Workshop on Indoor Air Quality

Review of Radon and Lung Cancer Risk

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Radon, a long-established cause of lung cancer in uranium and other underground miners, has recently emerged as a potentially important cause of lung cancer in the general population. The evidence for widespread exposure of the population to radon and the well-documented excess of lung cancer among underground miners exposed to radon decay products have raised concern that exposure to radon progeny might also be a cause of lung cancer in the general population. To date, epidemiological data on the lung cancer risk associated with environmental exposure to radon have been limited. Consequently, the lung cancer hazard posed by radon exposure in indoor air has been addressed primarily through risk estimation procedures. The quantitative risks of lung cancer have been estimated using exposure–response relations derived from the epidemiological investigations of uranium and other underground miners. We review five of the more informative studies of miners and recent risk projection models for excess lung cancer associated with radon. The principal models differ substantially in their underlying assumptions and consequently in the resulting risk projections. The resulting diversity illustrates the substantial uncertainty that remains concerning the most appropriate model of the temporal pattern of radon-related lung cancer. Animal experiments, further follow-up of the miner cohorts, and well-designed epidemiological studies of indoor exposure should reduce this uncertainty.

KEY WORDS: Radon; radon decay products; lung cancer; indoor air pollution.

1. INTRODUCTION

As information on air quality in indoor environments accumulated during the 1970s, it became apparent that radon and its decay products were invariably present indoors, and that concentrations reach unacceptably high levels in some dwellings.[(1)] The evidence for widespread exposure of the population to radon and the well-documented excess of lung cancer among underground miners exposed to radon decay products [(2)] have raised concern that exposure to radon decay products might also cause lung cancer in the general population.

Radon is an inert gas which is a naturally occurring decay product of radium-226, the fifth daughter of uranium-238. After radon forms from decay of radium-226, some of the radon molecules leave the soil or rock and enter the surrounding air or water.[(3)] As a result, radon is ubiquitous in indoor and outdoor air. Radon decays with a half-life of 3.82 days into a series of solid, short-lived radioisotopes. Two of these decay products emit alpha particles, high-energy and high-mass particles, which are highly effective in damaging tissues. When these alpha emissions take place within the lung as inhaled radon progeny decay, cells lining the airways may be damaged and lung cancer may result.

The measure of occupational exposure to alpha radiation from radon decay products is the "Working Level

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Month'' (WLM). One Working Level (WL), a concentration unit, is any combination of short-lived radon decay products in 1 L of air which results in the release of 1.3×10^5 MeV of potential alpha energy. The WLM, a cumulative measure of exposure, is the product of radon decay products concentration in WL and duration in working months of 170 hr.

Concentrations in homes are most often reported as pCi/L; a curie is a measure of the rate of radioactive decay. An indoor concentration of 100 pCi/L is approximately 0.5 WL, assuming a 50% equilibrium of radon with its decay products. Thus, the Environmental Protection Agency's guideline of 4 pCi/L translates to 0.02 WL; annual occupancy of a home at this concentration for 75% of time results in exposure of 0.8 WLM.

Epidemiological methods have been used to assess directly the lung cancer risk associated with exposure to radon decay products indoors. However, the available data on environmental radon are limited and preliminary, and the findings of epidemiological investigations cannot yet be used to characterize the risks of indoor radon. Consequently, the lung cancer hazard posed by radon exposure in indoor air has been addressed primarily through risk estimation procedures. The quantitative risks have been estimated using risk projection models incorporating exposure–response relationships derived from the epidemiological investigations of underground miners.

This presentation reviews currently applied risk projection models for lung cancer resulting from radon exposure. We initially consider the investigations of underground miners, and discuss the methodology and limitations of the principal studies. We then describe and compare the most widely used risk projection models.

2. INVESTIGATIONS OF MINERS

2.1. Introduction

Occupational lung disease associated with the mining of radioactive ores was documented as early as the fifteenth century among miners in the Erz Mountains of eastern Europe. In 1879, Harting and Hesse[(4)] reported that miners in this area developed cancer of the lung. During the twentieth century, it was recognized that these and other underground mines were contaminated with radon, and that the decay products of radon were the agents directly associated with the production of lung cancer.

At present, the health risk associated with exposure to radon decay products can be best characterized by examining the more informative epidemiologic studies of underground miners. We describe the methods and findings of five major studies. About 15 additional populations of radon-exposed miners have been investigated. The report of the Biological Effects of Ionizing Radiation Committee (BEIR) IV provides a comprehensive review.[(2)]

2.2. Czechoslovakian Uranium Miners

The latest update of the Czechoslovakian study reported on four cohorts of uranium miners with follow-up ending December 31, 1980 (Table I).[(5)] The groups had exposures to radon decay products ranging from an average of 3.2–303 WLM, and varying follow-up, ranging from 6–30 years. To date, excess lung cancer mortality has been found principally in the cohorts with highest exposure and longest follow-up.

The most recent follow-up has detected significantly elevated risk of lung cancer from exposures as low as 50–99 WLM.[(5)] Risk estimates were reported as either attributable or absolute risks, and are therefore difficult to compare to studies reporting estimates as relative risks. The overall attributable risk of lung cancer was estimated to be 20.0 per WLM/10^6 person years.

The Czech study also identified several factors that modify the exposure–response relationship of lung cancer risk with cumulative exposure. The attributable risk of lung cancer was found to increase with age at initial exposure, although lung cancers were found at young ages (before 40 years). An exposure rate effect was identified; low exposures for long duration produced higher risk than high exposures for short duration when cumulative exposure was equal. The joint effect of cigarette smoking and exposure to radon decay products was approximately additive. Finally, the investigators examined mortality for other causes of death and found a

Table I. Czechoslovakian Uranium Miners Study

	Study group			
	A	B	C	D
No. of miners	2194	1849	3799	1561
Mean exposure (WLM)	303	134	6.1	3.2
Mean length of follow-up (yrs)	30	25	10	6
Attributable risk (per WLM per 10^6 PYRS[a])	23.0	19.1	20.9	NA

[a] PYRS = person-years.

statistically significant risk of basal cell carcinoma of the skin.

One of the strongest features of the Czech study is the large size of the cohorts (Table 1). The exposure data for these miners are also very extensive. The average number of measurements in each mine ranged from 101–690 per year. The follow-up period was also quite long (25–30 years) for two of the four groups. The low exposure groups may be informative in the future. Since over 5000 miners have average exposures below 10 WLM, further follow-up of this group could provide invaluable information concerning the effects at levels that are near the average lifetime exposure in the U.S. homes.

Interpretation of the Czech study has been made difficult by the analytical methods employed and the manner in which the results have been presented; as a result, comparison with other studies has been difficult. While methodology used in early analyses of the Czech data was apparently different from that used in other studies of miners, the latest analysis was based on an approach comparable to the widely used modified life table approach.

The exposure databases are also limited by the measurement, before 1960, of radon rather than decay products. Accurate estimates of concentrations of radon decay products can only be obtained if the equilibrium ratio of radon to its decay products is known. Smoking information was also incomplete on the cohorts with the highest exposures and the longest follow-up.

2.3. Ontario Uranium Miners

The study includes 15,984 uranium miners who had no known asbestos exposure.[7] Requirements for entry into the study included receiving a miner's physical exam between 1955–1977 and working at least 1 month underground. Exposure estimates were made by combining WL measurements with work history information for experience before 1968. After 1968, exposure was obtained directly from the mining companies. The exposure estimates were made in two ways: "Standard" WL values were obtained by averaging quarterly measurements in each year; "special" WL values were obtained by weighing the measurements toward the highest levels found. The "special" WL values were regarded as upper bounds of the actual exposures experienced by the miners. The mean cumulative exposure levels in this cohort were about 40 WLM for "standard" values and 90 WLM for "special" values (Table II).

Lung cancer mortality was analyzed using a modified life table approach and found to be significantly increased for exposures in the categories of 40–70 WLM (mean = 53 standard WLM) and higher. A linear dose–response model was employed; the model estimated the excess lung cancer risk to be 1.3% per WLM for the "standard" values. The latest analyses also showed a decrease in risk with time since last exposure to radon decay products.

Table II. Ontario Uranium Miners Study

No. of miners	15,984
Mean length of follow-up (yrs)	15.1
Mean exposure	
Standard WLM	40
Special WLM	90
Percent excess relative risk/ WLM	
Standard WLM	1.3
Special WLM	0.5
Attributable risk (per WLM per 10^6 PYRS)	
Standard WLM	7
Special WLM	3

This study is important because of the large number of miners with relatively low exposures, and for the consideration given to exposures received in other types of hard-rock-mining. In addition, appropriate analytical methods have been used, and the dose–response relationship has been estimated.

At the end of follow-up in 1981, the cohort was relatively young, with median age of 49 years. Since lung cancer mortality rates increase sharply in the fifth and sixth decades, this cohort has not yet been followed for sufficient time for description of the full temporal expression of excess lung cancer risk associated with exposure to radon decay products. Information on cigarette smoking is not available for cohort members; however, the investigators are addressing this potential limitation by conducting a case-control study within the cohort. The exposure database may be limited by reliance on the opinions of mining engineers for exposure estimates for some mines in the years before 1968.

2.4. New Mexico Uranium Miners

This cohort consists of approximately 3500 underground uranium miners who had worked at least 1 year underground prior to December 31, 1976 (Table III).[8] This study group includes only about 100 members of the Colorado Plateau cohort; in comparison with the earlier Colorado Plateau cohort, its members are younger and received lower cumulative exposures. At the most

Table III. New Mexico Uranium Miners Study, Colorado Plateau Uranium Miners Study, Swedish Iron Miners Study

	New Mexico uranium miners	Colorado Plateau uranium miners	Swedish iron miners
No. of miners	3500	3346	1415
Mean follow-up (yrs)	18	22	44
Mean exposure (WLM)	113	821	81
Median exposure (WLM)	36	430	—
Attributable risk (per WLM per 10^6 PYRS)	—	6.3	19.0
% excess relative risk/WLM	1.1	1.2	3.6

recent follow-up, which extended through 1985, the mean exposure was 113 WLM and the mean follow-up interval was 17.7 years. The latest analysis was a nested case-control study involving 65 lung cancer cases and 230 controls. A proportional hazards model was used to estimate relative risk. The effect of cumulative exposure was found to be curvilinear downward at the highest exposure interval. Subsequent analyses were restricted to total cumulative exposures less than 1000 WLM. A linear model fit the data well in this range, with a relative risk increase of 1.1% per WLM. A multiplicative relationship between cigarette smoking and exposure to radon decay products was also found. Relative risk was estimated to decline with increasing age at risk. In contrast to the Ontario and Colorado Plateau studies, relative risk did not vary significantly during the first 15 years after ceasing to work in the mine, but was found to increase 15 years or more after cessation of exposure.

Since average exposures in the New Mexico study were approximately 20% of the mean exposures in the Colorado Plateau study, extension of risk estimates from this study to the indoor environment requires less extrapolation than from studies with substantially higher exposures. Also, because the New Mexico miners worked more recently than the Colorado Plateau miners, the exposure levels for the New Mexico study tend to be better documented. Cigarette smoking histories are available for most of the subjects.

The case-control analysis must be interpreted with caution until results from the full cohort are available. By contrast, the Colorado Plateau analysis used the entire cohort of 3346 miners, including 256 lung cancer cases. Given the high relative risks seen in both of these groups, a case-control design with less than four controls per case might not produce risk estimates with the same degree of precision as estimates from analysis of data from the full cohort.

2.5 Swedish Iron Miners

This is a study of 1415 Swedish iron miners born between 1890 and 1919, who were alive in 1930 and worked at least 1 year underground between 1897 and 1976 (Table III).[9] Exposures ranged from 2–300 WLM with an average exposure rate of 4.8 WLM per year. The average cumulative exposure was reported to be 81.4 WLM, which was calculated with a lag of exposure by 5 years to account for cancer latency. The average total cumulative exposure without discarding any exposure was 93.7 WLM.

Of the 1415 miners, 1294 were observed between 1951 and 1976, and 50 lung cancer deaths occurred during this period. The expected number of deaths based upon Swedish national mortality rates was calculated to be 14.6 (standardized mortality ratio [SMR] =342 for lung cancer). With control for cigarette smoking, the SMR increased to 391. Significant excess risk was shown for exposures above 80 WLM. The attributable risk was estimated as 19.0 per 10^6 person-years per WLM (Table III).

An attempt was made to consider the confounding effects of such co-carcinogens as cigarette smoking, diesel exhaust, arsenic, chromium, and nickel. On the basis of an informal statistical analysis that required many assumptions, the joint effect of cigarette smoking and exposure to radon decay products was considered to be additive. The effects of the other potential confounding exposures were discounted because of the small concentrations found to be present in the mines in this study. Indoor radon exposures were not considered to be of consequence because of low lung cancer rates in the surrounding communities.

This cohort has the most lengthy follow-up of the five studies considered here. The average time in the study was 44 years, with 99.5% ascertainment of vital status. The confirmation of cause of death was thorough, since approximately one half of all deaths in Sweden are followed by autopsy. Also, the exposures were relatively low with an average rate of 4.8 WLM per year.

This study is potentially limited by the sparse data from which cumulative exposures of individual miners were assigned. Reconstruction of past concentrations of radon was based upon measurements first taken in 1968, information on ventilation conditions in prior years, and consistency of radon measurements in groundwater between 1915 and 1975. Although the investigators consider that exposures were accurate to ±30%, the exposure estimates could not be validated and their accuracy is uncertain.

Analyses related to smoking are potentially flawed because smoking histories were not available for all subjects. A sample of the responses to a 1972–1973 survey of active miners and surface workers and from a 1977 survey of retirees were considered. Smoking histories for the lung cancer cases were obtained primarily from surrogate sources.

Differential exposure misclassification may have been introduced by the method used to assign exposure. Exposure assignment for lung cancer cases was apparently done differently from that for noncases. A detailed history of each mine area worked was obtained for lung cancer cases only, whereas noncases were assigned exposure based upon a weighted average of annual mine exposure levels. Any differential treatment of cases and noncases can potentially introduce a bias into the risk estimates.

2.6 Colorado Plateau Uranium Miners

The U.S. Public Health Service conducted a study of 4127 underground uranium miners with at least 1 month of underground exposure between 1950 and 1964. These miners worked in the four-state area of Colorado, New Mexico, Arizona, and Utah. The risk assessment conducted by the National Institute for Occupational Safety and Health (NIOSH) was confined to 3346 white male miners.[10] As shown in Table III, the average exposure was 821 WLM (median of 430 WLM), the highest of the five studies considered. Follow-up began as early as 1950 and ended December 31, 1982, with an average length of 22 years.

The NIOSH risk assessment used a generalized version of the Cox proportional hazards model to estimate relative risk and to identify factors potentially influencing the risk estimates. Over the full range of exposure (1–10,000 WLM), the dose–response function was found to be nonlinear, with a decreasing trend at the higher exposure levels. However, in the range of current interest in relation to indoor air (below 600 WLM), the risk model was essentially linear with excess risk estimated as 1.2% per WLM.

Other factors found to influence the exposure–risk relationship included age at initial exposure, time since last exposure, exposure rate, and cigarette smoking. Miners first exposed at older ages were at increased risk of lung cancer compared to those first exposed at younger ages. Relative risk was found to decrease with time since cessation of exposure. Exposures received at low exposure rates over long duration were more hazardous than high exposure levels for short duration, cumulative exposure being equal. Finally, cigarette smoking had a synergistic relationship with exposure to radon decay products. The relationship appeared to be closer to multiplicative, with the most likely estimate being slightly submultiplicative.

The Colorado Plateau and New Mexico studies are only large studies of underground miners with cigarette smoking information for most cohort members. The cohort is relatively large and has been followed closely since the study's initiation in 1950.

The primary weakness of this study in relation to current risk assessment needs is the high cumulative exposures received by most subjects. Risks estimated at lower levels therefore depend to some degree upon trends found at higher levels of exposure. Some of the exposure data may be biased on the high side due to the use of exposure measurements for years after 1960 that were made by mine inspectors who usually oversampled high exposure areas. Smoking data were obtained on all miners, but the last update of this data was in 1969. Therefore, the cumulative cigarette consumption of miners who quit smoking after this date will be overestimated by extrapolation of the smoking histories.

2.7 Discussion

Although the five studies were conducted on different cohorts of miners, using different analytical approaches and varying amounts of data, the findings demonstrate several consistent patterns. Each study showed an exposure–response relationship between the lung cancer excess and cumulative exposure to radon decay products. Table IV presents the relative risk estimates for each study in relation to cumulative exposure. The excess relative risk per WLM ranges from 3.6% per WLM for the Swedish miners to 1.1% per WLM in the New Mexico uranium miners. These estimates are not strictly comparable since they are based upon different analytical techniques, different treatment of the exposure data, and varying degrees of adjustment for cigarette smoking. However, considering the differences among the five studies, the risk estimates are remarkably homogeneous. In fact, the BEIR IV Committee analyzed data from three of these five cohorts (Sweden, Ontario, and Colorado Plateau) and found that the relative risk in the Swedish cohort was approximately 1.6% per WLM.[2] In addition, BEIR IV found no significant differences among the risk coefficients derived from the

Table IV. Comparison of Relative Risk Coefficients for Lung Cancer Among Five Studies of Underground Miners

Study	Excess relative risk/100 WLM
Czechoslovakian uranium miners	1.5
Ontario uranium miners	1.3[a]
New Mexico uranium miners	1.1
Swedish iron miners	3.6[b]
Colorado Plateau uranium miners	1.2

[a] Based upon "standard" WLM values.
[b] This estimate was calculated by discarding the first 10 years of exposure and lagging by 5 years. When the first 10 years exposure was included, RR dropped to 1.6 as estimated by BEIR IV Committee.

four cohorts for which data were analyzed. The Committee concluded that the overall relative risk coefficient from the four studies was approximately 1.5% per WLM.

Several factors other than cumulative exposure appear to influence the risk of lung cancer. The Czech and Colorado Plateau studies demonstrated an increasing risk with older age at initial exposure. A decrease in relative risk with time since last exposure was found in the Colorado Plateau and Ontario studies. The Colorado Plateau and Czech studies showed an exposure-rate effect in which lower exposure rates for longer duration were more hazardous than higher exposure rates for shorter duration when cumulative exposure was equal. A similar dose-rate effect has been found in a number of animal studies of exposure to radon decay products although at very high exposures.[11,12] Finally, all five studies found an increased risk of lung cancer among smoking miners compared to nonsmoking miners, at least to the degree that the data permitted. The joint effect of radon decay products exposure and cigarette smoking ranged from additive in the Swedish and Czech studies to approximately multiplicative in the Colorado Plateau and New Mexico studies.

3. RISK ASSESSMENT MODELS

3.1 Introduction

Protection of the health of underground miners and of the general population has provided a strong rationale for making quantitative estimates of the lung cancer risk posed by radon. A risk projection model describes the temporal expression of the radon-associated lung cancer as well as the effects of potentially important cofactors, such as cigarette smoking, age at exposure, and age at risk. The two most widely applied models are the relative risk and attributable risk models; the relative risk model assumes that the background risk is multiplied by the risk of radon, whereas the attributable risk model assumes that the excess risk is additive to the background risk. A model may also describe the risk as varying with time since exposure. The manner in which radon exposure and cigarette smoking are assumed to interact strongly influences the results of risk estimation models for radon. If a multiplicative interaction is assumed, then the risks for smokers, already much greater than for nonsmokers, are multiplied by the risk from radon exposure. If an additive interaction is assumed, then the same excess risk is added to the background rates for smokers and for nonsmokers. The interaction between the two agents might plausibly take some form other than purely additive or purely multiplicative.

Diverse risk projection models have been developed.[2,13–16] Models for environmental radon were recently published by the National Council for Radiation Protection and Measurements (NCRP),[13] the International Commission on Radiological Protection (ICRP),[14] the Environmental Protection Agency (EPA),[16] the National Institute for Occupational Safety and Health (NIOSH),[15] and the Biological Effects of Ionizing Radiation Committee (BEIR IV) of the National Research Council[2] (Table V). Each of the models estimates lung cancer risk on the basis of the epidemiological evidence from underground miners, but the assumptions underlying the models and the resulting risk projections differ. In this paper, we focus on the NCRP, ICRP, and BEIR IV models because these models are most widely used for assessing the risks of environmental radon. The EPA and NIOSH models are briefly described.

3.2 NCRP Model

NCRP Report No. 78 describes an attributable risk model adapted from an earlier report by Harley and Pasternack.[17] The annual attributable risk is calculated as:

$$A\ (t/t_0) = R\ (Pt/Pt_0)\ e^{-\lambda(t-t_0)}$$

where $A\ (t/t_o)$ is the attributable annual lung cancer rate at age t for 40 years and above due to a single annual exposure at age t_o; R is the risk coefficient; P_t/P_{t_o} is the lifetable correction and $\lambda(\lambda = \ln 2/20\ \text{yr}^{-1})$ describes the decrease in risk with time since exposure. The risk coefficient (R), 10×10^{-6} per year per working level month (WLM), represents the arithmetic average of coefficients available when the report was prepared.

Table V. Recent Risk Projection Models for Radon and Lung Cancer

Agency	Type of model	Source of risk estimate
National Council on Radiation Protection and Measurements[13]	Attributable risk, time-dependent	Average risk coefficient from principal studies of miners
International Commission on Radiological Protection[14]	Constant relative risk	Adjusted risk coefficient from 3 studies of miners
Environmental Protection Agency[16]	Constant relative risk	Range of coefficients based on studies of miners
National Institute for Occupational Safety and Health[15]	Relative risk, time-dependent	Risk based on Colorado Plateau uranium miners
National Research Council[2]	Relative risk, time-dependent	Risk based on analysis of 4 studies of miners

The absolute risk model was selected by the NCRP committee as appropriate for describing the appearance of lung cancer in uranium miners; additionally, the comparability of additive risks in smoking and nonsmoking Swedish miners employed at the Malmberget mines and studied by Radford and Renard was cited. The term $e^{-\lambda(t-t_0)}$ was included to describe loss of transformed cells by repair, cell death, or other mechanisms. Because lung cancer is infrequent before age 40 years, the model did not project cancers until age 40. In this model, correction for higher bronchial doses in children did not greatly change risk projections, and, accordingly, a single dose conversion factor was use for males and females of all ages.

For an average annual exposure of 0.2 WLM, the model estimates the increment in lifetime risk as 0.18%. If expressed uniformly over a 45-year period (ages 40 through 85 years), then the model projects 9000 radon-attributable lung cancer deaths annually in the U.S.

3.3 ICRP Model

ICRP Publication 50 details a constant relative risk model for lung cancer resulting from radon, and applies this model to a reference population with lung cancer mortality and activity patterns representative of more developed countries. The ICRP committee justified the choice of the constant relative risk approach on data from studies of miners and the atomic bomb survivors. The best estimate of the relative excess risk was derived from the studies of Colorado Plateau uranium miners, Czechoslovakian uranium miners, and Ontario uranium miners. The average from these studies, 1.0% per WLM, was adjusted to 0.64% to account for contributions from carcinogens other than radon in the mining environment and for differing dosimetry in homes and mines. For exposure received before age 20 years, a threefold increase in effect was assumed on the basis of the pattern of age-dependence in the atomic bomb survivors and of the increased bronchial dose in children.

The model was then used to estimate the lung cancer risk associated with constant lifetime exposure. The reference population for this analysis was assumed to be in a steady state with lung cancer frequency of 60 per 100,000 among males and 12 per 100,000 among females. The analysis assumed that 65% of time was spent indoors at home, 20% in other indoor locations, and 15% outdoors. For this population at exposure rates less than 3 WLM annually, the attributable relative risk was 0.5 per WLM per year. Assuming an indoor exposure of about 1 pCi/L, approximately 10% of the lung cancer in the reference population was attributable to indoor radon.

BEIR IV Model

The BEIR IV Committee obtained data from four studies of underground miners: U.S. uranium miners in the Colorado Plateau; underground uranium miners in Saskatchewan and in Ontario, Canada; and underground metal miners in Sweden. The committee first carried out separate but parallel analyses of the four data sets and then a formal analysis of the combined data. The analysis used relative risk models for the age-specific lung cancer mortality rates that incorporated terms for potential modifying factors, such as age at first exposure and age at risk, as well as for exposure to radon decay products.

The models were fit to the individual studies and then to the combined data set using Poisson regression. In analyzing the data sets, the committee used a form of relative risk model which was termed the Time-Since-Exposure model. Rather than considering cumulative exposure prior to age at observation, this model estimates the effects of exposures received in distinct time windows before the age at risk. The version of the model used by the committee estimated the effects during three windows: exposures received from the fifth through the ninth year before age at risk, from the tenth through the fourteenth year, and from the fifteenth year and beyond. The general form of this model is

$$r(a) = r_0(a)\ [1 + \beta\ \gamma\ (a)\ (d_1 + \theta_2 d_2 + \theta_3 d_3)]$$

where d_1, d_2, d_3 are the exposures received during the three windows, and 0_2 and 0_3 represent variation in the effects of exposure among the windows.

The analyses showed reasonable consistency among the cohorts; the final model was

$$r(a) = r_0(a)\ [1 + 0.025\gamma(a)\ (W_1 + 0.5W_2)]$$

where $r_0(a)$ is the age-specific baseline rate; $\gamma(a)$ is 1.2 for (a) less than 55 years, 1.0 for (a) 55–64 years, and 0.4 for (a) 65 years or more; W_1 is WLM of exposure received 5–15 years before age (a) and W_2 is WLM received 15 years or more before age (a). This model departs from the widely used constant relative risk model, in which the increase in relative risk associated with a given exposure is constant over time after exposure. The BEIR IV Time-Since-Exposure model implies that the effect of exposure wanes as the interval since exposure lengthens.

3.5 EPA Model

The EPA used a constant relative risk model to predict that radon causes 5000–20,000 lung cancer deaths annually. Based on the studies of miners, a range of relative risks from 1–4% per WLM was assumed. The model also adjusted for differences in breathing rates of miners (30 l per minute) and of average adults (15.3 l per minute), assuming that dose varies directly with minute ventilation.

3.6 NIOSH Model

NIOSH used a generalized form of the Cox proportional hazards model to account for possible departures from a constant relative risk.[15] The NIOSH modeling approach described lung cancer mortality patterns as a function of cumulative exposure to radon decay products, exposure rate, age, cigarette smoking, and time since last exposure without making assumptions about exposure effects regarding nonmining populations. The NIOSH model showed a decreasing effect of exposure above 2000 WLM, but the model was essentially linear below that level with a relative risk coefficent of 1.2% per WLM. An exponential decrease in relative risk after cessation of exposure was found with relative risk reduced by 50% 14 years after leaving the mines.

4. COMPARISON OF THE NCRP, ICRP, AND BEIR IV MODELS

Although each uses risk coefficients which are derived from the studies of miners, the three models differ substantially in describing the expression of excess risk associated with radon exposure (Tables VI and VII). The NCRP model generally projects the lowest excess risk because it is an additive model, and the radon-associated excess declines over time. The ICRP model, a constant relative risk model, projects the highest risks. Exposures received by age 20 years lead to a particularly large excess because of the threefold higher risk assumed up to age 20 years than in subsequent ages. In the BEIR IV model, the percent excess risk varies with both age and time since exposure.

When smokers and nonsmokers are considered separately, the substantial difference between assuming an additive or a multiplicative interaction between smoking and radon exposure is evident (Table VIII). The additive NCRP model projects small increments for smokers in comparison with the multiplicative ICRP and BEIR IV models. Lifetime excess lung cancer risks for smokers estimated by the models are markedly different. For example, Land [18] has calculated the excess lung cancer risk per 100,000 smokers exposed to 1 WLM at age 15 as: NCRP—7.4, ICRP—278.7, BEIR IV—114.5; for exposure to 1 WLM at age 35 years, the corresponding estimates are 15.5, 94.3. and 129.4.

5. CONCLUSIONS

For some dimensions of the radon problem, the degree of uncertainty is minimal. The causal association

Table VI. Features of Selected Risk Projection Models for Radon and Lung Cancer

	NCRP	ICRP	BEIR IV
Form of model	Attributable risk	Relative risk	Relative risk
Time-dependent	Yes; risk declines exponentially after exposure	No	Yes; risk declines as time since exposure lengthens
Lag interval	5 years	10 years	5 years
Age at exposure	No effect of age at exposure	3-fold increased risk for exposures before age 20 years	No effect of age at exposure
Age at risk	Risk commences at age 40 years	Constant relative risk with age	Lower risks for ages 55 years and older
Dosimetry adjustment	Increased risk for indoor exposure	Decreased risk for indoor exposure	No adjustment
Risk coefficient	10×10^{-6}/year/WLM	Excess relative risks: 1.9%/WLM at ages 0–20 years and 0.64%/WLM for ages 21 years and above	Excess relative risk of 2.5%/WLM but modified by time since exposure

of radon with lung cancer has been amply documented by studies of underground miners and by complementary animal studies.[2] Both the epidemiological and the animal data show that lung cancer risk increases with increasing exposure to radon or its decay products. The epidemiological evidence also indicates synergism between exposure to radon decay products and cigarette smoking, although the extent of the synergism is uncertain.[2] Epidemiological studies have not yet empirically demonstrated that radon in indoor environments causes lung cancer, but current understanding of the dosimetry of radon decay products in the respiratory tract indicates that radon should have approximately equivalent carcinogenic potency in homes and in mines.[2]

Substantial uncertainties remain, however, with regard to other facets of the radon problem. The quantitative relationship between exposure to radon and radon decay products and lung cancer risk has not been precisely described, and uncertainties about the effects of age, gender, cigarette smoking, and other factors on this relationship await resolution. Extrapolation of risk estimates based on studies of miners to the general public requires assumptions in areas of uncertainty. We also lack exposure information based on a large and representative sample of the nation's homes.

The studies of uranium and other underground miners have provided a relatively extensive database for estimating the exposure–response relationship between exposure to radon decay products and lung cancer risk. Although the populations of miners studied to date have been diverse and methodology has varied among the epidemiological studies, the risk coefficients derived from the miners are remarkably consistent (Table IV).[2] The range of the coefficients covers approximately one order of magnitude, in spite of potential bias from differential and nondifferential misclassification of exposure to radon decay products and of the diagnosis of lung cancer.

Recently published risk projection models for lung cancer associated with environmental radon have incorporated risk coefficients based on the studies of miners.

Table VII. Increments[a] in Lung Cancer Risks for One WLM Projected by NCRP, ICRP, and BEIR IV Models

Increment at age (years)	NCRP[a] (%) Male	NCRP[a] (%) Female	ICRP (%)	BEIR IV (%)
	Exposure at age 15 years			
35	0	0	1.9	1.5
50	0.3	0.7	1.9	1.5
65	0.05	0.2	1.9	0.5
85	0.02	0.1	1.9	0.5
	Exposure at age 35 years			
50	0.6	1.4	0.6	3.0
65	0.1	0.4	0.6	0.5
85	0.05	0.2	0.6	0.5

[a] The excess is additive for the NCRP model. The percent excess relative risk was calculated for illustration using sex-specific lung cancer mortality rates for the U.S., 1980–1984. The additive increments are 3.0×10^{-6}, 1.8×10^{-6}, and 0.9×10^{-6} for ages 50, 65, and 85 years, respectively, for exposure at age 15 years; and 6.0×10^{-6}, 3.5×10^{-6}, and 1.8×10^{-6}, respectively, for exposure at age 35 years.

Table VIII. Lung Cancer Mortality Rates per 100,000 Projected for Nonsmoking and Smoking Males at Age 65 Years by NCRP, ICRP, and BEIR IV Models[a]

	NCRP	ICRP	BEIR IV
Exposure to 10 WLM at age 15 years			
Nonsmoking	59.8	69.0	60.9
Smoking	698.3	828.8	731.3
Exposure to 10 WLM at age 35 years			
Nonsmoking	61.5	61.5	60.9
Smoking	700.0	738.3	731.3

[a] Background lung cancer mortality rates estimated as 58.0×10^{-5} for nonsmokers and 696.5×10^{-5} for smokers.[2]

The principal models differ substantially in their underlying assumptions and consequently in the resulting risk projections (Tables VI–VIII). The committees that developed these models offered rationales for the assumed pattern of temporal expression of excess risk that were based on biological mechanisms and epidemiological evidence. The resulting diversity illustrates the substantial uncertainty that remains concerning the most appropriate model of the temporal pattern of radon-related lung cancer. Animal experiments and further follow-up of the miner cohorts should reduce this uncertainty.

At present, however, risk modeling remains the principal approach for quantifying the hazard of environmental radon. Which risk model should be chosen for this task? While we cannot justify the choice of a particular model, we consider that the epidemiological data from miners are not consistent with an additive model, such as that published by the NCRP.[13] The largest data set, which is based on the Colorado Plateau uranium miners, indicates synergism between smoking and exposure to radon decay products, and the data reject an additive model for the two exposures.[10] The evidence from a recent study of New Mexico uranium miners is consistent.[8] The epidemiological data also support a declining effect as the time since exposure lengthens.[2,10] Thus, a constant relative risk model, such as that published by the ICRP,[14] may not be biologically appropriate. The BEIR IV model describes the effect of radon exposure on lung cancer risk as varying with time since exposure; the BEIR IV model also assumes a multiplicative interaction between smoking and radon exposure. Use of the BEIR IV model for environmental radon, however, requires the extrapolation of risks from four cohorts of adult male miners observed over particular age and time spans to the general population. New epidemiological and experimental data should provide more refined risk models with less uncertainty.

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