RESIDENTIAL RADON AND LUNG CANCER:
END OF THE STORY?

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The earliest evidence of increased lung cancer risk associated with radon came largely from
studies of highly exposed underground miners. In the United States, concerns about residential
exposures became prominent in the early 1980s with the identification of the Watras home,
which had remarkably elevated radon concentrations. By then, the problem of indoor radon
was already recognized in Europe and the first epidemiological studies on indoor radon had
been reported. The concern about the risk of indoor radon motivated a series of case-control
studies of residential radon and lung cancer in the United States, Canada, China, and a
number of European countries. In 1999, the U.S. National Research Council Committee on the
Biological Effects of Ionizing Radiation (BEIR VI) weighed the scientific evidence available at that
time on this issue and concluded that residential radon was an important contributor to the
lung cancer burden and that risks were appropriately estimated by a linear non-threshold
model. Since individual case-control studies have not provided consistent direct evidence of
excess lung cancer risk at residential exposure levels, combined analyses of residential radon
studies have been undertaken in both North America and Europe. These combined analyses,
including the North American pooled analysis described in this issue, represent an important
complement to the findings of the miner studies and further support the linear no-threshold
model for cancer risk adopted by the BEIR VI Committee and other groups.

In considering the findings of the pooled case-control studies of indoor
radon included in this special issue of the Journal of Toxicology and Environ-
mental Health, we should turn back 20 years ago to the early 1980s, when
concern about indoor radon first swept the United States. The problem surged
to national attention with the identification of the Watras home in the early
1980s, a home with an indoor radon concentration orders of magnitude greater
than the mean concentrations found in the studies reported in this issue. The
contamination of indoor environments by radon had been recognized earlier,
particularly in Scandinavia, and, in an article in Science in 1986, Nero and col-
leagues reported a geometric mean indoor residential concentration for U.S.
homes of 33 Bq/m³ (Nero et al., 1986). The first large-scale national survey of
residential radon levels was carried out in Canada in 1977–1978 (McGregor
et al., 1980). Additionally, by the early 1980s, the epidemiological studies of
underground miners, along with compelling experimental evidence, had

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provided convincing evidence that radon progeny could cause lung cancer (NRC, 1988). As national programs for testing and mitigation were implemented, critics questioned whether the scientific evidence on risks of residential radon was sufficiently certain to justify programs of this scale.

In response to the need for information on risks from indoor exposure, epidemiological studies directed at lung cancer in the general population were initiated in the 1970s and 1980s. The first wave of studies was largely ecological in design and provided mixed findings because of inherent flaws of this approach (Stidley & Samet, 1993). Case-control studies of lung cancer, a more appropriate design, were also implemented in the United States, Europe, and elsewhere. Some of the first studies did not incorporate measurements of indoor radon, as do those reported in this issue of the *Journal of Toxicology and Environmental Health*. Rather, they used surrogate measures, such as type of housing construction, and the resulting data could not provide the quantitative estimates of risk needed for policy purposes.

By the mid to late 1980s, many studies of more sophisticated design with larger sample sizes were undertaken. The data for individuals in these studies, since completed, have now been pooled. The findings in this issue, although having the inherent limitation of exposure measurement error, generally support the carcinogenicity of radon exposure in homes and are consistent with expectations of risk based on downward extrapolation of models based on the miner data.

The new findings support the national programs for radon measurement and mitigation that have long been in place. When the case-control studies were implemented, it was with the expectation that forthcoming evidence would reduce uncertainties about the carcinogenicity of indoor radon and offer an alternative basis for risk estimation, beyond applying the risks observed in the underground miners to the general population. As the case-control studies were implemented and planned, the challenge of obtaining the certainty sought by policymakers was quickly apparent. While the individual studies were designed primarily to test the hypothesis that radon was a cause of lung cancer, the more relevant question for setting policy direction was whether reliance on risk assessments using the miner data would exaggerate or underestimate the actual risks to the population. Addressing this question is more demanding of study design than the less relevant test of the null hypothesis that indoor radon does not cause lung cancer.

The scientific impetus for the pooling of the case-control studies began with discussions among members of the Biological Effects of Ionizing Radiation (BEIR) IV Committee during the mid-1980s (NRC, 1988). The committee reviewed the small number of published case-control studies and those planned, and two of its members, Jay Lubin and myself, joined Clarice Weinberg to publish a paper on sample size needs for case-control studies of indoor radon (Lubin et al., 1990). The potential limitations of the planned and in-progress studies were immediately evident: in the face of plausible levels of measurement error, the needed sample sizes were generally much greater than those...
of the individual studies, particularly for evaluation of possible differences in the risks for exposures in homes and in mines.

Planning for pooling of the individual studies was proposed as the best solution to the unavoidable problem of measurement error and the inadequate sample sizes of the individual studies. Two of the major funders of radon research at the time, the U.S. Department of Energy and the Commission of European Communities, were easily convinced that a planning effort should be put in place for eventual pooling of the case-control studies of indoor radon and lung cancer around the world. Together, they supported three investigator workshops, which took place in 1989, 1991, and 1995. The investigators carrying out the case-control studies were eager participants in the workshops and quickly established the collaborations that continued separately in North America and Europe and that will eventually lead to a pooling of all of the major studies. The investigators are to be congratulated for participating in this collaborative project that will give the most precise estimates possible of the lung cancer risk associated with indoor radon. The funders, both of the subsequent workshops and of the pooling efforts, also should be acknowledged.

**CURRENT DEVELOPMENTS**

In the last several decades, there have been many scientific advances around radon and lung cancer that have reduced some of the uncertainties that first prompted the case-control studies. First, the data from 11 cohort studies of underground miners have been pooled and exposure-response relationships have been characterized; the sample size also made possible analyses in never smokers in the cohorts, and in those having low exposures (<400 WLM) (NRC, 1999). The analyses of the underground miners having the lowest levels of exposure indicate a linear relationship of exposure with risk. Second, increasingly elegant experimental studies have documented the occurrence of permanent damage to a cell from just one hit by an alpha particle (NRC, 1999). This experimental finding suggests that assuming a linear nonthreshold relationship between exposure and risk at the levels found indoors is biologically appropriate. In this same type of experimental system, a bystander mutagenic effect has been demonstrated that affects cells adjacent to a cell damaged by a single alpha particle (Hall & Hei, 2003). This effect may amplify the risks of radon exposure beyond those anticipated based on the construct that passage of an alpha particle through a cell damages only that cell. Third, the results of the present analysis were anticipated with the earlier meta-analyses of the indoor studies (NRC, 1999).

Nonetheless, the pooled analysis reported in this issue of the Journal offers support from another line of investigation for use of a linear, nonthreshold relationship in estimating the risk of indoor radon. The findings of the North American pooling are mirrored by those of the just-reported pooling of 13 European studies involving 7148 cases and 14,208 controls (Darby et al., 2005). The risk for lung cancer was estimated to increase by 8.4% per 100 Bq/m³,
compared with 11% in the North American data. The dose-response relationship appeared linear and without indication of a threshold.

The policy implications of a linear, nonthreshold, dose-response relationship are substantial, and finding support in general population studies further reduces uncertainty on the risk of residential radon exposure. With completion of the European pooling and then the global pooling, this part of the radon story will be finished, as further lung cancer case-control studies are not in progress. There is strong coherence of the epidemiological data on lung cancer risk from studies of miners and the general population with the experimental data from animal and cellular models. Policies for testing and control can be based with confidence in the assumption that risk increases with concentration and that a “safe” concentration cannot be specified.

Is further research needed? Taken together, the epidemiological studies of miners and the general population, along with laboratory evidence and biophysical theory, give a strong foundation for presently used risk models. In fact, there are few environmental carcinogens for which human data are so abundant and the mechanism of carcinogenicity so well understood.

There are a few remaining details, however. Follow-up of the miner cohorts should be maintained so that the excess lung cancer risk caused by radon can be charted across the life span. These high-risk cohorts might also be informative on the genetic basis of susceptibility to radon. Presumably, another pooled analysis of the miner studies will soon be warranted. I also look to the experimentalists to continue to refine our understanding of how radon causes lung cancer. Work still in progress is refining the exposure measures in some of the case-control studies using surface radioactivity of glass as an index of cumulative exposure. There is also the possibility of exploring genetic modifiers of risk from residential exposure. However, I do not anticipate new research findings that would move us away from the present strategy of measurement and mitigation. And finally, no more case-control studies of lung cancer, please!

REFERENCES

