RADIATION RESEARCH

Volume 2
Congress Proceedings

Edited by

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11th INTERNATIONAL CONGRESS OF RADIATION RESEARCH

Dublin, Ireland
July 18–23, 1999

Radon in Houses and Risk of Lung Cancer: Direct Evidence for a Significant Association

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Radioactive radon is an inert gas which can migrate from radium-bearing rocks and accumulate in enclosed areas, such as mines and houses. Cohort studies of underground miners are unambiguous in showing that inhalation of radon and its decay products increases risk of lung cancer (1). More controversial is whether and to what extent radon exposure from houses, whose concentrations are on average much lower than mines, increases risk of lung cancer. Results from a meta-analysis of eight case–control studies of residential radon and lung cancer have shown a statistically significant excess risk of lung cancer with long-term residence in high-radon houses (2). This excess was consistent with risks for miners exposed to low doses; their cumulative exposures were similar to those received by long-term residents of houses, and with extrapolations from miners developed using the full range of miner exposures.

Since the meta-analysis, additional information from indoor radon studies is available, including corrected data for a Finnish study (3) and a new study from Cornwall/Devon in the United Kingdom (4). There are currently nine studies of indoor radon and lung cancer, with a total of 5,122 cases and 9,679 controls (Table 1). (Preliminary results from five other studies in the U.S. and Germany have been presented at conferences, but are not included since they have yet to appear in peer-reviewed journals.)

TABLE 1

Relative Risks (RR) and 95% Confidence Interval (CI) for Indoor Radon Case–Control Studies

Study	RR[a]	95% CI	Cases	Controls
Finland I	1.22	1.1–1.4	164	334
Finland II[b]	1.13	1.1–1.3	517	517
New Jersey, U.S.	1.69	1.1–2.5	433	402
Shenyang, China	0.90	0.8–1.0	308	356
Winnipeg, Canada	0.98	0.9–1.0	698	738
Stockholm, Sweden	1.50	1.2–1.8	201	378
Sweden	1.13	1.1–1.2	1,281	2,576
Missouri, U.S.	1.07	0.9–1.2	538	1,183
Cornwall/Devon, UK	1.12	1.0–1.3	982	3,195
Total			5,122	9,679

Note. Table modified from (2).

[a]RR at 100 Bq/m^3 from a log-linear model, $RR(x) = \exp[\beta(x - x_0)]$, fitted to each study, where x was mean radon level and x_0 was the mean of the lowest category.

[b]RR estimates and 95% CIs from corrected data in erratum (3).

Improvements in Study Design

The earliest studies of residential radon and lung cancer were targets of opportunity, with radon measurements added to ongoing studies. While additions of a measurement protocol to existing studies were not inherently limiting or biased, studies were not designed specifically to assess residential radon and so may have had incomplete data on recent exposures and on housing patterns or other pertinent information.

More recent studies have improved designs that have increased completeness and accuracy of radon exposure. Some of the important design improvements include: minimum time of residence in the current house; restrictions on the number of houses lived in; direct measurements of cumulative exposure (5); estimates of exposure from diverse sources (all rooms in houses, outdoors and workplaces); occupancy within rooms; and more information on housing modifications. Additional information improves exposure accuracy and enables explicit account of exposure error. For both the UK study (4) and the Swedish study (6), investigators found that adjustment for exposure misclassification increased risk estimates about 50%. Thus, in future analyses, it will be important to account for exposure measurement errors in both residential studies and miner studies.

Indoor Radon Studies and Meta-Analysis Estimates

As in ref. (2), a log-linear model, $RR(x) = \exp[\beta(x - x_0)]$, was fitted to the category-specific RRs for each study, where x was the mean radon level and x_0 was the mean of the lowest category (Table 1). The summary RR estimate at 100 Bq/m^3 based on a random effects model was 1.15 with 95% CI (1.0, 1.3), indicating an overall significant trend in risk of lung cancer from indoor radon. This estimate updates the estimate of 1.12 at 100 Bq/m^3 from Lubin and Boice (2). The observed risks from the indoor radon studies are consistent with predicted risks from miner-based models and consistent with RRs observed in miners with low exposures and with cumulative those similar to exposures experienced by long-term residents in high-radon houses (1).

Comparison of Analytical and Ecological Studies

In ecological studies, area disease rates are regressed on area level descriptive variables. Ecological analyses are often easy to carry out and inexpensive, but potentially suffer from severe methodological limitations, such as cross-level bias, which cannot be fully addressed using area-level variables. Thus ecological studies are not used to validate risk associations (7–9). In a large ecological study, Cohen shows that U.S. county lung cancer mortality rates exhibit a linear-quadratic relationship with county mean radon level, with a protective effect at radon levels below about 250–300 Bq/m^3 (10). Although analytical epidemiological studies do not indicate a protective effect, Cohen suggested that his linear-quadratic ecological model fit the RRs from the indoor radon studies.

In spite of Cohen's assertion, the ecological model provides a poor characterisation of lung cancer mortality compared with the more analytically sound indoor radon studies (Figure 1, see also ref. 11). Adjusting the models to pass through 22 Bq/m^3, the lowest radon category, Figure 1 shows little evidence of a protective effect for radon.

Three regression models were compared with the RRs in each study: 1) the log-linear model; 2) Cohen's linear-quadratic ecological regression model; and 3) BEIR VI model. The simplest method for comparing model fit counts the number of RRs falling below and above the various prediction lines. The study-specific log-linear models provided very good fits to the RRs, and 15 of 28 RRs fell below the prediction lines. Based on a binomial distribution, the P value of observing this number or a number more extreme is 0.43. For the miner model, 15 of 29 points fell below the prediction lines with P = 0.50. For Cohen's model, 7 of 31 fell below the prediction lines with P = 0.002, indicating a poor fit to the data.

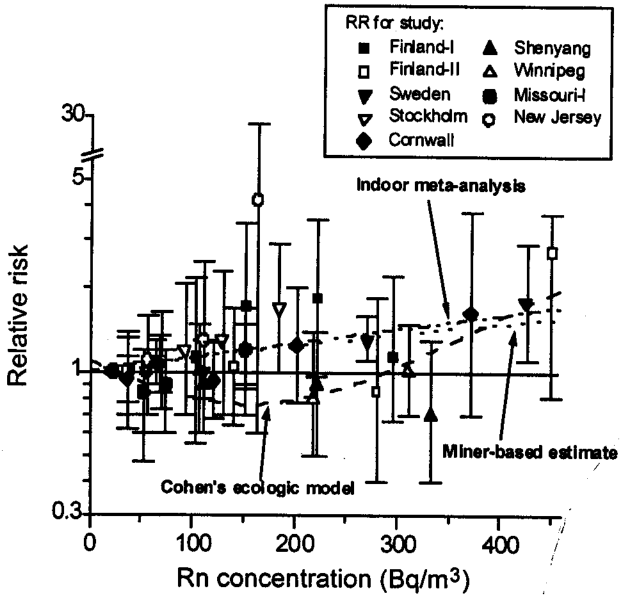

Figure 1. RRs from indoor radon studies, and estimates from a meta-analysis, miner-based model (1) and ecological model (10).

Using residual sums of squares, F statistics were calculated comparing the fit of the indoor meta-analysis model, the BEIR VI model, and the Cohen's model to the study-specific log-linear model. For 7 of 9 studies, the F statistic for the Cohen model exceeded the values for the other models, again indicating a poorer model fit compared to the other models. Similar results were obtained using Pearson χ^2 goodness-of-fit statistics.

In ecological studies, average dose does not determine average risk, and therefore the functional relationship between average dose and average risk provides no direct information about the relationship between dose and risk for the individual. Conversely, except in limited situations not applicable with radon and lung cancer, given a risk model for individual exposures, the county-level model cannot be deduced without specific information on the joint distribution of all risk factors within each county. Thus no valid inference can be made from a county-level relationship to the individual exposure–response relationship.

Conclusion

Results from the current case–control studies of indoor radon continue to support the existence of a small, statistically significant, excess lung cancer risk to the general population from residential radon. This excess is consistent with extrapolations using models developed in miners.

References

1. National Research Council, Committee on the Health Effects of Ionizing Radiations, Health Effects of Exposure to Radon (BEIR VI). National Academy Press, Washington, DC, 1999.
2. J. H. Lubin, J. D. Boice, Jr., J. Natl. Cancer Inst. 89, 49–57 (1997).
3. A. Auvinen, Lancet 348, 1662–1663 (1996). [letter]
4. S. Darby, E. Whitley, P. Silcocks, B. Thakrar, M. Green, R. Doll, Br. J. Cancer 78, 394–408 (1998).
5. J. A. Mahaffey, M. A. Parkhurst, T. E. Hui, R. C. Brownson, M. C. Alavanja, J. Expo. Anal. Environ. Epidemiol. 6, 425–437 (1996).
6. F. Lagarde, G. Pershagen, G. Akerblom, O. Axelson, U. Baverstam, G. A. Swedjemark, Health Phys. 72, 269–276 (1997).
7. S. Greenland, J. Robins, Am. J. Epidemiol. 139, 747–760 (1994).
8. S. Piantadosi, D. P. Byar, S. B. Green, Am. J. Epidemiol. 127, 893–904 (1988).
9. J. H. Lubin, Health Phys. 75, 4–10 (1998).
10. B. L. Cohen, Health Phys. 76, 437–439 (1999).
11. J. H. Lubin, Health Phys. 77, 330–332 (1999).