

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/m³ in the Germany western study to 500 Bq/m³ 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/m³ and >500 Bq/m³. When all of the studies were considered together, the overall mean TWA observed residential radon concentration was 105 Bq/m³, the median value was 63 Bq/m³, and the range was 1–4606 Bq/m³. 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/m³ (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/m³ (table 6). The estimated common difference between the TWA observed radon concentration for the lung cancer cases and the controls was 6.8 Bq/m³, 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/m³. For the controls, the corresponding weighted means were 96, 97, and 98 Bq/m³. 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/m ³)								
	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/m ³	566	7.9	1 474	10.4
25–49 Bq/m ³	1 999	28.0	3 905	27.5
50–99 Bq/m ³	2 618	36.6	5 033	35.4
100–199 Bq/m ³	1 296	18.1	2 247	15.8
200–399 Bq/m ³	434	6.1	936	6.6
400–799 Bq/m ³	169	2.4	498	3.5
800–1599 Bq/m ³	53	0.7	104	0.7
≥1600 Bq/m ³	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.

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

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/m ³)	Years with measurement (%)	Mean radon concentration (Bq/m ³)
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).

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 non-smokers (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/m³ 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/m³ 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 $\beta=0$ (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, ≥ 10 years), 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 $\times$ 2–other)	0.057	1.10	0.025	0.016–0.112	8.51
6 groups: (never–current $\times$ 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 subdividing current smokers by age started (<15, 15–17, 18–20, ≥ 21 years) separately for smokers of <15, 15–24, and ≥ 25 cigarettes/day, and subdividing 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/m³ 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/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 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/m ³ at:			
				100 Bq/m ³	200 Bq/m ³	500 Bq/m ³	1000 Bq/m ³
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

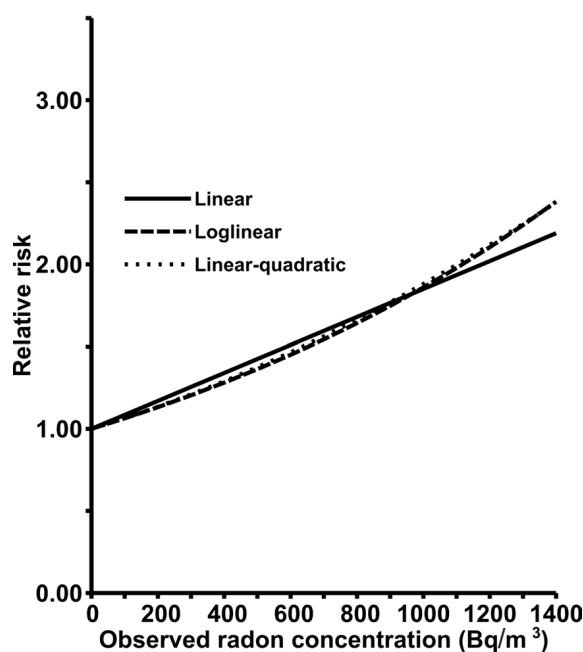


Figure 1. Comparison of different models for the relationship between the observed radon concentration and the risk of lung cancer. The equations for the fitted models are: linear $RR = 1 + 0.000844 X$, log-linear: $RR = \exp(0.000621 X)$, and linear-quadratic: $RR = 1 + 0.000622 X + 0.000000258 X^2$.

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

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/m ³	566	1 474	17	1.00	0.87–1.15
25–49 Bq/m ³	1999	3 905	39	1.06	0.98–1.15
50–99 Bq/m ³	2618	5 033	71	1.03	0.96–1.10
100–199 Bq/m ³	1296	2 247	136	1.20	1.08–1.32
200–399 Bq/m ³	434	936	273	1.18	0.99–1.42
400–799 Bq/m ³	169	498	542	1.43	1.06–1.92
≥800 Bq/m ³	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.

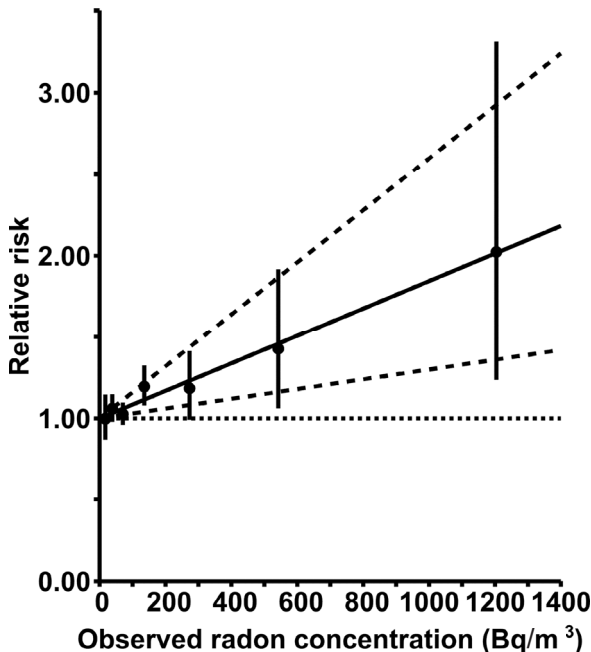


Figure 2. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration after stratification by study, age, sex, region of residence, and smoking habits. The relative risks and 95% confidence intervals are shown for the categories <25, 25–49, 50–99, 100–199, 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.

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.

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 $RR = 1 + \beta x$ 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 $RR = 1 + \beta x$ 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 $\beta=0$		
					Chi-squared	df	P-value
<800 Bq/m ³ only	7082	14 093	0.078	0.012–0.164	5.59	1	0.02
<400 Bq/m ³ only	6913	13 595	0.095	0.005–0.206	4.34	1	0.04
<200 Bq/m ³ only	6479	12 659	0.140	0.004–0.309	4.12	1	0.04
<100 Bq/m ³ 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 ($P=0.44$),

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 non-smokers. (95% CI = 95% confidence interval)

Observed radon concentration ^a	Cases (N)	Controls (N)	Mean observed radon concentration (Bq/m ³)	Relative risk ^b	95% CI ^c
<i>Current cigarette smokers</i>					
<25 Bq/m ³	281	335	17	0.92	0.72–1.19
25–49 Bq/m ³	975	808	39	1.00	0.86–1.17
50–99 Bq/m ³	1304	1071	72	1.05	0.93–1.19
100–199 Bq/m ³	654	595	136	1.24	1.03–1.51
200–399 Bq/m ³	234	294	275	1.19	0.86–1.64
≥400 Bq/m ³	127	219	652	1.48	0.92–2.35
Total	3575	3322	115	–	–
<i>Ex-smokers</i>					
<25 Bq/m ³	198	621	18	0.94	0.75–1.18
25–49 Bq/m ³	750	1515	38	1.10	0.97–1.24
50–99 Bq/m ³	898	1734	70	1.03	0.92–1.15
100–199 Bq/m ³	431	680	135	1.18	0.99–1.41
200–399 Bq/m ³	127	251	266	1.08	0.78–1.49
≥400 Bq/m ³	61	129	689	1.45	0.86–2.42
Total	2465	4930	90	–	–
<i>Lifelong nonsmokers</i>					
<25 Bq/m ³	56	467	17	1.06	0.78–1.45
25–49 Bq/m ³	222	1443	38	1.07	0.90–1.26
50–99 Bq/m ³	332	2023	71	1.02	0.90–1.16
100–199 Bq/m ³	170	866	135	1.23	1.02–1.48
200–399 Bq/m ³	63	362	278	1.37	1.00–1.90
≥400 Bq/m ³	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.

and the estimated upper 95% confidence limit for a possible threshold was 150 Bq/m³.

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 non-smokers, 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

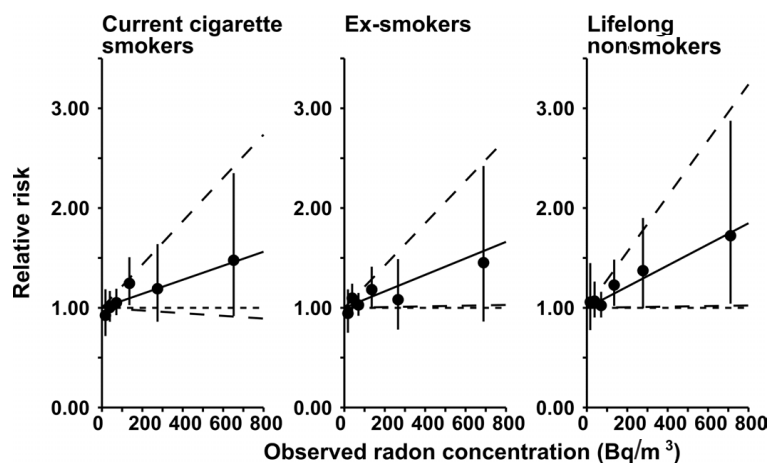


Figure 3. Relative risk of lung cancer according to the time-weighted average observed residential radon concentration by smoking status. The relative risks and 95% floated confidence intervals are shown for the categorical analyses, as are the estimated linear relationships (solid lines) and 95% confidence 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 $\beta = 0.127$, 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 $\beta = -0.070$, 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 $\beta = 0.304$, 95% CI 0.100–0.641) than for those who slept with it open (estimate of $\beta = 0.010$, 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	2955	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	5.46	1	0.02
Change in β for some urban residence	845 ^c	1300 ^c	-0.234	– ^b			
Change in β for window closed	1340 ^d	2569 ^d	0.067	– ^b			

^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).