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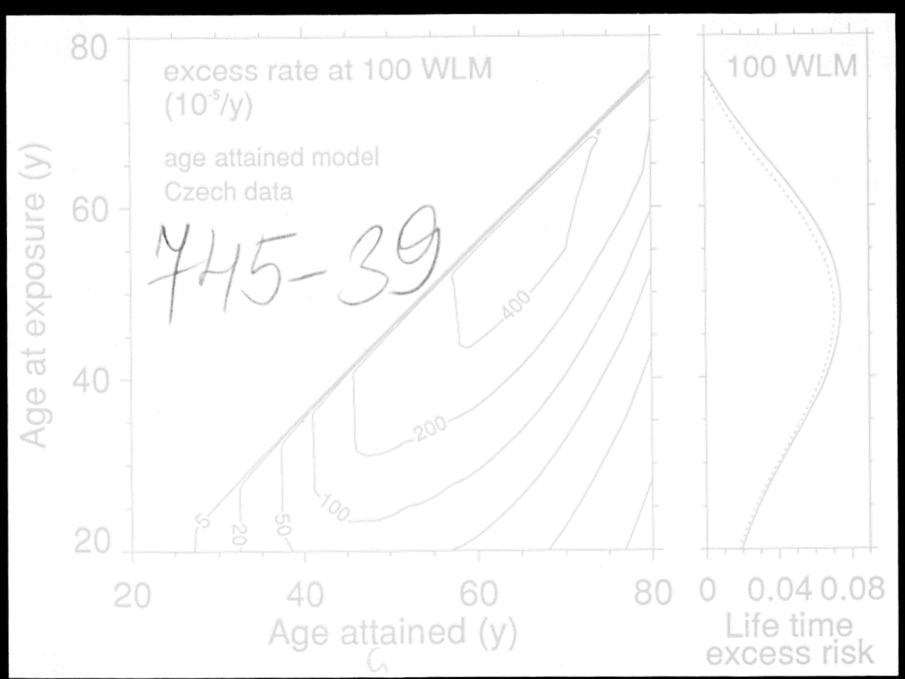

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CONTENTS

(Continued)

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CONTENTS *(continued)*

OTHER CONTENT

On the cover: Risk from exposure to radon progeny. See paper by D. Chmelevsky et al. on p. 15 for more details!

EDITORIAL ANNOUNCEMENT

Kenneth L. Miller has been selected to succeed Richard J. Vetter as Editor-in-Chief of *Health Physics*. All new manuscripts should be submitted to him for consideration at the following address:

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Paper

PROBABILITY OF CAUSATION FOR LUNG CANCER AFTER EXPOSURE TO RADON PROGENY: A COMPARISON OF MODELS AND DATA#

D. Chmelevsky,* D. Barclay,† A. M. Kellerer,‡§ L. Tomasek,‖ E. Kunz,‖ and V. Placek¶

Abstract—**The estimates of lung cancer risk due to the exposure to radon decay products are based on different data sets from underground mining and on different mathematical models that are used to fit the data. Diagrams of the excess relative rate per 100 working level months in its dependence on age at exposure and age attained are shown to be a useful tool to elucidate the influence that is due to the choice of the model, and to assess the differences between the data from the major western cohorts and those from the Czech uranium miners. It is seen that the influence of the choice of the model is minor compared to the difference between the data sets. The results are used to derive attributable lifetime risks and probabilities of causation for lung cancer following radon progeny exposures.**
Health Phys. 67(1):15–23; 1994

Key words: lungs, human; cancer; radon; uranium mines

INTRODUCTION

THE DECAY products of radon are the major contributors to the radiation exposure of the population. They have also been the main contributor to occupational exposure in a large number of underground miners, especially uranium miners, in different countries. The assessment of the risk of lung cancer due to radon progeny exposures is, consequently, one of the central issues of radiation protection.

Several cohorts of uranium miners have been followed, and the resulting knowledge has been reviewed and translated into risk estimates in several major studies (NCRP Report 78 1984; ICRP Publication 50 1986; National Research Council BEIR IV 1988). The NCRP publication used an absolute risk model modified by a term depending on time since exposure. The ICRP used the relative risk model that was applied to the data from the atomic bomb survivors. More recently, the BEIR IV Committee of the U.S. National Academy of Sciences performed a pooled analysis of four major cohorts of western miners** and employed somewhat different relative risk models. Finally the ICRP (1994) utilizes in its new recommendations on radon a more detailed relative risk model developed by Jacobi et al. (1992). The degree of equivalence between the different approaches cannot always be readily judged. This makes it desirable to compare the results and assess the influence that the choice of models may have. For this purpose illustrative diagrams will be used that facilitate the comparison of models and data sets. In the comparison of models, the familiar approaches will be referred to, but added models that are more suitable for the derivation of tables of probability of causation will also be considered. The comparison of data will set the western cohorts that have been analyzed by ICRP and the BEIR IV Committee against a recent evaluation of the S cohort of Czech uranium miners (Sevc et al. 1993).

Probabilities of causation, for those instances where the occurrence of a cancer raises the question of a causal relation to a foregoing radiation exposure, were first derived by a committee of the U.S. National Institutes of Health (NIH) (1985). In the parts that deal with lung cancer and radon progeny exposures, the radioepidemiological tables were based on fairly simple approximations. Jacobi et al. (1992) have recently improved the tables for radon progeny exposures and it is, therefore, of particular interest to compare the result of this approach to the Czech data.

BASIC CONCEPTS RELEVANT TO THE PROBABILITY OF CAUSATION

The NIH committee has defined the probability of causation (PC) as:

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** The study included two Canadian cohorts of uranium miners (Eldorado Beaverlodge and Ontario), the U.S. cohort of uranium miners from the Colorado Plateau, and the Malmberget cohort of Swedish iron miners.

$$PC = \frac{\Delta r(D, a)}{\Delta r(D, a) + r_0(a)}, \quad (1)$$

where $r_0(a)$ is the age-specific incidence rate of the specified cancer at age a. This rate, usually expressed as the expected number of cases per year and per 100,000 persons of the specified age, is obtained from national statistics or from the statistics for specified ethnic groups. $\Delta r(D, a)$ is the excess rate at age attained, a, i.e., the increase of the lung-cancer rate due to the irradiation. It is computed, according to an assumed risk model, for a known or estimated dose, D. A number of factors apart from dose and age attained need to be considered in the model; however, additional factors, such as age at exposure, are omitted here in the argument of the quantity.

The probability of causation can be understood as the fraction of the actual risk of an individual that is attributable to the radiation exposure. The definition of the probability of causation reflects the fact that a radiation-induced cancer cannot be recognized as such and that, consequently, it is only possible to attribute to a particular case a probability that the cancer was caused by irradiation. The term probability is used loosely here without the implication that the quantity has all the properties of a probability in the mathematical sense.

The NIH committee has used, for solid tumors except bone tumors and for a one-time exposure, a relative risk model that is still largely supported by the existing data among the atomic bomb survivors. In this model, sometimes termed the *age-at-exposure model*, the excess rate equals

$$\Delta r(D, a) = f(D, e)\, r_0(a), \quad (2)$$

where the *excess relative rate*, $f(D, e)$, depends (apart from the dose, D) on the age at exposure, e. As recently shown for the mortality from solid cancers among the atomic bomb survivors (Kellerer and Barclay 1992), an *age-attained model*,

$$\Delta r(D, a) = f(D, a)\, r_0(a), \quad (3)$$

is equally consistent with the data. In the subsequent considerations it will be seen that a similar equivalence pertains to the application of the models to the follow-up of uranium miners.

For radon and radon progeny exposures the formulation is somewhat more complicated because it requires integration over extended exposure periods. Furthermore, the term "dose" is not referred to because the dosimetric models for radon progeny exposure are still uncertain. Instead of using the dose to the lung, calculations use the exposure which is defined as the product of duration and radon-progeny concentration, with the conventional unit working level month (WLM).

The ICRP (1986) applied a relative risk model, as in eqn (2), to radon exposures (i.e., the relative risk function was treated as a function of the exposure, C, to radon progeny and as a function of the age at exposure, e). On the other hand, the BEIR IV Committee has, in detailed numerical calculations, employed a somewhat different model with a dependence on age attained, a, and time since exposure, $t = a - e$ [see eqn (4)]. For both models the actual analysis included additional factors which will be considered subsequently.

The choice of an age-attained model, instead of an age-at-exposure model, by the BEIR IV Committee has partly been a matter of numerical convenience. The committee performed maximum likelihood fits to the numerical data from four major western cohorts of radon-exposed miners. In the case of protracted exposures, the BEIR IV approach allows such computations with the available software[††] while a maximum likelihood evaluation in terms of other models would be more difficult.

The NIH committee included smoking as the dominant confounding factor. It was noted that the information on the influence of smoking on lung-cancer rates and its possible synergism with radiation exposure is too scarce to permit reliable quantification. While among the survivors of the atomic bombs the combined influence of smoking and irradiation appears to follow an additive risk model (Prentice et al. 1983; Blot et al. 1984; Kopecky et al. 1986), several studies of uranium miners (Whittemore and McMillan 1983; Hornung and Meinhardt 1987; Saccomano et al. 1988; Müller et al. 1985, 1989) suggest a multiplicative or nearly multiplicative interaction. In view of this contradictory evidence, the NIH committee did not recommend a particular alternative but described the formalism to be used either with the additive or with the multiplicative model.

The BEIR IV Committee, on the other hand, decided to choose a multiplicative model although, as stated in the report, the limited available data on smoking habits among uranium miners point towards a submultiplicative interaction. The committee warned that the multiplicative model was chosen partly to limit the inherent number of parameters in the equations, and it emphasized that a more complex model with a submultiplicative combination of the two risk factors, radiation exposure and smoking, may be closer to reality. This is supported by a recent study of Chinese tin miners (Zhen et al. 1993).

In subsequent considerations, excess relative rates will be quoted that pertain to the population as a whole. If the multiplicative model applies, the values are equally valid for smokers and nonsmokers. If a less-than-multiplicative model applies, the quoted values are overestimates for the smokers and underestimates for the nonsmokers. Accordingly, the PC values

[††] All maximum likelihood computations were performed with the software package EPICURE (Preston, D. L.; Lubin, J. H.; and Pierce, D. D. EPICURE). Generalized regression models for epidemiological data (1991). Software from Hirosoft International, Suite 103, 1463 E Republican, Seattle, WA 98112.

derived under the multiplicative assumption would favor the smokers and put the nonsmokers at a disadvantage. The error introduced by the assumption of multiplicativity would depend on the relative fractions of smokers and nonsmokers in the group of miners from which the excess relative rate is estimated and also on the degree of the deviation from the multiplicative model, the largest error resulting if a purely additive model holds, appearing to fit the Japanese data.

A COMPARISON BETWEEN MODELS AND BETWEEN DATA SETS

Two models applied to the major western cohorts

The treatment in BEIR IV. The BEIR IV Committee used, in its analysis, an age-attained model with an added dependence on time since exposure. This time dependence accounted for the observation that, at a given age attained, the excess rate decreases when the exposure lies further back. A simple summation replaces the integration over the period of exposure:

$$r(a, C) = r_0(a)\left(1 + \alpha\gamma_j \sum_i \beta_i C_i\right). \quad (4)$$

The dependence on time since exposure is introduced by subdividing the cumulative exposure C into different components, C_i. In its final simplified treatment, the BEIR IV Committee used only two components. The component C_1 refers to the exposure in the period 5–15 y prior to age attained, a; C_2, is the sum of earlier exposures. Exposures in the 5 y prior to age attained are disregarded; this lagging accounts for a minimum latent time between exposure and appearance of a lung cancer. The dependence on age attained is also represented by a step function, γ_j. The BEIR IV Committee proposed the following values of the parameters:

$$\alpha = 0.025$$
$$\beta_1 = 1;\ \beta_2 = 0.5$$
$$\gamma = \begin{cases} 1.2 & a < 55 \\ 1 & 55 \le a \le 64 \\ 0.4 & 64 < a \end{cases} \quad (5)$$

where the ages are expressed in years and the exposures in the unit WLM.

Accordingly, the excess relative rate in the BEIR IV model depends on age attained, a, and time since exposure $t = a - e$. For a hypothetical short-term exposure of magnitude C, the excess relative rate is thus:

$$f(C) = \alpha\beta_i\gamma_j C. \quad (6)$$

A short-term exposure is, of course, of little practical relevance but it serves as a convenient reference in the comparison of different models or of different data sets fitted by the same type of model. The $(a–e)$ diagram in Fig. 1 depicts the essentials of the BEIR IV model. It gives, according to eqns (5) and (6), areas of equal relative excess rate, $f(C)$, due to an instantaneous exposure $C = 100$ WLM. For an actual protracted exposure, the summation in eqn (4) is all that is needed. The $(a–e)$ diagram is a useful tool for the ready visual comparison of different models and different data sets, and its use will be exemplified in the subsequent treatment.

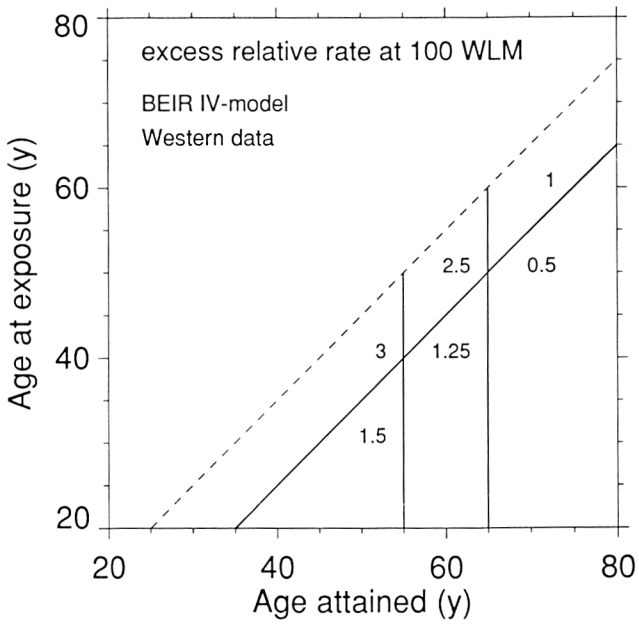

Fig. 1. Regions, in the age-attained vs. age-at-exposure plane, of constant excess relative rate after a single exposure to 100 WLM, according to the preferred model of the BEIR IV Committee [eqns (4) and (5)].

A modified treatment for the calculations of probabilities of causation. The BEIR IV model is satisfactory for the computation of lifetime attributable risks but it is unsuitable for probability of causation tables, where the step function leads to dependencies of the probability of causation on age attained that have marked discontinuities at ages 55 and 64 y. In practice this would not be acceptable.

Jacobi et al. (1992) have considered this difficulty in a recent analysis and have represented the same numerical results by a modified expression that avoids the marked discontinuities in the dependence of $f(C)$ on a and e. In line with the earlier treatment by the ICRP, they have chosen an age-at-exposure model. They based their model on the BEIR IV results without performing new maximum likelihood computations. Their expression for the excess relative rate is

$$f(C) = g(e)b(t)C, \quad (7)$$

with a continuous dependence on time since exposure, t, and age at exposure, e, that has minor discontinuities:

$$g(e) = \begin{cases} 0.036 & e < 25 \\ 0.032 & 25 \le 2 < 30 \\ 0.03 & 30 \le e < 35 \\ 0.0285 & 35 \le e < 40 \\ 0.027 & 40 \le e < 45 \\ 0.0255 & 45 \le e < 50 \\ 0.022 & 50 \le e < 55 \\ 0.018 & 55 \le e \end{cases} \quad (8)$$

$$b(t) = \begin{cases} 0 & t \le 4 \\ t/4 - 1 & 4 < t < 8 \\ 1 & 8 \le t < 12 \\ e^{-0.0693(t-12)} & 12 \le t \end{cases} .$$

The exposures are given in WLM, and t and e are given in years.

Fig. 2 gives the (a–e) diagram of this model for the same western data that were used in BEIR IV. Eqns (7) and (8) do not lead to large areas of constant excess relative rates. The diagram is therefore given in terms of lines of constant relative rates. A comparison to Fig. 1 shows good overall agreement; however, the new model provides a smooth dependency that is suitable for calculations of probabilities of causation. The result for a protracted exposure is, as with eqn (4), obtained by summing over the period of exposure, i.e., the excess relative rate at age attained, a, is

$$f = \sum_{i=e_1}^{a-L} g(i)b(a-i)C_i, \quad (9)$$

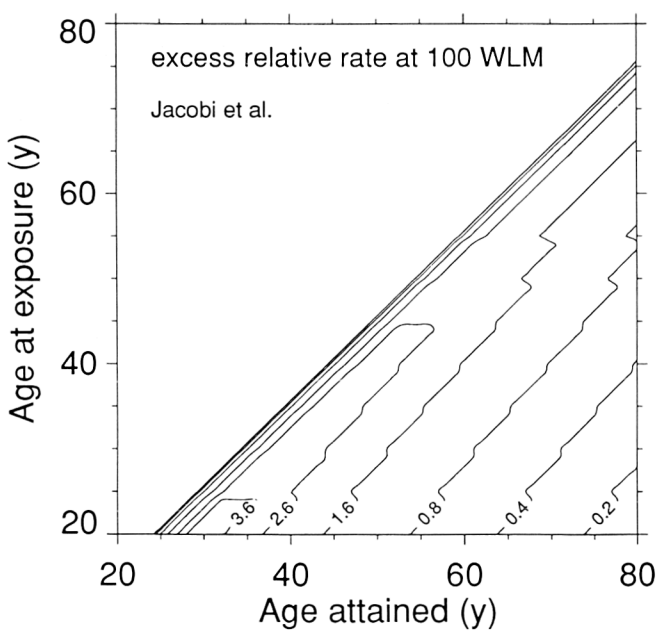

Fig. 2. Lines (in the age-attained vs. age-at-exposure plane) of constant excess relative rate after a single exposure to 100 WLM, according to the model developed by Jacobi et al. (1992) [eqns (7) and (8)].

where C_i is the exposure at age i, e_1 is the age at first exposure, and L is the latency period.

The comparison of the BEIR IV approach with the modified model of Jacobi et al. (1992) shows that the same data basis and essentially the same results can adequately be expressed by different models. This comparison does not refer to results that are derived by separate maximum likelihood computations; however, an independent computation in terms of Jacobi's model, if it were numerically feasible, would also lead to values for $g(e)$ and $b(t)$ that are essentially in line with the trends in the BEIR IV model. Some of the subsequent computations will support this point.

After this first consideration of models, the next section will deal with a comparison of the results from the western cohorts with those of the Czech uranium miners.

A COMPARISON OF THE BEIR IV DATA TO THE CZECH DATA

Results for the S cohort in terms of the BEIR IV model

The follow-up of the major Czech cohort of uranium miners (S cohort) provides an alternate basis for calculations of probabilities of causation. Based on a recent analysis (Sevc et al. 1993), a comparison can be made to the BEIR IV results and their evaluation by Jacobi et al. (1992).

The S cohort of uranium miners has been described in a number of publications (Kunz et al. 1978, 1979; Sevc et al. 1988) to which the reader is referred. The analysis of the cohort has shown, in agreement with the study of the BEIR IV Committee, that age attained and cumulated exposure (with a lag period of 5 y) are the two main parameters to determine the excess relative rates of lung cancer. Results in terms of the BEIR IV model and of models that are more suitable for the computation of probabilities of causation will be presented in this section.

For a direct comparison of the Czech data (follow-up to 1985) to the BEIR IV analysis of the western cohorts of miners, a maximum likelihood analysis, in terms of eqn (4), has been performed (Sevc et al. 1993) with the resulting best fit parameters:

$\alpha = 0.028$

$$\beta_i = \begin{cases} 0 & t < 5 \\ 1 & 5 \le t < 15 \\ 0.68 & 15 \le t < 25 \\ 0.1 & 25 \le t \end{cases} \text{ and } \gamma_j = \begin{cases} 2.2 & a < 55 \\ 1 & 55 \le a \le 64 \\ 0.64 & 64 < a \end{cases} . \quad (10)$$

The excess relative rate, $f(C)$, at $C = 100$ WLM, is represented in the (a–e) diagram of Fig. 3. As a difference to the results from the pooled western cohorts, it is notable that at young ages and short times after exposure the relative rates are higher. On the other hand, it will be seen in a subsequent section that the lifetime attributable risks obtained with the S cohort are nearly the same as with the evaluation of

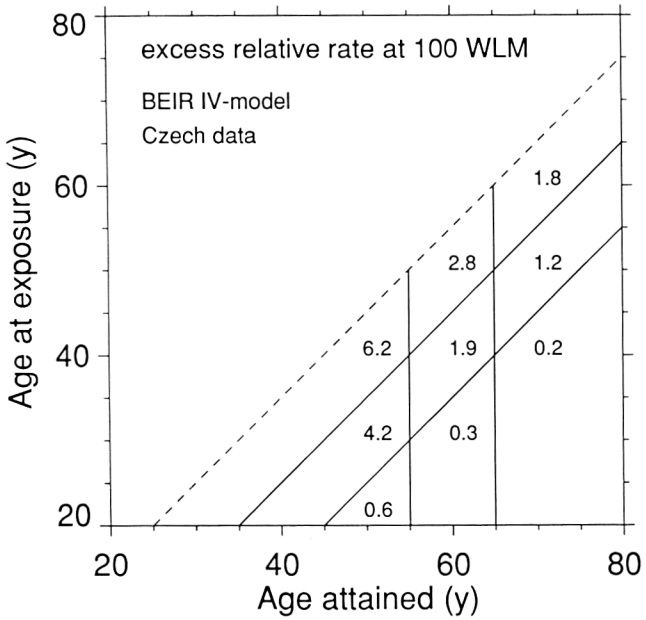

Fig. 3. Regions, in the age-attained vs. age-at-exposure plane, of constant excess relative rate after a single exposure to 100 WLM. The values have been derived for the Czech S cohort with the BEIR IV model [eqn (4)] and the parameters of eqn (10).

the BEIR IV Committee and with the model of Jacobi et al. (1992).

The solution of eqn (10) is suitable for comparison purposes, but it shares with the original BEIR IV treatment the problem of the discontinuities that make it unsuitable for the derivation of probabilities of causation. Added maximum likelihood computations have, therefore, been performed with a model that utilizes smooth analytical dependencies on a and t. The results of these calculations will permit a comparison to the model chosen by Jacobi et al. (1992).

Results for the S cohort in terms of an analytical model

A characteristic of the Czech data is their seeming nonlinearity, i.e., an apparent trend of higher excess risk per unit exposure at lower exposures which is found in analyses based on national rates of lung cancer. As indicated in the earlier report, the nonlinearity may be an artifact, at least in the initial part of the exposure response relationship. It could partly be a reflection of substantially higher baseline lung cancer rates among the miners relative to the national rates.[‡‡]

[‡‡] Increased domestic radon exposures have been invoked, in the review of this article, as a possible cause for the seemingly higher baseline rates among the miners. This possibility has been considered in the earlier article (Sevc et al. 1993), and a rough calculation has led to the conclusion that an average domestic exposure of 100 WLM would be required. Such an average domestic exposure appears unlikely in view of the fact that most of the miners did not come from the region of the mines and that they had lodgings of light construction that were unlikely to have excessive radon levels.

In the range of higher exposures, an exposure rate effect may be present—low exposure rates being more efficient. A linear model will be used here for the derivation of probabilities of causation. How to account, in a possible future improvement, for a dependence on dose rate or duration of exposure is left open.

In a maximum likelihood evaluation of the Czech data a solution has been obtained that depends on age attained, a, and on time since exposure, t. For a hypothetical brief exposure the excess relative rate at age attained a is

$$f(C) = 0.5Ce^{-0.05a - 0.09\eta}, \qquad (11)$$

where (for $t \geq 5$)

$$\eta = \begin{cases} 0 & 5 \leq t \leq 15 \\ (t - 15) & 15 < t \end{cases},$$

and where C is the exposure received at age $e = a - t$.

To facilitate the maximum likelihood calculation for the actual protracted exposures of the miners, eqn (11) has not actually been integrated over the distribution of times since exposure, t. The distribution has, instead, been approximated by assigning, at any age attained, the lagged cumulated exposure, $C(a)$, to the age, $e_m(a)$, when one-half of the exposure $C(a)$ had been received. e_m is termed the age at median exposure.

The maximum likelihood solution according to eqn (11) is depicted in the $(a$–$e)$ diagram of Fig. 4. As this figure is based on an analytical approach, it is most readily compared to the model of Jacobi et al. (1992) in Fig. 2. It shows the same differences between the

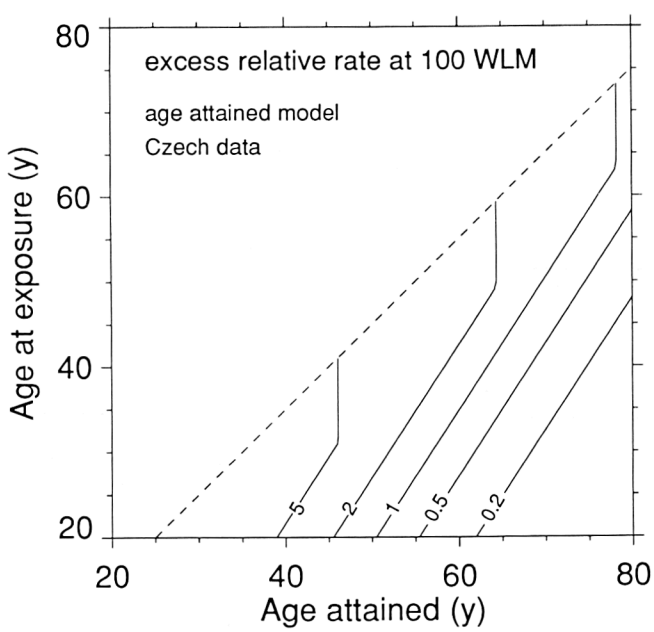

Fig. 4. Lines, in the age-attained vs. age-at-exposure plane, of constant excess relative rate after a single exposure to 100 WLM. The dependencies are derived for the Czech S cohort with the age-attained model [eqn (11)].

Czech data and the data from the western cohorts (i.e., higher excess relative rates per 100 WLM at young ages and short times after exposure).

As in the comparison of Figs. 1 and 2, the choice of different models for the same data set does not lead to very different results. A further comparison between models has been performed for the Czech data with added maximum likelihood calculations in terms of an analytical age-at-exposure model that is fairly close to the one chosen by Jacobi et al. (1992). The result is shown in the Appendix. The conclusion is the same—the difference between the western data and the Czech data prevails; the influence of the model is minor.

Lifetime attributable risks

Figs. 1–4 represent relative rates in their dependence on age attained and age at exposure. For a more complete comparison of risk estimates, lifetime attributable risks are needed. For their calculation, absolute excess rates are required. The subsequent calculations are analogous to those performed by Land and Sinclair (1991) for the ICRP, i.e., they are based on the age-specific lung cancer rates and the life expectancies given in Land and Sinclair (1991) for the U.S. population with a lifetime lung cancer risk of 0.065.

Figs. 5 and 6 give the absolute excess rates due to 100 WLM at the specified age at exposure and age attained. Fig. 5 represents these values for Jacobi's model (Jacobi et al. 1992) and Fig. 6 gives the results obtained with eqn (11) and the Czech data. At the right-hand side of each graph, excess lifetime attributable risks are given which result from a single exposure to 100 WLM at the specified ages at exposure. For comparison, results are also given with dotted lines for the BEIR IV model in Fig. 5 and for the age-at-exposure model [eqn (A1)] in Fig. 6. In spite of the differences between the dependencies on age and time for the two data sets, the overall lifetime risks, in their dependence on age at exposure, are strikingly similar.

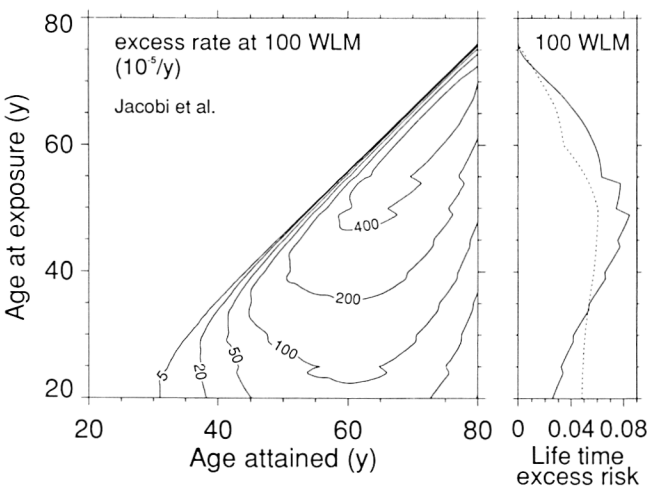

Fig. 5. Left panel: Lines, in the age-attained vs. age-at-exposure plane, of constant excess rate per 100,000 males and year after a single exposure to 100 WLM. The dependencies are derived with the model of Jacobi et al. (1992). Right panel: Excess lifetime attributable risk following an exposure to 100 WLM at the specified age; full line: Jacobi's model; dotted line: BEIR IV model. The values are obtained with baseline rates for lung cancer mortality and with life expectancies for the U.S. male population (see Land and Sinclair 1991).

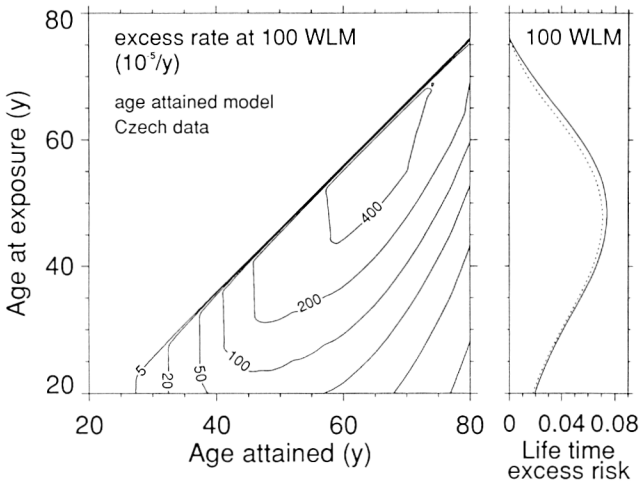

Fig. 6. Left panel: Lines, in the age-attained vs. age-at-exposure plane, of constant excess rate per 100,000 males and year after a single exposure to 100 WLM. The dependencies are derived for the Czech S cohort with the age-attained model [eqn (11)]. Right panel: Excess lifetime attributable risk following an exposure to 100 WLM at the specified age; full line: age-attained model [eqn (11)]; dotted line: age-at-exposure model [eqn (A1)]. The values are obtained with baseline rates for lung cancer mortality and with life expectancies for the U.S. male population (see Land and Sinclair 1991).

The risk estimates would decrease if, in the analysis of the Czech data, a model were used that includes higher spontaneous rates. On the other hand, the response in the high exposure range could increase for lower exposure rates. It is therefore conceivable that the overall effect of the two corrections would be minor with respect to risk estimates.

PROBABILITIES OF CAUSATION

The (*a*–*e*) diagrams have indicated differences between the results for the western cohorts and the Czech uranium miners. The BEIR IV Committee deduced its model and the value of the parameters from a comparison between several cohorts of uranium miners and from a joint analysis of these cohorts. The results of this pooled analysis differ, in some regards, from the results for the Czech miners; however, upon closer examination there are similar, if not bigger, differences between the western cohorts themselves. The Malberget cohort appears to be the only one that shows, beyond the dependence on time since exposure, also a marked decrease of the relative risk

with age attained. Similarly the decrease of the excess rate with time after exposure is not present to the same degree in the four western cohorts; it is most clearly seen in the Eldorado cohort. It is possible to conclude that the results of the BEIR IV Committee represent an average but that there are substantial differences. While these differences could be a matter of the magnitude of the exposures in the different cohorts, this does not establish a clear-cut difference. In fact, the Czech cohort, with its high exposures, resembles more (in its results) the low-exposure western cohorts, namely the Malberget and the Eldorado cohorts. In view of these complexities it may be safer, for the computation of probabilities of causation, to weigh more heavily the low-exposure cohorts or the low-exposure parts of the cohorts. This would seem to support the dependencies that are seen in the Czech cohort and in the low-exposure western cohorts.

Fig. 7 exemplifies the probabilities of causation for an assumed exposure of 100 WLM over 20 y (upper panel) and 5 y (lower panel) with different ages at start of exposure. These results are given for the western cohorts in terms of Jacobi's model (1992) (solid lines) and for comparison with dotted lines, for the BEIR IV model. Analogous plots are given for the Czech data in Fig. 8. It is seen that the two models of eqns (11) and (A1) are nearly equivalent; it is also seen that the probabilities of causation at young ages are substantially larger.

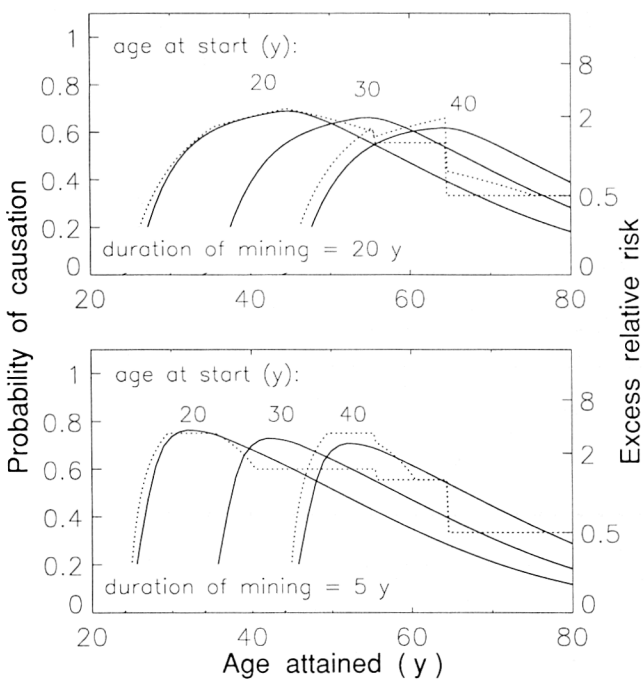

Fig. 7. Probability of causation (left ordinate) and the corresponding excess relative rate (right ordinate) for a total cumulated exposure of 100 WLM; full lines: Jacobi's model; dotted lines: model of the BEIR IV committee. A duration of exposure of 20 y (upper panel) or 5 y (lower panel) is assumed.

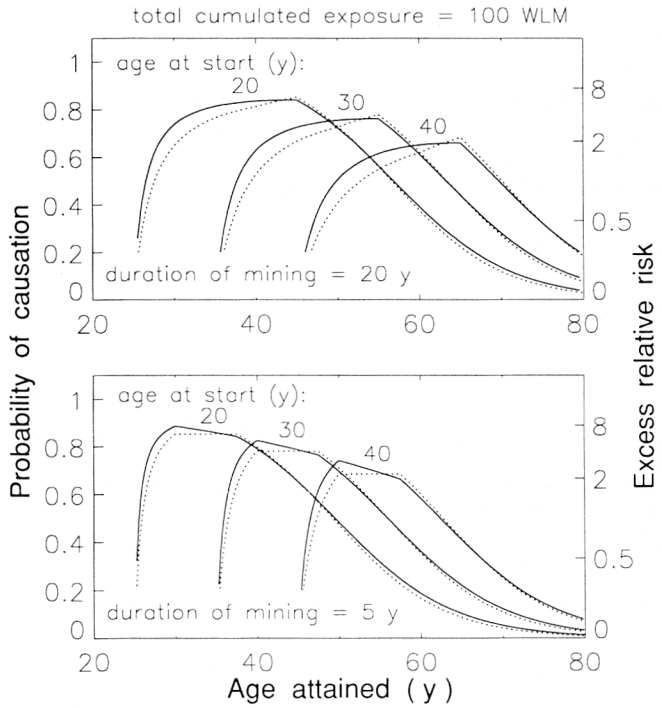

Fig. 8. Probability of causation (left ordinate) and the corresponding probability of causation (right ordinate) for the models with dependence on age-attained [eqn (11), full lines], or on age at exposure [eqn (A1), dotted lines]. The values are based on the analysis of the Czech S cohort. A duration of exposure of 20 y (upper panel) or 5 y (lower panel) is assumed.

CONCLUSION

The results obtained by the BEIR IV Committee for the main western cohorts of radon-exposed miners are compared with an analysis, in terms of linear models, of the S cohort of Czech uranium miners, and this comparison is extended to the derivation of probabilities of causation. Also included in the comparison is the new model of Jacobi et al. (1992). The analysis of the S cohort shows, in agreement with the results of the BEIR IV Committee, that the two parameters—age attained and time since exposure—are, apart from the cumulated exposures, the main parameters that determine the excess relative risk. The dependencies obtained with the S cohort are, however, more markedly dependent on age and on time since exposure than those obtained by the BEIR IV Committee. According to the Czech data, the excess risks decrease faster with time after exposure, although this may partly reflect the fact that a number of lung cancer deaths were still unreported in the follow-up period from 1980–1985.

The marked dependence on time after exposure is in line with the treatment by the BEIR V Committee (1990) of the lung cancer risk among the survivors of the atomic bombs. For lung cancer, the committee recommended a relative risk model with no depen-

dence on age at exposure or age attained but with a term for time after exposure which is not far from the decrease obtained with the S cohort, i.e., a decline by a factor of 5 over the period 10–30 y after exposure.

Fits of similar quality and with nearly the same results are obtained from an age-at-exposure model with a dependency on time after exposure. The age-attained model is, in the present analysis, preferred for computational convenience.

Lifetime attributable risks obtained from the BEIR IV analysis, from Jacobi's model, and from the 1985 follow-up of the S cohort are nearly equal. There exist, nevertheless, differences that are important for the determination of probabilities of causation in the rare cases of lung cancer at young ages. The Czech data indicate higher excess relative rates for lung cancers at younger ages than deduced by the BEIR IV Committee. For cases of lung cancer diagnosed between ages 40 and 60 y, probabilities of causation in excess of 0.5 are inferred from the Czech data for lagged cumulated exposures below 100 WLM. For higher ages and longer times after exposure the Czech data suggest somewhat lower excess rates than the BEIR IV Committee, but this may partly be a matter of an incomplete follow-up in the last period of the Czech study. Similar conventions for compensation are thus suggested by the western data and the Czech data for the majority of the lung cancers that occur at ages beyond 60 y. For the early, infrequent lung cancers, the Czech data suggest a more liberal compensation practice.

In all epidemiological studies, with the exception of the Chinese tin miners' study (Zhen et al. 1993), the majority of miners were adults at the start of mining. It must thus be noted that the present results, while they indicate reduced lifetime attributable risks for young ages at exposure, cannot be extrapolated to ages below 20 y.

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APPENDIX
Comparison of the Age-at-Exposure Model with the Age-Attained Model for the Czech Data

Maximum likelihood computations with the age-at-exposure model are difficult for protracted exposures with the available software.[††] The following simplified form of an age-at-exposure model has therefore been chosen. For a brief exposure, the analogue compared to the age-attained model of eqn (11) is

$$f(C) = \alpha C e^{-\gamma e - \beta \eta} \tag{A1}$$

with the same relation as in eqn (11). Using the same numerical approximation in terms of age at median exposure as with eqn (11), the maximum likelihood solution is obtained:

$$f(C) = 0.25 C e^{-0.049 e_m - 0.15 \eta}. \tag{A2}$$

As before, the exposure is given in WLM, and a, e_m, and t are given in years. The results are illustrated in Fig. 1A. The comparison with Fig. 4 shows that the excess relative rates are nearly the same with the two models. This again shows that the choice of the model is rather uncritical.

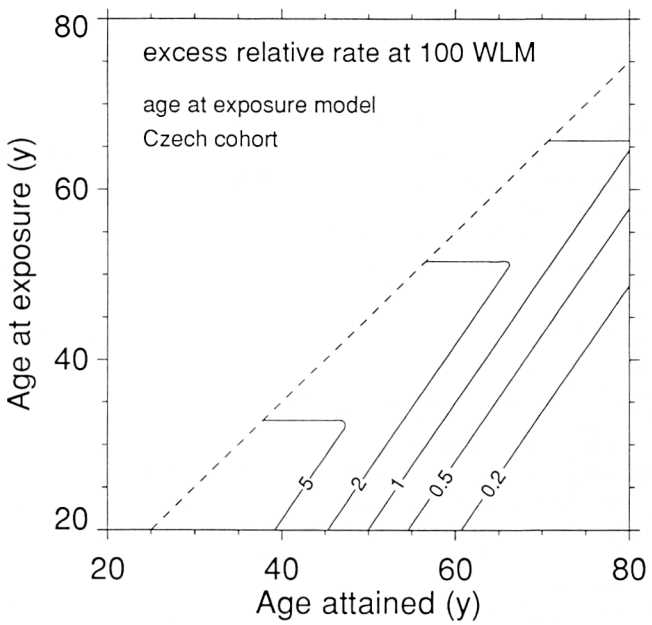

Fig. A1. Lines in the age-attained vs. age-at-exposure plane of constant excess relative rate after a single exposure to 100 WLM. The dependencies are derived for the Czech S cohort with the age-at-exposure model [eqn (A1)].

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