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Radon Progeny Exposure and Lung Cancer Risk: Analyses of a Cohort of Newfoundland Fluorspar Miners

by

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RADON PROGENY EXPOSURE AND LUNG CANCER RISK: ANALYSES OF A COHORT OF NEWFOUNDLAND FLUORSPAR MINERS

A report prepared by H.I. Morrison and P.J. Villeneuve, Health Canada, under contract to the Atomic Energy Control Board.

ABSTRACT

A cohort study of the mortality experience (1950-1990) of 1744 underground miners and 321 millers or surface workers has been conducted. Excess mortality among underground miners was noted for cancers of the lung, buccal cavity, pharynx and mouth, urinary tract and for silicosis and pneumoconioses. A highly statistically significant relationship was noted between radon daughter exposure and risk of dying of lung cancer; the small numbers of buccal cavity/ pharynx cancers (n = 6) precluded meaningful analysis of exposure-response. No statistically significant excess was found for any cause of death among surface workers.

The exposure-response data for lung cancer were fitted to various mathematical models. The model selected included terms for attained age, cumulative dose, dose rate and time since last exposure. Because risk varies according to each of these factors, a single summary risk estimate was felt to be misleading. The joint effects of radon and smoking could not be adequately assessed using this cohort.

RÉSUMÉ

On a effectué une étude de cohorte sur le taux de mortalité (1950-1990) de 1 744 mineurs de fond et 321 mineurs de surface. Chez les mineurs de fond, on a observé une surmortalité par cancers du poumon, de la cavité buccale, du pharynx et de la bouche et des voies urinaires, ainsi que par silicose et pneumoconiose. Une corrélation hautement significative sur le plan statistique a été établie entre l'exposition aux produits de filiation du radon et le risque de décès par cancer du poumon; à cause du faible nombre de cancers de la cavité buccale et du pharynx (n = 6), il n'a pas été possible de procéder à une analyse efficace du rapport exposition-effet. Aucune surmortalité statistiquement significative n'a été enregistrée chez les mineurs de surface, quelle que soit la cause de décès.

Les données sur la relation exposition-effet pour le cancer pulmonaire ont été soumises à différents modèles mathématiques. Le modèle retenu comprenait les termes pour l'âge atteint, la dose cumulative, le débit de dose et le temps écoulé depuis la dernière exposition. Comme

le risque varie selon chacun de ces facteurs, on a jugé qu'une estimation globale unique du risque pourrait induire en erreur. Les effets combinés du radon et du tabagisme n'ont pu être convenablement appréciés sur cette cohorte.

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TABLE OF ABBREVIATIONS

AR	Attributable Risk
BEIR IV	National Academy of Sciences Committee on the Biological Effects of Ionizing Radiations
ER	Excess or absolute risk
ERR	Excess relative risk
LET	Linear energy transfer
LR	Likelihood ratio test
SMR	Standardized Mortality Ratio
TSE	Time since last radon exposure
WL	Working Level
WLM	Working Level Month

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CHAPTER 1

BACKGROUND

1.1 Study goals

The goal of this report is to estimate the increased risk of lung cancer among a cohort of Newfoundland fluorspar miners exposed to radon daughter products. Further mortality follow-up and new smoking information collected in 1993 allow for improved risk estimates compared to previously published analyses of this cohort. From a public health perspective, an understanding of the exposure-response relationship will aid in the formulation of regulations to protect miners from levels of radiation that are associated with a significantly increased risk of lung cancer.

Specifically, our analysis focused on:

(1) Summarizing the mortality experience of the fluorspar cohort between 1950 and 1990;

(2) estimating the nature of the exposure response relationship and the excess relative risk (ERR) per working level month (WLM);

(3) assessing the variation of ERR\WLM with attained age, and age at first exposure;

(4) assessing the joint effects of smoking and Radon progeny exposure on ERR\WLM;

(5) examining the effect of exposure rate on ERR\WLM;

(6) assessing the variation of ERR\WLM by time since an exposure occurred and time since exposure ceased.

Analyses presented in this report are based primarily on Poisson regression analysis. Previous analyses have relied primarily on the use of external comparison populations using standardized mortality ratios. This approach has limitations for adequately characterizing an exposure response relationship, particularly in the presence of secondary variables such as age at risk, smoking and so on.

Improved estimation of the exposure-response relationship of radon progeny and lung cancer is important for assessing regulatory levels of radon concentrations in mines, those exposed in the past to high levels of radon and to extrapolate to the general population exposed to radon in their homes. Further questions to be answered include whether exposures in early life are particularly hazardous, analyses of whether smoking multiplies or adds to the risk from radon progeny exposure, and the impact of smoking cessation on risk.

1.2 Health effects of radon daughters

Radon (Rn^{222}) is a radioactive decay product of radium (Ra^{226}), which in turn is the fifth decay progeny of uranium (U^{238}). At normal temperature and pressure, radon is an inert gas. Both U^{238} and Ra^{226} are ubiquitous in the earth's crust, with highly variable concentrations. As radon forms from the decay of Ra^{226}, it leaves soil or rock and enters surrounding air or water. Radon decays with a half-life of 3.82 days into a series of isotopes that are called radon daughters or progeny. Two isotopes of polonium (Po^{218} and Po^{214}), formed in the decay process, release alpha particles as they in turn decay. Po^{218} and Po^{214} are short lived with half-lives of 3 minutes and 1.6×10^{-6} seconds respectively.

Alpha particles can damage the cells lining the airways, which may ultimately result in lung cancer. Similarly, radiation may be absorbed in the nasal cavity. However, not as much genetic damage is likely to occur, as the mucosal layer provides some protection.

Increased risk of lung cancer due to radon exposure was first noted in mining populations. Improvements in ventilation and development of occupational standards have dramatically reduced the radon exposure levels in mines. In mines, radon arises principally from the decay of radium in ore. Exposures may also result from radon dissolved in water.

Interest in the biological effects of radon exposure was heightened with the discovery that radon in homes can accumulate to high levels, sometimes exceeding those in mines. Domestic radon levels were first systematically measured in Scandinavia in the 1970's and in the 1980's in the U.S. In 1988, the U.S. Environmental Protection Agency (EPA) and the US Centers for Disease Control (CDC) recommended that nearly all homes be tested for radon.

An important source of domestic exposure of radon results from the seepage of water in which radon has been dissolved through cracks in the foundation of homes. Indoor exposure can also result from radon being released from building materials, as well as from radon dissolved in drinking water or natural gas. The radon levels in homes vary due to variation of radium in subsoils, construction materials used and source of water. Private wells in particular have the potential to contain significant amounts of radon. Air exchange plays a role, although to a lesser degree, in determining domestic Rn levels.

Exposure to radon is measured by the amount of alpha energy that will be emitted by short-lived radon daughters in a quantity of air. This is typically measured by a "working level" (WL) which is any combination of radon daughters in one litre of air that will result in the ultimate emission of $1.3x10^5$ million electron volts (MeV). Two alternate measures of domestic Rn are pCi/L and becquerels per cubic metre (Bq/m^3). One WL≈100 pCi/L of Rn in equilibrium with its short-lived progeny, and one pCi/L = 37 Bq/m^3. For occupational studies, Rn exposure is typically measured in working levels months. One working level month is equivalent to being exposed to 1 working level (WL) for 170 hours.

In a survey measuring radon in households in communities across Canada, mean radon levels varied from 5.2 to 57.0 Bq/m^3 (Le84). The average level in U.S. homes is 1.5 pCi/L (56 Bq/m^3) (Ne86). The EPA recommends action for Rn exposure when levels exceed 4 pCi/L (148 Bq/m^3) (Sa90). Approximately 8% of all households are above this level (Ne86).

As the lifetime risk of developing lung cancer is significantly elevated among cigarette smokers (Vi95), radon risk should be assessed separately by smoking status. The Rn dose received by smokers may be greater than that received by non-smokers due to greater central deposition of the lung, increased permeability and slowed mucosal transport. Furthermore, the components of smoke might also interact with alpha particles in the process of carcinogenesis. Environmental tobacco smoke also contributes to the development of lung cancer in active and non smokers exposed to radon.

1.3 Studies of mining populations

In the 1950's there was a large increase in the demand for uranium, both for the construction of nuclear weapons and for the production of electricity (Th82). Consequently, uranium mining greatly expanded, most notably in the Colorado Plateau region of western United States (Ho87, Sa91), Czechoslovakia (Še88), Ontario (Ku93), France (Ti93), South Australia (Wo91), Saskatchewan (Ho86) and the Northwest Territories of Canada (Ho87). Other cohorts of radon exposed miners include tin miners from China (Xu93), iron miners in Sweden (Ra84) and fluorspar miners in Newfoundland (Mo88). These 11 cohorts have recently been the subject of a pooled analysis by the U.S. National Cancer Institute (Lu94).

1.31 Previous studies of the St. Lawrence fluorspar miners

The first published report examining the mortality experience of the fluorspar miners in St. Lawrence, Newfoundland was by de Villiers and Windish in 1964 (de64). They calculated age-specific standardized mortality ratios (SMRs) for fluorspar miners using mortality rates for the Burin Peninsula excluding St. Lawrence to generate expected values. Numbers of deaths from various causes were also compared between St. Lawrence and a control town, Grand Bank. Mean latency for lung cancer was calculated by plotting age at first exposure by age at death. De Villiers and Windish found that the number of lung cancer deaths among fluorspar miners was far in excess of that expected, with SMRs varying from 7.9 to 43.2, depending on the age group.

A second paper, by Parsons et al. (Pa64), examined the prevalence of respiratory symptoms among miners and concluded that levels of pneumoconiosis and bronchitis were comparable to those reported among other groups of hard rock miners. The role of cigarette smoking in the induction of lung cancer among fluorspar miners was addressed, with the conclusion that, although smoking was a factor in the very high levels of lung cancer noted among the miners, most of the excess was radiation-related.

The first attempt to examine the Rn progeny exposure-response relationship was in a paper published in 1971 by de Villiers and colleagues (de71). The number of hours worked underground was used as a surrogate for actual exposure in WLM. A plot of lung cancer deaths by number of hours worked revealed an exponential relationship. To adjust for the variable radiation exposure of differing occupations, hours were weighted according to occupation. Drifters and stope workers were assigned a radiation level of 8 WL, muckers, trammers, and chute operators were assigned a level of 4 WL and shaftmen were assigned a level of 2 WL. With the assignment of these weights, the exposure-response relationship became linear.

In 1977, Wright and Couves published a paper (Wr77) which was restricted to examining the histology and survival rates of lung cancer cases among the miners. In 1981, an update of the 1971 paper by de Villiers et al. was published (Mo81) which extended the mortality follow-up to 1978. Estimates of radon daughter levels were based on those used in

the 1971 paper. These estimates were based on occupation and hours worked only. Mine site and annual exposure data were not used.

In 1985, a further update was published which extended the follow-up period to 1981 (Mo85). This analysis, like previous ones, used a modified person-years approach. Expected numbers of deaths were generated from an internal control group of surface workers unexposed to radiation. Unlike previous analyses, cigarette smoking and latency were taken into account. In addition, excess risks were estimated.

In 1988, modelling of the exposure-response relationship using an external control group was performed to estimate attributable and additive relative risk[1] coefficients (Mo88a,b). New radon exposure estimates were used (Co84). Attributable and relative risk coefficients were examined by attained age, age first exposed and smoking status. In addition, lifetime risk of lung cancer mortality was assessed using both the relative and attributable risk models.

[1] The term additive relative risk was coined by Breslow and Day (Br87), and is mathematically equivalent to excess relative risk.

CHAPTER 2

MATERIALS AND METHODS

2.1 Study population

The initial cohort of miners consisted of 2,111 underground miners and 550 surface workers employed by either the St. Lawrence Fluorspar Company or by Newfoundland Fluorspar Limited. Miners who lacked adequate personal identifying information or who had died before 1950, were dropped from analysis. Most of those excluded from analysis were short-term workers during World War II. The remaining 1,772 underground miners and 352 surface workers were those analyzed in the 1988 AECB report (Mo88b). For this analysis, a further 28 underground miners and 31 surface workers who were born before 1900 for whom no death information was available were dropped. The final cohort of miners included 1,744 underground miners and 321 millers or surface workers. Details regarding how the initial cohort was assembled are contained in the 1988 AECB report by Morrison and colleagues (Mo88a).

2.2 Radon daughter exposure

Working level month estimates according to year, mine and occupation between 1933-1960 were provided by the Atomic Energy Control Board of Canada (Co84). These were based on measured (1960) levels, a review of working conditions of the mine, and mine architecture. From 1960 to 1967 the average exposure was 0.5 WL. From 1968 onwards, radiation levels were measured more frequently. In 1969, daily exposures for each worker were recorded based on radiation levels in the place worked on a given day. Cumulative

exposures were expressed in working level months (one working level month is equivalent to exposure to one working level for 170 hours). Based on previous studies and analytical support, a lag interval of 5 years was incorporated into the calculation of cumulative exposure (Lu94). Thus radon exposure within the previous five years was assumed to be unrelated to risk of lung cancer. The mean cumulative exposure for underground workers was 382.8 WLM over an average of 5.7 years of exposure.

2.3 Cigarette smoking information

A survey was conducted in 1993 to update previously collected data on the smoking habits of the fluorspar miner cohort. Previous surveys to determine smoking behaviour were conducted in 1960, 1966 and 1970 in St. Lawrence, Newfoundland by Health and Welfare Canada and in 1978 by the Atomic Energy Control Board. Smoking information was available for 65% of the cohort exposed to radon.

2.4 Ascertainment of vital status

The mortality experience of the cohort was updated from the 1988 AECB report (Mo88b) to reflect deaths occurring between 1984 and 1990. This involved manually tracing all members of the cohort through the Canadian Mortality Database operated by Statistics Canada. The linkage was performed by employees who were blind as to exposure status. Copies of microfilmed death certificates were obtained and the underlying causes of death were coded according to the 8th revision of the International Classification of Diseases by the Nosology Reference Centre of Statistics Canada. As with previous analyses, persons not

found were assumed to be alive for the purposes of analysis. Those born before 1900 for whom no death information was available were dropped from analysis.

The smoking survey, conducted by Health Canada in 1993, was in some instances helpful in determining vital status. For some members of the cohort in which personal identifying information was sparse, data gathered in the survey was useful in determining vital status. This aided in identifying several members of the cohort who had died before 1984 including 8 lung cancer deaths that were overlooked in previous analyses. As vital status was recorded on the smoking survey up to 1993, data collected will also aid in future mortality updates.

2.5 Statistical analysis

Mortality was analyzed from the beginning of 1950 to the end of 1990. Mortality before 1950 was not examined to facilitate comparisons with previously published results. Furthermore, the quality of Newfoundland death certificates before 1950 precluded their use (Mo88b).

2.5.1 Creation of person-year tables

Poisson regression models were used to fit relative and absolute excess risk models. Cross tabulations of data consisting of lung cancer deaths, person-years and summary variables were entered into the Poisson regression program. Person-years were calculated using a program analogous to that outlined by Pearce (Pe87). Data were cross classified by

attained age (<45, 45-55, 55-65, 65-75, 75+) and period (1950-59, 1960-1969, 1970-1979, 1980+) and estimated WLM (0, >0 - < 25, 25-<200, 200-<500, 500-<1000, 1000-<1500, 1500- <2000, 2000- <2500, 2500-3500, 3500+ WLM). As the number of deaths in each strata followed a Poisson distribution with variance estimated by the predicted number of deaths, WLM's were categorized in a manner such that the number of lung cancer deaths occurring in each dose category was about the same. In so doing, parameter estimates of the fitted model will have approximately the same standard error. The AMFIT program of the software package EPICURE was used to do all Poisson regression modelling (Pr90).

2.5.2 Poisson regression modelling

Models were fitted to grouped data using Poisson regression analyses. This method models the logarithm of either incidence or mortality rates as a linear regression of the independent variables, including interactions if necessary. The regression coefficients provide estimates of the relative risks for the independent variables.

The general form of the Poisson regression model (Br83) is:

$$\frac{\lambda}{\lambda_0} = \exp\left(b_1 X_1 + b_2 X_2 + \ldots b_k X_k\right)$$

where X_1, $X_2 \ldots X_k$ are a set of predictor variables.

λ =the mortality rate for persons with specified values $X_1, X_2, \ldots, X_k$

λ_0=the baseline mortality rate

$b_1, b_2, \ldots b_k$ are parameters to be estimated from the data

The general method of fitting a Poisson regression model is to use the Poisson model formulation to derive a likelihood function that can then be maximized using an iteratively reweighted least squares method so that parameter estimates, estimated standard errors, maximized likelihood statistics (deviances) and other information can be obtained.

The deviance provides a measure of the amount of residual, or unexplained, variation, and is a measure of how well a model fits. The deviance is asymptotically distributed as a chi-square variable. As such, changes in deviance can be compared to the chi-square distribution to assess the goodness of fit of a particular model (Kl88).

Relative risks were estimated for each WLM category adjusting for attained age and calendar period. Poisson regression models in which the risk of lung cancer mortality was assumed to increase exponentially with cumulative dose were fitted to the data. A linear excess relative risk (ERR) model was fitted to the mean WLM of each dose category weighted by person-years. This model was specifically,

$$\text{(I)} \qquad RR=1+\beta WLM$$

where β measured a unit increase in ERR per unit increase in cumulative WLM. The addition of a quadratic term to the above model was assessed using standard likelihood procedures. The linear excess relative risk model was modified to allow for an arbitrary intercept. As outlined by Lubin (Lu94), this model is expressed mathematically by the equation,

$$\text{(II)} \qquad RR=\theta'(1+\beta WLM)$$

where f is a binary variable indicating exposure to radon progeny. The intercept (θ), measures the relative difference between exposed and nonexposed workers. In addition a linear exponential model, which included a cell-killing parameter was fitted (Lu94).

$$\text{(III)} \quad RR=(1+\beta WLM)e^{\theta(WLM)}$$

Absolute excess risk is an alternative way of assessing risk. In this instance, the effect of exposure adds to the background lung cancer mortality rate. The following model was fitted to the data:

$$\text{(IV)} \quad ER=r(x,w)-r_0(x) = \beta WLM$$

where $r(x,w)$ = mortality rate of miners at age x exposed at dose w

$r_0(x)$ = mortality rate of non-exposed miners at age x

All fitted models were adjusted for age and calendar period. The fits of the models were compared with each other using the deviances from the models.

2.5.3 Assessment of effects of smoking

Miners were categorized in three smoking categories: never, former and current. Smoking status was determined from the last interview for which smoking status was reported. To assess the joint effect of smoking and WLM exposure, the number of exposure categories was reduced from ten to four.

Initially, relative risks were estimated within categories of WLM and the smoking variable. RR's were then estimated for each cell of the two-way table of WLMs by smoking status. Thus, for three levels of smoking and four levels of WLM, eleven relative risk estimates were produced. The twelfth estimate was the baseline which was set to one. This was the full model against which an additive and multiplicative relationship of smoking and radon were tested. The multiplicative model was:

$$(V) \quad RR=\theta_s (1+\beta_d)$$

where 'd' denotes exposure category and 's' smoking category. The additive model was:

$$(VI) \quad RR=(\theta_s+\beta_d).$$

Finally, the geometric model for categories of the WLM and smoking variables:

$$(VII) \quad RR=[\theta_s(1+\beta_d)\,]^{\lambda}\,[\theta_s+\beta_d\,]^{1-\lambda}.$$

The geometric model allows for relationships between additivity and multiplicativity. With a multiplicative association, the greater background risk of lung cancer among smokers results in a radiogenic excess that is substantially greater in smokers than in non-smokers.

2.5.4 Attained age

To assess the effect of attained age, a linear excess relative risk model (I) $RR=1+\beta\times WLM$ was initially fitted. The significance of attained age was assessed by comparing (I) with the model $RR=1+\beta_j\times WLM$ where *j* denoted the categories of attained age. In our analyses attained age was categorized as: < 50, 50-<60, 60-<70, 70+ years. The difference in the deviances of the two models can be approximated by a χ^2 distribution with three degrees of freedom.

2.5.5 Time since first exposure

To assess the effect of time since first exposure to radon, a linear excess relative risk model (I) $RR=1+\beta\times WLM$ was initially fitted. The significance of dose rate was assessed by comparing (I) with the model $RR=1+\beta_j\times WLM$ where *j* denoted the categories of age at first exposure. In our analyses age at first exposure was categorized as: < 25, 25-<40 and 40+ years. The difference in the deviances of the two models can be approximated by a χ^2 distribution with two degrees of freedom.

2.5.6 Exposure windows

As in the BEIR(IV) Report (NR88) cumulative WLM exposure was divided into time since exposure windows. Cumulative exposure was partitioned as follows:

$$w=w_{5\text{-}14} + w_{15\text{-}24} + w_{25\text{-}34} + w_{35+}$$

where $w_{5\text{-}14}$ was the cumulative exposure received 5-14 years prior to the specific age, $w_{15\text{-}24}$ was the cumulative exposure received 15-24 years prior to the specific age, etc. The excess relative risk model took the form:

$RR=1+\beta\ (\theta_1 w_{5\text{-}14}+\theta_2 w_{15\text{-}24}+\theta_3 w_{25\text{-}34}+\theta_4 w_{35+})$ where θ_1 was set equal to one.

The above model was compared with $RR=1+\beta WLM$ (where WLM is cumulative lifetime exposure) to test the homogeneity of estimates of time since exposure effects. Details are found in Appendix B. Because it proved to be impossible to attain model

convergence using the joint effects model with exposure windows, this issue was also examined by modelling time since last exposure (<15 years versus 15+ years).

2.5.7 Assessment of exposure rate and duration

Previous studies have noted an inverse exposure-rate response relationship with radon daughter exposure (Lu94). Specifically, those exposed to low doses over a long period are at increased lung cancer risk compared to those exposed to an equivalent cumulative lifetime dose but at higher rates over a shorter duration.

To assess this inverse exposure-rate response relationship, a linear excess relative risk model (I) $RR=1+\beta \times WLM$ was initially fitted. The significance of dose rate was assessed by comparing (I) with the model $RR=1+\beta_j \times WLM$ were j denoted the categories of exposure duration. In our analyses exposure duration was categorized as:< 10, 10-<20 and 20+ years. The differences in the deviances of the two models can be approximated by a χ^2 distribution with two degrees of freedom.

2.5.8 Lifetime risk estimates

A relative risk model, which accommodated the effects of cumulative WLM, attained age, exposure duration and time since last exposure was used to model lifetime risk of lung cancer mortality. To do this, Newfoundland all cause and lung cancer mortality data between 1985 and 1989 were used. Lifetime risks were compared to those derived using the

BEIR IV model (see Appendix C). Lifetime risks were estimated at the current occupational exposure limit standard of 4WLM/year under varying durations of employment.

CHAPTER 3

RESULTS

The mortality experience of 1,744 underground and 321 surface miners was examined. Among the underground miners, 577 deaths were observed between 1950 and 1990 (Table 1). Of these, 229 were from cancer, of which 139 were from lung cancer. Observed numbers of death from cancers of the lung, buccal cavity, salivary gland and urinary tract were significantly elevated when compared to the mortality experienced by Newfoundland males between 1950 and 1990. A significant excess number of deaths were also noted for infective and parasitic diseases, silicosis, accidental drownings and falls. Only eight lung cancer deaths were observed among surface workers.

Lung cancer mortality by cumulative radiation exposure is presented in Table 2. Approximately 60,000 person-years of follow-up were noted. Relative risk estimates for categorical WLM estimates, when adjusted for attained age and period, increased with increasing cumulative dose and were statistically significant for cumulative doses exceeding 200 WLM. The Poisson model used to estimate these risks yielded a deviance value of 404.9 with 716 degrees of freedom (Table 3). When a regression line of excess relative risks by mean categorical WLM, using a constrained intercept was fitted, the relative risk coefficient was estimated at 0.66 per cent per working level month (Figure 1). The cell killing effect was not found to be statistically significant at the $\alpha = 0.05$ level. The attributable risk coefficient for continuous WLM was estimated as 6.3 deaths per working level month per million person-years (Table 3).

ERR/WLM% declined with increasing attained age (Table 4), whereas ERR/WLM% did not vary by age at first exposure (Table 5). Smoking information was available for 65% of the exposed miners (Table 6). Almost 90% of those of known smoking status were either current or former cigarette smokers. However, the prevalence of current cigarette smokers has decreased over the past 15 years. Based on the 1978 AECB and 1993 Health Canada smoking surveys, 32% of those smoking in 1978 had quit smoking by 1993. Only three members of the 1993 cohort questioned about their smoking status began smoking after 1978.

Models were created to examine the relationship between cigarette smoking, radon and lung cancer risk. Cigarette smoking was modelled two ways: by number of cigarettes per day (Appendix A) and by smoking status (current, former, never). Table 7 displays relative risks based on additive and multiplicative models which account for smoking status. Relative risks of over 50 were observed for men who were never or current smokers exposed to 2500+ WLM. Further analyses based on number of cigarettes smoked per day and smoking status are found in Appendix A.

Models were constructed in which the effects of WLM, cigarette smoking status, and background (age and period effects) were assessed (Table 8). It was not possible to differentiate in terms of statistical fit between the full model (details of which are presented in Table 10) and models based on a mixture of multiplicative and additive (geometric model), or multiplicative or additive effects. Excess relative risk per WLM increased with increasing

length of duration of exposure (Table 9), indicating that risk per unit dose decreased with increasing dose rate.

Table 10 displays the final, selected model. Besides terms for radon progeny exposure and baseline risk, this model includes terms for attained age, duration of exposure and time since last exposure. A term for period was not included because (i) the model would not converge with period in the model and (ii) the effect of period was not statistically significant. The number of categories for each effect was reduced to attain convergence.

Table 11 displays the lifetime risk of exposure to radon based on various exposure scenarios. A miner occupationally exposed to 4 WLM per year for forty years has a relative risk of approximately 1.7 of lung cancer mortality. Attributable risks (AR) for the cohort by smoking status are displayed in Table 12. For the cohort as a whole, the AR resulting from radon exposure was 0.64. Attributable risks were higher for smokers (0.69) than for non-smokers (0.59).

CHAPTER 4

4.1 DISCUSSION AND RECOMMENDATIONS

As expected, the risk of dying of lung cancer was found to be strongly associated with cumulative radon daughter exposure. Miners who smoked cigarettes and were exposed to 2500 or more WLMs had a more than 50-fold increased risk of dying of lung cancer.

The excess relative risk coefficient for the cohort (0.66% per WLM) suggests that the dose required to double the risk of lung cancer is 152 working level months. This is higher than previous analyses (112 WLM). Lubin et al., in a joint analyses of 11 miner cohorts (Lu94), estimated the excess relative risk coefficient to be 0.49% per WLM for all eleven cohorts, and 0.76% per WLM for the fluorspar cohort. The estimate for all eleven cohorts combined produces a doubling in risk after an exposure of 204 WLM. However, because risk varies strongly with attained age and exposure rate, and to a lesser extent, by time since last exposure, a single summary risk measure may be misleading.

4.2 Effects of attained age

Excess relative risks per WLM were found to decrease dramatically with attained age. This agrees with the findings of Lubin et al. in their 11 cohort analysis (Lu94). Relative risks often decline with age (Se88). The interaction of radon and lung cancer risk with age may lie somewhere between additivity and multiplicativity.

4.3 Effect of dose rate

Excess relative risk per WLM increased with increasing length of duration of exposure, suggesting that those exposed to lower doses or for longer periods of time have a greater risk than those exposed to an equivalent cumulative lifetime dose but at higher doses over a shorter period.

Decreasing ERR/WLM with increased duration of exposure was previously observed in the 11 cohort study by Lubin and colleagues (Lu94). Whittemore & McMillan (Wh83) both found that lower dose rates were more damaging per unit of exposure than higher dose rates. This finding was also reported by Kunz et al. in Czechoslovakian miners (Ku79). This concept is biologically plausible. At high dose rates, alpha radiation may be less effective in inducing cancer because there is an increased probability that multiple "hits" will kill cells. Many mathematical models of carcinogenesis include a cell-killing term (Th82).

If correct, the public health significance of this finding is considerable. It suggests that the low exposure rates likely to be experienced in a residential setting may have greater biological significance than would otherwise be expected.

An alternate explanation for the inverse dose rate effect is that the finding is an artefact resulting from greater non-differential exposure misclassification at higher dose rates than at lower dose rates. In the Newfoundland cohort, high dose rates occurred prior to 1960. Because pre-1960 data were extrapolated, there is likely to have been a much higher degree

of misclassification of these exposures compared to 1960+ exposures. The effect of non-differential misclassification should be to bias risk estimates towards the null, resulting in this case in a greater reduction in risk estimates at high dose rates compared to low dose rates.

It is not known to what extent this bias may have produced the observed "inverse dose rate" effect in the Newfoundland cohort. When we attempted to restrict our analysis to include only those individuals first exposed after 1960, there were too few to allow model convergence. The eleven-study analysis by Lubin and colleagues (Lu94) found that the "inverse dose rate" effect did not vary by year first exposed, suggesting that the degree of misclassification of exposure did not vary significantly over the three time periods examined. However, the most recent calendar period examined (first exposed $\geq$ 1955) may have been too broad, as it included both men for whom exposures were well characterized as well those likely to have been significantly misclassified.

If the "inverse dose rate" effect is the result of bias, then the estimated study ERR is an underestimate. The significant random exposure misclassification which would be the basis of the bias should also have biased the overall ERR towards 0.0.

4.4 Effect of age at first exposure

Our analysis found no effect for age at first exposure. The 1988 AECB fluorspar miner report (Mo88b) also noted no significant difference by age at first exposure. As well, the combined 11 cohort study by Lubin and colleagues noted no age at first exposure effect

(Lu94). Although there is evidence of an increased risk of certain cancers resulting from exposure to gamma radiation in childhood, there is only limited evidence for lung cancer and high LET radiation. Differences in risk between adults and children are the primarily the result of differences in lung morphology and physiology and breathing rates. In mining populations, this expected increase in risk would be small, as few begin employment before their teenage years. It is estimated that this expected increase would be roughly 10-20% (Lu94). The power of this study to detect such a difference in risk is limited due to uncertainties in WLM exposure, smoking patterns and the control of other covariates. The Chinese tin miner cohort noted a stronger effect for those exposed before age twenty (Lu94). However, the age of first exposure was much lower in this cohort; fifty-four lung cancer cases were observed among those who were first exposed before age ten (Lu94).

4.5 Time since exposure

We included in our final model a parameter for time since last radiation exposure. This parameter had a large standard error, but was included because the point estimate showed a decline in risk with increasing time since last exposure that was consistent with our previously published results (Mo88b), and with the model selected by Lubin (Lu94).

4.6 Lifetime risk estimates

Lifetime risk estimates were lower than those observed using the BEIR IV model. This occurred primarily because the relative risk decreased much more rapidly with attained

age in the parameter estimates of our model as compared to the BEIR IV model. The BEIR IV analysis did not use the fluorspar cohort.

4.7 Effects of smoking

Statistically significant differences were detected in the ERR/WLM between smokers, former smokers and non-smokers. A limitation of the analyses by smoking status was that smoking categories were fixed (i.e., we didn't have sufficient information to determine changes in smoking status over the follow-up period).

Thomas et al. (Th85), analyzing data from the Colorado Plateau miners cohort, concluded that the interaction between smoking and radiation may be intermediate between additive and multiplicative. This finding was supported by the multi-cohort analysis by Lubin (Lu94). The present findings, based on the very small number of non-smokers in the cohort are subject to considerable variability and should be viewed cautiously.

4.8 Differences in lung cancer risk

This analysis of the fluorspar cohort noted an excess relative risk for lung cancer of 0.66% per WLM. This is slightly lower than what was observed by Lubin and colleagues (Lu94) in their analysis of the fluorspar cohort. The difference resulted from the current analysis having been based on a longer follow-up time (1990 versus 1984). The value of 0.66% per WLM is similar to that noted by Lubin for all eleven mining cohort studies combined (0.49% per WLM).

The cohort specific ERR/WLM varied considerably across the eleven studies, reflecting significant effect modification by dose rate. Some differences across the various mining cohort studies also resulted from inaccuracies in the exposure estimates. Uncertainties in exposure estimates are inherent in the nature of occupational epidemiology. Regulatory agencies or mining companies are unlikely to monitor a factor that is not believed to be present in the mines or one that is not believed to be harmful at the levels detected if known to be present. Each of the radiation mining studies has had to estimate personal exposures to radon daughters for at least part of the follow-up time.

A small advantage that this study has over most other studies of radiation-exposed mining populations results from the fact that the source of radiation in the fluorspar mines was from ground water and not from radioactive ore. Because of this, it was possible to exclude the effects of gamma radiation, thoron and radioactive dust. This was not possible in the cases of the Czechoslovakian, Ontario and Colorado Plateau uranium mining studies.

Another advantage that the present study has compared with some others is that fluorspar miners were almost without exception, local men with no previous mining experience who, upon ceasing to mine fluorspar, went back to non-mining professions. In contrast, many Ontario uranium miners worked as gold miners either before or after their uranium mining experience (Mu83). Gold-quartz mining is itself an occupation associated with an increased risk of lung cancer (Mu85).

However, like most other hardrock mining cohorts, the current cohort was exposed to silica. Evidence of this is the large excess of deaths attributable to silicosis. There is limited evidence that silica is a human carcinogen (IA87); some excess lung cancer attributed to radon may reflect silica exposure.

From a public health perspective, the dose-response relationship below 100 WLM is of greatest importance, given the present Canadian standard of 4.0 WLM per year for uranium miners (Do79) and a hypothetical likely maximum working life expectancy of 25 years as a miner. Fortunately, few workers are exposed anywhere near the current standard of 4.0 WLM per year (Do79). Unfortunately, evidence from this study and others suggests that the effectiveness of low dose-rate radiation may be greater per unit dose than that of high dose-rate radiation.

There are many problems in attempting to estimate the effects of low level radiation. Cohorts of miners exposed to measured levels of radon daughters are typically exposed to relatively "safe" low levels of radiation. Studies of such cohorts are important in that they look at low-level doses to which miners working at the present may be exposed. As well, they can be used to look at risks at low doses without having to rely on mathematical extrapolation from high dose data models. However, such studies tend to have difficulty finding effects because of sample size limitations. These limitations arise because sample size requirements are dependent on the size of the relative risks. At low doses, relative risks associated with radiation exposure are of course much smaller than at higher doses.

Studies such as the present one that examine populations exposed to high level radiation have no trouble finding an effect. However, the model that is chosen will have important implications in estimating risk at low doses. As well, doses are invariably based, at least to some extent, on estimated rather than measured radiation exposure. As a result, there is still considerable controversy regarding the nature of the dose-response relationship at low doses (Th85).

4.9 Choice of analytic methods

The method selected to analyze the fluorspar cohort was Poisson regression. The Poisson distribution is often used to model rare events such as cancer incidence rates and has found its most frequent application in occupational epidemiology (Ch89). It is ideally suited to handle complex forms of interaction, such as nonlinear relationships (Br83).

One benefit of Poisson regression analysis is that it makes comparisons using an internal comparison group. The use of an internal control population should largely remove the "healthy worker effect" which is a common problem when analyzing occupational cohorts (We83). While it is conceivable that employees not healthy enough to work in the mines were assigned to surface work, surface workers were still healthy enough to be employed. It is likely that surface workers resembled underground workers to a greater extent than did the entire male population of Newfoundland. Both surface and underground workers lived in the same locality; smoking levels appear comparable and socio-economic status between the two groups, at least as indicated by wage scales, were fairly similar.

A further advantage to an internal control group is the potential of including in the analysis detailed auxiliary variables such as cigarette smoking, which are usually not available for an external control group.

The current analysis suggested that 64% of the lung cancer among this cohort could be attributed to the effects of radon progeny exposure. The full model couldn't be used because of convergence difficulties, so a model based on a multiplicative effect between radon and smoking was used. The current analysis r ɔted lower attributable risks (AR) among never smokers. Lubin (Lu94) also found a lower AR among never smokers in this cohort compared to smokers (0.65 vs. 0.86). Most studies report higher AR for non-smokers compared to smokers. In Lubin's analysis, the combined AR for all studies reporting smoking information were 0.73 and 0.39 for never-smokers and smokers respectively. The discrepancy between the current study and others reflects the very small number of lung cancer cases among non-smokers in the Newfoundland cohort (n=4), which resulted in quite imprecise estimates.

4.10 Conclusions and Recommendations

The mortality experience of 2,065 fluorspar miners, millers and surface workers has been updated to the end of 1990. The risk of lung cancer mortality was related to cumulative radon daughter exposure. Excesses were noted for cancers of the lung, buccal cavity and mouth, urinary tract and for silicosis and pneumoconioses. The exposure-response data for lung cancer were fitted to various mathematical models. The model selected included terms for attained age, dose, dose rate and time since last exposure. Because risk varies according to each of these factors, a single summary risk estimate is misleading. It is unlikely that the joint effects of radon progeny exposure and smoking can be assessed using this cohort.

Recommendations for further work include using the risk estimates derived from this study to examine risks resulting from exposure to household (indoor) radon.

Table 1

Mortality among underground fluorspar miners, Newfoundland, 1950-1990

Cause of Death	Observed	Expected	SMR	95% confidence limits
All Causes	577	501.73	1.15	(1.07,1.23)
Infective and parasitic diseases	17	9.34	1.82	(1.17,2.75)
Neoplasms	229	116.60	1.96	(1.76,2.19)
Buccal Cavity and pharynx	6	2.52	2.38	(1.05,4.77)
Salivary Gland	2	0.20	10.00	(1.75,32.62)
Digestive Tract	43	46.53	0.92	(0.71,1.19)
Trachea, bronchus and lung	139	31.07	4.47	(3.87,5.15)
Prostate	10	7.28	1.37	(0.75,2.35)
Urinary tract	11	5.96	1.85	(1.04,3.08)
Brain, nervous system	3	2.89	1.04	(0.29,2.76)
Lymphatic and hematopoietic	6	6.76	0.89	(0.39,1.78)
Endocrine/nutritional/metabolic diseases	3	8.53	0.35	(0.10,0.93)
Mental Diseases	5	3.55	1.41	(0.56,3.02)
Diseases of nervous system sense organs	3	7.41	0.40	(0.11,1.08)
Diseases of circulatory system	209	234.55	0.89	(0.79,1.00)
Ischemic Heart disease	149	148.33	1.01	(0.87,1.15)
Cerebrovascular disease	16	22.52	0.71	(0.45,1.09)
Nonmalignant respiratory disease	40	37.67	1.06	(0.80,1.39)
Chronic bronchitis, emphysema and asthma	23	15.37	1.50	(1.03,2.13)
Silicosis and anthrasilicosis	7	0.12	58.33	(27.70,111.08)
Digestive system diseases	10	14.92	0.67	(0.37,1.15)
Genitourinary diseases	2	8.17	0.24	(0.04,0.80)
Symptoms ill-defined	1	10.14	0.10	(0.00,0.50)
Accidents, poisonings, violence	56	36.28	1.54	(1.22,1.93)
Traffic accidents	14	9.66	1.45	(0.88,2.28)
Accidental falls	7	2.73	2.56	(1.22,4.88)
Accidental drowning	8	4.29	1.86	(0.94,3.41)
Suicide	5	4.45	1.12	(0.45,2.41)

** Expected number of deaths calculated based on male Newfoundland age-specific mortality rates between 1950-90

Table 2

Lung cancer mortality by cumulative radiation exposure, fluorspar miner cohort, Newfoundland, 1950-1990

Cumulative exposure (WLM)[†]	Mean exposure (WLM)	Person-years	Lung cancer deaths	Relative Risk (95% C.I.)[‡]
0	0	14763	8	1.0 --
>0-<25	4.66	17731	19	1.92 (0.82,4.48)
25-<200	90.06	9892	15	2.15 (0.91,5.10)
200-<500	329.52	6978	16	3.34 (1.43,7.77)
500-<1000	698.84	3236	13	4.94 (2.01,12.15)
1000-<1500	1238.26	1703	16	14.03 (6.07,32.44)
1500-<2000	1742.46	1238	17	18.85 (8.15,43.61)
2000-<2500	2184.44	700	13	22.07 (8.97,54.27)
2500-<3500	3006.58	578	13	29.55 (12.18,71.66)
3500+	3913.33	361	17	47.96 (20.16,114.10)

[†]WLM-working level months. A lag interval of 5-years was incorporated into the calculation of cumulative exposure.

[‡]Relative risks were adjusted for age and calendar period

Table 3

Results of fitting several relative risk models† to Newfoundland fluorspar mining cohort mortality 1950-1990.

Equation for RR or ER as a function of cumulative WLM(x)	Degrees of freedom[a]	Deviance	Parameter Estimate	Standard Error
Separate RR for each dose group	716	402.86	(See figure 1)	
$RR=\exp(\beta x)$	724	419.87	0.89×10^{-3}	0.60×10^{-4}
$RR=\exp(\beta x+\gamma x^2)$	723	401.01	$0.18\times10^{-2}(\beta)$ $-0.25\times10^{-6}(\gamma)$	0.21×10^{-3} 0.58×10^{-7}
$RR=(1+\beta x)$	724	402.86	0.66×10^{-2}	0.17×10^{-2}
$RR=(1+\beta x+\gamma x^2)$	723	402.70	$0.39\times10^{-2}(\beta)$ $0.12\times10^{-5}(\gamma)$	0.17×10^{-2} 0.62×10^{-6}
$RR=(1+\beta x)e^{\gamma x}$	723	399.60	$0.42\times10^{-2}(\beta)$ $0.16\times10^{-3}(\gamma)$	0.16×10^{-2} 0.10×10^{-3}
$ER=\beta x$	724	394.75	0.63×10^{-5}	0.74×10^{-6}

ER Absolute Excess risk
RR Relative risk
† All models adjusted for age and period
a Degrees of freedom is equal to the number of observations in the person year tables minus the number of parameters to be estimated.

Table 4

Excess relative risk percent of lung cancer[†], per WLM, by attained age, Newfoundland fluorspar miners, 1950-1990

Attained Age	Lung Cancer Cases	ERR/WLM%	Standard Error	P[‡]
< 50	39	3.60	0.22×10^{-1}	<0.001
50-<60	56	0.62	0.26×10^{-2}	
60-<70	37	0.32	0.15×10^{-2}	
70+	15	0.20	0.16×10^{-2}	

[†] background rates adjusted for age and period

[‡] P-value for test of homogeneity of ERR/WLM

Table 5

Excess relative risk percent of lung cancer†, per WLM, by age at first exposure, Newfoundland fluorspar underground miners, 1950-1990

Age first exposed	Lung cancer cases	ERR/WLM%	Standard Error	P‡
< 25	64	0.70	0.19×10^{-2}	0.38
25-<40	51	0.51	0.16×10^{-2}	
40+	24	0.87	0.41×10^{-2}	

† background rates adjusted for age and period
‡ P-value for test of homogeneity of ERR/WLM

Table 6

Prevalence of cigarette smoking among those of known smoking status, underground versus surface workers, Newfoundland fluorspar cohort, by percentage

Smoking status	Underground	Surface
	%	%
Never Smoker	10.8	18.0
Current Smoker	29.7	36.1
Former Smoker	59.5	45.9

Smoking status was unknown for 81% of surface workers and 35% of underground miners. Smoking status was determined from date last interviewed.

Table 7

Relative risk of lung cancer, Newfoundland fluorspar miners, by cumulative radon progeny exposure and smoking status

Smoking status		Cumulative WLM			
		< 400	400-<1500	1500-<2500	2500+
Never	n	1	1	1	1
	RR	1.0	4.71	30.72	52.74
Former	n	6	6	7	6
	RR	2.02	6.42	19.57	42.07
Current	n	30	24	18	17
	RR	5.72	19.17	39.97	51.72
Total	n	37	31	26	24
	RR[a]	1.0	9.51	28.79	47.00
	RR[b]	1.0	3.33	6.84	11.27

n = number of lung cancer cases
RR is the relative risk estimated fitted with the full model
RR[a] is the relative risk estimate fitted with an additive model
RR[b] is the relative risk estimate fitted with a multiplicative model

Table 8

Results of Model Fitting, by cigarette smoking status

Model	Deviance	Degrees of Freedom	p-value‡
Full	209.09	298	-
Mixture(λ=0.4)	211.20	303	0.91
Multiplicative	212.98	304	0.69
Additive	214.75	304	0.46
WLM	230.69	306	<0.01
Smoking status	302.62	307	0.00
Background	302.85	309	0.00

‡p-value of model relative to full model

Table 9

Excess Relative Risk per WLM by exposure duration*

Exposure duration	Number of lung cancer cases	ERR/WLM%
0-<10	57	0.125
10-<20	61	0.657
20+	39	0.828
Overall	147	0.658

p-value for test of homogeneity ($p<0.0001$)
* adjusted for attained age and period

Table 10

Relative Risk Model

Relative risk was estimated with the following model:

$$RR = 1+\beta \times WLM \times \varphi_{age} \times \gamma_{dur} \times \tau_{tse}$$

where

φ_{age} =	1.00	for age < 50
	0.23	for 50 $\leq$ age < 70
	0.10	for age $\geq$ 70
γ_{dur} =	1.00	for duration <10 years
	6.89	for 10 $\leq$ duration < 20 years
	8.71	for duration $\geq$ 20 years
τ_{tse} =	1.0	for time since exposure < 15 years
	0.83	for time since exposure $\geq$ 15 years
β =	0.0031	

Table 11

The lifetime relative risk[‡] of lung cancer mortality for a miner occupationally exposed to radon at 4WLM/year

Age first employed	Age last employed	Model	
		Fluorspar[§]	BEIR IV[¥]
20	30	1.14	1.31
20	45	1.44	1.80
20	60	1.68	2.30

[‡]calculated using Newfoundland all-cause and lung cancer mortality rates over the period 1985-1989

[§]a description of this model is found in Table 10

[¥]a description of this model is found in Appendix C

Table 12

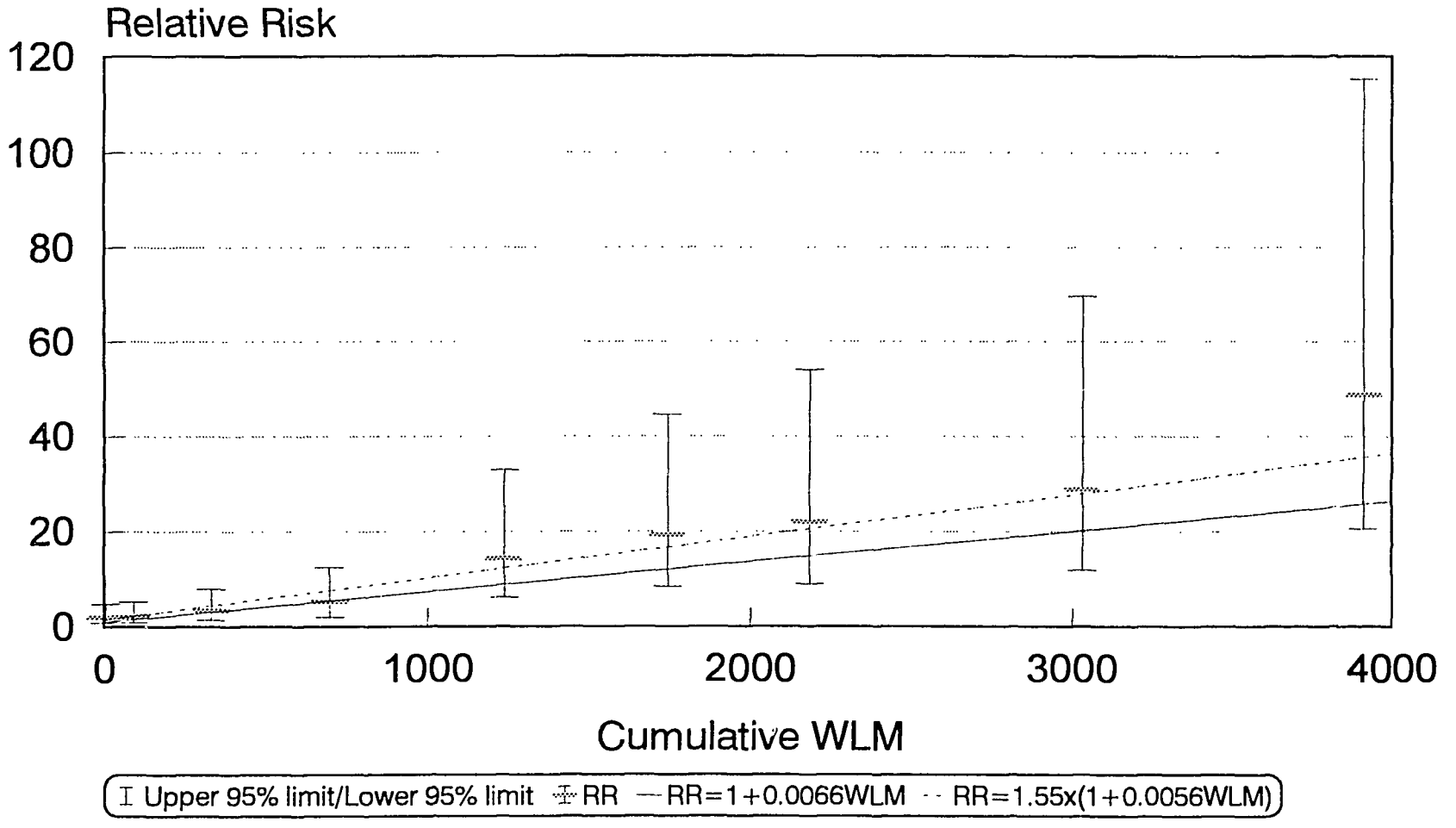
Attributable risk* of lung cancer due to radon progeny exposure by smoking status

	Excess number of cases	Estimated number of cases	Attributable Risk
Entire Cohort*	84.36	131.96	0.639
Never smokers[@]	1.99	3.39	0.59
Former smokers[@]	16.82	24.82	0.68
Current smokers[@]	59.79	86.52	0.69

* Entire cohort: model included terms for attained age, duration exposed, time since exposure, adjusted for background rates.

[@] Smoking model included terms for cumulative exposure, attained age, and multiplicative smoking effect (smoking status: never, former, current) adjusted for background rates.

Figure 1: Relative risk of lung cancer*, by cumulative Rn dose, Newfoundland fluorspar miners, 1950-1990



*RR's plotted at mean WLM for each category and were adjusted for age and period

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APPENDIX A

Table A1

Relative risk of lung cancer, Newfoundland fluorspar miners, by cumulative radon progeny exposure and cigarettes smoked per day

Cigarettes per day	Cumulative WLM				Total Cases			
	< 400	400-<15000	1500-<2500	2500+		RR	RR[a]	RR[b]
0-<20	4	6	12	9	31	1.0	1.0	1.0
	1.0	3.42	18.53	21.58				
20-<30	14	15	9	8	46	1.38	3.14	1.24
	2.71	9.60	14.00	13.88				
30+	6	4	5	6	21	2.01	2.92	2.09
	2.30	7.04	31.14	60.21				
Total Cases	24	25	26	23	98			
RR	1.0	3.00	8.26	11.82				
RR[a]	1.0	5.89	18.98	24.17				
RR[b]	1.0	3.45	9.43	11.77				

RR[a] is the relative risk estimate fitted with an additive model
RR[b] is the relative risk estimate fitted with a multiplicative model

Table A2

Results of Model Fitting using cigarettes per day

Models	Deviance	Degrees of Freedom	p-value‡
Full	215.61	293	-
Mixture (λ=0.13)	226.14	298	0.07
Multiplicative	226.58	299	0.09
Additive	226.29	299	0.10
WLM only	231.93	301	0.04
cigarettes/day only	298.83	302	0.00
Background	302.85	304	0.00

‡ p-value of model relative to full model

Table A3

Excess relative risk per WLM (x100) of lung cancer by cigarettes smoked per day for the Newfoundland cohort by attained age*

Cigarettes smoked per day	Person Years	Lung Cancer Deaths	(ERR/WLM)%	p†
ALL AGES				
Overall	24257	98	0.63	
0-<20	8817	31	2.10	0.12
20-<30	11008	46	0.27	
≥30	4432	21	0.93	
AGE < 55 yrs				
Overall	19588	52	1.57	
0-<20	7023	17	∞	0.43
20-<30	8836	24	0.85	
≥30	3729	11	1.30	
AGE ≥55 yrs				
Overall	4007	46	0.21	
0-<20	1794	14	0.43	0.08
20-<30	2172	22	0.03	
≥30	703	10	0.74	

† p-value for test of homogeneity of ERR/WLM
* All models adjusted for age, period and smoking.

Table A4

Excess relative risk per WLM (x100) of lung cancer by smoking status for the Newfoundland cohort. All models adjusted for age, period and smoking.

Smoking Status	Lung Cancer Deaths	(ERR/WLM)%	Standard Error	p[†]
Never	4	0.26	0.22	
Former	25	0.27	0.12	
Current	89	0.65	0.22	
Overall	118	0.44	0.15	0.01

[†] p-value for test of homogeneity of ERR/WLM

Appendix B

Examination of Various Time Windows of Exposure

Details of Fitted Model

1. **Parameter Estimates**

   θ_1=1.0, θ_2=0.77, θ_3=0.72, θ_4=0.13
   ERR/WLM%=0.9318 at 5-14 years since exposure (This is β)

   where θ_1 corresponds to 5-14 years since exposure
   θ_2 corresponds to 15-24 years since exposure
   θ_3 corresponds to 25-34 years since exposure
   θ_4 corresponds to 35+ years since exposure

2. **Number of Cases=147**
3. **Model Deviance 666.559, DF=2467**
4. **Test for homogeneity:**

   LR statistic=12.57 on 3 df-------> p=0.0057

Appendix C

BEIR IV Model

The BEIR IV committee, upon analysis of four mining cohorts, adopted the following mathematical model to estimate the probability of dying of lung cancer at age *a*:

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

where,

- $r(a)$ is the lung cancer mortality rate at age *a* observed in the mining cohorts
- $r_0(a)$ is the baseline lung-cancer mortality rate of the U.S. population
- $\gamma(a)$ is 1.2 for ages less than 55 years, 1.0 for ages 55-64 years, and 0.4 for age 65 years and over
- W_1 is cumulative radiation exposure in WLM 5 to 15 years before age *a*
- W_2 is cumulative radiation exposure in WLM 15 years or more before age *a*