Radiation Protection Dosimetry (2007), pp. 1–11 doi:10.1093/rpd/ncm330

SCIENTIFIC NOTES

CASE-CONTROL STUDY OF RADON AND LUNG CANCER IN NEW JERSEY

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Received April 10 2007, revised April 10 2007, accepted May 24 2007

Radon is known to cause lung cancer in humans; however, there remain uncertainties about the effects associated with residential exposures. This case-control study of residential radon and lung cancer was conducted in five counties in New Jersey and involved 561 cases and 740 controls. A yearlong α-track detector measurement of radon was completed for ~93% of all residences lived in at the time of interview (a total of 2063). While the odds ratios (ORs) for whole data were suggestive of an increased risk for exposures >75 Bq m^{-3}, these associations were not statistically significant. The adjusted excess OR (EOR) per 100 Bq m^{-3} was −0.13 (95% CI: −0.30 to 0.44) for males, 0.29 (95% CI: −0.12 to 1.70) for females and 0.05 (95% CI: −0.14 to 0.56) for all subjects combined. An analysis of radon effects by histological type of lung cancer showed that the OR was strongest for small/oat cell carcinomas in both males and females. There was no statistical heterogeneity of radon effects by demographic factors (age at disease occurrence, education level and type of respondent). Analysis by categories of smoking status, frequency or duration did not modify the risk estimates of radon on lung cancer. The findings of this study are consistent with an earlier population-based study of radon and lung cancer among New Jersey women, and with the North American pooling of case control radon seven studies, including the previous New Jersey study. Several uncertainties regarding radon measurements and assumptions of exposure history may have resulted in underestimation of a true exposure–response relationship.

INTRODUCTION

Radon is a well-established human lung carcinogen based on experimental evidence using *in vivo* and *in vitro* cell culture and mutagenesis studies[1,2] and epidemiologic cohort studies on miners[1,3–5]. The International Agency for Research on Cancer[6] considered that there is sufficient evidence for the carcinogenicity of radon and its decay products to humans. Additionally, the US National Research Council on the Biological Effects of Radiation (BEIR VI) concluded that residential radon was an important contributor to the total burden of lung cancer[1].

Downward extrapolation of data from studies on miners exposed to high levels of radon suggests that 8–15% of total lung cancer deaths in the US and Canada can be attributed to radon exposure in homes[1,7,8]. However, such extrapolation raises serious complications regarding differences between the mine and the home environments (exposure levels and confounding factors), difficulty in extrapolating miner data to females and children and differences in physical factors such as breathing rates, size distribution of aerosol particles and fraction of unattached radon progeny.

To overcome these uncertainties, many studies have been conducted to estimate directly the health risks associated with residential radon exposures in the general population. To date, more than 20 case-control studies of residential radon and lung cancer have been completed[9–27]. The results of these individual studies have been inconsistent due, in part, to inadequate sample sizes and the inherent uncertainties in radon measurements. Although the excess odds ratios (EORs) for all but two studies were positive, most of these studies did not show statistically significant effect of radon on lung cancer. Combined analysis of seven of these studies (a total of 3662 cases and 4966 controls) in North America[28,29]

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and 13 studies (involving 7148 cases of lung cancer and 14 208 controls) in Europe[30,31] provided the opportunity to better characterise risk estimates by increasing the number of subjects available for analysis and improving accuracy in radon dosimetry (through data restriction). In North American pooling study, the estimated odds ratio (OR) after exposure to radon at a concentration of 100 Bq m^{-3} in the exposure time window (ETW) 5–30 y before the index date was 1.11 (95% CI = 1.00–1.28), while in the European pooling, the OR for lung cancer was 1.08 (with 95% CI = 1.03–1.16) per 100 Bq m^{-3} increase in measured radon. Collectively, these pooled analyses indicated the appreciable risk of lung cancer from exposures to residential radon with estimates consistent with the predicted EOR of 0.12 (0.02–0.25) per 100 Bq m^{-3} based on a linear model developed by the BEIR VI[1] using data on low-exposed miners whose exposures were similar to long-term residents of high-radon homes.

An earlier study (also known as NJ–I study) to examine indoor radon exposure and lung cancer risk in women was conducted in New Jersey for the period 1982–84[9] and was an extension of a previously completed statewide population-based lung cancer study[32]. The results from New Jersey's first radon study showed a significant trend in odds ratios (ORs) with increasing radon concentration (one-sided $p = 0.04$), and the trend was strongest among light smokers (less than 15 cigarettes per day, one-sided $p = 0.01$). The trend for lung cancer risk with estimated cumulative radon exposure was weaker (one-sided $p = 0.09$). Unfortunately, the possibility of selection biases, the small number of high exposures and other uncertainties necessitate caution in the interpretation of these data. Additional radon monitoring increased the eligible subjects to 922 (480 cases and 442 controls) from 835 (433 cases and 402 controls) in the initial analysis, but did not substantially change the study results or their interpretation in relation to radon-related lung cancer risk[33]. The data from the first New Jersey study have been re-analysed as part of combined analysis of North American studies of residential exposure to radon and lung cancer[28,29].

The current study (NJ–II study) is the next phase of the New Jersey radon project and is intended to build on the findings of the previous study and address some of its limitations. For this study, both male and female subjects living in five rural counties in New Jersey known to have relatively high levels of radon were recruited between 1989 and 1992. The analyses presented in this paper have been undertaken to characterise the risk in this study population. The data from the second New Jersey study will be added to the global pooling, which is underway to combine all case-control studies of residential radon and lung cancer conducted throughout the world.

SUBJECTS AND METHODS

This study was based in five counties in New Jersey City (Hunterdon, Somerset, Morris, Sussex and Warren). The counties are located on the 'Reading Prong' characterised the low population density and relatively high radon distribution. Eligible cases were male and female residents of the five counties diagnosed with primary, histologically confirmed lung cancer. Male cases were drawn between 1 September 1989 and 30 April 1991, whereas female cases had an extended recruitment period from 1 September 1989 to 30 April 1992. There were no exclusions based on smoking status. Controls were frequency matched to cases by sex, race, 5-y age groups and smoking status (ever smoker, never smoker). Controls were selected from the five county study areas. Controls for cases aged <65 y were identified by random digit dialling, whereas controls for cases aged >65 were identified from files of the Health Care Finance Administration (Medicare) comprising almost all individuals in the US of age ≥ 65.

From a pool of initially identified cases and controls ~80%, a total of 1683 subjects, have consented to participate in the study and completed the interviews. All homes lived in by subjects for a minimum of 2 y were targeted for radon monitoring. Owing to high mobility of some subjects and refusal to place the dosemeters by current occupants, no a yearlong α-track detector (ATD) measurements were available within the 5–30 y (from 5 to 29 y inclusive) of ETW for 133 cases (17%) and 155 controls (17%). These subjects were excluded from the analyses of this study. Additionally, four subjects were excluded because no smoking data were available (Table 1). A total of 651 cases and 740 controls contributed to the current analysis of radon exposure and risk of lung cancer.

RADON EXPOSURE ASSESSMENT

The targeted ETW was 5–30 y prior to diagnosis for both cases and controls. Restriction of radon exposure assessment to this period presumes that the risk of lung cancer is most biologically relevant to radon exposure in this time window, with 5 y latency from the onset of exposure to disease formation[1]. Residence inclusion criteria for the subjects were all homes with a minimum of 2 y of residency that could be monitored. A yearlong ATD measurement of radon (type SF; Terradex Radon Detection Products, Glenwood, IL, USA) was conducted in the living area (in the living room and in the master bedroom in some cases). For ~10% of the houses, another ATD was paired with the first one as quality control check on the measurement precision.

Cumulative radon exposure (in Bq m^{-3}) was estimated from the living area radon concentrations and

Table 1. Availability of residential radon measurements and smoking information.

Sex	Number of subjects		Number of subjects excluded				Number of subjects retained for analysis	
			No smoking data		No radon data[a]			
	Cases	Controls	Cases	Controls	Cases	Controls	Cases	Controls
Males	401	455	1	1	82	93	349	392
Females	386	441	2		51	62	302	348
All Subjects	787	896	3	1	133	155	651	740

[a]Yearlong ATD measurements within 5–30 y ETW.

the number of years the subject lived in the index residence during the period of 5–30 y prior to diagnosis or selection. Average radon exposures were calculated first by treating all exposures occurring in the 5–30 y ETW as equally important (time weighted average) and then by treating exposures occurring farther in the past as decreasing in importance (BEIR VI weighted average). In the latter case, exposures occurring 5–14, 15–24 and 25 y or more prior to the index date were assigned weights of 1.0, 0.8 and 0.3, respectively[1].

STATISTICAL METHODS

The data analysis was conducted using conditional likelihood regression for matched or stratified data[34]. This approach has been used for the combined analysis of North American studies[28,29]. The stratification variables in the model consistent with those used in the combined analysis have used. The analysis was stratified by sex, age, number of cigarettes smoked per day, duration of cigarette smoking, number of residences occupied (1, >1) and years with ATD (<25, >24 y). These factors included as stratification variables in the regression model.

Analyses were based on a linear model for the OR of the form

$$\mathrm{OR}(x) = 1 + \beta x,$$

where x is the radon concentration (in Bq m^{-3}) and β is the EOR for each unit increase in x. This model was fit using the PECAN module in the Epicure software package, which calculates parameter estimates under conditional analytic methodology[35]. The model is fit using categories of radon concentration. The categories were selected to be consistent with North American poling analyses[28,29].

DATA RESTRICTIONS

Main analyses of this study are based on the full dataset. In addition, sensitivity analyses were also performed on restricted datasets for which more accurate radon dosimetry was available. The restriction criteria proposed in the North American pooling analysis[28,29] is used. The restricted analysis was based on the completeness of monitoring where the subjects' prior residences were monitored for 20 y or more with ATDs in the 5–30 y ETW. Furthermore, subjects eligible for the restricted analysis occupied only one or two residences in the ETW. There were 326 cases and 418 controls available for the restricted analysis.

RESULTS

A total of 1391 subjects were available for analysis, 651 incident lung cancer cases and 740 matched controls. There were 302 male and 349 female cases of lung cancer. The majority of the cases were >65 y, with between 8 and 13 y of education. Proxies (next of keen or other person living with a subject) were used to complete the interviews when subjects were unavailable. There were only 51 (7%) proxy interviews in the control sample out of 740 interviews. The case group had 285 (44%) proxy interviews. A large majority of cases and controls smoked tobacco products at some time in their lives (Table 2). A higher percentage of cases were cigarette smokers. The histological breakdown of the lung cancer cases includes: 166 squamous cell carcinomas, 105 small/oat cell carcinomas, 271 adenocarcinomas, 34 large cell carcinomas and 75 other histological types (data not shown).

Nine hundred and twenty-eight case residences and 981 control residences had α-track measurements completed, and a total of 2063 residences were available for analysis with measured or imputed data (Table 3). The average number of residences per subject for the case group was 1.5 and for the control group 1.4 (data not presented). Similar percentage of houses for cases and controls were covered by ATD radon measurements (Table 3). Among cases, the mean exposure level was higher for females. Male and female controls' mean exposures were similar: 46.8 and 45.8 Bq m^{-3}, respectively (Table 3).

Table 2. Characteristics of study subjects in the NJ-II study.

Characteristic	Cases		Controls	
	Number	Percentage	Number	Percentage
Sex				
Males	302	46	348	47
Females	349	54	392	53
Age at disease occurrence (y)				
<60	173	26.6	182	25
60–64	118	18.1	126	17
70–74	125	19.2	156	21
>75	134	20.6	163	22
Education (y)				
<7	32	4.9	16	2
8–13	435	66.8	437	59
>14	180	27.6	284	38
Unknown	4	0.6	3	0.4
Source of interview				
Subject	366	56.2	689	93
Proxy	285	43.8	51	7
Lifetime smoking status				
Never smoked	40	6.1	116	16
Smoked cigarettes only	521	80.0	513	69
Smoked pipe/cigar	1	0.2	0	0
Mixed smoking habit	89	13.7	111	15
Total	651		740	

Overall, no significant increases of risks of lung cancer with increasing levels of radon concentrations were observed (Table 4). The ORs for the combined male and female groups showed a tendency of increase with elevated radon exposure up to the 100–149 Bq m^{-3} exposure category. The adjusted EOR per 100 Bq m^{-3} was −0.13 (95% CI: −0.30 to 0.44) for males, 0.29 (95% CI: −0.12 to 1.70) for females and 0.05 (95% CI: −0.14 to 0.56) for the total subjects. The highest exposure level (≥150 Bq m^{-3}) had few cases and the ORs were generally smaller than in the lower exposure categories. The summary estimates of EOR per 100 Bq m^{-3} did not materially differ after data in the ≥150 exposure groups were removed (values not shown).

Restricting analysis to those with more accurate exposure information (one or two residences and ≥20 y of α-track monitoring) slightly changed point estimates. However, the overall results remained non-significant for males, females and all subjects combined.

Table 5 shows the unstratified OR for different histological type of lung cancer by radon exposure categories in males and females. In male cases, radon exposure showed stronger effects with small/oat cell carcinomas and squamous cell carcinomas. Similar effects were seen in females with a tendency of increasing risk of small/oat cell carcinoma with increasing levels of radon exposure. More detailed analysis of trends for specific histological type was difficult because of small number of cancers in the dataset.

Table 6 examines the risk of lung cancer associated with demographic factors and radon concentration by males and females. There was no

Table 3. Outcome of radon monitoring in residential houses of the study subjects in the 5–30 y of ETW.

Outcome of measurement attempt	Lung cancer cases			Controls		
	Males	Females	Total	Males	Females	Total
Houses covered						
Total number of residences radon measured or imputed	529	476	1005	567	491	1058
Number of residences with radon measured using α-track dosimeters[a] (%)	487 (92)	441 (93)	928 (92)	525 (93)	456 (93)	981 (93)
Estimated residential radon concentrations in the 5–30 ETW						
Time weighted average[b] (Bq m^{-3})	41.9	50.7	46.0[c]	46.8	45.8	46.4[c]
BEIR VI Weighted Average[d] (Bq m^{-3})	32.9	40.1	36.2[c]	36.8	36.0	36.4[c]

[a]Of the total number of houses radon measured or imputed in the corresponding categories.
[b]Exposure determined using weights of 1.0 for exposures received in each year.
[c]Estimated residential radon concentrations for male and female subjects combined.
[d]Exposures determined using weights of 1.0, 0.8 and 0.3 for exposures received 5–14, 15–24 and 25 y and more prior to the index date, respectively.

Table 4. ORs of lung cancer (95% CI) for males, females and total study group in the total study group and in the restricted study group.

	Time weighted average radon concentration (Bq m^{-3})						$\beta^b \times 100$
	<25 Case/controls OR[a]	25–49 Case/controls OR (95% CI)	50–74 Case/controls OR (95% CI)	75–99 Case/controls OR (95% CI)	100–149 Case/controls OR (95% CI)	≥150 Case/controls OR (95% CI)	
All study groups							
Males ($n = 741$)	105/122, 1.00	162/169, 0.90 (0.58–1.39)	43/54, 1.13 (0.62–2.07)	19/21, 1.12 (0.45–2.79)	13/10, 1.70 (0.59–4.88)	7/16, 0.45 (0.16–1.30)	−0.13 (−0.30 to 0.44)
Females ($n = 650$)	95/120, 1.00	119/135, 0.89 (0.53–1.49)	45/51, 0.93 (0.50–1.73)	18/17, 1.52 (0.59–3.94)	12/13, 1.14 (0.34–3.76)	13/12, 1.38 (0.45–4.23)	0.29 (−0.12 to 1.70)
Total ($n = 1391$)	200/242, 1.00	281/304, 0.90 (0.64–1.25)	88/105, 1.02 (0.66–1.57)	37/38, 1.31 (0.68–2.53)	25/23, 1.40 (0.64–3.09)	20/28, 0.76 (0.36–1.61)	0.05 (−0.14–0.56)
Restricted group (one or two residences only and ≥20 y of α-track monitoring)							
Males ($n = 403$)	69/88, 1.00	62/70, 1.03 (0.53–1.99)	19/31, 1.18 (0.50–2.79)	15/13, 1.66 (0.44–6.21)	10/8, 1.92 (0.52–7.06)	4/14, 0.33 (0.08–1.30)	−0.17 (−0.30 to 0.42)
Females ($n = 341$)	62/89, 1.00	38/51, 1.07 (0.49–2.32)	20/26, 0.72 (0.28–1.83)	10/9, 1.44 (0.37–5.57)	8/8, 0.84 (0.16–4.31)	9/11, 0.93 (0.23–3.66)	0.02 (−0.15 to 0.99)
Total ($n = 744$)	131/177, 1.00	100/121, 1.03 (0.63–1.70)	39/57, 0.92 (0.49–1.73)	25/22, 1.58 (0.62–4.04)	18/16, 1.36 (0.50–3.69)	13/25, 0.54 (0.21–1.40)	−0.05 (−0.15 to 0.71)

ORs stratified by sex and categories of age, duration of smoking, number of cigarettes smoked per day, number of residences occupied and years with α-track monitoring.
[a]Reference category.
[b]Excess OR (β) based on the linear model: $OR(x) = 1 + \beta(x)$, where x is the mean radon concentration in the 5–30 y ETW.

Table 5. OR for various histological types of lung cancer by different radon exposure categories in males and females.

	Total number of cases	ORs					
		Radon concentration exposure category (Bq m^{-3})					
		0–24	25–49	50–74	75–99	100–149	>150
Males							
Squamous cell	114	1.00	1.47	1.42	0.86	2.26	1.69
Small/oat cell	51	1.00	1.04	0.42	1.82	3.05	0.00
Adenocarcinoma	127	1.00	0.89	0.92	0.92	0.83	0.17
Large cell	18	1.00	2.17	0.00	1.45	3.05	0.00
Other	39	1.00	0.93	0.81	0.83	0.00	0.00
Females							
Squamous cell	52	1.00	1.30	1.10	1.88	0.62	2.00
Small/oat cell	54	1.00	1.01	1.25	2.82	2.46	2.67
Adenocarcinoma	144	1.00	1.05	1.01	1.15	0.75	0.82
Large cell	16	1.00	1.56	1.76	0.00	2.31	2.50
Other	36	1.00	1.11	1.18	0.00	1.54	0.83

statistically significant heterogeneity of radon effects by the demographic factors of age at disease occurrence, education level or type of respondent (p-values for the test of homogeneity were not significant in the males, females or in the combined male and female groups).

Analysis by smoking factors (smoking status, frequency or duration) showed that risk estimates did not differ by various smoking categories (Table 7). However, never-smokers in the combined male and female groups had a higher risk of lung cancer (EOR = 0.28) compared with ever-smokers (EOR = 0.15) although the test of homogeneity was insignificant ($p = 0.85$). The number of cigarettes per day, duration of smoking and years since smoked did not affect the association between radon and lung cancer.

DISCUSSION

Overall, no significant increases of risks of lung cancer with increasing levels of radon concentrations were observed. Results of this study are consistent with the majority of worldwide case-control studies in showing slight increase in risk without statistical significance[10–12,14–16,18–21,23,24]. Only four studies reported statistically significant increased risk in the EOR[13,17,25,27], whereas in only two studies[22,26], the EORs were negative.

This case-control study of lung cancer among New Jersey males and females combined showed a slight increase (although no association or an inverse association is consistent with the 95% CIs) in the risk of lung cancer (overall EOR = 0.05 per 100 Bq m^{-3}, 95% CI: −0.14 to 0.56). The EOR for females was 0.29 (95% CI: −0.12 to 1.70). The EOR in the first New Jersey[9] study, which was conducted in females only, was 0.56 (95% CI: −0.22 to 2.97). The NJ-I study included subjects form urban areas and densely populated counties known to have low radon levels, while the current study (NJ-II study) was based on subjects residing in five rural counties with relatively high radon concentrations.

Restricting the analysis to those with less radon exposure misclassification did not markedly change the risk estimates. Data restriction to those with one or two residences and ≥20 y of α-track monitoring probably had little effect because the average number of residences per person was low (about 1.5 for all subjects). More importantly, 1909 (92%) of the 2063 residences occupied by the subjects were measured using ATDs.

As noted above, the results did not differ by demographic factors such as age and education. Never-smokers had higher EOR than ever-smokers although the test for heterogeneity was not significant. The possibility of selection bias among heavy smokers and misclassification of smoking by proxy interviews mean that the differences by smoking may be spurious. Proxies were more represented in the case group than in the control group. Proxy interviews may also influence information related to residential histories, mobility, house occupancy, education and consequently affect accuracy of information used for adjustment of radon measurements. In the study conducted in Missouri[21], the trend in relative risks was greater when the interview respondent was the subject rather than a next-of-kin, suggesting the possibility of recall bias for smoking.

The BEIR Committee suggested that the apparent inconsistency in findings among residential case-control studies was largely a consequence of exposure misclassification[1]. This factor is inherent

Table 6. Excess ORs of lung cancer (95% CI) by demographic factors.

Factors	Males				Females				Total			
	Case	Control	$\beta \times 100$[a]	p[b]	Case	Control	$\beta \times 100$[a]	p[b]	Case	Control	$\beta \times 100$[a]	P[b]
Radon exposure	349	392	−0.13 (−0.30 to 0.44)		302	348	0.29 (−0.12 to 1.70)		651	740	0.05 (−0.14 to 0.56)	
Age at disease occurrence												
<60	80	87	−0.12		93	95	1.33		173	182	−0.03	
60–64	69	65	−0.27		49	48	−0.34		118	113	−0.40	
65–69	60	74	0.12		41	52	0.40		101	126	0.19	
70–74	82	71	0.03		54	74	0.06		125	156	0.20	
>75	69	84	0.06	0.69	65	79	0.26	0.78	134	163	0.18	0.29
Highest grade level of education												
0–7	21	10	—		11	6	−3.43		53	26	−0.04	
8–13	222	212	−0.07		213	225	−0.05		657	649	−0.05	
>14	105	168	0.01	0.76	75	116	0.60	0.58	285	452	0.20	0.82
Type of respondent												
Subject	191	367	−0.36		175	322	0.52		366	689	−0.02	
Surrogate	158	25	2.02	0.39	127	26	−1.13	0.28	285	51	0.34	0.82

[a]Based on the linear OR model: $\mathrm{OR}(x) = 1 + \beta(x)$, where x is the mean radon concentration in the 5–30 y ETW. Models stratified by sex, age, duration of smoking and number cigarettes smoked per day. Combined estimates based on the fixed effects modelling. Number of cases and controls vary due to missing data.
[b]Test of homogeneity of β.

Table 7. Excess ORs by categories of cigarette smoking-related factors.

Factors	Males				Females				Total			
	Case	Control	$\beta \times 100$[a]	p[b]	Case	Control	$\beta \times 100$[a]	p[b]	Case	Control	$\beta \times 100$[a]	p[b]
Radon exposure	262	281	0.01 (−0.29 to 1.10)		299	348	0.29 (−0.12 to 1.70)		561	629	0.16 (−0.13 to 0.89)	
Smoking status												
Never-smoked	11	43	−0.29		29	73	1.18		40	116	0.28	
Ever-smoked	251	238	0.03	0.77	270	275	0.23	0.57	521	513	0.15	0.85
Number cigarettes per day												
1–9	5	25	−0.45		16	71	−0.42		21	96	−0.84	
10–19	50	93	0.01		117	133	0.34		167	226	0.28	
20–29	106	59	−0.01		88	51	0.27		194	110	0.17	
>30	90	61	0.14	0.98	49	20	−0.90	0.87	139	81	0.04	0.89
Years of cigarette smoking												
1–24	17	49	−0.30		24	57	0.78		41	106	0.29	
25–34	39	40	−0.04		58	71	4.31		97	111	0.93	
35–44	77	59	0.04		82	69	−0.33		159	128	−0.19	
>45	118	90	0.09	0.98	106	78	0.40	0.56	224	168	0.28	0.89
Years since smoked												
0	120	108	−0.31		158	37	0.02		278	245	−0.31	
1–9	75	51	0.14		74	60	0.04		149	111	0.14	
10–19	26	24	2.25		22	27	−0.39		48	51	2.25	
>20	30	55	−0.20	0.40	16	51	0.13	—	46	106	−0.20	0.40

[a]Data limited to never and cigarette-only smokers.
[b]Test of homogeneity of β for never-smokers and levels of cigarette smoking variables.

in radon studies that usually estimate historical radon exposure in the 25-y period of ETW by 1-y measurement of radon in current residences. Changes to homes due to structure aging, remoulding, new furnaces, storm windows and other changes introduce systematic bias even with complete coverage[12]. Other important source of exposure misclassification is subject's mobility, which increases the difficulty in monitoring multiple residences and necessitates imputing data for missing homes[29]. Year-to-year variation of radon concentration is another important factor contributing to the error in radon exposure estimation. Lagarde *et al.*[36] reported that the main contributor to random errors in exposure estimation is the variation in radon levels over calendar years.

Data of this study showed that the EOR was positive for females and negative for males. Similar findings were reported in studies conducted in Utah and Connecticut[4], where the EOR was -0.006 for males and 0.061 for females. In the combined North American analysis[28], no apparent heterogeneity in the EOR by sex was observed ($p = 0.21$), although EOR was 0.19 for males and 0.03 for females. Similarly, the combined analysis in Europe[30] and studies in China[37] did not show effect modification by sex. It is possible that male and female discrepant results in this study were caused by chance. Models estimating attributable risk for lung cancer from residential exposure to radon assume that radon increases background lung cancer rates by the same factor for males and females.

The previous New Jersey study[9] also suggested a tendency for small cell carcinoma to have the strongest association with radon exposure. In the current study, too, radon exposure showed stronger association with small/oat cell carcinomas than with other histological types. Radon exposure was also found to be strongly associated with small lung cancer compared with other types[15, 22]. Pershagen *et al.*[16] provided evidence of stronger effects for small cell lung cancer and squamous cell carcinomas in a study conducted in Swedish women, while another Swedish report[17] found largest effects among small cell lung cancer and adenocarcinoma. Similarly, pooled analysis of the North American[28] and the European studies found that the largest EOR was for small cell carcinoma (0.23 and 0.31 per 100 Bq m^{-3}, respectively). Studies on uranium miners also showed stronger association with small cell carcinoma[1,38,39].

The average radon exposure was $\sim$46 Bq m^{-3} for both cases and controls (Table 3) and a large percentage of subjects were in the 10–50 Bq m^{-3} exposure range (distribution of radon exposure is not shown). Because of the small risk of radon on lung cancer, detection of any effect of radon at this relatively low level of exposure would be challenging. This might have contributed to the limited statistical power. Inaccuracy of radon exposure assessment increases if the variation in exposure within the population is low. Furthermore, if a large number of subjects are in the lower exposure categories then the results would more likely to be biased towards null[22].

In conclusion, in isolation, the current study showed a nonsignificant small effect of residential radon exposure on the risk of lung cancer. Its findings are in statistical agreement with the earlier New Jersey radon study and with the North American pooled analysis that included the earlier New Jersey study and six others conducted in other states or provinces. However, several uncertainties regarding radon measurements and assumptions of exposure history may have resulted in underestimation of a true exposure–response relationship. The effect of large radon exposures in causing lung cancer remains clear, having been demonstrated extensively in mining and animal studies. Furthermore, conclusion of the North American and European pooling suggested that an appreciable fraction of lung cancer may be caused by prolonged exposure to radon in homes. However, questions still exist around the presence of a threshold, an exposure level above which carcinogenic effects are observed. Establishment of appropriate and safe levels of household radon, if any, still remains to be completed.

Global pooling of all studies on residential radon is underway and the results of this study will be used along with data from the previous case-control studies to add to the current evidence of effects of residential radon on lung cancer.

ACKNOWLEDGEMENTS

This work was supported by the National Institute of Environmental Health Sciences (NIEHS), grant no. RO1-ES05079. This research was also supported by grants from the Canadian Institutes of Health Research (formerly the Medical Research Council of Canada) and the Natural Sciences and Engineering Research Council of Canada to D. Krewski, who currently holds the NSERC/SSHRC/McLaughlin Chair in Population Health Risk Assessment at the University of Ottawa.

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