impact of exposure to radon and its daughters in dwellings. Scand J Work Environ Health 1979;5:10–15.
44. Axelson O, Edling C, Kling H, Andersson L. Lung cancer and radon in dwellings [letter]. Lancet 1981;318:995–6.
45. Edling C, Kling H, Axelson O. Radon in homes—a possible cause of lung cancer. Scand J Work Environ Health 1984;10:25–34.
46. Damber LA, Larsson LG. Lung cancer in males and type of dwelling. Acta Oncol 1987;26:211–5.
47. Svensson C, Eklund G, Pershagen G. Indoor exposure to radon from the ground and bronchial cancer in women. Int Arch Occup Environ Health 1987;59:123–31.
48. Axelson O, Andersson K, Desai G, Fagerlund I, Jansson B, Karlsson C, et al. Indoor radon exposure and active and passive smoking in relation to the occurrence of lung cancer. Scand J Work Environ Health 1988;14:286–92.
49. Poffijn A, Mak R, Van-Hoorne M, Weynants P, Prignot J. Indoor radon exposure and lung cancer in Belgium. Arch Belg 1989;47:104–6.
50. Deri ZS, Takacs S, Csige I, Hunyadi I. A case-control study of radon and lung cancer in eastern Hungary. Radiat Prot Dosim 1992;45:695–8.
51. Zaridze DG, Zemlyanaya G. Relationship between radon concentration in living premises and risk of lung cancer. Med Radiol Radiolog Safety 1995;40:44–7.
52. Magnus K, Engeland A, Green BM, Haldorsen T, Muirhead CR, Strand T. Residential radon exposure and lung cancer—and epidemiological study of Norwegian municipalities. Int J Cancer 1994;58:1–7.
53. Pressyanov D, Minev L, Uzunov P, Danon S, Valerianova Z. Excess lung cancer incidence and radon indoors in a Bulgarian town. J Epidemiol Community Health 1999;53:448.
54. Pisa FE, Barbone F, Betta A, Bonomi M, Alessandrini B, Bovenzi M. Residential radon and risk of lung cancer in an Italian alpine area. Arch Environ Health 2001;56:208–15.
55. Conrady J, Martin K, Lembcke J. The true size of the lung cancer risk from indoor radon: hidden behind a smoke screen? In: Bayer A, editor. Proceedings of the 5th International Conference on High Levels of Natural Radiation and Radon Areas, Radiation Dose and Health Effects; 2000 Sep; München, Germany. Amsterdam (North-Holland): Elsevier; 2000. Excerpta Medica International Congress Series (ICS 1225) p 253–8.
56. Krewski D, Lubin JH, Zielinski JM, Alavanja M, Catalan VS, Field RW, et al. Residential radon and risk of lung cancer. A combined analysis of seven North American case-control studies'. Epidemiology. 2005;16:137–45.
57. Wang Z, Lubin JH, Wang L, Zhang S, Boice JD Jr, Cui H, et al. Residential radon and lung cancer risk in a high-exposure area of Gansu Province, China. Am J Epidemiol 2002;155:554–64.
58. Blot WJ, Xu ZY, Boice JD Jr, Zhao DZ, Stone BJ, Sun J, et al. Indoor radon and lung cancer in China. J Natl Cancer Inst 1990;82:1025–30.
59. Lubin JH, Boice JD Jr. Lung cancer risk from residential radon: meta-analysis of eight epidemiologic studies. J Natl Cancer Inst 1997;89:49–57.
60. Xu ZY, Blot WJ, Xiao HP, Wu A, Feng YP, Stone BJ, et al. Smoking, air pollution and the high rates of lung cancer in Shenyang, China. J Natl Cancer Inst 1989;81:1800–6.
61. Lubin JH, Wang ZY, Boice JD, Yi Xu Z, Blot WJ, Wang LD et al. Risk of lung cancer and residential radon in China: pooled results of two studies. Int J Cancer 2004;109:132–7.
62. Pavia M, Bianco A, Pileggi C, Angelillo IF. Meta-analysis of residential exposure to radon gas and lung cancer. Bull World Health Organ 2003;81:732–8.
63. Lubin JH. Indoor radon and risk of lung cancer. Radiat Res 1999;151:105.
64. Yarmoshenko IV, Kirdin IA, Zhukovsky MV, Astrakhantseva SY. Meta-analysis of twenty radon and lung cancer case-control studies. In: Simopoulos ES, editor. Radioactivity in the environment, volume 7. Oxford (UK): Elsevier; 2004. p 762–71.
65. National Council on Radiation Protection and Measurements. Evaluation of the linear-nonthreshold dose-response model for ionizing radiation. Bethesda (MD): National Council on Radiation Protection and Measurements; 2001. NCRP report no 136.
66. Lubin JH, Boice JD Jr, Edling C, Hornung RW, Howe GR, Kunz E, et al. Lung cancer in radon-exposed miners and estimation of risk from indoor exposure. J Natl Cancer Inst 1995;87:817–27.
67. Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, et al. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. Proc Natl Acad Sci USA 2003;100:13761–6.
68. Hall EJ. The bystander effect. Health Phys 2003;85:31–5.
69. Brenner DJ, Sachs RK. Domestic radon risks may be dominated by bystander effects—but the risks are unlikely to be greater than we thought. Health Phys 2003;85:103–8.
70. Cohen BL. Lung cancer rate vs mean radon level in US counties of various characteristics. Health Phys 1997;72:114–9.
71. Heid IM, Gerken M, Wellmann J, Küchenhoff H, Kreienbrock L, Wichmann HE. On the potential of measurement error to induce differential bias on odds ratio estimates: an example from radon epidemiology. Stat Med 2002;21:3261–78.
72. Schaffrath Rosario A, Wellmann J, Heid IM, Wichmann HE. Radon epidemiology: continuous and categorical trend estimators when the exposure distribution is skewed and outliers may be present. J Toxic Environ Health. In press.
73. Tomášek L, Plaček V, Müller T, Heribanová A, Matzner J, Burian I, et al. Czech studies of lung cancer risk from radon. Int J Low Radiat 2003;1:50–62.
74. Krewski D, Lubin JH, Zielinski JM, Alavanja M, Catalan VS, Field RW, et al. A combined analysis of North American case-control studies of residential radon and lung cancer. J Toxicol Health. In press.
75. Lubin JH, Tomášek L, Edling C, Hornung RW, Howe G, Kunz E, et al. Estimating lung cancer mortality from residential radon using data for low exposures of miners. Radiat Res 1997;147:126–34.
76. Haerting FH, Hesse W. Der Lungenkrebs, die Bergkrankheit in den Schneeberger Gruben (Lung cancer, the mountain disease in the Schneeberg mines). Vierteljahresschr Gerichtl Med Öff Sanitätswes 1879;30:296–309; 31:102–32,312–37.
77. Pirchan A, Sikl H. Cancer of the lung in the miners of Jachymov (Joachimsthal). Am J Cancer 1932;4:681–722.
78. Sikl H. The present status of knowledge about the Jachymov disease (cancer of the lungs in the miners in the radium mines). Acta Unio Int Contra Cancrum 1950;6:1366–75.
79. Tomášek L, Plaček V. Radon exposure and lung cancer risk: Czech cohort study. Radiat Res 1999;152:S59–S63.
80. Horáček J, Placek V, Ševc J. Histologic types of bronchogenic cancer in relation to different conditions of radiation expo-

sure. Cancer 1977;40:832–5.
81. Saccomanno G, Auerbach O, Kuschner M, Harley NH, Michels RY, Anderson MW, et al. A comparison between the localization of lung tumors in uranium miners and in nonminers from 1947 to 1991. Cancer 1996;77:1278–83.
82. Yao SX, Lubin JH, Qiao YL, Boice JD Jr, Li JY, Cai SK, et al. Exposure to radon progeny, tobacco use and lung cancer in a case–control study in southern China. Radiat Res 1994;138:326–36.
83. Land CE, Shimosato Y, Saccomanno G, Tokuoka S, Auerbach O, Tateishi R, et al. Radiation-associated lung cancer: a comparison of the histology of lung cancers in uranium miners and survivors of the atomic bombings of Hiroshima and Nagasaki. Radiat Res 1993;134:234–43.
84. Kreuzer M, Müller KM, Brachner A, Gerken M, Grosche B, Wiethege T, et al. Histopathologic findings of lung carcinoma in German uranium miners. Cancer 2000;89:2613–21.
85. Bochicchio F, Campos Venuti G, Nuccetelli C, Piermattei S, Risica S, Tommasino L, et al. Results of the representative Italian national survey on radon indoors. Health Phys 1996;71:741–8.
86. Hubbard LM, Swedjemark GA. Challenges in comparing radon data sets from the same Swedish houses: 1955–1990. Indoor Air 1993;3:361–8.
87. Samuelsson C. Retrospective determination of radon in houses. Nature 1988;334:338–40.
88. Mahaffey JA, Parkhust MA, James AC, Cross FT, Alavanja MCR, Boice JD, et al. Estimating past exposure to indoor radon from household glass. Health Phys 1993;64:381–91.
89. Samuelsson C, Falk R, Roos B. Alpha particle emission from reference glass surfaces implanted with 210Po. Sci Total Environ 2001;272:175–9.
90. Alavanja MC, Lubin JH, Mahaffey JA, Brownson RC. Residential radon exposure and risk of lung cancer in Missouri. Am J Public Health 1999;89:1042–8.
91. Lagarde F, Falk R, Almrén K, Nyberg F, Svensson H, Pershagen G. Glass-based radon-exposure assessment and lung cancer risk. J Expo Anal Environ Epidemiol 2002;12:344–54.
92. Bochicchio F, McLaughlin JP, Walsh C. Comparison of radon exposure assessment results: ^{210}Po surface activity on glass objects *vs* contemporary air radon concentration. Radiat Meas 2003;36:211–5.
93. Steck DJ, Alavanja MCR, Field RW, Parkhurst MA, Bates DJ, Mahaffey JA. ^{210}Po implanted in glass surfaces by long term exposure to indoor radon. Health Phys 2002; 83: 261–71.
94. Field RW, Smith BJ, Steck DJ, Lynch CF. Residential radon exposure and lung cancer: variation in risk estimates using alternative exposure scenarios. J Expo Anal Environ Epidemiol 2002;12:197–203.
95. Pierce DA, Sharp GB, Mabuchi K. Joint effects of radiation and smoking on lung cancer risk among atomic bomb survivors. Radiat Res 2003;159:511–20.
96. Brenner DJ, Sachs RK. Do low dose-rate bystander effects influence domestic radon risk? Int J Radiat Biol 2002;78:593–604.
97. Rogel A, Laurier D, Tirmarche M, Quesne B. Lung cancer risk in the French cohort of uranium miners. J Radiol Prot 2002;22:A101–A106.
98. Stram DO, Langholz B, Huberman M, Thomas DC. Correcting for exposure measurement error in a reanalysis of lung cancer mortality for the Colorado plateau uranium miners cohort. Health Phys 1999;77:265–75.

Appendix A: additional methodological information

Table A1. Summary of the design of each study. [See also the list of references at the end of appendix A]

Study	Summary of design
Austria [Oberaigner et al, 2002 (1)]	The study was carried out in the district of Imst in Tyrol, Austria. The cases were persons having died from lung cancer in 1970–1992, taken from the official mortality statistics file for Austria. The controls were a random sample of decedents (excluding persons who had died from smoking-related causes) in the same period taken from the same source, individually matched by sex, age, and year of the decedents. Only German-speaking people for whom a next-of-kin could be found were selected for the study. There was no review of pathological material. The index year was the year of death.
Czech Republic [Tomášek et al, 2001 (2)]	The study was based on a cohort study of the population of the Middle Bohemian Pluton. The cohort study population included inhabitants of the area (80 villages), who had resided there for at least 3 years (including at least 1 year after 1960), a total of 12 004 people. The follow-up was from 1960 to 1999. Information on vital status and causes of death was obtained from local authorities and from the national population registry. Smoking status was available for 206 of the 210 who died from lung cancer and 70% of the population as a whole. The case–control study comprised the 206 lung cancer cases, together with 4 controls per case selected at random from people who were alive at the time of death of the case and for whom smoking information was available, matched for sex and year of birth (±5 years). There was no review of pathological material. For the cases, the index year was the year of death, and for the controls it was the year of death of the matched case.
Finland nationwide [Auvinen et al, 1996 (3)]	All persons residing in the same single-family house from 1 January 1967 or earlier, until the end of 1985 were identified from the Finnish Population Register. In this group, all of the cases of lung cancer diagnosed from 1 January 1986 through 31 March 1992 were identified from the Finnish Cancer Register. There was no specific review of pathological material. One control matched by year of birth and sex was identified from the same cohort for each case, the control had to be alive at the time of the diagnosis for the corresponding case. In the event that no information was available for the primary control another control was identified.The index year was the year of diagnosis for the cases. For the controls it was the year of diagnosis of the matched case or, if this information was not available, the mean year of diagnosis for the cases with the same sex and year of birth.
Finland southern [Ruosteenoja et al, 1996 (4)]	Nineteen rural municipalities in southern Finland with high radon levels were included in the study. All men with lung cancer diagnosed in the resident population in these municipalities during 1980–1985 were identified through the Finnish Cancer Register (1980–1982) or through hospitals in the study area with diagnostic and treatment facilities for lung cancer (1983–1985). The cases were excluded from the study if they were institutionalized, had migrated to the study area after 1 January 1980, had been diagnosed prior to 1980, had a lung metastasis only secondary to another primary site, or had missing case records. There was no specific review of pathological material. A random sample of men resident in the study municipalities on 1 January 1980 and balanced according to the age distribution of the cases was drawn from the National Population Register. The controls were excluded from the study if they were institutionalized, deceased with no next of kin, or had been diagnosed with lung cancer. A questionnaire on smoking was sent to the remainder. Among those who replied, all current smokers were selected for the study, as were random samples of approximately 10% each of ex-smokers and lifelong nonsmokers.The index date was the year of diagnosis for the cases and the mean year of diagnosis of the cases (1982) for the controls.
France [Baysson 2004 et al, (5)]	The study was undertaken in five radon-prone regions (Auvergne, Brittany, Languedoc, Limousin and Ardennes). In each participating hospital where the investigation and treatment of lung cancer is carried out, all persons diagnosed with primary lung cancer during 1992–1998 and under 75 years of age on their date of diagnosis were identified by local interviewers and interviewed within 6 months of diagnosis. Persons were eligible for the study if they had lived in the study areas for at least 25 out of the last 35 years. There were no exclusion criteria based on occupation or nationality. There was no specific review of pathological material. For each case, two controls were identified from the pool of hospital patients of the same region who satisfied the study residence requirements and who had not been hospitalized for a disease strongly related to tobacco. Within each region the controls were individually matched to the cases for sex and age (± 5 years). In each region, attempts were made to include patients with a wide variety of diseases in the hospital control group. The index year was the year of diagnosis for both the cases and the controls.
Germany eastern [Wichmann et al, 1999 (6); Kreuzer et al, 2003 (7); Wichmann et al, 2005 (8)]	The cases were recruited in five hospitals in Thuringia and Saxony from October 1990 to March 1997 and were eligible if they currently resided in the study area, had lived in Germany since 1965, were aged 75 years or less, had microscopically confirmed lung cancer with no evidence of tuberculosis, could be interviewed within 3 months of the initial diagnosis, had never worked in the SDAG (Die Sowjetisch-Deutsche Aktiengesellschaft) Wismut uranium mining industry, and were well enough to be interviewed personally. Histological material was reviewed by one pathologist and cytological material by another. Histological and/or cytological material was available for all the cases; a review of the histological material by one reference pathologist and of the cytolgical material by another was performed for 61% of the cases. Population controls were recruited during 1990–1997 using a two-stage process. First, a random sample of about 30 000 people was selected from the central registration office of the former German Democratic Republic. Then people were selected at random with frequency matching to the cases for sex, age (six 5-year groups), and 10 matching regions. The eligibility criteria were similar to those for the cases.The index year was the year of interview (for the cases within 3 months of diagnosis). Exclusion criteria were as for the Germany western study.
Germany western [Wichmann et al, 2005 (8); Wichmann et al, 1998 (9); Kreienbrock et al,2001 (10)]	The study was carried out in the rural areas of Eifel, Westerwald/Hunsrueck, and Upper Palatinate/Lower Bavaria and also in neighboring urban areas (the industrialized Ruhr area, Rhineland and the Saar region). The cases were recruited in 9 hospitals from October 1990 to October 1995 and were eligible if they currently resided in the study area, had lived in Germany since 1965, spoke German, were aged 75 years or less, had microscopically confirmed lung cancer with no evidence of tuberculosis, could be interviewed within 3 months of the initial diagnosis, and had never worked in the SDAG (Die Sowjetisch-Deutsche Aktiengesellschaft) Wismut uranium mining industry. Histological and/or cytological material was available for all of the cases; a review of the histological material by one reference pathologist and of the cytological material by another was performed for 75% of the cases. People were excluded when the current address had been occupied for less than a year or when the subject had spent less than 25% of his or her time at home. Population controls were selected at random from registers of residents or by random digit dialing, were frequency matched to the cases for sex, age (six 5-year groups), and 13 matching regions. The eligibility criteria were similar to those for the cases. The index year was the year of interview (for the cases within 3 months of diagnosis).

(continued)

Table A1. Continued.

Study	Summary of design
Italy [Bochicchio et al, 2005 (11)]	The study was based on patients admitted to one of the main hospitals of the metropolitan area of Rome during November 1993–June 1996. The participants were Caucasians, aged at least 35 years, resident in the Lazio region for at least 25 years of the 35 years before the year of interview. The cases were those with a final diagnosis of lung cancer. The controls were selected from the following wards: general surgery, orthopedics, ear, nose & throat, and general medicine. They were frequency-matched to the cases for sex and age (5-year groups). People admitted to the hospital for conditions related to smoking or diet, including most cancers, respiratory diseases, diabetes, and cardiovascular, digestive and renal diseases, were not included as controls. There was no specific review of pathological material.
Spain [Barros-Dios et al, 2002 (12)]	The study was carried out in the Santiago de Compostela Public Health District in northwest Spain and was population-based. All of the cases of lung cancer diagnosed in the period 1992–1994 were identified from the pathology departments of the local hospitals. There was no specific review of pathological material for this study. The controls were selected at random from the 1991 census, subject to frequency matching to the cases by geographic area (comarca) of current residence and sex. Exclusion criteria were age under 35 years, current residence less than 5 years' duration or having undergone major structural alterations recently, cases without histological confirmation and/or undergoing occupational or therapeutic radiation, controls with respiratory tract disease or previous cancer. The interviews took place during the period 1992–1995 and were carried out by two specially trained interviewers, either with the subject in person or, if he or she had died, with their closest surviving relative or cohabitant. The index date was the mean year of diagnosis of the cases (1993) for all the participants.
Sweden nationwide [Pershagen et al, 1994 (13); Lagarde et al, 1997 (14)]	The study was carried out in 109 municipalities in Sweden, of which 56 had been selected as high-radon areas and the remainder as low-radon areas. The base population for the study included all persons 35 to 74 years of age who had lived in one of these municipalities at some time from 1 January 1980, through 31 December 1984, and who had been living in Sweden on 1 January 1947. All of the cases of lung cancer diagnosed in the base population from 1 January 1980 through 31 December 1984 were selected from the Swedish Cancer Register. There was no specific review of pathological material. Two control groups representing the base population for the study were selected from the population registers of Statistics Sweden. The first control group was frequency-matched with the case group for age and calendar year of residence in the study area.The second group was selected according to the same criteria used to select the first group, except that, in addition, it was frequency-matched for vital status on 1 December 1986. The index year was the year of diagnosis for the cases and the frequency-matched year of selection for the controls.
Sweden never-smokers [Lagarde et al, 2001 (15)]	Participants were recruited from five case–control studies carried out for other reasons. All never-smoker cases in these studies were included provided their year of diagnosis was 1980 or later. Up to twice as many never-smoker controls were selected, matched for birth year (within 3 years), sex, and study. Additional relevant details for each substudy follow: *Study 1* [Nyberg et al, 1998 (16)]: a study of exposure to environmental tobacco smoke and lung cancer among never-smokers resident in Stockholm county. The cases were recruited between 1 October 1989 and 30 September 1995 among patients referred to the three main hospitals treating lung cancer. About twice as many controls were selected from the population registers, frequency-matched by age group (30–49, 50–69, ≥70 years), sex, and hospital catchment area. *Study 2* [Gustavsson et al, 2000 (17)]: never-smokers were selected from a case–control study of air pollution and lung cancer. The cases were selected from those diagnosed between 1 January 1985 and 31 December 1990 in the Stockholm County regional cancer registry and were included if they were aged 40–75 years, resident in Stockholm county at some time between 1 January 1985 and 31 December 1990, with no more than 5 years of residence outside the county between 1950 and 1990. About twice as many controls were randomly selected in 1992 from population registers of Stockholm county for the corresponding years, frequency-matched for age at calendar-year of diagnosis. About half of the controls were additionally frequency-matched to the cases for vital status in 1990, excluding those with a smoking-related cause of death. *Study 3* [Pershagen et al, 1995 (18)]: a study designed to assess lung cancer risk from environmental emissions from a large smelting plant in northern Sweden recruited cases and controls from men and women who died in the Skellefteå Municipality between 1961 and 1990, excluding those who worked at the plant or as miners. Two controls per case were selected, matched for birth year and sex. For the present study 40 never-smoking cases, 78 never-smoking controls who had died in the period 1980–1990 were selected. *Study 4* [Axelsson et al, 1996 (19)]: a case–control study of environmental factors and lung cancer was conducted among people aged less than 75 years and living at the time of the study in one of 26 municipalities in Göteborg and Bohus county or Älvsborg county in southwest Sweden. The cases were recruited from the three local regional hospitals from January 1989 to June 1994. The controls were selected from population registers matching for county, sex and birth date. All 49 never-smoker cases and twice as many never-smoker controls were selected for the present study. *Study 5*: A case–control study investigated the association between occupational exposure and lung cancer in the county of Västernorrland, where many paper and pulp mills are situated. The cases were men diagnosed with lung cancer between 1978 and 1991, as recorded in the Umeå Regional Cancer Register, who died before 1 September 1992. There was no pathological review specifically for the present study. With the controls for each study one control group was selected from the National Cause-of-death Register (excluding deaths from suicide or lung cancer) and matched to cases on year of birth, year of death and municipality of residence at the time of diagnosis of the matched case. A second control group was selected from persons alive at the time of diagnosis of the case using the national population register, matching for year of birth and municipality of residence. All 25 never-smoker cases diagnosed in 1980 or later and twice as many controls were included in the study. For all these five component studies the index year was the year of diagnosis for the cases. For the controls it was the year of diagnosis of the case for living controls who died less than 3 years before their matched case and the year of death for the controls who died more than 3 years before the year of diagnosis of the matched case.
Sweden Stockholm [Svensson et al, 1989 (20); Pershagen et al, 1992 (21)]	Females referred with suspected lung cancer were interviewed at all the clinical departments of pulmonary medicine and thoracic surgery at hospitals in Stockholm county from September 1983 through December 1985. The final diagnosis was obtained from hospital records. Those subsequently found not to have lung cancer constituted the hospital group. There was no specific review of pathological material for this study. For each case of lung cancer a population control was randomly selected from Stockholm County population registers from women who were born on the same day as the case. The index year was the year of interview for both the cases and controls.
United Kingdom [Darby et al, 1998 (22)]	The study was carried out in Devon and Cornwall, the two counties in Great Britain with the highest average residential radon concentrations. People under 75 years of age who were referred with suspected lung cancer during a 4-year period were identified at five hospitals in Devon and Cornwall, where lung cancers are investigated and treated. They were eligible for the study if they were current residents of Devon or Cornwall and had lived in either county for at least 20 years during the 30-year period ending 5 years previously. Only those who were ethnically white were included in the study. Pathological specimens were reviewed by one pathologist. For each person with suspected lung cancer, a control was sought from hospital patients of the same sex, born within 5 years of the case, who satisfied the study residence requirements, whose current hospital admission was for a disease not known to be strongly associated with smoking, and who lived in the same area as the case. For each hospital two or three areas were defined, one being the local area of the hospital and the other(s) more distant areas. A population-based group of controls was selected and was frequency-matched to the persons with suspected lung cancer by age, sex and county of current residence. The index year was year of the interview. For the cases this was always shortly after the diagnosis of lung cancer.

Table A2. Summary of the radon measurement procedure for each study. [See the list of references at the end of appendix A][L = living room, B = bedroom, TLD = thermoluminescent dosimeter, x = bedroom occupancy as a proportion of the total time spent at home]

Study	Dwellings targeted in 30 years	Detectors (N)	Type of detector	Place	Time period	Measurement formula (if >1 detector	Comment
Austria	Last available home occupied for at least 2 years	2	Closed CR-39 α-track detector [a]	1 in L; 1 in B	1 year (ie, 1 x 12 months) but shorter (minimum 1 month) with seasonal correction if concentration high	xL+(1−x)B [b]	For measurements in previous homes, changes due to alteration of the house or different ventilation practices of the study members and present inhabitants were taken into account by a multivariate model [Gerken et al (23)]
Czech Republic	All dwellings in study area	2	Open LR-115 α-track detector [c]	2 most occupied rooms in house	1 year (ie, 1 × 12 months)	Average	Original measurement on radon progeny; conversion factor to radon gas established by 652 simultaneous measurements of radon progeny by passive track detectors and radon gas by electrets
Finland nation wide	Index dwelling only	1	Closed Macrofoil α-track detector [d]	L or B	1 year	–	–
Finland southern	All dwellings occupied for at least 1 year during 1950–1975	1	Closed Macrofoil α-track detector [d]	L or B	Either 2 months winter only or 2 months winter and 2 months summer	–	Winter concentrations only were adjusted for seasonal correction [Arvela et al (24), Arvela (25), Castrén et al (26)]
France	All dwellings occupied for ≥1 year	2	Open LR-115 α-track detector [c]	1 in L; 1 in B	6 months	(L+B)/2	Seasonal adjustments shown to be less than 20% [Baysson et al (27)]
Germany western	All dwellings occupied for at least 1 year in previous 25 years	2 [e]	Closed CR-39 α-track detector [a]	1 in L; 1 in B	1 year ±2 months [e]	(1−x)L+xB [b]	Changes in building characteristics over time or differences in ventilation practice between the study participant and the current inhabitant were taken into account using a multivariate model [Gerken et al (23)]
Germany eastern	Only current dwelling considered in present exercise	2 [e]	Closed CR-39 α-track detector [a]	1 in L; 1 in B	1 year ±2 months [e]	(1−x)L+xB [b]	Changes in building characteristics over time or differences in ventilation practice between the study participant and the current inhabitant were taken into account using a multivariate model [Gerken et al (23)]
Italy	All dwellings in study area occupied for at least 1 year	8	Closed LR-115 α-track detector [f]	2 x 2 in L; 2 x 2 in B	1 year (comprising 2 consecutive 6-month periods)	(L+B)/2	Some proxy measurements made for apartments above ground level; proxy dwelling was always in same building and generally on same floor as target dwelling [Bochicchio et al (28)]
Spain	Current dwelling open	1	Closed α-track detector [g]	B	5 months on average (minimum 3 months)	–	–
Sweden never-smokers	All dwellings occupied for at least 2 years	2	Closed CR-39 α-track detector [h]	1 in L; 1 in B	3 months winter	(L+B)/2	Seasonal correction of 10% [Pershagen et al (13)]
Sweden nation-wide	All dwellings occupied for at least 2 years	2	Closed CR-39 α-track detector [h]	1 in L; 1 in B	3 months winter	(L+B)/2 or L or B	Seasonal correction of 10% [Pershagen et al (13)]
Sweden Stockholm	All dwellings occupied for at least 2 years	2	Closed LR-115 α-track detector [i] (62.7% of years of interest)	1 in L; 1 in B	1 year (ie, 1 × 12 months	(L + B)/2or L or B	Some proxy measurements made for apartments; the proxy dwelling was always in the same building and on the same floor as the target dwelling
		1	or TLD [j] (14.3% of years of interest)	1 week L, then 1 week B	2 weeks	0.9×TLD+0.44	TLD measurements transformed to α-track using the regression equation empirically derived by Svensson et al (30)
United Kingdom	All dwellings in study area occupied for at least 1 year	2	Closed CR-39 α-track detector [k]	1 in L 1 in B	6 months	0.4×L+0.55×B	Seasonal adjustment as in Pinel et al 1995 (31); weights for L and B taken from Wrixon et al (32).

[a] Manufactured by Bayer.
[b] Bedroom occupancy was estimated individually for each dwelling from questionnaire information. If either the bedroom or the living room measurement was missing, it was imputed from the other measurement corrected for the systematic difference between the bedroom and living room radon levels.
[c] Manufactured by Kodak.
[d] Manufactured at Finnish Centre for Radiation and Nuclear Safety.
[e] For houses with radon concentrations over 400 Bq/m^3, as identified by initial spot measurement, several detectors were placed consecutively over a 1-year period. For other houses, the detectors were left in place for 12 months.
[f] Manufactured by Istituto Superiore di Sanita/Italian Institute of Health using LR-115 bought from Dosirad, France.
[g] Supplied by Radiation Safety Services Inc, Illinois (US Environmental Agency approved laboratory).
[h] Manufactured by Swedish Radiation Protection Authority [Mellander & Enflo (29)].
[i] Manufactured by Terradex Corporation type SF.
[j] Thermoluminescence detectors designed by Swedish Radiation Protection Authority and calibrated yearly.
[k] Manufactured by National Radiological Protection Board, United Kingdom.

Table A3. Common data format for the European Collaborative Analysis. Missing or inapplicable variables have 9 for all digits (eg, 9999 or 99.9, etc). (ID = identification number)

Variable description	Variable name	Codes
Constant variables		
Study	study	01, 02, 03, ...etc.
Status	status	1=case, 2=hospital control, 3 & 4=population control
Study specific ID number	unique	
Include in analysis	include	1=yes, 2=no: no radon measurement in period 5–35 years before index date, 3=no: incomplete smoking data, 4=no: neither radon nor smoking data, 5=no: diagnosis not eligible (eg, carcinoid, etc)
Interview type	int_type	1=subject, 2=surrogate, 3=combination of 1 and 2
Interview method	int_mtd	1=in person or by phone, 2=postal questionnaire, 3=combination of 1 and 2
Sex	Sex	1=male, 2=female
Index year	ind_year	Last 2 digits of index year
Age in index year	ind_age	Integer value
Region of residence in index year	region	Integer value
Histological type	his_typ	1=squamous, 2=small cell, 3=adeno, 4=other (including undifferentiated and microscopically confirmed but histological type unspecified), 5=no microscopic confirmation, 8=control
Diagnosis of hospital controls	icd	ICD9 3 digit code
Smoking category	smoking	1=lifelong nonsmoker (ie, people who have never smoked as much as 1 cigarette per day for as long as a year, who have never smoked a pipe or cigars regularly, and who have smoked a lifetime total of less than 400 cigarettes or equivalent in other tobacco); 2=current cigarette smoker (<15 per day); 3=current cigarette smoker (15–24 per day); 4=current cigarette smoker (≥25 per day); 5=ex-smokers <10 years; 6=ex-smoker ≥10 years; 7=others (ie, occasional cigarette smokers and current smokers of pipe, cigars, cigarillos but not of cigarettes)
Age started smoking cigarettes	age_cig	Integer value (88: lifelong nonsmoker)
Number of cigarettes smoked/day during the active smoking period where available; otherwise number of cigarettes last smoked regularly	aver_cig	Integer value (30 grams of pipe tobacco per week assumed to have the same effect as 2 cigarettes per day) (88: lifelong nonsmoker)
Years prior to index date when last smoked cigarettes regularly	last_cig	Integer value (00: current cigarette smokers, 88: lifelong nonsmokers)
Social status	soc_stat	Up to 3 levels for each country, based either on occupation or on education
Occupational lung cancer risk (of duration at least 1 year)		
Radon	occ_rad	1=yes, 2= no
Asbestos	occ_asb	1=yes, 2=no
Other established occupational lung cancer risk	occ_oth	1=yes, 2=no
Average occupancy (ie, estimated average proportion of 24-hour day spent at home during 30-year period of interest)	aver_occ	Proportion in range 0.0 to 1.0
Urban–rural indicator	u_r_ind	Proportion in range 0.0 to 1.0 (0.0=rural all 30 years, 1.0=urban all 30 years)
Usually slept with the window open?	win_open	1=yes, 2=no
Married to a smoker (lifelong nonsmokers only)	ets_home	1=yes, 2=no
Exposed to environmental tobacco smoke at work (lifelong nonsmokers only)	ets_work	1=yes, 2=no
Year-by-year variables		
Study	study	As in constant variables above
Status	status	As in constant variables above
Study specific ID number (unique when taken in combination with status)	unique	As in constant variables above
Year	year	1,2,...,30 (earliest year=1)
Address	add	1,2,...(earliest year=1)
Annual radon gas concentration Bq/m³, long-term measurement	radon_m	Integer value 99999=no measurement
Annual radon gas concentration Bq/m³, estimate	radon_e	integer value 99999=measurement available

Table A4. Coverage of the target population in each study. (N/A = not available) [See the list of references at the end of appendix A]

Study	Lung cancer cases		Population controls		Hospital controls		All participants	
	N	%	N	%	N	%	N	%
Austria [Oberaigner et al, 2002 (1)]								
Persons initially selected	355	.	432	.	–	.	787	.
Found not to belong to target population	14	.	17	.	–	.	31	.
Persons belonging to target population	341	.	415	.	–	.	756	.
Included in Collaborative Analysis	183	.	188	.	–	.	371	.
Coverage of target population	–	54	–	45	–	.	–	49
Czech Republic [Tomášek et al, 2001 (2)]								
Persons initially selected	210	.	12 004	.	–	.	–	.
Found not to belong to target population	–	.	–	.	–	.	–	.
Persons belonging to target population	210	.	12 004	.	–	.	–	.
Included in Collaborative Analysis	171	.	713 [a]	.	–	.	884	.
Coverage of target population	–	81	–	70 [a]	–	.	–	72
Finland nationwide [Auvinen et al, 1996 (3)]								
Persons initially selected	2563	.	3 354	.	–	.	5 917	.
Found not to belong to target population	6	.	.	.	–	.	6	.
Persons belonging to target population	2557	.	3 354	.	–	.	5 911	.
Included in Collaborative Analysis	881	.	1 435	.	–	.	2 316	.
Coverage of target population	–	34	–	43	–	.	–	39
Finland southern [Ruosteenoja et al, 1996 (4)]								
Persons initially selected	318	.	1 500	.	–	.	1 818	.
Found not to belong to target population	29	.	918 [b]	.	–	.	947	.
Persons belonging to target population	289	.	582	.	–	.	871	.
Included in Collaborative Analysis	160	.	328	.	–	.	488	.
Coverage of target population	–	55	–	56	–	.	–	56
France [Baysson et al, 2004 (5)]								
Persons initially selected	688	.	–	.	1428	.	2 116	.
Found not to belong to target population	0	.	–	.	0	.	0	.
Persons belonging to target population	688	.	–	.	1428	.	2 116	.
Included in Collaborative Analysis	571	.	–	.	1209	.	1 780	.
Coverage of target population	–	83	–	.	–	85	–	84
Germany eastern [Wichmann et al, 1999 (6); Kreuzer et al, 2003 (7); Wichmann et al, 2005 (8)]								
Persons initially selected	3 960	.	5 192	.	–	.	9 152	.
Found not to belong to target population	1 384	.	954	.	–	.	2 338	.
Persons belonging to target population	2 576	.	4 238	.	–	.	6 814	.
Included in Collaborative Analysis	1 788 [c]	.	1 927 [c]	.	–	.	3 715 [c]	.
Coverage of target population	–	69	–	45	–	.	–	55
Germany western [Wichmann et al, 2005 (8); Wichmann et al, 1998 (9); Kreienbrock et al, 2001 (10)]								
Persons initially selected	4 307	.	12 825	.	–	.	17 132	.
Found not to belong to target population	1 322	.	4 684	.	–	.	6 006	.
Persons belonging to target population	2 985	.	8 141	.	–	.	11 126	.
Included in Collaborative Analysis	2 294 [c]	.	2 488 [c]	.	–	.	4 872 [c]	.
Coverage of target population	–	77	–	31	–	.	–	43
Italy [Bochicchio et al, 2005 (11)]								
Persons initially selected	918	.	–	.	599	.	1 517	.
Found not to belong to target population	248	.	–	.	–	.	248	.
Persons belonging to target population	670	.	–	.	599	.	1 269	.
Included in Collaborative Analysis	384	.	–	.	405	.	789	.
Coverage of target population	–	57	–	.	–	68	–	62
Spain [Barros-Dios et al, 2002 (12)]								
Persons initially selected	257	.	500	.	–	.	757	.
Found not to belong to target population	25	.	109	.	–	.	134	.
Persons belonging to target population	232	.	391	.	–	.	623	.
Included in Collaborative Analysis	156	.	235	.	–	.	391	.
Coverage of target population	–	67	–	60	–	.	–	63
Sweden nationwide [Pershagen et al, 1994 (13); Lagarde et al, 1997 (14)]								
Persons initially selected	1 500	.	1 500 [d]	.	1500 [d]	.	4 500	.
Found not to belong to target population	140	.	76	.	77	.	293	.
Persons belonging to target population	1 360	.	1 424	.	1423	.	4 207	.
Included in Collaborative Analysis	960	.	978	.	1067	.	3 005	.
Coverage of target population	–	71	–	69	–	75	–	71

(continued)

Table A4 Continued.

Study	Lung cancer cases		Population controls		Hospital controls		All participants	
	N	%	N	%	N	%	N	%
Sweden never-smokers [Lagarde et al, 2001 (15)]								
Persons initially selected	N/A[e]	.	N/A[e]	.	–	.	N/A[e]	.
Found not to belong to target population	N/A[e]	.	N/A[e]	.	–	.	N/A[e]	.
Persons belonging to target population	N/A[e]	.	N/A[e]	.	–	.	N/A[e]	.
Included in Collaborative Analysis	258	.	487	.	–	.	745	.
Coverage of target population	–	N/A[e]	–	N/A[e]	–	.	–	N/A[e]
Sweden Stockholm [Svensson et al, 1989 (20); Pershagen et al, 1992 (21)]								
Persons initially selected	N/A[f]	.	242	.	N/A[f]	.	N/A[f]	.
Found not to belong to target population	4	.	0	.	0	.	4	.
Persons belonging to target population	N/A[f]	.	242	.	N/A[f]	.	N/A[f]	.
Included in Collaborative Analysis	196	.	196	.	179	.	571	.
Coverage of target population	–	N/A[f]	–	81	–	N/A[f]	–	N/A[f]
United Kingdom [Darby et al, 1998 (22)]								
Persons initially selected	2 959	.	5 223	.	2401	.	10 583	.
Found not to belong to target population	1 609[g]	.	2 939	.	919	.	5 150	.
Persons belonging to target population	1 350	.	2 284	.	1799[g]	.	5 433	.
Included in Collaborative Analysis	960	.	1 477	.	1649	.	4 086	.
Coverage of target population	–	71	–	65	–	92	–	75

[a] In the Czech Republic study, the original study was a cohort study. The controls were selected from the 70% of the population for whom smoking information was available.
[b] Includes 825 people who responded to the initial smoking questionnaire but who were not selected.
[c] The number of persons after exclusions during the analysis in the Germany eastern study was 945 for the lung cancer cases, 1516 for the population controls, and 2461 for all the participants; and in the Germany western study the corresponding numbers were 1323, 2146 and 3469, respectively.
[d] In the Sweden nationwide study both control groups were population based. The first was matched for vital status and the second was not.
[e] Participation rates among the never-smokers in the five component studies were: study 1: 85.5% of cases of lung cancer, 82.9% of controls of those screened for never-smoking status (6.1% of the controls were potentially eligible as never-smokers could not be contacted, even for screening for never-smoking status). Study 2: cases 87%, controls matched for vital status 82%, controls not matched for vital status 88%. Study 3: cases 94%, controls about 93%. Study 4 cases 86%, controls 75%. Study 5: cases 88%, controls 84% [Lagarde et al (15)]. A further 13 persons with lung cancer and 40 controls were excluded from the analysis as no radon measurement was available during the period of interest.
[f] It was not possible to interview 2.9% of the cases of suspected lung cancer referred to the relevant clinical departments. Cases of suspected lung cancer whose final diagnosis was not lung cancer formed the hospital control group.
[g] In the United Kingdom Southwest England study 317 persons were initially referred with suspected lung cancer but had a final diagnosis that was a disease that was not strongly related to smoking. These were transferred to the hospital control group.

Table A5. Smoothed lung cancer death rates per 10^5 person-years for lifelong nonsmokers during years 3–6 (1984–1988) of the second cancer prevention study of the American Cancer Society. Data based on study by Peto et al (33).

Age	Rate per 10^5 years	
	Males	Females
35–39 years	2	2
40–44 years	3	3
45–49 years	5	4
50–54 years	7	7
55–59 years	10	10
60–64 years	14	14
65–69 years	20	19
70–74 years	27	26
75–79 years	35	34
≥80 years	46	44

References for appendix A

1. Oberaigner W, Kreienbrock L, Schaffrath Rosario A, Kreuzer M, Wellmann J, Keller G, et al. Radon und Lungenkrebs im Bezirk Imst/Österreich [Radon and lung cancer in the district of Imst, Austria]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 2002. Fortschritte in der Umweltmedizin.
2. Tomášek L, Müller T, Kunz E, Heribanová A, Matzner J, Plaček V, et al. Study of lung cancer and residential radon in the Czech Republic. Centr Eur J Public Health 2001;9:150–3.
3. Auvinen A, Mäkeläinen I, Hakama M, Castrén O, Pukkala E, Reisbacka H, et al. Indoor radon exposure and risk of lung cancer: a nested case-control study in Finland. J Natl Cancer Inst 1996;88:966–72. Erratum J Natl Cancer Inst 1998; 90:401–2.
4. Ruosteenoja E, Mäkeläinen I, Rytömaa T, Hakulinen T, Hakama M. Radon and lung cancer in Finland. Health Phys 1996;71:185–9.
5. Baysson H, Tirmarche M, Tymen G, Gouva S, Caillaud D, Artus JC, et al. Case-control study on indoor radon and lung cancer in France. Epidemiology 2004;15:709–16
6. Wichmann HE, Gerken M, Wellmann J, Kreuzer M, Kreienbrock L, Keller G, et al. Lungenkrebsrisiko durch Radon in der Bundesrepublik Deutschland (Ost) – Thüringen und Sachsen [Lung cancer risk due to radon in the Federal Republic of Germany (East)—Thuringia and Saxony]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 1999. Fortschritte in der Umweltmedizin.
7. Kreuzer M, Heinrich J, Wölke G, Schaffrath Rosario A, Gerken M, Wellmann J, et al. Residential radon and risk of lung cancer in Eastern Germany. Epidemiol 2003;14:559–68.
8. Wichmann HE, Rosario AS, Heid IM, Kreuzer M, Heinrich J, Kreienbrock L. Increased lung cancer risk due to residential radon in a pooled and extended analysis of studies in Germany. Health Phys. 2005;88:71–9.
9. Wichmann HE, Kreienbrock L, Kreuzer M, Gerken M, Dingerkus G, Wellmann J, et al. Lungenkrebsrisiko durch Radon in der Bundesrepublik Deutschland (West) [Lung cancer risk due to radon in the Federal Republic of Germany (West)]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 1998. Fortschritte in der Umweltmedizin.
10. Kreienbrock L, Kreuzer M, Gerken M, Dingerkus G, Wellmann J, Keller G, et al. Case-control study on lung cancer and residential radon in Western Germany. Am J Epidemiol 2001;153:42–52.
11. Bochicchio F, Forastiere F, Farchi S, Quarto M, Sera F, Axelson O. Indoor radon and lung cancer: a case-control study in a Mediterranean region. Int J Cancer. 2005;114:983-91.
12. Barros-Dios JM, Barreiro MA, Ruano-Ravina A, Figueiras A. Exposure to residential radon and lung cancer in Spain: a population-based case-control study. Am J Epidemiol 2002;156:548–55.
13. Pershagen G, Åkerblom G, Axelson O, Clavensjö B, Damber L, Desai G, et al. Residential radon exposure and lung cancer in Sweden. N Engl J Med 1994;330:159–64.
14. Lagarde F, Pershagen G, Åkerblom G, Axelson O, Bäverstam U, Damber L, et al. Residential radon and lung cancer in Sweden: risk analysis accounting for random error in the exposure assessment. Health Phys 1997;72:269–76.
15. Lagarde F, Axelsson G, Damber L, Mellander H, Nyberg F, Pershagen G. Residential radon and lung cancer among never-smokers in Sweden. Epidemiology 2001;12:396–404.
16. Nyberg F, Agrenius V, Svartengren K, Svensson C, Pershagen G. Environmental tobacco smoke and lung cancer in non-smokers: does time since exposure play a role? Epidemiology 1998;9:301–8.
17. Gustavsson P, Jakobsson R, Nyberg F, Pershagen G, Järup L, Schéele P. Occupational exposure and lung cancer risk – a population-based case-referent study in Sweden. Am J Epidemiol 2000;152:32–40.
18. Pershagen G, Nyberg F. Luftföroreningar och lungcancer I Rönnskärsområdet [Air pollution and lung cancer in the Rönnskär area]. Stockholm: Institutet för miljömedicin, Karolinska Institutet; 1995. IMM-rapport 1/95.
19. Axelsson G, Liljeqvist T, Andersson L, Bergman B, Rylander R. Dietary factors and lung cancer among men in West Sweden. Int J Epidemiol 1996;25:32–9.
20. Svensson C, Pershagen G, Klominek. Lung cancer in women and type of dwelling in relation to radon exposure. Cancer Res 1989;49:1861–5.
21. Pershagen G, Liang Z-H, Hrubec Z, Svensson C, Boice Jr JD. Residential radon exposure and lung cancer in Swedish Women. Health Phys 1992;63:179–86.
22. Darby S, Whitley E, Silcocks P, Thakrar B, Green M, Lomas P, et al. Risk of lung cancer associated with residential radon exposure in south-west England: a case-control study. Br J Cancer 1998;78:394–408.
23. Gerken M, Kreienbrock L, Wellmann J, Kreuzer M, Wichmann HE. Models for retrospective quantification of indoor radon exposure in case-control studies. Health Phys 2000;78:268–78.
24. Arvela H, Voutilainen A, Mäkeläinen I, Castrén O, Winqvist K. Comparison of predicted and measured variations of indoor radon concentration. Radiat Prot Dosim 1988;24: 231–5.
25. Arvela H. Seasonal variation in radon concentrations of 3000 dwellings with model comparison. Radiat Prot Dosim 1995;59:33–42.
26. Castrén O, Arvela H, Mäkeläinen I, Voutilainen A. Indoor radon survey in Finland: methodology and applications. Radiat Prot Dosim 1992;45:413–18.
27. Baysson H, Billon S, Laurier D, Rogel A, Tirmarche M. Seasonal correction factors for estimating radon exposure in dwellings in France. Radiat Prot Dosim 2003;104:245–52.
28. Bochicchio F, Forastiere F, Farchi S, Marocco D, Quarto M, Sera F. Quality assurance program for LR 115 based radon concentration measurements in a case-control study: description and results. Radiat Meas 2003;36:205–10.
29. Mellander H, Enflo A. The alpha track method used in the Swedish radon epidemiology study. Radiat Prot Dosim 1992;45:65–71.
30. Svensson C, Pershagen G, Hrubec Z. A comparative study on different methods of measuring radon concentrations in homes. Health Phys 1988;55:895–902.
31. Pinel J, Fearn T, Darby SC, Miles JC. Seasonal correction factors for indoor radon measurements in the United Kingdom. Radiat Prot Dosim 1995;58:127–32.
32. Wrixon AD, Green BM, Lomas PR, Miles JC, Cliff KD, Driscoll CM, et al. Natural Radiation exposure in UK dwellings. London: Her Majesty's Stationery Office; 1988. National Radiological Protection Board report NRPB-R190,
33. Peto R, Lopez A, Boreham J, Thun M, Heath C. Mortality from tobacco in developed countries: indirect estimation from national vital statistics. Lancet 1992;339:1268–78.

Appendix B: characteristics of the cases and controls

Table B1. Numbers of persons by case-control status, study, and interview type.

Study	Interview type					
	Cases			Controls		
	Subject	Surrogate	Not known	Subject	Surrogate	Not known
Austria	·	183	·	·	188	·
Czech Republic	43	128	·	376	337	·
Finland nationwide	157	724	·	1286	149	·
Finland southern	24	136	·	274	54	·
France	571	·	·	1 209	·	·
Germany eastern	945	·	·	1516	·	·
Germany western	1323	·	·	2146	·	·
Italy	384	·	·	405	·	·
Spain [a]	·	·	156	·	·	235
Sweden nationwide	85	875	·	981	1064	·
Sweden never-smokers	169	89	·	371	116	·
Sweden Stockholm	196	·	·	375	·	·
United Kingdom	960	·	·	3126	·	·
Total	4857	2135	156	12 065	1908	235

[a] Spain study included both participant and surrogate interviews.

Table B2. Numbers of persons by case-control status, study, and interview method.

Study	Interview method					
	Cases			Controls		
	In person/ by phone	By mail	Both	In person/ by phone	By mail	Both
Austria	183	·	·	188	·	·
Czech Republic	171	·	·	713	·	·
Finland nationwide	·	881	·	·	1435	·
Finland southern	159	1	·	325	3	·
France	571	·	·	1 209	·	·
Germany eastern	945	·	·	1516	·	·
Germany western	1323	·	·	2146	·	·
Italy	384	·	·	405	·	·
Spain	156	·	·	235	·	·
Sweden nationwide	·	960	·	·	2045	·
Sweden never-smokers	184	60	14	352	112	23
Sweden Stockholm	196	·	·	375	·	·
United Kingdom	960	·	·	3126	·	·
Total	5232	1902	14	10 590	3595	23

Table B3. Numbers of persons by case-control status and age at index date.

Age at index date	Cases	Controls	Total
20–24 years	1	2	3
25–29 years	3	4	7
30–34 years	13	47	60
35–39 years	69	178	247
40–44 years	136	357	493
45–49 years	306	717	1 023
50–54 years	572	1 277	1 849
55–59 years	1013	2 054	3 067
60–64 years	1493	2 764	4 257
65–69 years	1652	3 203	4 855
70–74 years	1399	2 686	4 085
75–79 years	319	634	953
80–84 years	130	205	335
85–89 years	40	70	110
90–94 years	2	7	9
95–99 years	·	3	3
Total	7148	14 208	21 356

Table B4. Numbers of persons by case-control status, study, and social status. In the analysis, social status was assumed to be unknown in the Austrian study, as nearly all persons were in the same category.

Study	Social status							
	Cases				Controls			
	Lower	Intermediate	Higher	Not known	Lower	Intermediate	Higher	Not known
Austria	178	1	1	3	185	1	.	2
Czech Republic	.	.	.	171	.	.	.	713
Finland nationwide	.	.	.	881	.	.	.	1435
Finland southern	136	24	.	.	276	52	.	.
France	370	132	52	17	816	232	124	37
Germany eastern	767	130	48	.	1086	258	167	5
Germany western	1111	136	72	4	1347	451	346	2
Italy	251	82	50	1	228	99	75	3
Spain	6	137	13	.	22	189	24	.
Sweden nationwide	72	517	365	6	164	1142	717	22
Sweden never-smokers	83	63	106	6	147	104	229	7
Sweden Stockholm	86	64	40	6	169	124	71	11
United Kingdom	265	498	197	.	713	1479	934	.
Total	3325	1784	944	1095	5153	4131	2687	2237

Table B5. Numbers of persons by case-control status, region of current residence, and study. (CR = region of current residence, CA = cases, CO = controls)

CR	Study																									
	Austria[a]		Czech Republic[b]		Finland, nationwide		Finland, southern[c]		France[d]		Germany, eastern		Germany, western[e]		Italy[f]		Spain[g]		Sweden, nationwide[h]		Sweden, never-smokers[i]		Sweden, Stockholm[j]		United Kingdom[k]	
	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO	CA	CO
1	25	4	86	315	881	1435	46	101	100	195	945	1516	655	1033	250	329	34	54	88	157	48	110	103	148	273	728
2	158	184	46	240	.	.	87	161	202	417	.	.	361	621	10	16	6	28	.	.	53	73	93	227	687	2398
3	.	.	32	112	.	.	27	66	99	190	.	.	307	492	56	40	15	30	27	48	22	47	.	.	.	.
4	.	.	7	46	.	.	.	.	89	186	.	.	.	.	47	11	35	43	53	82	32	62	.	.	.	.
5	.	.	.	.	.	.	.	.	81	221	.	.	.	.	21	9	66	80	12	45	34	65	.	.	.	.
6	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	1	3	33	71	.	.	.	.
7	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	33	90	13	17	.	.	.	.
8	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	38	87	1	1	.	.	.	.
9	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	15	45	2	3	.	.	.	.
10	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	39	68	6	18	.	.	.	.
11	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	29	63	8	6	.	.	.	.
12	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	162	272	6	14	.	.	.	.
14	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	54	108	.	.	.	.	.	.
15	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	41	120	.	.	.	.	.	.
16	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	58	141	.	.	.	.	.	.
17	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	71	175	.	.	.	.	.	.
18	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	63	124	.	.	.	.	.	.
19	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	29	51	.	.	.	.	.	.
20	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	28	64	.	.	.	.	.	.
21	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	80	183	.	.	.	.	.	.
22	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	5	24	.	.	.	.	.	.
23	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	29	82	.	.	.	.	.	.
24	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	5	11	.	.	.	.	.	.
25	.	.	.	.	.	.	.	.	.		.	.	.	.	.	.	.	.	.	2	.	.	.	.	.	.
Total	183	188	171	713	881	1435	160	328	571	1209	945	1516	1323	2146	384	405	156	235	960	2045	258	487	196	375	960	3126

[a] 1 residing in Umhausen, 2 residing elsewhere in the Imst region.
[b] 1 residing in high radon area, 2 residing in medium radon area, 3 residing in low radon area, 4 currently residing outside study area.
[c] 1 residing in high radon area, 2 residing in medium radon area, 3 residing in low radon area.
[d] 1 residing in Auvergne, 2 residing in Bretagne, 3 residing in Languedoc, 4 residing in Limousin, 5 residing in Ardennes.
[e] 1 residing in high radon area, 2 residing in medium radon area, 3 residing in low radon area.
[f] 1 residing in Rome city, 2 residing in Rieti and Viterbo provinces, 3 residing in Rome province, 4 residing in Frosinone province, 5 residing in Latina province.
[g] 1 residing in Santiago, 2–5 residing in a municipality to the southeast, northeast, northwest or southwest of Santiago.
[h] Regions are the 25 counties of Sweden.
[i] 1–3 geographic areas of the original study 1, 4 in the original study 2, 5 in the original study 3, 6–7 geographic areas of the original study 4, 8–12 geographic areas of the original study 5.
[j] 1 residing in the municipality of Stockholm, 2 residing outside the municipality of Stockholm.
[k] 1 residing in county of Cornwall, 2 residing in county of Devon.

Table B6. Lung cancer cases by histological type.

Study	Histological type of lung cancer				
	Squamous cell	Small cell	Adenocarcinoma	Other	No microscopy
Austria	·	·	·	·	183
Czech Republic	·	·	·	·	171
Finland nationwide	316	111	140	73	241
Finland southern	66	45	17	25	7
France	237	135	139	18	42
Germany eastern	370	250	280	45	·
Germany western	486	279	471	87	·
Italy	187	43	64	40	50
Spain	77	41	27	11	·
Sweden nationwide	323	222	274	141	·
Sweden never-smokers	36	15	144	61	2
Sweden Stockholm	54	50	68	21	3
United Kingdom	327	188	74	232	139
Total	2479	1379	1698	754	838

Table B7. Numbers of male and female cases and controls by study and smoking status.

Sex	Smoking status													
	Cases							Controls						
	Never-smokers	<15 cigarettes/day	15–24 cigarettes/day	≥25 cigarettes/day	Ex <10 years	Ex ≥10 years	Other	Never-smokers	<15 cigarettes/day	15–24 cigarettes/day	≥25 cigarettes/day	Ex <10 years	Ex ≥10 years	Other
Men														
Austria	3	9	36	49	37	25	2	21	16	27	28	21	31	20
Czech Republic	16	13	59	46	16	9	·	239	84	150	78	38	67	1
Finland nationwide	36	59	207	89	189	198	20	515	54	95	30	88	472	23
Finland southern [a]	3	24	33	36	40	22	2	33	82	68	60	50	31	4
France	11	51	152	83	116	88	8	235	113	124	52	131	350	75
Germany eastern	19	170	253	36	188	152	15	349	174	130	8	140	495	26
Germany western	23	113	305	178	301	188	9	409	150	200	68	196	658	60
Italy	6	22	66	90	70	71	·	41	24	64	37	30	90	10
Spain	2	3	19	46	75	·	·	74	27	33	18	53	·	8
Sweden nationwide	32	101	109	61	104	40	99	372	132	88	33	94	181	117
Sweden never-smokers	114	·	·	·	·	·	·	220	·	·	·	·	·	·
United Kingdom	3	125	122	67	143	137	57	380	219	165	61	335	758	155
Total	268	690	1361	781	1279	930	212	2888	1075	1144	473	1176	3133	499
Women														
Austria	19	1	1	1	·	·	·	20	·	2	1	1	·	·
Czech Republic	12	·	·	·	·	·	·	56	·	·	·	·	·	·
Finland nationwide	52	6	11	3	5	5	1	145	2	3	·	3	5	·
France	28	2	14	7	4	4	3	89	7	6	1	6	7	13
Germany eastern	61	17	13	1	12	8	·	147	17	1	·	11	18	·
Germany western	66	33	46	19	27	15	·	244	40	21	5	29	66	·
Italy	22	9	14	5	5	3	1	61	8	15	7	5	11	2
Spain	10	·	1	·	·	·	·	20	1	·	1	·	·	·
Sweden nationwide	143	118	84	18	41	6	4	784	113	35	6	47	32	11
Sweden never-smokers	144	·	·	·	·	·	·	267	·	·	·	·	·	·
Sweden Stockholm [b]	36	57	56	19	15	13	·	181	70	48	9	26	41	·
United Kingdom	23	68	83	36	67	26	3	516	102	89	20	91	222	13
Total	616	311	323	109	176	80	12	2530	360	220	50	219	402	39

[a] Finland southern study had no women.
[b] Sweden Stockholm study had no men.

Table B8. Numbers of persons by case-control status, and number of cigarettes per day (current cigarette smokers only). (cig = cigarettes)

Study	Cases								Controls							
	<8 cig	8–12 cig	13–17 cig	18–22 cig	23–27 cig	28–32 cig	≥33 cig	Not known[a]	<8 cig	8–12 cig	13–17 cig	18–22 cig	23–27 cig	28–32 cig	≥33 cig	Not known[a]
Austria	3	5	12	21	15	13	28	·	7	6	9	19	9	8	16	·
Czech Republic	·	13	·	59	·	46	·	·	·	84	·	150	·	78	·	·
Finland nation-wide	·	·	·	·	·	·	·	375	·	·	·	·	·	·	·	184
Finland southern	·	·	·	·	·	·	·	93	·	·	·	·	·	·	·	210
France	13	22	54	121	19	28	51	1	47	50	52	95	17	18	24	·
Germany eastern	40	95	141	166	27	13	8	·	65	94	81	77	8	4	1	·
Germany western	26	64	169	196	105	75	59	·	63	83	114	127	46	23	28	·
Italy	4	22	31	55	25	19	50	·	12	27	29	42	12	16	17	·
Spain	·	·	·	·	·	·	·	69	·	·	·	·	·	·	·	80
Sweden nation-wide	65	172	31	163	14	46	·	·	107	150	23	94	8	25	·	·
Sweden Stockholm	13	42	39	24	10	3	1	·	26	50	32	15	3	1	·	·
United Kingdom	·	·	·	·	·	·	·	501	·	·	·	·	·	·	·	656
Total	164	435	477	805	215	243	197	1039	327	544	340	619	103	173	86	1130

[a] For persons classified as not known in this table, smoking status is available for the groupings shown in table B7.

Table B9. Numbers of persons by case-control status, study, and age when smoking started (current cigarette smokers only).

Study	Cases					Controls				
	<15 years of age	15–17 years of age	18–20 years of age	≥21 years of age	Not known	<15 years of age	15–17 years of age	18–20 years of age	≥21 years	Not known
Current smokers of <15 cigarettes/day only										
Austria	2	2	4	2	·	3	1	9	3	·
Czech Republic	·	·	6	7	·	·	8	39	37	·
Finland nationwide	2	12	24	23	4	3	5	20	26	2
Finland southern	4	2	5	12	1	8	12	26	36	·
France	6	15	20	12	·	13	36	38	33	·
Germany eastern	6	43	79	59	·	12	42	87	50	·
Germany western	9	42	56	39	·	6	40	72	72	·
Italy	8	8	10	5	·	8	8	5	11	·
Spain	·	1	·	2	·	6	3	6	11	2
Sweden nationwide	22	47	77	73	·	7	72	65	101	·
Sweden Stockholm	1	7	12	37	·	2	16	18	34	·
United Kingdom	70	51	42	30	·	83	98	80	60	·
Total	130	230	335	301	5	151	341	465	474	4
Current smokers of 15–24 cigarettes/day only										
Austria	5	12	18	2	·	·	9	13	7	·
Czech Republic	1	10	30	18	·	·	15	96	39	·
Finland nationwide	26	69	67	49	7	6	22	35	34	1
Finland southern	4	13	8	8	·	7	14	17	30	·
France	27	34	77	28	·	25	37	53	15	·
Germany eastern	13	99	105	49	·	10	50	50	21	·
Germany western	21	118	142	70	·	17	71	87	46	·
Italy	26	26	15	13	·	27	22	15	14	1
Spain	7	7	5	1	·	5	5	13	10	·
Sweden nationwide	29	52	59	53	·	5	50	34	34	·
Sweden Stockholm	1	19	19	17	·	2	15	15	16	·
United Kingdom	60	82	39	24	·	65	102	55	32	·
Total	220	541	584	332	7	169	412	483	298	2

(continued)

Table B9. Continued.

Study	Age when smoking started									
	Cases					Controls				
	<15 years of age	15–17 years of age	18–20 years of age	≥21 years of age	Not known	<15 years of age	15–17 years of age	18–20 years of age	≥21 years	Not known
Current smokers of ≥25 cigarettes/day only										
Austria	7	18	17	8	·	5	7	12	5	·
Czech Republic	·	5	31	10	·	2	11	49	16	·
Finland nationwide	13	29	24	21	5	1	8	10	11	·
Finland southern	9	8	9	10	·	4	14	26	16	·
France	18	24	31	17	·	16	18	11	8	·
Germany eastern	7	13	12	5	·	·	3	3	2	·
Germany western	19	75	63	40	·	6	21	21	25	·
Italy	43	28	17	6	1	19	15	6	4	·
Spain	25	11	5	5	·	5	5	4	4	1
Sweden nationwide	20	16	20	23	·	5	19	6	9	·
Sweden Stockholm	2	8	4	5	·	·	3	3	3	·
United Kingdom	38	36	23	6	·	24	30	11	16	·
Total	201	271	256	156	6	87	154	162	119	1

Table B10. Numbers of cases and controls by study and years since last smoked (ex-smokers only).

Study	Years since last smoked													
	Cases							Controls						
	<5 years	5–9 years	10–14 years	15–19 years	20–24 years	≥25 years	Not known [a]	<5 years	5–9 years	10–14 years	15–19 years	20–24 years	≥25 years	Not known [a]
Austria	27	10	12	2	3	8	·	11	11	9	7	9	6	·
Czech Republic	11	5	4	·	3	2	·	8	30	20	18	14	15	·
Finland nationwide	120	72	64	56	38	42	5	38	51	70	120	74	212	3
Finland southern	23	16	7	5	7	4	·	45	4	7	4	2	19	·
France	63	57	40	29	14	9	·	51	86	93	70	73	121	·
Germany eastern	124	76	55	43	35	27	·	71	80	87	106	111	209	·
Germany western	229	99	82	53	37	31	·	116	109	153	153	135	283	·
Italy	39	36	27	18	14	15	·	11	24	22	24	11	44	·
Spain	·	·	·	·	·	·	75	·	·	·	·	·	·	53
Sweden nationwide	45	20	19	6	7	12	82	42	46	39	28	24	48	127
Sweden Stockholm	5	10	7	2	2	2	·	13	13	13	6	4	18	·
United Kingdom	115	72	65	46	30	42	3	154	183	206	160	190	471	42
Total	801	473	382	260	190	194	165	560	637	719	696	647	1446	225

[a] For persons classified as not known in this table, smoking status was available for the groupings shown in table B7.

Table B11. Numbers of ex-smokers by case-control status, study, and number of cigarettes per day when last smoked regularly.

Study	Number of cigarettes per day							
	Cases				Controls			
	<15 cigarettes	15–24 cigarettes	≥25 cigarettes	Not known	<15 cigarettes	15–24 cigarettes	≥25 cigarettes	Not known
Ex-smokers of <10 years duration only								
Austria	7	14	16	·	10	6	6	·
Czech Republic	1	5	10	·	14	17	7	·
Finland nationwide	42	96	28	28	31	42	9	9
Finland southern	8	19	12	1	20	17	13	·
France	23	55	42	·	41	54	42	·
Germany eastern	75	91	34	·	70	61	20	·
German western	78	108	142	·	75	87	63	·
Italy 11	24	40	·	12	9	14	·	

(continued)

Table B11. Continued.

Study	Cases: <15 cigarettes	Cases: 15–24 cigarettes	Cases: ≥25 cigarettes	Cases: Not known	Controls: <15 cigarettes	Controls: 15–24 cigarettes	Controls: ≥25 cigarettes	Controls: Not known
	Number of cigarettes per day							
Spain	7	29	38	1	13	26	13	1
Sweden nationwide	42	26	39	38	64	22	24	31
Sweden Stockholm	9	5	1	.	16	8	2	.
United Kingdom	64	78	65	3	162	144	104	16
Total	367	550	467	71	528	493	317	57
Ex-smokers of ≥10 years' duration only								
Austria	9	8	8	.	14	10	7	.
Czech Republic	2	4	3	.	21	32	14	.
Finland nationwide	49	100	24	30	168	197	59	53
Finland southern	2	13	6	1	15	9	5	2
France	26	36	30	.	125	118	114	.
Germany eastern	65	78	17	.	314	145	54	.
Germany western	74	67	62	.	344	184	196	.
Italy 16	24	34	.	52	29	19	1	
Sweden nationwide	14	10	10	12	98	21	30	64
Sweden Stockholm	12	1	.	.	30	8	3	.
United Kingdom	31	61	70	1	469	284	195	32
Total	300	402	264	44	1650	1037	696	152

Table B12. Numbers of ex-smokers by case-control status, study, and age when smoking started.

Study	Cases: <15 years	Cases: 15–17 years	Cases: 18–20 years	Cases: ≥21 years	Cases: Not known	Controls: <15 years	Controls: 15–17 years	Controls: 18–20 years	Controls: ≥21 years	Controls: Not known
	Age started smoking									
Ex-smokers of <10 years' duration only										
Austria	5	14	14	4	.	2	6	9	5	.
Czech Republic	1	2	8	5	.	.	8	22	8	.
Finland nationwide	24	37	54	56	23	4	12	27	43	5
Finland southern	4	12	15	9	.	7	7	18	18	.
France	20	38	41	21	.	18	47	49	23	.
Germany eastern	11	55	84	50	.	3	48	62	38	.
Germany western	14	101	134	79	.	14	61	90	60	.
Italy	31	20	13	11	.	7	9	12	6	1
Spain	.	.	.	.	75	.	.	.	.	53
Sweden nationwide	21	34	43	41	6	10	43	34	52	2
Sweden Stockholm	1	4	3	7	.	.	5	11	10	.
United Kingdom	54	78	47	28	3	82	159	103	67	15
Total	186	395	456	311	107	147	405	437	330	76
Ex-smokers of ≥10 years' duration only										
Austria	2	7	11	5	.	5	9	8	9	.
Czech Republic	.	1	7	1	.	.	8	40	19	.
Finland nationwide	19	36	54	69	25	19	73	154	227	4
Finland southern	3	5	7	7	.	4	5	10	12	.
France	11	28	39	14	.	53	88	157	59	.
Germany eastern	5	54	71	30	.	19	152	237	105	.
Germany western	6	56	90	51	.	23	214	295	192	.
Italy 19	24	21	10	.	28	32	22	19	.	
Sweden nationwide	6	10	13	15	2	8	62	79	57	7
Sweden Stockholm	.	2	2	9	.	.	4	13	24	.
United Kingdom	41	61	45	16	.	155	387	280	131	27
Total	112	284	360	227	27	314	1034	1295	854	38

Table B13. Numbers of life-long nonsmokers by case-control status, study, and exposure to tobacco smoke from spouse or at work.

Study	Exposure to tobacco smoke from spouse						Exposure to tobacco smoke at work					
	Cases			Controls			Cases			Controls		
	Yes	No	Not known	Yes	No	Not known	Yes	No	Not known	Yes	No	Not known
Austria	.	.	22	.	.	41	.	.	22	.	.	41
Czech Republic	22	6	.	164	131	.	.	.	28	.	.	295
Finland nationwide	36	40	12	243	393	24	.	.	88	.	.	660
Finland southern	.	.	3	.	.	33	.	.	3	.	.	33
France	15	24	.	69	255	.	5	34	.	59	265	.
Germany eastern	34	46	.	105	360	31	33	47	.	238	226	32
Germany westerm	46	43	.	206	447	.	49	40	.	375	278	.
Italy	18	9	1	50	50	2	4	23	1	22	78	2
Spain	.	.	12	.	.	94	.	.	12	.	.	94
Sweden nationwide	79	96	.	435	687	34	.	.	175	.	.	1156
Sweden never-smokers	100	155	3	175	306	6	.	.	258	.	.	487
Sweden Stockholm	21	15	.	108	73	.	.	.	36	.	.	181
United Kingdom	18	8	.	373	523	.	9	1	16	249	73	574
Total	389	442	53	1928	3225	265	100	145	639	943	920	3555

Table B14. Numbers of persons by case-control status, study, and occupational exposure.

Study	Cases			Controls		
	Yes	No	Not known	Yes	No	Not known
Occupational exposure (all types)						
Austria	4	179	.	6	182	.
Czech Republic	.	.	171	.	.	713
Finland, nationwide	190	691	.	242	1193	.
Finland, southern	23	137	.	48	280	.
France	280	291	.	544	665	.
Germany eastern	332	613	.	457	1059	.
Germany western	453	870	.	460	1686	.
Italy 69	315	.	65	340	.	
Spain	48	108	.	66	169	.
Sweden nationwide	71	889	.	93	1952	.
Sweden never-smokers	11	247	.	17	470	.
Sweden Stockholm	.	.	196	.	.	375
United Kingdom	194	766	.	611	2515	.
Total	1675	5106	367	2609	10511	1088
Occupational exposure to radon						
Austria	.	183	.	.	188	.
Czech Republic	.	.	171	.	.	713
Finland nationwide	.	881	.	.	1435	.
Finland southern	.	160	.	.	328	.
France	11	560	.	20	1 189	.
Germany eastern	.	945	.	.	1516	.
Germany western	.	1323	.	.	2146	.
Italy	.	384	.	.	405	.
Spain	.	.	156	.	.	235
Sweden nationwide	.	.	960	.	.	2045
Sweden never-smokers	.	258	.	.	487	.
Sweden Stockholm	.	.	196	.	.	375
United Kingdom	17	943	.	33	3093	.
Total	28	5637	1483	53	10 787	3368

(continued)

Table B14. Continued.

Study	Cases			Controls		
	Yes	No	Not known	Yes	No	Not known
Occupational exposure to asbestos						
Austria	.	.	183	.	.	188
Czech Republic	.	.	171	.	.	713
Finland nationwide	155	483	243	195	1014	226
Finland southern	23	127	10	48	277	3
France	57	514	.	96	1113	.
Germany eastern	249	696	.	366	1150	.
Germany western	347	976	.	345	1801	.
Italy 1	383	.	.	405	.	
Spain	.	.	156	.	.	235
Sweden nationwide	.	.	960	.	.	2045
Sweden never-smokers	.	.	258	.	.	487
Sweden Stockholm	.	.	196	.	.	375
United Kingdom	183	777	.	591	2535	.
Total	1015	3956	2177	1641	8295	4272
Other occupational exposure						
Austria	4	179	.	6	182	.
Czech Republic	.	.	171	.	.	713
Finland nationwide	61	820	.	70	1365	.
Finland southern	.	.	160	.	.	328
France	271	300	.	526	683	.
Germany eastern	83	862	.	91	1425	.
Germany western	106	1217	.	115	2031	.
Italy 69	315	.	65	340	.	
Spain	48	106	2	66	169	.
Sweden nationwide	71	887	2	93	1938	14
Sweden never-smokers	11	241	6	17	463	7
Sweden Stockholm	.	.	196	.	.	375
United Kingdom	.	960	.	.	3126	.
Total	724	5887	537	1049	11 722	1437

Table B15. Numbers of persons by case-control status, study, and percentage of time usually spent indoors at home.

Study	Time indoors at home							
	Cases				Controls			
	<50%	50–74%	≥75%	Not known	<50%	50–74%	≥75%	Not known
Austria	15	138	26	4	15	154	18	1
Czech Republic	·	·	·	171	·	·	·	713
Finland nationwide	302	479	49	51	554	752	60	69
Finland southern	·	·	·	160	·	·	·	328
France	79	348	139	5	135	800	265	9
Germany eastern	221	698	26	·	368	1103	45	·
Germany western	265	1014	44	·	423	1617	106	·
Italy	92	184	34	74	93	181	39	92
Spain	·	·	·	156	·	·	·	235
Sweden nationwide	113	542	127	178	216	1005	395	429
Sweden never-smokers	·	·	·	258	·	·	·	487
Sweden Stockholm	·	106	89	1	·	172	200	3
United Kingdom	·	543	417	·	·	1783	1343	·
Total	1087	4052	951	1058	1804	7567	2471	2366

Table B16. Numbers of persons by case-control status, study, and residence in rural or urban areas during period of interest

Study	Rural or urban area					
	Cases			Controls		
	All rural	Some urban	Not known	All rural	Some urban	Not known
Austria	183	·	·	188	·	·
Czech Republic	158	13	·	661	52	·
Finland nationwide	·	·	881	·	·	1435
Finland southern	160	·	·	328	·	·
France	418	153	·	888	321	·
Germany eastern	718	227	·	1108	408	·
Germany western	705	618	·	1118	1028	·
Italy	107	277	·	58	347	·
Spain	111	45	·	177	58	·
Sweden nationwide	808	152	·	1835	210	·
Sweden never-smokers	118	140	·	215	272	·
Sweden Stockholm	93	103	·	227	148	·
United Kingdom	574	386	·	1908	1218	·
Total	4153	2114	881	8711	4062	1435

Table B17. Numbers of persons by case-control status, study, and usual position of bedroom window at night

Study	Bedroom window open at night					
	Cases			Controls		
	Yes	No	Not known	Yes	No	Not known
Austria	33	150	·	26	162	·
Czech Republic	·	·	171	·	·	713
Finland nationwide	·	·	881	·	·	1435
Finland southern	·	·	160	·	·	328
France	129	341	101	319	655	235
Germany eastern	753	192	·	1062	454	·
Germany western	939	384	·	1379	767	·
Italy	134	178	72	136	183	86
Spain	·	·	156	·	·	235
Sweden nationwide	259	580	121	597	1206	242
Sweden never-smokers	·	·	258	·	·	487
Sweden Stockholm	·	·	196	·	·	375
United Kingdom	·	·	960	·	·	3126
Total	2247	1825	3076	3519	3427	7262

Appendix C: residential radon concentrations

Table C1. Effect of using geographic areas to estimate radon concentrations that could not be measured.

Study	MSE_u/MSE_a [a]	Description of areas used
Austria	1.68	Umhausen and remainder of Imst region
Czech Republic	1.22	10 administrative districts
Finland nationwide	– [b]	– [b]
Finland southern	1.02	High, medium and low radon areas
France	1.05	Auvergne, Bretagne, Languedoc, Limousin, Ardennes
Germany eastern	1.01	High and low radon areas
Germany western	1.05	High, medium and low radon areas
Italy	1.14	Districts of Rome, grouped into 5 categories according to geometric mean radon concentration, plus 5 provinces
Spain	1.02	Santiago, and southeast, northeast, northwest, and southwest Galicia
Sweden nationwide	1.02	High, medium and low radon areas
Sweden never-smokers	1.01	5 categories, based on original study
Sweden Stockholm	1.04	Single family houses, multifamily houses without ground contact, and multifamily houses with ground contact
United Kingdom	1.21	6 area groupings, derived according to average geometric mean radon concentration

[a] MSE_u is the mean squared error of prediction without subdivision by area, and MSE_a is the mean squared error of prediction after subdivision by area. A value of 1.05 means that subdivision by area improved the mean squared error of prediction by 5%. In each case the MSE was calculated as $[\Sigma(x_m - x_p)^2]/N$, where x_m is the measured value, and x_p is the predicted value based either on the overall control mean or on the area-specific control means and omitting the value x_m from the calculation of the means.

[b] No information regarding area was available for this study.

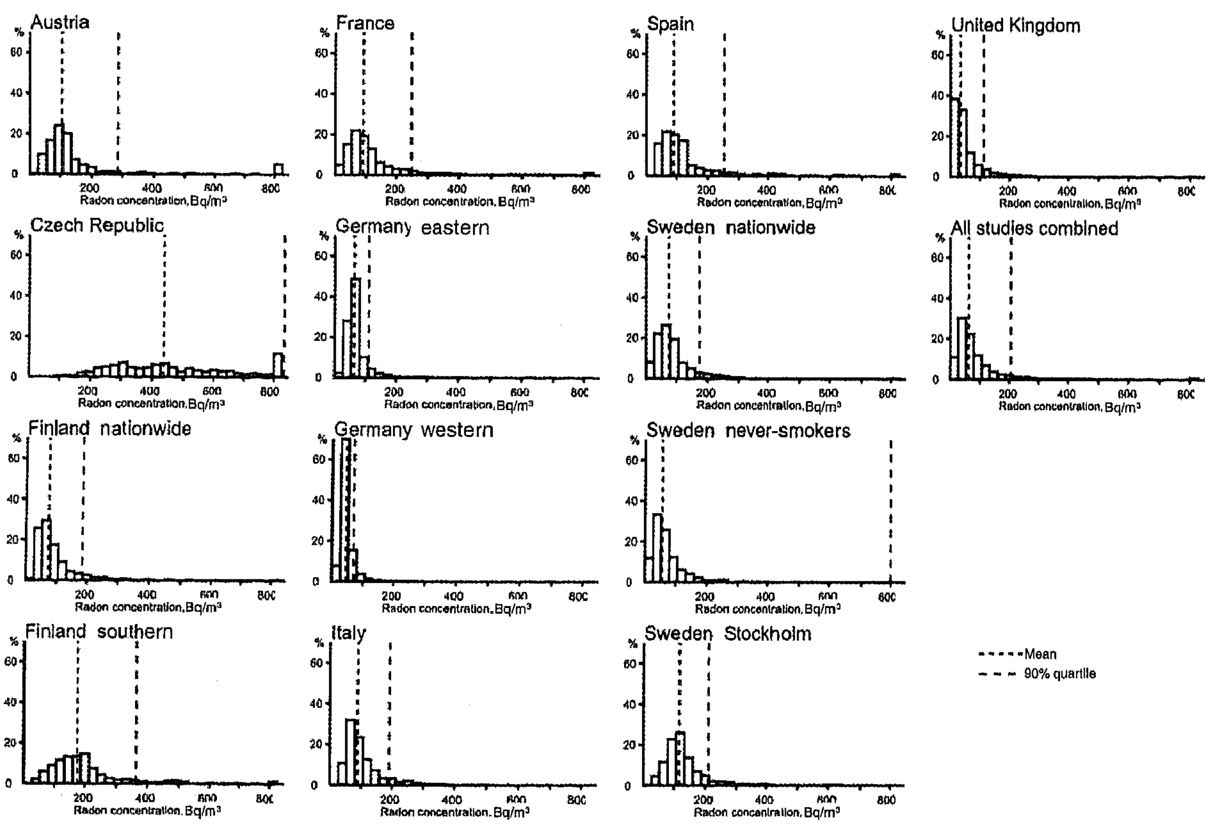

Figure C1. Distribution of the time-weighted average observed radon concentrations by study, based on the measured values and estimates when no measurements could be obtained.

Table C2. Numbers of addresses reported and measured per person and number of years for which measurements were available in each study.

Study	Cases						Controls					
	Addresses reported (N)		Addresses measured (N)		Years for which measurements available (N)		Addresses reported (N)		Addresses measured (N)		Years for which measurements available (N)	
	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range
Austria	1.6	1–3	1.0	1–1	21	1–30	1.5	1–3	1.0	1–1	24	2–30
Czech Republic	1.4	1–4	1.2	1–2	28	6–30	1.4	1–5	1.2	1–3	27	1–30
Finland nationwide	1.5	1–3	1.0	1–1	26	1–30	1.4	1–3	1.0	1–1	27	1–30
Finland southern	3.0	1–8	1.4	1–4	22	2–30	2.9	1–10	1.3	1–4	22	1–30
France	2.4	1–10	1.5	1–5	24	1–30	2.4	1–8	1.5	1–5	24	1–30
Germany eastern	2.2	1–8	1.0	1–1	20	1–30	2.3	1–10	1.0	1–1	20	1–30
Germany western	2.5	1–10	1.0	1–4	19	1–30	2.8	1–12	1.1	1–4	18	1–30
Italy	2.8	1–8	2.1	1–7	27	1–30	2.9	1–9	2.2	1–6	27	1–30
Spain	2.0	2–2	1.0	1–1	21	7–25	2.0	2–2	1.0	1–1	20	7–25
Sweden nationwide	3.8	1–12	2.3	1–7	23	1–30	3.6	1–11	2.2	1–8	23	1–30
Sweden never-smokers	2.8	1–9	2.1	1–6	25	2–30	2.8	1–8	2.2	1–7	25	1–30
Sweden Stockholm	3.4	1–10	2.4	1–6	24	1–30	4.0	1–10	2.4	1–6	23	1–30
United Kingdom	3.2	1–14	2.3	1–10	26	1–30	3.2	1–15	2.3	1–12	26	1–30
All studies	2.6	1–14	1.5	1–10	23	1–30	2.7	1–15	1.6	1–12	24	1–30

Table C3. Completeness of residential radon measurements by case-control status, study, and time period.

Study	Percentage of years with measurement							
	Cases				Controls			
	5–14 years [a]	15–24 years [a]	25–34 years [a]	All years	5–14 years [a]	15–24 years [a]	25–34 years [a]	All years
Austria	92	71	52	72	93	81	63	79
Czech Republic	95	93	91	93	91	89	88	89
Finland nationwide	99	96	70	88	99	97	73	90
Finland southern	88	76	52	72	90	80	52	74
France	94	86	58	79	92	86	64	81
Germany eastern	89	66	45	67	91	67	42	67
Germany western	89	64	37	63	89	61	32	61
Italy	96	93	80	89	96	95	81	91
Spain	98	81	35	71	96	72	30	66
Sweden nationwide	90	80	63	78	89	80	65	78
Sweden never-smokers	90	84	74	83	89	86	79	85
Sweden Stockholm	85	80	73	79	87	77	68	77
United Kingdom	94	90	73	86	94	90	75	87

[a] Numbers of years prior to the index date.

Table C4. Mean time-weighted average observed residential radon concentration (Bq/m^3) by case-control status and study, based on measured values and estimates when no measurement could be made.

Study	Mean radon concentration (Bq/m^3)							
	Cases				Controls			
	5–14 years [a]	15–24 years [a]	25–34 years [a]	All years	5–14 years [a]	15–24 years [a]	25–34 years [a]	All years
Austria	270	271	261	267	126	130	133	130
Czech Republic	535	528	522	528	491	493	496	493
Finland nationwide	105	105	101	104	103	103	103	103
Finland southern	215	223	226	221	223	202	209	212
France	129	137	148	138	120	128	145	131
Germany eastern	76	78	80	78	73	74	76	74
Germany western	48	49	50	49	50	51	51	51
Italy	107	112	121	113	95	99	113	102
Spain	116	121	132	123	141	135	134	137
Sweden nationwide	104	102	92	99	92	95	95	94
Sweden never-smokers	78	81	78	79	72	73	71	72
Sweden Stockholm	132	130	130	131	142	139	128	136
United Kingdom	58	59	54	57	57	55	51	54

[a] 5–14, 15–24, and 25–34 are numbers of years prior to the index date.

Table C5. Distribution of the time-weighted average observed residential radon concentration for the cases and controls by study, based on measured values and estimates when no measurement could be obtained.

Study	Time-weighted average residential radon (Bq/m³)													
	Cases							Controls						
	Mean	SD	Minimum	Quartiles			Maximum	Mean	SD	Minimum	Quartiles			Maximum
				1st	2nd	3rd					1st	2nd	3rd	
Austria	267	460	25	90	111	164	2649	130	176	18	70	98	132	2173
Czech Republic	528	280	158	310	446	660	1647	493	271	81	309	435	602	2209
Finland nationwide	104	124	19	50	73	107	2225	103	125	19	53	74	112	3244
Finland southern	221	162	24	140	188	228	1189	212	214	33	121	171	232	2823
France	138	239	6	60	94	147	4606	131	155	6	60	89	136	1541
Germany eastern	78	110	14	50	65	77	2867	74	60	16	51	64	76	980
Germany western	49	33	10	36	45	52	674	51	36	9	37	45	52	818
Italy	113	73	28	69	94	131	529	102	65	28	63	83	115	456
Spain	123	100	33	63	96	147	955	137	149	30	60	88	129	939
Sweden nationwide	99	107	1	50	76	113	1792	94	114	4	47	73	102	2253
Sweden never-smokers	79	69	2	38	59	97	497	72	63	6	37	57	88	596
Sweden Stockholm	131	67	22	94	117	158	622	136	82	30	92	118	149	636
United Kingdom	57	94	1	20	32	59	1700	54	73	3	21	33	60	1266
All studies	104	161	1	42	64	107	4606	105	149	3	40	62	105	3244

Table C6. Distribution of the $\log_e$(time-weighted average observed radon concentration) for the cases, controls, and cases and controls combined by study, based on measured values and estimates when no measurement could be obtained. (Min = minimum, Max = maximum)

Study	$\log_e$ (time-weighted average of the residential radon concentration)																				
	Cases							Controls							Cases and controls combined						
	Mean	SD	Min	Quartiles			Max	Mean	SD	Min	Quartiles			Max	Mean	SD	Min	Quartiles			Max
				1st	2nd	3rd					1st	2nd	3rd					1st	2nd	3rd	
Austria	4.96	0.93	3.22	4.50	4.71	5.10	7.88	4.62	0.61	2.89	4.25	4.58	4.88	7.68	4.78	0.80	2.89	4.36	4.65	4.98	7.88
Czech Republic	6.14	0.50	5.06	5.74	6.10	6.49	7.41	6.08	0.49	4.39	5.73	6.08	6.40	7.70	6.09	0.50	4.39	5.73	6.08	6.42	7.70
Finland nationwide	4.37	0.64	2.94	3.91	4.29	4.67	7.71	4.39	0.62	2.94	3.97	4.30	4.72	8.08	4.38	0.63	2.94	3.95	4.30	4.70	8.08
Finland southern	5.22	0.57	3.18	4.94	5.24	5.43	7.08	5.14	0.60	3.50	4.80	5.14	5.45	7.95	5.17	0.60	3.18	4.82	5.17	5.45	7.95
France	4.56	0.77	1.79	4.09	4.54	4.99	8.44	4.53	0.78	1.79	4.09	4.49	4.91	7.34	4.54	0.78	1.79	4.09	4.51	4.93	8.44
Germany eastern	4.17	0.51	2.64	3.91	4.17	4.34	7.96	4.17	0.47	2.77	3.93	4.16	4.33	6.89	4.17	0.49	2.64	3.93	4.16	4.33	7.96
Germany western	3.79	0.42	2.30	3.58	3.81	3.95	6.51	3.82	0.42	2.20	3.61	3.81	3.95	6.71	3.81	0.42	2.20	3.61	3.81	3.95	6.71
Italy	4.59	0.51	3.33	4.23	4.54	4.88	6.27	4.48	0.51	3.33	4.14	4.42	4.74	6.12	4.53	0.51	3.33	4.17	4.48	4.83	6.27
Spain	4.62	0.58	3.50	4.14	4.56	4.99	6.86	4.60	0.72	3.40	4.09	4.48	4.86	6.84	4.61	0.67	3.40	4.14	4.50	4.89	6.86
Sweden nationwide	4.32	0.73	0.00	3.91	4.33	4.73	7.49	4.26	0.72	1.39	3.85	4.29	4.62	7.72	4.28	0.73	0.00	3.87	4.32	4.65	7.72
Sweden never-smokers	4.09	0.75	0.69	3.64	4.08	4.57	6.21	4.04	0.68	1.79	3.61	4.04	4.48	6.39	4.06	0.70	0.69	3.61	4.06	4.50	6.39
Sweden Stockholm	4.76	0.47	3.09	4.54	4.76	5.06	6.43	4.79	0.47	3.40	4.52	4.77	5.00	6.46	4.78	0.47	3.09	4.52	4.77	5.02	6.46
United Kingdom	3.57	0.89	0.00	3.00	3.47	4.08	7.44	3.60	0.83	1.10	3.04	3.50	4.09	7.14	3.59	0.84	0.00	3.04	3.50	4.09	7.44
All studies	4.23	0.82	0.00	3.74	4.16	4.67	8.44	4.21	0.87	1.10	3.69	4.13	4.65	8.08	4.22	0.85	0.00	3.71	4.14	4.66	8.44

Table C7. Numbers of persons by the time-weighted average observed radon concentration (Bq/m³) and study for the cases and controls.

Study	Residential radon concentration																	
	Cases									Contols								
	<25	25–	50–	100–	200–	400–	800–	≥1600	Total	<25	25–	50–	100–	200–	400–	800–	≥1600	Total
Austria	.	10	52	86	11	7	12	5	183	1	13	89	64	16	4	.	1	188
Czech Republic	.	.	.	5	60	79	25	2	171	.	.	3	32	267	337	69	5	713
Finland nationwide	5	208	412	180	54	18	3	1	881	5	299	690	321	94	22	3	1	1435
Finland southern	1	1	18	72	54	11	3	.	160	.	7	51	156	87	24	1	2	328
France	21	77	216	173	63	15	4	2	571	50	161	487	335	127	34	15	.	1209
Germany eastern	20	215	587	98	16	7	1	1	945	23	332	974	147	32	6	2	.	1516
Germany western	92	854	328	39	9	1	.	.	1323	117	1372	570	66	18	2	1	.	2146
Italy	.	25	190	130	34	5	.	.	384	.	41	227	105	30	2	.	.	405
Spain	.	14	70	55	14	2	1	.	156	.	40	99	59	20	14	3	.	235
Sweden nationwide	53	196	423	212	59	14	2	1	960	150	396	954	403	110	24	6	2	2045
Sweden never-smokers	26	77	92	52	8	3	.	.	258	50	148	205	65	16	3	.	.	487
Sweden Stockholm	1	9	52	111	22	1	.	.	196	.	11	109	210	38	7	.	.	375
United Kingdom	347	313	178	83	30	6	2	1	960	1078	1085	575	284	81	19	4	.	3126
Total	566	1999	2618	1296	434	169	53	13	7148	1474	3905	5033	2247	936	498	104	11	14 208

Table C8. Distribution of the time-weighted average corrected residential radon concentration for the cases and controls by study, based on measured values and estimates when no measurement could be obtained and corrected for uncertainties in both the measurements and estimates. (Min = minimum, Max = maximum)

Study	Time-weighted average residential radon (Bq/m³)													
	Cases							Controls						
	Mean	SD	Min	Quartiles			Max	Mean	SD	Min	Quartiles			Max
				1st	2nd	3rd					1st	2nd	3rd	
Austria	170	189	38	93	108	141	1083	113	80	30	76	100	125	939
Czech Republic	467	134	166	372	458	562	841	448	136	125	355	442	538	928
Finland nationwide	81	16	46	71	78	87	201	82	16	54	71	79	89	229
Finland southern	176	63	52	141	166	190	485	170	69	64	130	157	191	777
France	123	157	9	61	90	139	2797	118	114	9	63	87	128	1084
Germany eastern	66	36	20	52	61	69	754	66	27	26	53	60	70	376
Germany western	45	14	17	38	43	47	231	45	15	17	39	43	48	260
Italy	111	65	30	70	94	129	463	101	59	31	63	83	112	407
Spain	112	82	31	63	88	137	746	120	118	28	60	83	116	735
Sweden nationwide	90	75	2	51	73	104	1038	86	78	5	49	70	96	1300
Sweden never-smokers	71	50	3	40	59	88	357	67	46	8	40	56	81	416
Sweden Stockholm	122	44	33	97	114	145	408	125	52	43	96	115	138	418
United Kingdom	51	67	3	22	31	55	1117	49	53	6	22	31	54	778
All studies	90	100	2	44	65	95	2797	94	109	5	41	63	94	1300

Table C9. Distribution of the $\log_e$(time-weighted average corrected radon concentration) for the cases, controls, and cases and controls combined by study, based on measured values and estimates when no measurement could be obtained and corrected for uncertainties in both the measurements and estimates. (Min = minimum, Max = maximum)

Study	$\log_e$ (time-weighted average residential radon)																				
	Cases							Controls							Cases and controls combined						
	Mean	SD	Min	Quartiles 1st	Quartiles 2nd	Quartiles 3rd	Max	Mean	SD	Min	Quartiles 1st	Quartiles 2nd	Quartiles 3rd	Max	Mean	SD	Min	Quartiles 1st	Quartiles 2nd	Quartiles 3rd	Max
Austria	4.84	0.65	3.64	4.53	4.68	4.95	6.99	4.62	0.43	3.40	4.33	4.60	4.82	6.84	4.73	0.56	3.40	4.41	4.64	4.88	6.99
Czech Republic	6.10	0.30	5.11	5.92	6.13	6.33	6.73	6.05	0.34	4.83	5.87	6.09	6.29	6.83	6.06	0.33	4.83	5.88	6.09	6.30	6.83
Finland nationwide	4.38	0.18	3.83	4.26	4.36	4.47	5.30	4.39	0.17	3.99	4.26	4.37	4.49	5.43	4.39	0.18	3.83	4.26	4.36	4.48	5.43
Finland southern	5.12	0.33	3.95	4.95	5.11	5.24	6.18	5.07	0.34	4.16	4.87	5.06	5.25	6.66	5.09	0.34	3.95	4.89	5.08	5.25	6.66
France	4.54	0.68	2.20	4.11	4.50	4.93	7.94	4.51	0.68	2.20	4.14	4.47	4.85	6.99	4.52	0.68	2.20	4.13	4.48	4.88	7.94
Germany eastern	4.13	0.34	3.00	3.95	4.11	4.23	6.63	4.13	0.31	3.26	3.97	4.09	4.24	5.93	4.13	0.32	3.00	3.97	4.09	4.23	6.63
Germany western	3.76	0.26	2.83	3.64	3.76	3.85	5.44	3.78	0.25	2.83	3.66	3.76	3.87	5.56	3.77	0.26	2.83	3.64	3.76	3.87	5.56
Italy	4.58	0.48	3.40	4.25	4.54	4.86	6.14	4.49	0.48	3.43	4.14	4.42	4.72	6.01	4.53	0.48	3.40	4.20	4.48	4.80	6.14
Spain	4.56	0.55	3.43	4.14	4.48	4.92	6.61	4.52	0.66	3.33	4.09	4.42	4.75	6.60	4.54	0.62	3.33	4.14	4.45	4.80	6.61
Sweden nationwide	4.29	0.63	0.69	3.93	4.29	4.64	6.95	4.24	0.63	1.61	3.89	4.25	4.56	7.17	4.25	0.63	0.69	3.91	4.26	4.58	7.17
Sweden never-smokers	4.07	0.63	1.10	3.69	4.08	4.48	5.88	4.03	0.57	2.08	3.69	4.03	4.39	6.03	4.05	0.59	1.10	3.69	4.04	4.42	6.03
Sweden Stockholm	4.74	0.35	3.50	4.57	4.74	4.97	6.01	4.76	0.35	3.76	4.56	4.74	4.93	6.04	4.76	0.35	3.50	4.56	4.74	4.93	6.04
United Kingdom	3.58	0.75	1.10	3.09	3.43	4.01	7.02	3.59	0.70	1.79	3.09	3.43	3.99	6.66	3.59	0.72	1.10	3.09	3.43	3.99	7.02
All studies	4.21	0.70	0.69	3.78	4.17	4.55	7.94	4.19	0.77	1.61	3.71	4.14	4.54	7.17	4.19	0.75	0.69	3.74	4.16	4.55	7.94

Table C10. Numbers of cases and controls by the time-weighted average corrected radon concentration and study.

Study	Residential radon concentration (Bq/m³)																
	Cases									Controls							
	<25	25–	50–	100–	200–	400–	800–	≥1600	Total	<25	25–	50–	100–	200–	400–	800–	Total
Austria	.	3	55	96	13	12	4	.	183	.	5	89	84	8	1	1	188
Czech Republic	.	.	.	1	52	117	1	.	171	.	.	.	32	229	447	5	713
Finland nationwide	.	1	778	101	1	.	.	.	881	.	.	1262	172	1	.	.	1 435
Finland southern	.	.	9	116	33	2	.	.	160	.	.	26	229	70	3	.	328
France	13	70	242	183	47	12	3	1	571	31	153	554	324	111	31	5	1 209
Germany eastern	2	189	686	58	9	1	.	.	945	.	280	1129	95	12	.	.	1 516
Germany western	22	1048	240	12	1	.	.	.	1323	27	1659	434	25	1	.	.	2 146
Italy	.	17	196	138	29	4	.	.	384	.	31	238	108	27	1	.	405
Spain	.	14	75	51	15	1	.	.	156	.	40	111	51	23	10	.	235
Sweden nationwide	31	190	476	212	44	5	2	.	960	101	416	1057	375	79	14	3	2 045
Sweden never-smokers	15	85	108	42	8	.	.	.	258	31	161	227	60	6	2	.	487
Sweden Stockholm	.	4	51	130	10	1	.	.	196	.	3	107	236	28	1	.	375
United Kingdom	320	364	180	67	24	4	1	.	960	978	1285	554	245	55	9	.	3 126
Total	403	1985	3096	1207	286	159	11	1	7148	1168	4033	5788	2036	650	519	14	14 208

Appendix D: additional results

Table D1. Results of previous analyses of studies included in the Collaborative Analysis with comments. Where previous analyses have been carried out based on a continuous measure of radon exposure, the relative risks at 100 Bq/m³ have been quoted. Most of such analyses were based on a log-linear rather than a linear model. In such a log-linear model the fitted relative risk at 100 Bq/m³ tends to be somewhat lower than for the corresponding linear model (see figure 1 in main text).

Study	Results of previous analyses and comment
Austria	Results of previous analysis: relative risk of lung cancer increased by 0.25 (95% CI 0.08–0.43) per 100 Bq/m³ in a log-linear risk model and by 0.43 (95% CI 0.11–1.53) per 100 Bq/m³, conditional on study, age, sex, and year of death with adjustment for smoking and occupational exposure to established lung carcinogens [Oberaigner et al (1) and Oberaigner et al, personal communication] Comment: results were similar in the two analyses.
Czech Republic	Results of previous analysis: relative risk of lung cancer increased by 0.09 (95% CI 0.02–0.21) per 100 Bq/m³ based on a Poisson regression model with a linear term in radon and adjustment for age, sex, and calendar period based on national lung cancer rates [Tomášek et al (2)]. Comment: results differed somewhat between the two analyses, with a higher risk estimate and wider confidence interval in the Collaborative Analysis. These differences were chiefly due to the finer level of stratification, especially for smoking, in the Collaborative Analysis.
Finland nationwide	Results of previous analysis: relative risk of lung cancer increased by 0.11 (95% CI -0.06–0.31) per 100 Bq/m³ based on a log-linear model and conditional on matched pairs with adjustment for smoking; matching was by age and sex [Auvinen et al (3)]. Comment: results differed somewhat in the two analyses. This was to be expected, given that only complete matched pairs were included in the previous analysis. The numbers of cases and controls included in the collaborative analysis were substantially greater.
Finland southern	Results of previous analysis: relative risks of lung cancer of 1.0, 1.8 (95% CI 0.9–3.5) and 1.5 (95% CI 0.8–2.9), for persons with average observed radon concentrations of <95, 95–185, and ≥186 Bq/m³, respectively, with adjustment for smoking intensity and quitting [Ruosteenoja et al (4)]. Comment: results were similar in the two analyses.
France	Results of previous analysis: relative risk of lung cancer increased by 0.04 (95% CI -0.01–0.11) per 100 Bq/m³ based on a log-linear model and adjustment for age, sex, region, cigarette smoking, and occupational exposure. Cigarette smoking was taken into account both continuously by log(pack-years +1) and by smoking status in four categories (lifelong nonsmoker, current smoker, ex-smoker <10 years, ex-smoker >10 years). Occupational exposure was taken into account with two binary variables: ever–never exposed to asbestos, ever–never exposed in an occupation of the A list [Baysson et al (5)]. Comment: results were similar in the two analyses.
Germany eastern	Results of previous analysis: relative risk of lung cancer increased by 0.04 (95% CI -0.04–0.12) per 100 Bq/m³ in a log-linear model conditional on age, sex, and region and adjusted for pack-years of smoking, years since stopping smoking, and occupational exposure to asbestos, and based on the data used in the Collaborative Analysis (ie, restricted to radon measurements in the last dwelling) [Wichmann et al, 1999 (6)]. The relative risk of lung cancer increased by 0.08 (95% CI -0.03–0.20) per 100 Bq/m³ in a log-linear model and based on a data set that included additional radon measurements and focused on the last 5–35 years before the interview [Kreuzer et al (7)]. Comment: results of the Collaborative Analysis and of Wichmann et al (6) differed as those of Wichmann et al were based on a log-linear model rather than a linear model for radon, and they were adjusted for smoking rather than stratification being used. An additional analysis including the studies in both eastern and western Germany, with some extra persons and more complete measurement data has also been carried out [Wichmann et al (8)].
Germany western	Results of previous analysis: relative risk of lung cancer changed by -0.12 (95% CI -0.26–0.04) per 100 Bq/m³ based on a log-linear model conditional for age, sex, region, and exposure to asbestos and adjusted for pack-years of smoking [Kreienbrock et al (9)]. Comment: results were similar in the two analyses, bearing in mind the differences between the fitted models. An additional analysis including the studies in both eastern and western Germany, with some extra persons and more complete measurement data has also been carried out [Wichmann et al (8)].
Italy	Results of previous analysis: relative risk of lung cancer increased by 0.14 (95% CI -0.11–0.46) per 100 Bq/m³ based on a log-linear model and adjusted for age, sex, sex × age, smoking, area of residence at index date, and diet. A higher excess relative risk of 0.32 (95% CI -0.19–1.16) was estimated for low-medium consumption of dietary antioxidants [Bochicchio et al (10)]. Comment: results were similar in the two analyses, bearing in mind the differences in the fitted models, in the approach to confounders, and in the confounders themselves.
Spain	Results of previous analysis: relative risks of lung cancer 1.00, 2.73 (95% CI 1.21–6.18), 2.48 (95% CI 1.12–5.48), and 2.96 (95% CI 1.29–6.79) for persons with average observed radon concentrations of <36.9, 37.0–55.1, 55.2–147.9, and ≥148.0 Bq/m³, respectively, with adjustment for age, sex, pack-years of cigarettes, family history, and area of residence [Barros-Dios et al (11)]. Comment: the estimated linear relationship between the relative risk of lung cancer and the observed residential radon concentration in the Collaborative Analysis appeared to differ substantially from the recently published results, which were based on quartiles of the radon distribution. In that analysis the relative risks of lung cancer were reported as 1.00, 2.73 (95% CI 1.21–6.18), 2.48 (95% CI 1.12–5.48), and 2.96 (95% CI 1.29–6.79) for persons with measured radon concentrations of <36.9, 37.0–55.1, 55.2–147.9, and ≥148.0 Bq/m³, respectively. The reason for the discrepancy is that the distribution of radon concentrations was highly skewed with a long upper tail (see figure C1). Therefore, when the total number of observations was relatively small, the values at the upper extreme of the distribution were highly influential in determining the estimated value of the linear relationship. Consequently, the linear relationship could be estimated only with great uncertainty, as indicated by its wide confidence interval. It was for this reason that Barros-Dios [Barros-Dios et al (11)] did not present a linear model in their original publication. For the Spanish study, 20 out of a total of 391 persons included in the present analysis had time-weighted average observed radon concentrations that were >400 Bq/m³ and, of these 20 persons, all but three were controls, although controls accounted for only 60% of the persons in the study as a whole (see Tables C7a and b). These 19 persons were responsible for the negative estimate of the linear relationship in the present analysis and, if they are excluded, the estimated linear relationship using the methodology of the Collaborative Analysis becomes positive. In the categorical analysis reported by Barros-Dios et al (11) the upper category of ≥148 Bq/m³ included 88 persons, of whom 42 were cases, and the very high proportion of controls among those with the highest radon concentrations was more than counter-balanced by the much higher proportion of cases in the remainder of the category.
Sweden nation-wide	Results of previous analysis: relative risk of lung cancer increased by 0.10 (95% CI 0.01–0.22) per 100 Bq/m³ based on a linear model conditional on age, sex, smoking, urbanization, and occupational exposure to established lung carcinogens. After correction for uncertanties in the assessment of radon exposure, the the increase in the relative risk per 100 Bq/m³ increased to about 0.15 to 0.20 [Pershagen et al (12); Lagarde et al (13)]. Comment: results were similar in the two analyses.

(continued)

Table D1. Continued.

Study	Results of previous analyses and comment
Sweden never-smokers	Results of previous analysis: relative risk of lung cancer increased by 0.28 (95% CI -0.05–1.05) per 100 Bq/m³ based on a log-linear model and conditional on study age, sex, and area of current residence with adjustment for exposure to environmental tobacco smoke, urbanization, and occupational exposure to established lung carcinogens [Lagarde et al (14)]. Comment: results were similar in the two analyses.
Sweden Stockholm	Results of previous analysis: relative risks of lung cancer of 1.00, 1.2 (95% CI 0.7–2.1), 1.3 (95% CI 0.7–2.3), and 1.7 (95% CI 1.0–2.9) for persons with average observed radon concentrations of <75, 76–110, 111–150, and ≥151 Bq/m³, respectively, with adjustment for age, smoking, and municipality of residence [Pershagen et al (15)]. Comment: results were similar in the two analyses.
United Kingdom	Results of previous analysis: relative risk of lung cancer increased by 0.08 (95% CI -0.03–0.20) per 100 Bq/m³ based on a log-linear model and adjustment for age, sex, smoking status, county of residence, and social class. After correction for uncertainties in the assessment of radon exposure, the relative risk increased to 0.12 (95% CI -0.05–0.33) [Darby et al (16)]. Comment: results were similar in the two analyses.

Table D2. Numbers of persons providing some information (PI) about β in the analysis by study and smoking status.

Study	Cases			Controls		
	Total number	PI about β		Total number	PI about β	
		N	%		N	%
Austria						
Current cigarette smokers	97	47	48	74	34	46
Ex-smokers	62	29	47	53	34	64
Lifelong nonsmokers	22	14	64	41	22	54
Others	2	2	100	20	5	25
Total	183	92	50	188	95	51
Czech Republic						
Current cigarette smokers	118	87	74	312	153	49
Ex-smokers	25	18	72	105	29	28
Lifelong nonsmokers	28	27	96	295	145	49
Others	0	.	.	1	0	0
Total	171	132	77	713	327	46
Finland nationwide						
Current cigarette smokers	375	304	81	184	175	95
Ex-smokers	397	370	93	568	550	97
Lifelong nonsmokers	88	87	99	660	646	98
Others	21	20	95	23	20	87
Total	881	781	89	1435	1 391	97
Finland southern						
Current cigarette smokers	93	59	63	210	91	43
Ex-smokers	62	37	60	81	36	44
Lifelong nonsmokers	3	3	100	33	5	15
Others	2	0	0	4	0	0
Total	160	99	62	328	132	40
France						
Current cigarette smokers	309	158	51	303	147	49
Ex-smokers	212	162	76	494	281	57
Lifelong nonsmokers	39	36	92	324	101	31
Others	11	8	73	88	19	22
Total	571	364	64	1209	548	45
Germany eastern						
Current cigarette smokers	490	431	88	330	308	93
Ex-smokers	360	348	97	664	626	94
Lifelong nonsmokers	80	80	100	496	491	99
Others	15	15	100	26	22	85
Total	945	874	92	1516	1 447	95
Germany western						
Current cigarette smokers	694	509	73	484	385	80
Ex-smokers	531	480	90	949	799	84
Lifelong nonsmokers	89	86	97	653	518	79
Others	9	8	89	60	25	42
Total	1 323	1083	82	2 146	1 727	80

(continued)

Table D2. Continued.

Study	Cases			Controls		
	Total number	PI about β		Total number	PI about β	
		N	%		N	%
Italy						
Current cigarette smokers	206	90	44	155	74	48
Ex-smokers	149	92	62	136	89	65
Lifelong nonsmokers	28	18	64	102	49	48
Others	1	0	0	12	0	0
Total	384	200	52	405	212	52
Spain						
Current cigarette smokers	69	5	7	80	3	4
Ex-smokers	75	27	36	53	27	51
Lifelong nonsmokers	12	5	42	94	10	11
Others	0	.	.	8	0	0
Total	156	37	24	235	40	17
Sweden nationwide						
Current cigarette smokers	491	130	26	407	145	36
Ex-smokers	191	51	27	354	49	14
Lifelong nonsmokers	175	171	98	1 156	676	58
Others	103	81	79	128	65	51
Total	960	433	45	2 045	935	46
Sweden never-smokers						
Current cigarette smokers	0	.	.	0	.	.
Ex-smokers	0	.	.	0	.	.
Lifelong nonsmokers	258	242	94	487	417	86
Others	0	.	.	0	.	.
Total	258	242	94	487	417	86
Sweden Stockholm						
Current cigarette smokers	132	90	68	127	76	60
Ex-smokers	28	25	89	67	32	48
Lifelong nonsmokers	36	36	100	181	158	87
Others	0	.	.	0	.	.
Total	196	151	77	375	266	71
United Kingdom						
Current cigarette smokers	501	427	85	656	543	83
Ex-smokers	373	362	97	1 406	1 197	85
Lifelong nonsmokers	26	26	100	896	580	65
Others	60	58	97	168	149	89
Total	960	873	91	3 126	2 469	79
All studies						
Current cigarette smokers	3 575	2 337	65	3 322	2 134	64
Ex-smokers	2 465	2 001	81	4 930	3 749	76
Lifelong nonsmokers	884	831	94	5 418	3 818	70
Others	224	192	86	538	305	57
Total	7 148	5 361	75	14 208	10 006	70

Table D3. Estimated log-linear relationship between the relative risk of lung cancer and the observed residential radon concentration for each study and for all studies combined. [exp(β) = risk of lung cancer at 100 Bq/m³ time-weighted average observed radon concentration relative to 0 Bq/m³, estimated after stratification by study, sex, region of residence, and smoking habits; 95% CI = 95% confidence interval; df = degrees of freedom]

Study	Estimate of exp(β)	95% CI for exp(β)
Austria	1.049	0.759–1.450
Czech Republic	1.088	0.998–1.186
Finland nationwide	1.029	0.949–1.115
Finland southern	1.044	0.846–1.288
France	1.067	0.989–1.152
Germany eastern	1.135	0.990–1.302
Germany western	0.981	0.774–1.244
Italy	1.084	0.743–1.581
Spain	0.822	0.511–1.320
Sweden nationwide	1.072	0.948–1.211
Sweden never-smokers	1.169	0.914–1.497
Sweden Stockholm	1.085	0.814–1.448
United Kingdom	1.050	0.940–1.173
All studies [a]	1.064	1.027–1.102

[a] Chi-squared for test of $\beta = 0$: 12.30, 1 df; P=0.0005. Chi-squared for heterogeneity between studies: 4.48, 12 df; P=0.97

Table D4. Influence analysis showing estimated log-linear relationship between relative risk of lung cancer and observed residential radon concentration omitting each study in turn. [exp(β) = risk of lung cancer at 100 Bq/m³ time-weighted average observed radon concentration relative to 0 Bq/m³, estimated after stratification by study, sex, region of residence, and smoking habits; 95% CI = 95% confidence interval]

Study omitted	Estimate of exp(β)	95% CI for exp(β)
Austria	1.064	1.028–1.103
Czech Republic	1.059	1.020–1.102
Finland nationwide	1.074	1.032–1.119
Finland southern	1.065	1.028–1.104
France	1.063	1.021–1.107
Germany eastern	1.058	1.020–1.098
Germany western	1.066	1.029–1.106
Italy	1.064	1.027–1.103
Spain	1.066	1.029–1.105
Sweden nationwide	1.063	1.026–1.104
Sweden never-smokers	1.062	1.025–1.101
Sweden Stockholm	1.064	1.027–1.103
United Kingdom	1.066	1.027–1.107
All studies included	1.064	1.028–1.103

Table D5. Values of the parameters used for the analyses correcting for uncertainties in the assessment of radon concentrations in the study dwellings in each area. (μ = mean of the logarithm of the true long-term average radon concentration, V_t = variance of the logarithm of the true long-term average radon concentration, V_m = variance of the logarithm of the measurement error in each study)

Study	Area [a]	Control measurements (N)	μ	V_t+V_m	V_m [b]
Austria	1	4	4.52 [c]	0.50 [c]	0.14
	2	184	4.52 [c]	0.50 [c]	0.14
Czech Republic	1	163	6.07	0.17	0.12
	2	46	5.75	0.17	0.12
	3	41	6.33	0.17	0.12
	4	53	6.06	0.17	0.12
	5	73	6.19	0.17	0.12
Czeck Republic	6	88	6.43	0.17	0.12
	7	65	5.75	0.17	0.12
	8	194	6.28	0.17	0.12
	9	66	5.95	0.17	0.12
	10	36	5.82	0.17	0.12
	11, 12 [d]	National survey [e]	4.70	0.24	0.12
Finland nationwide	1	1435	4.34	0.46	0.33
Finland southern	1	427	4.93	0.74	0.33
France	1	1847	4.26	1.04	0.14
Germany eastern	1	1516	4.03	0.40	0.14
Germany western	1	2262	3.69	0.36	0.14
Italy	1	48	4.97	0.36 [f]	0.03
	2	49	4.73	0.36	0.03
	3	299	4.42	0.36	0.03
	4	245	4.12	0.36	0.03
	5	100	4.30	0.36	0.03
	6 [g]	741 [h]	4.36	0.38	0.03
	7	76	4.69	0.36	0.03
	8	20	5.31	0.36	0.03
	9	17	3.89	0.36	0.03
	10	22	4.55	0.36	0.03
	11	15	4.62	0.36	0.03
	12 [i]	National survey [j]	4.04	0.48	0.03
	13 [k]	World estimate [l]	3.40	0.44	0.14
	99 [m]	National survey [j]	4.04	0.48	0.03
Spain	1	235	4.18	1.28	0.14
Sweden nationwide	1	4453	3.99	1.02	0.14
Sweden never-smokers	1	1050	3.80	0.87	0.14
Sweden Stockholm	1	918	4.59	0.56	0.14
United Kingdom	1	1058	2.79	0.52	0.20
	2	2213	3.15	0.61	0.20
	3	1778	3.32	0.66	0.20
	4	1232	3.83	0.93	0.20
	5	670	4.32	0.92	0.20
	6	293	4.91	1.01	0.20
	7 [n]	7244 [h]	3.43	0.98	0.20
	8 [o]	–	– [p]	–	–
	9 [q]	–	– [p]	–	–
	10 [r]	National survey [s]	2.71	0.60	0.20
	11 [t]	World estimate [l]	3.40	0.44	0.14

[a] For studies with more than one area, these are as defined in table C1 unless otherwise indicated.
[b] Observed values, as in table 30 used for Czech Republic, Finland, Italy, Sweden and United Kingdom. Median of the observed values used for other countries.
[c] For Austria, areas have been pooled as there were too few measurements even for estimating the mean for area 1.
[d] That is, outside study area.
[e] Values based on Tomášek et al (2) with estimate of V_m from study data for Czech Republic.
[f] Where number of measurements was less than 100 for some strata, values of V_t+V_m have been averaged within a study.
[g] That is, in Rome, but district unknown.
[h] That is, all measurements in the city of Rome for the Italian study; all measurements in the study area for the United Kingdom study.
[i] That is, Italy, but outside the study area.
[j] Bochicchio et al (17).
[k] That is, outside Italy.
[l] United Nations Scientific Committee on the Effects of Atomic Radiation, 2000 (18) with variance taken from areas in this study with a similar geometric mean level.
[m] That is, unknown area.
[n] That is, in study area but unknown location.
[o] That is, caravan.
[p] True values of radon concentrations taken to be 4 Bq/m³ in caravans and 0 Bq/m³ in ships.
[q] That is, ship.
[r] That is, in United Kingdom but outside the study area.
[s] Wrixon et al (19).
[t] That is, outside the United Kingdom.

Table D6. Distribution of time-weighted average corrected residential radon concentrations during the 30-year period of interest by study.

Study	Time-weighted average residential radon (Bq/m³)								
	Mean	SD	Geometric mean	Geometric SD	Minimum	Quartiles			Maximum
						1st	2nd	3rd	
Austria	141	147	113	1.37	30	82	104	131	1083
Czech Republic	452	136	429	1.12	125	357	444	542	928
Finland nationwide	82	16	80	1.03	46	71	78	88	229
Finland southern	172	67	162	1.12	52	133	160	191	777
France	120	129	92	1.59	9	62	88	131	2797
Germany eastern	66	31	62	1.11	20	53	60	69	754
Germany western	45	14	43	1.07	17	38	43	48	260
Italy	106	62	93	1.26	30	67	88	121	463
Spain	117	105	93	1.47	28	63	86	122	746
Sweden nationwide	87	77	70	1.48	2	50	71	98	1300
Sweden never-smokers	68	47	57	1.42	3	40	57	83	416
Sweden Stockholm	124	50	116	1.13	33	96	114	139	418
United Kingdom	50	57	36	1.67	3	22	31	54	1117
All Studies	92	106	66	2.11	2	42	64	95	2797

Table D7. Estimated linear relationship between the relative risk of lung cancer and the residential radon concentration for each study and for all of the studies combined, correcting for uncertainties in the assessment of radon concentrations using the method of regression calibration. (β = excess relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average corrected radon concentration, estimated after stratification by study, sex, region of residence, and smoking habits; 95% CI = 95% confidence interval; df = degrees of freedom)

Study	Estimate of β	95% CI for β
Austria	1.62	<-0.11 [a]–>5.00 [b]
Czech Republic	– [c]	0.06–>5.00 [b]
Finland nationwide	−0.02	−0.38–1.24
Finland southern	0.35	<-0.21 [a]–>5.00 [b]
France	0.17	−0.01–0.62
Germany eastern	0.38	−0.02–1.39
Germany western	0.15	−0.36–1.61
Italy	0.10	−0.20–1.68
Spain	−0.14	<-0.14 [a]–0.87
Sweden nationwide	0.17	−0.05–0.67
Sweden never-smokers	0.28	−0.12–1.26
Sweden Stockholm	0.17	−0.21–3.87
United Kingdom	0.05	−0.07–0.28
All studies [d]	0.16	0.05–0.30

[a] Values below these limits, but cannot be ascertained as lower values of β lead to negative fitted values for the probability of lung cancer.
[b] The upper 95% confidence limit is greater than 5.00.
[c] Likelihood for Czech Republic study had no maximum.
[d] Chi-squared for test of $\beta = 0$: 11.25, 1 df; P=0.0008; chi-squared for heterogeneity between studies: 7.47, 12 df; P=0.76.

Table D8. Estimated log-linear relationship between the relative risk of lung cancer and the residential radon concentration for each study and for all the studies combined, correcting for uncertainties in the assessment of radon concentrations, using the method of regression calibration. [exp(β) = risk of lung cancer at 100 Bq/m³ time-weighted average corrected radon concentration relative to 0 Bq/m³, estimated after stratification by study, sex, region of residence and smoking habits; 95% CI = 95% confidence interval; df = degrees of freedom]

Study	Estimate of exp(β)	95% CI for exp(β)
Austria	1.17	0.68–2.01

(continued)

Table D8. Continued.

Study	Estimate of exp(β)	95% CI for exp(β)
Czech Republic	1.30	1.03–1.65
Finland nationwide	0.97	0.51–1.85
Finland southern	1.15	0.70–1.89
France	1.11	0.99–1.23
Germany eastern	1.36	1.00–1.86
Germany western	1.12	0.62–2.02
Italy	1.09	0.71–1.67
Spain	0.81	0.46–1.41
Sweden nationwide	1.11	0.94–1.31
Sweden never-smokers	1.22	0.87–1.72
Sweden Stockholm	1.12	0.72–1.76
United Kigdom	1.06	0.90–1.24
All studies [a]	1.12	1.05–1.2

[a] Chi-squared for test of $\beta = 0$: 12.02, 1 df; P=0.0005, chi-squared for heterogeneity between studies: 5.69, 12 df; P=0.93

Table D9. Influence analysis showing the estimated linear relationship between the relative risk of lung cancer and the corrected residential radon concentration omitting each study in turn. (β = increase in the relative risk of lung cancer per 100 Bq/m³ increase in the time-weighted average observed radon concentration, estimated after stratification by study, age, sex, region of residence, and smoking history; 95% CI = 95% confidence interval)

Study omitted	Estimate of β	95% CI for β
Austria	0.153	0.050–0.297
Czech Republic	0.140	0.036–0.283
Finland nationwide	0.164	0.056–0.313
Finland southern	0.156	0.051–0.301
France	0.156	0.039–0.320
Germany eastern	0.141	0.038–0.287
Germany western	0.158	0.053–0.306
Italy	0.160	0.054–0.309
Spain	0.167	0.060–0.316
Sweden nationwide	0.156	0.045–0.315
Sweden never-smokers	0.151	0.046–0.298
Sweden Stockholm	0.158	0.052–0.305
United Kingdom	0.212	0.074–0.415
All studies included	0.158	0.054–0.303

Table D10. Relative risk of lung cancer according to time-weighted average observed residential radon for the categories <50, 50–79, 80–139, 140–399 and ≥400 Bq/m³. An analysis with these categories was requested by the investigators of the German studies at the outset of the Collaborative Analysis. The baseline is 0 Bq/m³. (95% CI = 95% confidence interval)

Observed radon concentration [a]	Persons with lung cancer (N)	Controls (N)	Average observed radon concentration [b] (Bq/m³)	Relative risk [c]	95% CI
<50 Bq/m³	2518	5 312	33	1.04	0.97–1.12
50–79 Bq/m³	1929	3 665	63	1.03	0.96–1.10
80–139 Bq/m³	1519	2 833	103	1.10	1.01–1.20
140–399 Bq/m³	946	1 785	220	1.22	1.08–1.38
≥400 Bq/m³	236	613	683	1.53	1.18–2.00
Total	7148	14 208	105	–	.

[a] Observed radon concentration for each address in the 30-year period ending 5 years prior to the index date weighted according to the length of time that the person lived there.

[b] Average corrected radon concentrations, after uncertainties in the assessment of radon concentrations were taken into account, were 36, 63, 94, 189, and 485 Bq/m³.

[c] Relative risks estimated using the method of floating absolute risks after stratification by study, age, sex, region of residence, and, for current and ex-smokers, detailed smoking history.

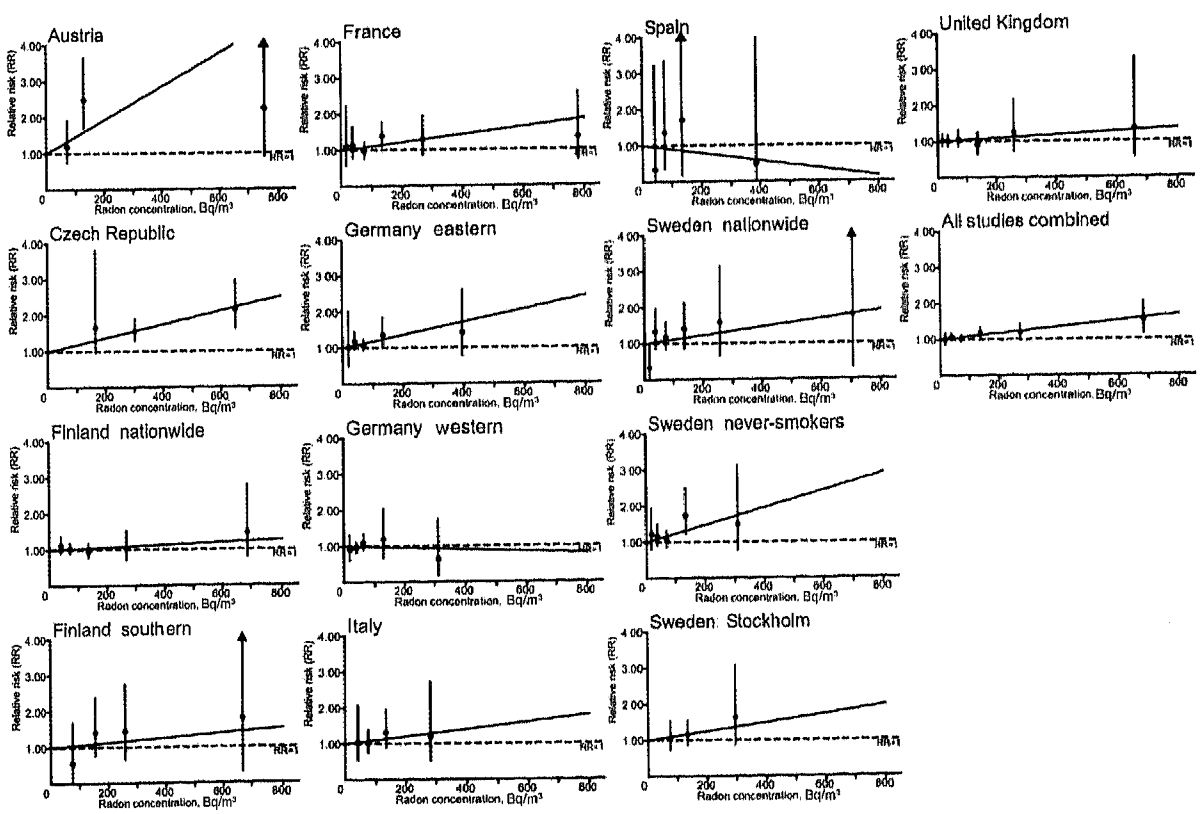

Figure D1. Relative risks, 95% confidence intervals (95% CI), and estimated linear relationships for lung cancer risk and the observed radon concentration by study. Radon concentrations and stratification as in figure 2 in the main text. Categories with fewer than 30 persons and categories 400–799 Bq/m³ and ≥800 Bq/m³ combined. The baseline is 0 Bq/m³.

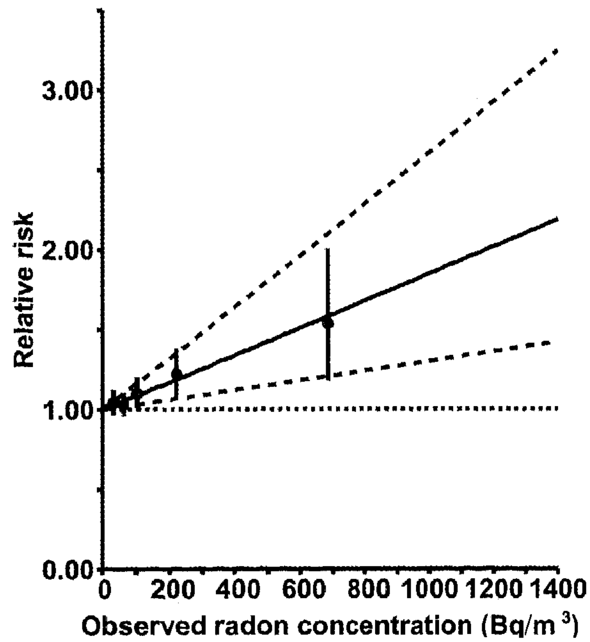

Figure D2. Relative risk of lung cancer according to the time-weighted average (Bq/m³) observed residential radon concentration after stratification by study, age, sex, region of residence, and smoking habits. Relative risks and 95% confidence intervals are shown for categories <50, 50–79, 80–139, 140–399 and ≥400 Bq/m³, and also the estimated linear relationship RR=1+0.00085 X (solid line), with 95% confidence intervals (dashed lines). Baseline is 0 Bq/m³. An analysis with these categories was requested by the investigators of the German studies at the outset of the Collaborative Analysis.

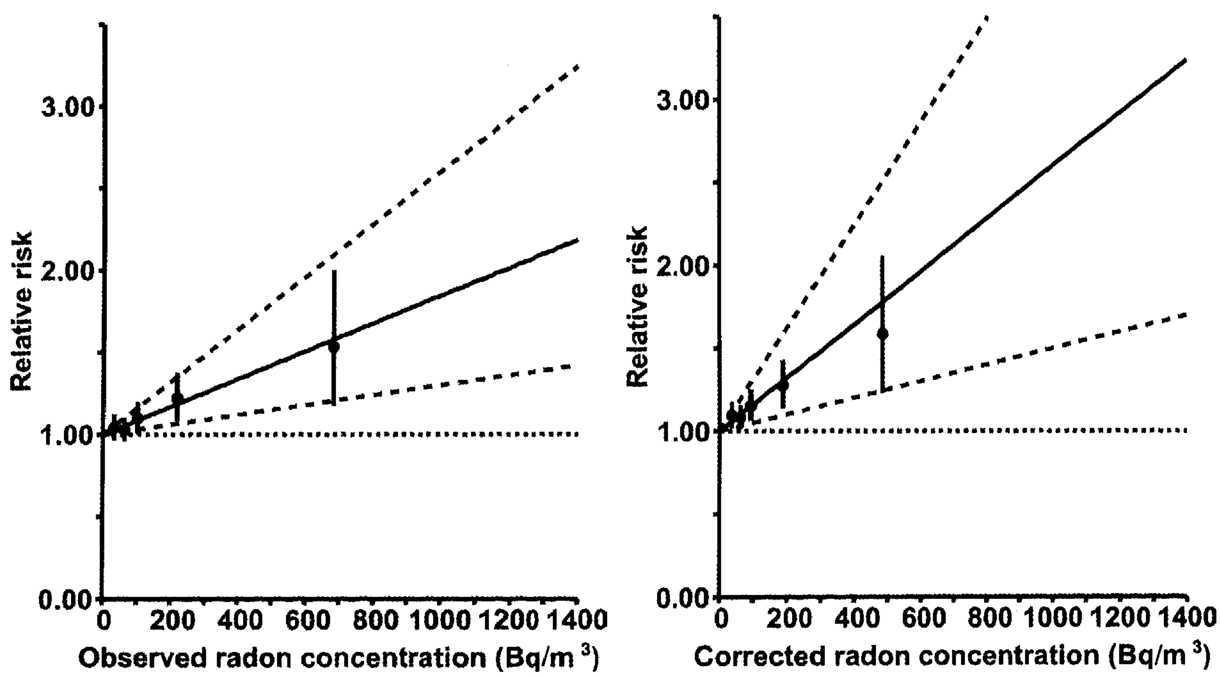

Figure D3. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration (on the left) and the time-weighted average corrected residential radon concentration (on the right). Relative risks and 95% confidence intervals are shown for the categorical analyses and also the estimated linear relationships (solid lines) with the 95% confidence intervals (dashed lines). The risks were calculated after stratification by study, age, sex, region of residence, and smoking habits. See figure 7 in the text for further methodological details. An analysis with these categories was requested by the investigators of the German studies at the outset of the Collaborative Analysis.

References for Appendix D

1. Oberaigner W, Kreienbrock L, Schaffrath Rosario A, Kreuzer M, Wellmann J, Keller G, et al. Radon and lung cancer in the district of Imst, Austria (Radon und Lungenkrebs im Bezirk Imst/Österreich). Landsberg am Lech, Germany: Ecomed Verlagsgesellschaft; 2002. Fortschritte in der Umweltmedizin.
2. Tomášek L, Müller T, Kunz E, Heribanová A, Matzner J, Plaček V, et al. Study of lung cancer and residential radon in the Czech Republic. Cent Eur J Public Health 2001;9:150–3.
3. Auvinen A, Mäkeläinen I, Hakama M, Castrén O, Pukkala E, Reisbacka H, et al. Indoor radon exposure and risk of lung cancer: a nested case-control study in Finland. J Natl Cancer Inst 1996;88:966–72. Erratum in J Natl Cancer Inst 1998; 90:401–2.
4. Ruosteenoja E, Mäkeläinen I, Rytömaa T, Hakulinen T, Hakama M. Radon and lung cancer in Finland. Health Phys 1996;71:185–9.
5. Baysson H, Tirmarche M, Tymen G, Gouva S, Caillaud D, Artus JC, et al. Case-control study on indoor radon and lung cancer in France. Epidemiology 2004;15:709–16.
6. Wichmann HE, Gerken M, Wellmann J, Kreuzer M, Kreienbrock L, Keller G, et al. Lungenkrebsrisiko durch Radon in der Bundesrepublik Deutschland (Ost) – Thüringen und Sachsen [Lung cancer risk due to radon in the Federal Republic of Germany (East)—Thuringia and Saxony]. Landsberg am Lech (Germany): Ecomed Verlagsgesellschaft; 1999. Fortschritte in der Umweltmedizin.
7. Kreuzer M, Heinrich J, Wölke G, Schaffrath Rosario A, Gerken M, Wellmann J, et al. Residential radon and risk of lung cancer in Eastern Germany. Epidemiology 2003;14:559–68.
8. Wichmann HE, Rosario AS, Heid IM, Kreuzer M, Heinrich J, Kreienbrock L. Increased lung cancer risk due to residential radon in a pooled and extended analysis of studies in Germany. Health Phys. 2005;88:71–9.
9. Kreienbrock L, Kreuzer M, Gerken M, Dingerkus G, Wellmann J, Keller G, et al. Case-control study on lung cancer and residential radon in Western Germany. Am J Epidemiol 2001;153:42–52.
10. Bochicchio F, Forastiere F, Farchi S, Quarto M, Axelson O. Residential radon exposure, diet and lung cancer: a case-control study in a Mediterranean region. Int J Cancer. 2005;114:983–91.
11. Barros-Dios JM, Barreiro MA, Ruano-Ravina A, Figueiras A. Exposure to residential radon and lung cancer in Spain: a population-based case-control study. Am J Epidemiol 2002;156:548–55.
12. Pershagen G, Åkerblom G, Axelson O, Clavensjö B, Damber L, Desai G, et al. Residential radon exposure and lung cancer in Sweden. N Engl J Med 1994;330:159–64.
13. Lagarde F, Pershagen G, Åkerblom G, Axelson O, Bäverstam U, Damber L, et al. Residential radon and lung cancer in Sweden: risk analysis accounting for random error in the exposure assessment. Health Phys 1997;72:269–76.
14. Lagarde F, Axelsson G, Damber L, Mellander H, Nyberg F, Pershagen G. Residential radon and lung cancer among never-smokers in Sweden. Epidemiology 2001;12:396–404.
15. Pershagen G, Liang Z-H, Hrubec Z, Svensson C, Boice Jr JD. Residential radon exposure and lung cancer in Swedish Women. Health Phys 1992;63:179–86.
16. Darby S, Whitley E, Silcocks P, Thakrar B, Green M, Lomas P, et al. Risk of lung cancer associated with residential radon exposure in south-west England: a case-control study. Br J Cancer 1998;78:394–408.
17. Bochicchio F, Campos Venuti G, Nuccetelli C, Piermattei S, Risica S, Tommasino L, et al. Results of the representative Italian national survey on radon indoors. Health Phys 1996;71:741–8.
18. United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). Sources and effects of ionizing radiation. New York (NY): United Nations; 2000. UNSCEAR 2000 report to the General Assembly, with scientific annexes, vol I: sources.
19. Wrixon AD, Green BM, Lomas PR, Miles JC, Cliff KD, Francis EA, et al. Natural radiation exposure in UK dwellings., London: Her Majesty's Stationery Office; 1988. National Radiation Protection Board Report NRPB-R190.