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A Comparison of Radiological Risk Assessment Models

Risk Assessment Models Used by the BEIR V Committee, UNSCEAR, ICRP, and EPA (for NESHAP)

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A COMPARISON OF RADIOLOGICAL RISK ASSESSMENT MODELS
Risk Assessment Models Used by the BEIR V Committee, UNSCEAR, ICRP, and EPA (for NESHAP)

by

Linnea E. Wahl

ABSTRACT

Radiological risk assessments and resulting risk estimates have been developed by numerous national and international organizations, including the National Research Council's fifth Committee on the Biological Effects of Ionizing Radiations (BEIR V), the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), and the International Commission on Radiological Protection (ICRP). A fourth organization, the Environmental Protection Agency (EPA), has also performed a risk assessment as a basis for the National Emission Standards for Hazardous Air Pollutants (NESHAP). This paper compares the EPA's model of risk assessment with the models used by the BEIR V Committee, UNSCEAR, and ICRP. Comparison is made of the values chosen by each organization for several model parameters: populations used in studies and population transfer coefficients, dose-response curves and dose-rate effects, risk projection methods, and risk estimates. This comparison suggests that the EPA has based its risk assessment on outdated information and that the organization should consider adopting the method used by the BEIR V Committee, UNSCEAR, or ICRP.

INTRODUCTION

Risk Assessments

Risk assessment has been defined by the National Research Council (NRC) as "... the characterization of the potential adverse health effects of human exposures to environmental hazards" (NRC 1983, p. 18). An assessment of the risks from all types of hazards, including radiological hazards, requires all or some of the following activities (NRC 1983):

- hazard identification, which is done to determine whether a particular hazard has a corresponding health effect;
- dose-response assessment, in which the relation between the magnitude of the dose and the probability that the health effect will occur is determined;
- exposure or dose assessment, which is the determination of the extent to which humans will be exposed to the hazard; and
- risk characterization, which describes the nature and the magnitude of the human risk, including uncertainties surrounding that risk.

It is this last activity, risk characterization, that integrates the results of the previous activities into a risk statement that includes one or more quantitative estimates of risk (Cohrssen and Covello 1989).

Radiological risk assessments and resulting risk estimates have been developed by numerous organizations. Some organizations, such as the NRC's fifth committee on the Biological Effects of Ionizing Radiations (BEIR V) and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), attempt to summarize the complex data available on the effects of radiation in a form that is easily applicable. Other organizations, such as the International Commission on Radiological Protection (ICRP), recommend a system of limits for controlling radiation doses. Each of these organizations regularly assesses new data on the risks of ionizing radiation and publishes risk estimates. Each also uses a slightly different method of calculating risk estimates.

A third type of organization uses the risk assessment information published by other organizations to set limits on radiation doses. This third type is exemplified by the Environmental Protection Agency (EPA), which regulates radioactive air emissions, among other hazardous air pollutants.

The National Emission Standards for Hazardous Air Pollutants

In 1977, Congress amended the Clean Air Act to address emissions of radioactive materials into the air, and in 1985, the EPA promulgated standards for regulating such emissions called the National Emission Standards for Hazardous Air Pollutants (NESHAP). The bases for these standards were published by the EPA in 1989 in three background information documents. Volume I, *Risk Assessments Methodology* (EPA 1989a), describes the results of the four risk assessment activities listed earlier. Volume II, *Risk Assessments* (EPA 1989b), describes each of four sources of radioactive air emissions and the technology used to control these emissions. Volume III, *Economic*

Assessment (EPA 1989c), considers the costs and benefits of controlling emissions from each source.

It is the EPA's risk assessment method, documented in Volume I, that is of interest in this paper. Specifically, this paper considers the parameters used by the EPA to calculate its risk estimates—the estimate of how many deaths from cancer or cases of serious genetic disease will occur in a general population that is exposed to a given amount of low linear energy transfer (LET) radiation. Because these risk estimates form the technical basis for setting radioactive air emissions limits, they are of most interest to those responsible for meeting the EPA's radioactive air emissions standards.

Comparing Risk Assessment Models

The model used to perform a risk assessment is a function of several parameters, including populations from which data are obtained, relationships between doses and effects, and methods used to project risks into the future. Because our knowledge of radiation effects is limited, there is much discussion among organizations about the interpretation of data and the choice of values for these parameters.

- Populations used in epidemiological studies and population transfer coefficients chosen vary among risk assessments. Some studies provide better data than others; some populations better represent the population of concern. In addition, differences in population characteristics (lifestyles, cancer rates, industrial exposures) must be considered in transferring results obtained from one population to another population. Approximating and applying a population transfer coefficient allows for such differences.
- The dose-response curve and dose-rate effect applied by various organizations can differ. For example, some organizations apply a linear-quadratic dose-response curve and assign no dose-rate effect to leukemias; others apply a linear relationship and a dose-rate effectiveness factor of 2–10. As more data are obtained, we can better predict the relationship between a given radiation dose and the biological response (death or disease). New data help us develop aspects of this relationship that were previously only guessed at.
- Risk projection methods used to predict the mortality from or incidence of cancer and genetic disease that will occur within a given population can be of several types. Cancer risk projections use additive or multiplicative methods; genetic risk projections may use direct or indirect methods. Each method requires, in turn, choices from among several additional parameters including death rates, specific causes of death, population statistics, and dose calculations.

Because of the wide variation in values used in risk assessments, the numerical risk estimates made by each organization differ. As with the EPA's radioactive air emission standards, these estimates are often used to set limits and thus affect the ways in which industry and the government run their operations.

This paper compares the values assigned to each of these major risk assessment parameters by the BEIR V Committee (NRC 1990), UNSCEAR (UNSCEAR 1988), and ICRP (ICRP 1991) with the values assigned by the EPA in preparing its radioactive air emission standards (EPA 1989a). The BEIR V and UNSCEAR reports are risk assessment documents; the ICRP report is a planning document based on a risk assessment; and the EPA report is a regulatory document, also based on a risk assessment.

Please note that this comparison is limited to the parameters used to develop risk estimates; other parameters, such as pathway analyses used to assess exposure potential, are not considered. Nor is it within the scope of this paper to consider the EPA's application of its risk estimates in setting radioactive air emission limits. These may, however, be useful topics of future research.

LITERATURE REVIEW

What previous comparisons have been made of radiological risk assessment methods? To answer this question, the literature was searched using various computer search programs: TOXLINE (searched for documents published from January 1965 through December 1992), DIALOG (searched for documents published from January 1974 through March 1993), and the NTIS technical report system (searched for documents published from January 1982 through March 1993). The key phrase used in these searches was *risk assessment*. These searches turned up surprisingly little and nothing that compared risk assessment methods.

The annual indexes of several leading radiological and risk analysis journals were searched going back through 1983: *Health Physics, Journal of Radiological Protection, Radiation Research, Applied Radiation and Isotopes, Journal of Environmental Radioactivity, Nuclear Technology,* and *Risk Analysis*. Of these, the first two were of most value; no comparisons of risk assessment methods were found in the others.

Other comparisons of radiological risk assessment methods turned up incidentally during the preparation of this paper or were recommended by colleagues. Of course, many standard texts (such as Till and Meyer 1983) cite the results of various organizations' risk assessments. The organizations themselves do an excellent job of comparing their methods and results with those of previous analyses.

One such recent report, National Council on Radiation Protection and Measurements (NCRP) Report No. 116 (NCRP 1993), reexamines earlier NCRP recommendations (NCRP 1987) in light of the risk assessments prepared by the BEIR V Committee (NRC 1990), UNSCEAR (1988), and ICRP (1991). The report is introduced with a table comparing the NCRP's current parameters with those chosen by the NCRP in its 1987 report and by the ICRP in its 1991 report. In general, the current parameters closely parallel those of the ICRP. The few differences are discussed in a brief appendix to the NCRP report.

In addition, several documents were located which, although they do not compare risk assessment methods, do discuss one or more specific parameters intrinsic to risk assessments. One such journal article by Fabrikant (1990) provides an excellent overview of the major risk assessment parameters, including dose-response curves; latent periods; population factors such as age at which a radiation dose was received, age at death, sex, and death rates; types of cancers; dosimetry; dose-rate effects; risk projection methods; and risk estimates. The author discusses the available data and the major sources of uncertainty for each of these parameters. He concludes that when these

data are simplified by organizations such as the BEIR V Committee, UNSCEAR, ICRP, and EPA in public statements about radiation risk, the results may be misleading. This underscores the importance of choosing parameter values and comparing risk assessments carefully.

Among the comparison documents reviewed was "Radon Risk Projection: Validating the NCRP and Other Models" by Harley (1989). In this paper, three models for projecting risk from radon are compared. These methods differ in the way in which they handle the reduction in relative (or multiplicative) risk with increasing time since the dose was received. The three methods, described and displayed as mathematical equations, are

- the NCRP method, which applies an exponential reduction in lung cancer risk with time since the radiation dose was received;
- the Ontario method, which assesses the reduction in lung cancer risk across three time segments; and
- the BEIR IV method, which assesses the reduction across two time segments.

To illustrate the differences between the three methods, the author plots the curves produced by each method for a single exposure to 1 working-level-month (WLM) in 1 year for a person at ages 20, 40, and 60. These curves plot attributable lung cancer cases per year per million people against attained age.

Further variations among the methods are apparent when the author validates the methods by calculating risks for various occupationally exposed cohorts (populations of miners from five different studies) and for typical indoor environments (populations of male smokers and nonsmokers exposed to indoor concentrations of 1 and 4 pCi/L). The percent excess lifetime risks of lung cancer projected by the different methods are compared for each validation situation.

The author's technique of applying each method using realistic parameter values provides a fair basis for comparison, especially in the absence of an experimental risk estimate. When such an estimate exists, as is expected from the case-control studies of radon-caused lung cancer currently underway in New Jersey and Pennsylvania, the applications of these three methods can be compared against this value and the validity of each method can be judged. When differences between the projections produced by the methods are identified, the individual parameters chosen for each method can be scrutinized to determine the cause of the discrepancy. The author does this to explain why the projections of the BEIR IV Committee's method are much greater than those of the other methods.

This is just the sort of scrutiny employed by Thomas et al. (1992) in "Definition and Estimation of Lifetime Detriment from Radiation Exposures: Principles and Methods." This article explains the different ways in which lifetable analyses have been applied by various organizations to estimate radiation risks. (The basic concepts of lifetable analysis are summarized in an appendix.) The authors also consider the most useful methods of measuring the effects of radiation on populations. They illustrate their points by comparing the risk assessment methods (based on multiplicative methods only) used by several BEIR committees with those used by the UNSCEAR in its 1988 report.

The parameters that differ the most from one organization's application of lifetable analyses to another's (and hence, have the greatest effect on the resulting risk assessments) include

- measures of lifetime risk and life expectancy,
- baseline death rates,
- population age distributions, and
- methods of projecting excess risks.

The authors present three different measures of lifetime risk, their mathematical expressions, and the advantages and disadvantages to using each. They present two different measures of life expectancy:

- loss of life expectancy, which is the difference between how long the mean exposed population will live and how long the mean unexposed population will live; and
- loss of life expectancy among exposure-induced deaths, which is the total loss of life expectancy divided by the fraction of the population suffering that loss.

As with the measures of lifetime risk, the authors present the mathematical expressions and advantages and disadvantages of using each measure of life expectancy.

Thomas et al. present two options for choosing death rate baselines: one uses the death rate among the population being studied as the baseline, and the other uses the death rate among a different population than the one being studied.

There are also two population age distribution options: one option, chosen by the BEIR V Committee, is to use the age distribution that will eventually result from a constant birth rate; the other option, chosen by the UNSCEAR, is to use the current age distribution of a real or hypothetical population. The authors point out that these two options result in risk estimates that differ considerably.

They discuss several multiplicative methods, providing mathematical expressions for each, and consider the effects of latency and plateau periods. The BEIR V Committee's variable multiplicative (or relative) risk method, which depends on age

and time, is compared with the constant multiplicative risk method used by the UNSCEAR. Thomas et al. conclude that there are probably many other parameters that strongly affect risk projections and when possible, these confounders and modifiers should be incorporated into risk projection methods.

The population transfer issue (how all the parameters used in risk assessment are applied or transported to a population that is unlike the original population) is another, "most important and most controversial" (p. 265), concern of the authors. They present the BEIR V Committee's conclusion, which was that multiplicative risks transfer better than do additive risks, but suggest that this conclusion is tentative.

Thomas et al. note that although the risk estimates by the BEIR V Committee and the UNSCEAR are remarkably similar, the comparison between them is confounded by the different methods they use; thus, any differences between the estimates cannot be attributed to differences in a particular factor. Indeed, the authors state that the similarities " . . . should be viewed as coincidence" (p. 270) and not as evidence that parameter choice is unimportant.

These risk estimates are the basis for the comparison presented by the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC) of the President's Office of Science and Technology Policy (CIRRPC 1992), which compares the cancer risk estimates calculated by the BEIR V Committee and UNSCEAR. This committee was requested by the U.S. Department of Defense to provide a consensus on risk estimates that could be applied to risk assessments performed by government agencies, and its objective was to identify areas in which the BEIR V Committee and UNSCEAR agreed.

In spite of the different methods these organizations used, the CIRRPC developed a technique for comparing their cancer risk estimates by applying a dose-rate effectiveness factor (see "Comparison of Risk Estimates" in the present paper). The committee also developed a statement on the uncertainty associated with these risk estimates and recommended that this statement accompany risk estimates that are provided for decision-making or public information purposes.

Another discussion of cancer risk projection methods is provided by Little and Charles (1989) in their article, "Estimation of Population Cancer Risks from the DS86 Bomb Survivor Data." By developing a cancer risk projection method that is a hybrid of the additive and multiplicative methods, Little and Charles claim in this paper to more accurately estimate cancer risks to the Hiroshima and Nagasaki survivors. They discuss several parameters that affect cancer risk projection methods and risk estimates, including transfer of data across populations, latency and plateau periods, dose-rate effect, and populations used as a basis for death rates. To validate their method, the

authors compare their results with cancer risk estimates obtained by other organizations.

Little and Charles argue for their hybrid risk projection method and the use of death rates from the population of Hiroshima and Nagasaki survivors by comparing the cancer risk estimates obtained using their method with estimates calculated by the BEIR III Committee and by the ICRP in its 1977 report. The estimate obtained using the hybrid method is the same as the BEIR III Committee's estimate and is four times the ICRP estimate. The authors' estimate, however, is based on 1986 estimates of doses received by the Hiroshima and Nagasaki survivors, while the BEIR III and ICRP estimates are based on 1965 dose estimates. It is not clear that these estimates can be compared. It is clear, however, that a proposed method can be effectively validated by comparing results obtained by that method with results obtained by methods of other organizations, provided the input data are comparable.

Genetic risk projection methods are the subject of an article by Abrahamson (1990) in "Risk Estimates: Past, Present, and Future." In this article, the author reviews some of the parameters used in assessing genetic risks from radiation, comparing past choices with current ones. These parameters include doubling dose and mutation component.

In discussing doubling dose, Abrahamson compares values chosen over the past 30 years by various NRC committees (the 1956 committee on the Biological Effects of Atomic Radiation [BEAR] and the BEIR I, III, and V Committees) with those chosen by the UNSCEAR in 1958 and 1988. He notes that the early estimates of doubling dose were inaccurate because they were based on a linear extrapolation from high doses to mice and did not recognize the dose-rate effect.

The mutation components for genetic diseases of complex etiology are also reviewed by this author. He compares the BEIR I Committee's estimate with estimates in past UNSCEAR reports (from 1972, 1977, 1982, and 1986). Interestingly, he states that neither the UNSCEAR in its 1988 report nor the BEIR V Committee used a mutation component; the latter statement does not seem to be true (see "Comparison of Genetic Risk Projection Methods" in the present paper).

By reviewing the logic of past and current choices, Abrahamson suggests the direction that future choices may take. He states that we would do well to base our genetic risk estimates on the most sensitive and accurately derived mutation rates of mice.

The measure chosen to represent cancer risks is the topic of "Widening the Discussion on Tolerability of Risk" (Hoaksey 1990). Hoaksey argues for the use of

measures of reduction in life span (loss of life-expectancy) over measures of probability of injury or death in an attempt to broaden the perspective of radiation risk and improve our basis for judging dose limits. In the course of this argument, the author discusses several parameters used in calculating both measures and reviews the parameter choices made by various organizations. These parameters include dose-rate effectiveness factor, cancer risk projection method, and risk estimates.

Using these parameters, Hoaksey compares probability of injury or death to loss of life-expectancy. He also discusses the differences between two variations of the loss of life-expectancy: individual and population-averaged. The author concludes that the use of population-averaged loss of life-expectancy is preferable to the use of probability of injury or death.

COMPARISON OF POPULATIONS USED IN STUDIES

Background

In choosing populations for study, epidemiologists consider several factors, including population size and apportionment. Increasing the size of the population improves the precision and reduces the random error in the data. In addition, reasonable precision (for a given resource expenditure) is achieved by dividing the population into equal numbers of cases and controls (Rothman 1986). Other considerations in choosing a population include the following (NRC 1983):

- how results were extrapolated from a small segment of a population to the entire population;
- how doses from radioactivity transported through environmental pathways were predicted;
- how variations in human activities, such as dietary habits and hobbies, were taken into account;
- whether point (single) estimates or ranges were used;
- how differences in timing and duration of dose and in age at which a dose was first received were estimated;
- how the size and features (for example, age structure) of the population were estimated;
- how doses to special risk groups, such as pregnant women and young children, were estimated; and
- whether exposures to other hazards (such as chemical carcinogens) were considered.

It is important to note that epidemiologists and risk assessors generally base dose assessments on data from several studies and hence, several different populations. This is in part because individual studies cannot be controlled in all respects and because interpretations of the results of individual studies may be complicated by issues such as confounding factors and control group selection. In addition, pooling data increases the population size, thereby improving precision and reducing random error, as discussed earlier.

Human vs. Animal Populations

Populations for epidemiological studies can be human or animal, depending on the type of data that is needed. Although data from human populations are preferred, deliberate irradiation of humans without diagnostic or therapeutic justification is unacceptable (in spite of the fact that we are all exposed to background radiation), and much of our radiological data are based on animal studies.

Data from human and animal populations are often complementary and are used to reinforce one another. For the following activities, the available human data are inadequate and must be interpreted using concepts developed from animal studies (NRC 1980):

- predicting the effects of high-LET external radiations, including neutrons;
- predicting the effects of low or varying dose rates and of various dose fractionation schemes;
- understanding the mechanisms of mutagenesis, carcinogenesis, and developmental damage; and
- predicting the uptake, distribution, retention, dose distribution, and biological effects of internally deposited radionuclides.

Animal studies, however, raise a number of concerns, including the validity of extrapolating from results obtained under experimental conditions to conditions relevant to population doses (using variables such as dose rates and fractionation schemes) and extrapolating from experimental organisms such as mice, in which radiation effects may be estimated with some confidence, to humans, in which there are wide variations in radiation sensitivity (NRC 1980).

Both the BEIR V Committee and EPA followed two general principles, first stated by the BEIR I Committee (NRC 1972), that relate to the difficulties of extrapolating from animal data to humans. These principles are that

- relevant data from all sources should be used, but human data should be emphasized when feasible; and
- reliable data from the lowest doses and dose rates should be used because these data are more relevant to the usual conditions of human irradiation.

Cancer Risk

In the assessments by the BEIR V Committee, UNSCEAR, ICRP, and EPA, cancer risks were based mainly on a few epidemiological studies and in particular, on data from residents of Hiroshima and Nagasaki in 1950 (the Life Span Study). To support these risk assessments, many more populations, both animal and human, were considered by each study.

It is important to note that although all four assessments are based on the same population of residents of Hiroshima and Nagasaki, the data from this population varies. For example, the EPA used data based on tentative dose estimates made in 1965 (the Tentative 1965 Dosimetry, Revised [T65DR]) (Auxier 1977), which overestimated the dose equivalent to organs. The BEIR V Committee, ICRP, and UNSCEAR used data based on dose estimates made in 1986 (the Dosimetry System 1986 [DS86]) (Shimizu et

al. 1987), which corrected some of the mistakes made in the earlier dosimetry system. This is discussed further in "Comparison of Cancer Risk Projection Methods" in the present paper.

Genetic Risk

The assessments for genetic risks by the BEIR V Committee, UNSCEAR, ICRP, and EPA relied on animal (especially mouse) data to supplement human data. To determine human genetic risk by extrapolating from animal data, three assumptions must be made (UNSCEAR 1986).

- The amount of genetic damage induced by a given type of radiation under given conditions in the animal species is the same in human germ cells.
- Biological factors (such as sex, germ cell stage, and age) and physical factors (such as quality of radiation and dose rate) similarly affect genetic damage in the animal species and in humans.
- The relationship between dose of low-LET radiation and frequency of genetic effects is linear at low doses and low dose rates (see "Comparison of Dose-Response Curves" in the present paper).

Genetic effects, by definition, require that at least one generation must pass before they are expressed, and their expression is affected by the exposed population's sex, age, and probability of having children. Genetic risks determined from human data are based on the assumption that all the exposed people were of reproductive age and wanted to have children. In the irradiation of an entire population, the reproducing people are a fraction of the total, and damage to the germ cells of the nonreproducing people in the population does not pose a genetic risk. If the irradiation is neither random nor uniform (as is true of the available human populations), the expression of genetic effects is difficult to quantify, and a reduction factor may be required to adjust genetic risk estimates (UNSCEAR 1988).

BEIR V Committee Populations

Cancer Risk

As noted earlier, the BEIR V Committee cancer risk assessments were based on a few major populations. To validate these assessments, however, studies of many additional animal and human populations were reviewed. For example, no fewer than 34 additional studies were cited in support of the risk assessment for breast cancer.

Human Populations. The BEIR V Committee estimated risks for breast cancer, respiratory tract cancer, digestive tract cancer, leukemia, and other nonleukemia cancers. Human populations were used and were chosen based on the type of cancer.

For breast cancer, four populations were used:

- residents of Hiroshima and Nagasaki in 1950, most of whom were exposed to the atomic bomb (the Life Span Study);
- women examined by fluoroscopy in Canada for tuberculosis from 1930 to 1952;
- women examined by fluoroscopy in Massachusetts from 1930 to 1956; and
- women treated with radiotherapy for postpartum mastitis in New York during the 1940s and 1950s.

For respiratory and digestive tract cancers, the population comprised residents of Hiroshima and Nagasaki in 1950 (the Life Span Study).

For leukemia, two populations were used:

- residents of Hiroshima and Nagasaki in 1950 (the Life Span Study) and
- people treated with radiotherapy for ankylosing spondylitis in the United Kingdom from 1935 to 1954.

A third population, women treated with radiotherapy in several countries for cervical cancer, may also have been used in leukemia risk calculations; the BEIR V Committee report is unclear on this point.

For all other cancers (except leukemias), the study population comprised residents of Hiroshima and Nagasaki in 1950 (the Life Span Study).

Animal Populations. In general, the BEIR V Committee cancer risk assessments considered animal populations only when necessary to validate or understand data from human populations.

Genetic Risk

Human Populations. The BEIR V Committee used several human populations, divided into three sets, to assess genetic risk. The first set consisted of people with genetic disorders resulting from spontaneous mutations. These disorders included dominant autosomal disorders, sex-linked recessive disorders, recessive autosomal disorders, chromosomal abnormalities, congenital abnormalities, and other multifactorial traits. Multifactorial traits is a group of disorders about which the exact mode of inheritance is unknown and includes such diseases as diabetes mellitus, gout, schizophrenia, affective psychoses, epilepsy, glaucoma, hypertension, varicose veins, asthma, psoriasis, ankylosing spondylitis, and juvenile osteochondrosis of the spine.

The second set consisted of people with genetic disorders resulting from several specific spontaneous mutations that were used to calculate mutation rates. The disorders included dominant autosomal disorders and recessive sex-linked disorders.

The third set was the Hiroshima and Nagasaki survivors and their children, including members of

- a pregnancy termination study,
- a cytogenetic study of the children of exposed parents,
- an investigation of rare electrophoretic variants in children of exposed parents, and
- doubling dose studies.

Animal Populations. In general, mouse populations were used to assess genetic risk when human data were unavailable or inappropriate; a few data points were taken from monkey and marmoset studies. The animals in these studies displayed a specific endpoint, such as dominant and recessive lethal and visible mutations, reciprocal and heritable translocations, congenital malformations, and aneuploidy; multilocus mutations were not included.

UNSCEAR Populations

Cancer Risk

Human Populations. The UNSCEAR considered several populations in determining cancer risks: survivors of the atomic bombings of Hiroshima and Nagasaki; observers of nuclear tests and those exposed to fallout; patients irradiated therapeutically to treat cancers or other disease conditions; workers in nuclear installations, miners, and radiologists; individuals exposed at home to elevated levels of background radiation; and individuals involved in nuclear accidents. Of these, three major populations provided most of the data:

- residents of Hiroshima and Nagasaki in 1950 (the Life Span Study),
- people treated with radiotherapy for ankylosing spondylitis in the United Kingdom from 1935 to 1954, and
- women treated with radiotherapy in several countries for cervical cancer.

Animal Populations. Animal populations were considered by the UNSCEAR in determining cancer risks only when necessary to validate or understand data from human populations.

Genetic Risk

Human Populations. Three different groups of children of Hiroshima and Nagasaki survivors were considered by the UNSCEAR to estimate genetic risks. These groups included

- children in a cytogenetic study,
- children investigated for rare electrophoretic variants, and
- children studied for deficiency variants of nine erythrocyte enzymes.

Animal Populations. The animal populations used by the UNSCEAR to determine genetic risks were those cited in their 1986 report (UNSCEAR 1986), which included mice, marmosets, and monkeys.

ICRP Populations

Cancer Risk

For cancer risk, the ICRP chose to follow the lead of the BEIR V Committee and UNSCEAR: the commission used the Hiroshima and Nagasaki survivors (the Life Span Study) as its major human study population for assessing cancer risks. Other populations were considered (such as patients treated for leukemia, Hodgkin's disease, tuberculosis, ankylosing spondylitis, ovarian cancer, and tinea capitis) to support estimates of organ-specific cancer risks.

The commission made little mention of animal studies in its cancer risk assessment. We can therefore assume that the ICRP, as well as the BEIR V Committee and UNSCEAR, considered animal populations only when necessary to support data from human populations.

Genetic Risk

The ICRP based its assessment of genetic risk on the assessments of the BEIR V Committee and UNSCEAR. As described previously, the human populations used for these assessments were people with genetic disorders resulting from spontaneous mutations and the Hiroshima and Nagasaki survivors and their children. The animal populations used for these assessments were primarily mice but also included marmosets and monkeys.

EPA Populations

Cancer Risk

Human Populations. The EPA based its cancer risk assessments on those used by the BEIR III Committee (NRC 1980), which relied mainly on two populations:

- residents of Hiroshima and Nagasaki in 1950 (the Life Span Study) and
- people treated with radiotherapy for ankylosing spondylitis in the United Kingdom from 1935 to 1954.

Other populations (patients therapeutically exposed to partial-body irradiation, uranium miners, and radium-dial painters) were considered but do not seem to have been used as a source of data.

Animal Populations. In general, the BEIR III Committee's cancer risk assessment considered animal populations only when necessary to validate or understand data from human populations (NRC 1980).

Genetic Risk

The EPA based its genetic risk assessment on the assessment performed by the BEIR III Committee (NRC 1980).

Human Populations. The BEIR III Committee (NRC 1980) used several human populations to assess genetic risk:

- live-born residents of British Columbia with hereditary defects;
- live-born infants in Northern Ireland with autosomal dominant, recessive, sex-linked, congenital, and other traits;
- children of Hiroshima and Nagasaki survivors, including members of a mortality study and a cytogenetic study (the primary population considered by the UNSCEAR in its 1977 report [UNSCEAR 1977]); and
- men who received testicular x-rays.

Animal Populations. The BEIR III Committee used two animal populations to assess genetic risk: mice and marmosets (NRC 1980).

Summary

Table I summarizes the major populations used in risk assessments performed by the BEIR V Committee, UNSCEAR, ICRP, and EPA, and a discussion of the EPA's choices follows.

Table I. Major Populations Used in Studies

Study Population	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Data on Cancer Risk				
Hiroshima and Nagasaki survivors	√	√	√	√
Ankylosing spondylitis patients	√	√	√	√
Fluoroscopy patients	√			
Mastitis patients	√			
Cervical cancer patients		√	√	
Data on Genetic Risk				
Children of Hiroshima and Nagasaki survivors	√	√	√	√
People with genetic disorders	√		√	√
Mice and marmosets	√	√	√	√
Monkeys	√	√	√	

For genetic risks, the EPA's populations included all of those used by the BEIR V Committee, UNSCEAR, and ICRP, except monkeys. This population, however, seems to have been used in only a few studies, whereas mice were used in multiple studies.

COMPARISON OF POPULATION TRANSFER COEFFICIENTS

Background

There are many uncertainties surrounding risk assessments. Some sources of uncertainty can be evaluated using conventional statistical theory and are incorporated into risk assessment parameters such as dose-response relationships and risk projection methods. Other sources of uncertainty cannot be captured by the usual statistical techniques. These uncertainties include assumptions made in estimating doses, in applying results from one nationality to another, and in choosing the "best" values for each parameter.

Not only are these uncertainties difficult to quantify, the approach to them taken by various organizations is difficult to compare. One uncertainty that has been considered by the BEIR V Committee, UNSCEAR, ICRP, and EPA is the uncertainty inherent in applying risks determined in one population to another population. Sometimes called the *transportation problem* or *population transfer coefficient*, this issue is of major concern because most of the organizations' risk assessments are based on results from the Hiroshima and Nagasaki survivors applied to U.S. populations. This extrapolation requires assumptions about diets, industrial exposures, cancer rates, and in general, lifestyles (NRC 1990). This issue is not confined to a population's geographic location; for example, risk assessments for one sex must sometimes be based on data obtained from the other. Indeed, this issue can be expanded to include the classic confounding factors, such as differences between smokers and nonsmokers, taken into consideration by epidemiologists (EPA 1989a).

BEIR V Committee Population Transfer Coefficient

The BEIR V Committee recognized the population transfer issue to be a fundamental problem and considerable source of uncertainty in estimating risks. The committee chose to evaluate this issue by ". . . a consensus of expert opinion as to the uncertainty, expressed in a number on a scale commensurate with ordinary statistical measures of variability" (NRC 1990, p. 220).

The committee obtained this number by judging the range within which it was believed with 95 percent credibility (where credibility is analogous to confidence) to lie. The committee obtained the standard deviation by dividing the width of the range by 3.92. In this way, all types of uncertainty (both statistically calculated and estimated by consensus) were evaluated together to obtain combined measurements of standard error and credibility intervals (analogous to confidence intervals in statistical analyses).

The committee thus estimated the uncertainty in population transfer to be 20%. In terms of geometric standard deviation, this is an uncertainty of 1.2.

UNSCEAR Population Transfer Coefficient

The UNSCEAR questioned the validity of using " . . . risk coefficients obtained from one population for predicting lifetime risks in any other population" (UNSCEAR 1988, p. 489) and attempted to address this concern by using death rates from reference populations (see "Comparison of Cancer Risk Projection Methods" in the present paper) that matched the populations being studied. Even within the same population, however, the committee acknowledged that baseline risks could vary; for example, risks to a resident of Hiroshima or Nagasaki under the stress of an atomic bomb during wartime are not the same as the risks to a generic Japanese resident of today.

To understand the impact of population transfer uncertainties, the committee compared lifetime risk estimates, using the same risk coefficients, for three different populations (having different death rates and demographic characteristics). The results suggested that, in general, lifetime risk projections are insensitive to population differences and that the committee's risk projections are applicable over a broad range of situations.

For these reasons, the committee chose not to deal explicitly with population transfer uncertainties.

ICRP Population Transfer Coefficient

The ICRP also recognized the impact of population differences on risk assessments. The commission suggested that this impact was even greater than that of sex, age, or choice of risk projection method, all of which it found to have considerable effect. The ICRP noted too the lack of general agreement among organizations as to which population transfer coefficient is preferred, whether the same value should be applied to each organ, and which specific population should serve as a reference.

In light of all these difficulties, the ICRP determined that population transfer effects can result in as much as 20% variation in risk assessments. This uncertainty was especially evident when a multiplicative risk projection method was used.

To address these uncertainties, the ICRP considered two transfer techniques: one that applies the absolute mortality rate per unit dose from one population to another population and one that uses the ratio of the increase in the mortality rate for each type of cancer between the two populations. Because the ICRP found no reason to prefer one method over the other, the commission chose to average the two methods, which

essentially averages the probabilities of cancer in each organ for each of several different populations (Japan, U.S., Puerto Rico, United Kingdom, and China). This resulted in a relative probability of cancer for a nominal world population.

EPA Population Transfer Coefficient

As with the BEIR V Committee and UNSCEAR, the EPA considered the problems in extrapolating risk assessments from a population being studied to the U.S. population. And as with other parameters, the EPA considered first the approach taken by the BEIR III Committee (NRC 1980). According to the EPA, the BEIR III Committee ". . . concluded, based largely on the breast cancer evidence, that the appropriate way to transport the Japanese risk to the U.S. population was to assume that the absolute [additive] risk over a given observation period was transferable but that relative [multiplicative] risk was not" (EPA 1989a, p. 6-30). This conclusion was based on the assumption that whatever the cause of variations in baseline cancer rates between Japanese and U.S. populations, these would have no effect on the incidence of radiation-induced cancers. Thus, the effects of radiation and population transfer uncertainties were assumed to be additive (see "Comparison of Cancer Risk Projection Methods" in the present paper).

The EPA also considered the variations in cancer rates for specific organs. For example, if lung cancer risks estimated by applying a multiplicative method to Japanese populations were transported to U.S. populations, the estimated whole-body risk would increase by 20%. On the other hand, if stomach cancer risks (which are relatively low in the Japanese population) estimated in the same way were transported to U.S. populations, the estimated whole-body risk would decrease by 8%.

The EPA concluded " . . . the amount of uncertainty introduced by transporting cancer risks observed in Japan to the U.S. population appears to be small compared to other sources of uncertainty" (EPA 1989a, p. 6-31) and thus apparently chose not to deal with population transfer uncertainties.

Summary

Table II summarizes the population transfer factors used in risk assessments performed by the BEIR V Committee, UNSCEAR, ICRP, and EPA, and a discussion of the EPA's choice follows.

Table II. Population Transfer Uncertainty

	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Population Transfer Uncertainty	20%	Not estimated	20%	Not estimated

The EPA's choice to ignore population transfer uncertainties, while at variance with the approaches taken by the BEIR V Committee and the ICRP, does not seem to be out of line with the choice made by the UNSCEAR. The UNSCEAR, however, chose to project cancer risks using both multiplicative and additive methods, whereas the EPA used additive methods to project only leukemia and bone cancer risks. Thus the EPA noted the BEIR III Committee's decision to transport only additive risks but then chose to transport multiplicative risks (for most cancers) without adjusting for population transfer uncertainties. This inconsistency suggests that uncertainties such as those inherent in the population transfer issue, while universally recognized, are not fully understood.

COMPARISON OF DOSE-RESPONSE CURVES

Background

A dose-response relationship (or curve) is determined by the change in effect (response, the dependent variable) with increasing amounts of radiation (dose, the independent variable). The relationship between dose and response is at the heart of the problem of understanding the health risks of radiation (Cohrssen and Covello 1989).

Determining radiation dose is difficult and the details of the process are beyond the scope of this paper. In general, however, a comprehensive dose assessment for radionuclides released to the environment includes the following steps (Till and Meyer 1983):

1. measuring or calculating the type and quantity of radionuclides emitted (developing the source term);
2. predicting the concentrations of radionuclides that will reach humans directly or indirectly through the atmosphere, surface water, and ground water;
3. determining the deposition of radionuclides onto terrestrial or aquatic environments and estimating their accumulation in plants and animals;
4. applying usage factors to estimate the quantity of each radionuclide entering the body; and
5. estimating the energy deposited in various organs of the body.

Determining the responses to radiation is equally demanding. Although somatic effects (such as cancer) and genetic effects are the major responses to radiation, many intermediate conditions or specific endpoints are used as measurements. Among the many endpoints that are considered in nonhuman studies are clonogenic survival of cultured cells and formation of tumors and death in test animals. In human studies, effects such as chromosome abnormalities, enzyme aberrations, tumorigenesis, and leukemia are considered. To ensure that effects are measured consistently and that results are reproducible, endpoints must be carefully and quantitatively defined.

The effects of cancer and genetic damage are presumed to be stochastic effects; that is, any level of irradiation increases the likelihood of inducing genetic damage or cancer. Thus the dose-response relationship we are interested in presumably begins at the level of the background radiation, which varies from place to place; only zero dose above background produces zero response beyond background (UNSCEAR 1986).

Because the effects of low doses of experimentally applied radiation are indistinguishable from those of natural background radiation, most experimental

studies are conducted using high doses.[1] These high doses are plotted against the responses to obtain a piece of the dose-response curve, and a mathematical relationship is used to determine the shape of the curve in the low-dose region.

Two mathematical relationships explain the two differently shaped dose-response curves most commonly applied to radiation data: linear and linear-quadratic. The linear relationship extrapolates high-dose data along a straight line into the low-dose region where response is proportional to dose. The linear-quadratic relationship is a straight line at low doses but begins to rise more steeply with increasing dose because of a squared term in the mathematical expression. Thus at high doses, response is proportional to the square of the dose. Both dose-response curves are expected to fall off quickly at very high doses because of cell killing (NRC 1990).

At low doses, the linear relationship predicts greater response than does the linear-quadratic relationship and is often seen as an upper limit (Rodricks 1992). Thus the linear relationship provides a conservative estimate of dose.

These mathematical expressions describe the role of dose, dose rate, and radiation quality. As the dose rate of low-LET radiation decreases, the slope of the linear dose-response curve also decreases. High-LET radiation seems to be unaffected by dose rate. This, however, is a simplification of the dose-response relationship. These mathematical relationships do not take into account, for example, the ways in which radiation affects hormones and immune response, which in turn affect cancer growth (UNSCEAR 1986).

BEIR V Committee Dose-Response Curves

The BEIR V Committee chose a linear dose-response curve for determining genetic risk and most cancer risk from low doses of radiation. For leukemia, however, the BEIR V Committee used a linear-quadratic dose-response curve, which better fit the DS86 dosimetry data from the residents of Hiroshima and Nagasaki.

UNSCEAR Dose-Response Curves

The UNSCEAR also chose a linear dose-response curve to determine genetic risk and nonleukemia cancer risks from low doses of radiation. In fact, a linear relationship is one of the basic assumptions the UNSCEAR uses in extrapolating from animal data to humans (see "Comparison of Populations Used in Studies" in the present paper).

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1 The UNSCEAR defines *low dose* as less than 0.2 Gy; *intermediate dose* as 0.2–2.0 Gy; *high dose* as 2.0–10 Gy; and *very high dose* as greater than 10 Gy.

The UNSCEAR based this decision on data published in its 1986 report (UNSCEAR 1986), which considered the characteristic dose-response curve for various types of tumor. This report determined that breast, thyroid, respiratory tract, and bone cancers fit a primarily linear dose-response curve, while leukemia was best described by a linear-quadratic relationship.

ICRP Dose-Response Curves

The ICRP, while it considered the decisions of the BEIR V Committee and UNSCEAR and DS86 dosimetry results from the Hiroshima and Nagasaki survivors, chose a "simple proportional relationship at all levels . . . below the dose limits recommended in this report" (ICRP 1991, p. 18). Although the commission concluded that the most probable dose-response relationship is linear-quadratic, this statement suggests that they applied a linear dose-response curve for determining all risks, genetic and cancer, and then approximated the low-dose portion of the curve by applying a dose-rate effectiveness factor (see "Comparison of Dose-Rate Effects" in the present paper).

EPA Dose-Response Curves

For all estimates of cancer and genetic risks to low doses of radiation, the EPA used a linear dose-response curve. In making this choice, the EPA used data from the DS86 dosimetry system applied to the residents of Hiroshima and Nagasaki, rather than the T65DR dosimetry system used by the BEIR III Committee to choose a linear-quadratic dose-response curve (NRC 1980). The EPA found the DS86 data to be more consistent with a linear dose-response curve than the T65DR dosimetry data. The EPA did not treat leukemia differently, as did the BEIR V Committee and UNSCEAR; it maintained that the linear and linear-quadratic curves derived from the DS86 dosimetry data were very similar at low doses for both leukemia and solid tumors.

Summary

Table III summarizes the dose-response curves used by the BEIR V Committee, UNSCEAR, ICRP, and EPA in their risk assessments, and a discussion of the EPA's choices follows.

Table III. Dose-Response Curves

Type of Cancer	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Solid tumors	Linear	Linear	Linear	Linear
Leukemia	Linear-quadratic	Linear-quadratic	Linear	Linear

The EPA's choice of a linear dose-response curve to estimate risks from leukemia, while in agreement with the ICRP's choice, may provide an unnecessarily conservative result that overestimates the risk. Both the BEIR V Committee and UNSCEAR judged that the DS86 dosimetry data from the Hiroshima and Nagasaki survivors warranted the application of a linear-quadratic relationship for leukemia risks, which are thus lower than they would be if a linear dose-response curve was chosen.

More importantly, however, is the EPA's decision to selectively apply DS86 dosimetry data in choosing a dose-response curve. This is a major departure for the EPA, which adopted the BEIR III Committee's choices (NRC 1980), all based on the T65DR dosimetry system, for other risk assessment parameters such as dose-rate effectiveness factor. Indeed, mixing data from two dosimetry systems (which results in different dose estimates) is an important inconsistency in the EPA's risk assessment method and calls into question its final risk estimates.

COMPARISON OF DOSE-RATE EFFECTS

Background

Because most of our data on radiation effects come from high doses (see "Comparison of Dose-Response Curves" in the present paper), we must extrapolate to obtain data that apply to low doses, which describe most human irradiation.[2] Evidence from biology and medicine suggests that as dose and dose rate decrease, the effect per unit dose also decreases (NCRP 1980). Thus high doses and dose rates are more effective at causing damage than low doses and dose rates, and this difference is called the dose-rate effectiveness factor (DREF) or dose and dose-rate effectiveness factor (DDREF).

The effect of dose rate has been widely studied. For low-LET radiation, the effect depends on several factors, including repair of sublethal damage, redistribution of cells in the mitotic cycle, and compensatory proliferation of cells during protracted irradiation. For high-LET radiation, the dose-rate effect is much reduced. The effect seems to apply both to cancer and genetic endpoints (NRC 1990).[3]

The dose-rate effectiveness factor is estimated using mouse or human data. With a linear-quadratic relationship, the dose-response curve is linear at low doses. With a linear relationship, the dose-response curve is also linear at low doses but because it is extrapolated from high-dose data along a straight line, it predicts greater response at a given dose than does the linear-quadratic relationship. The ratio of these two responses at low doses, the linear extrapolation overestimation factor, approximates the dose-rate effectiveness factor (Fabrikant 1990).

The most commonly cited range for dose-rate effectiveness factor is 2 to 10; that is, radiation at high doses and dose rates is from two to ten times more effective at causing damage than radiation at low doses and dose rates (NCRP 1980). Dose-rate effectiveness factors must be applied with care, however. When a linear-quadratic dose-response curve is used, a dose-rate effect is already implied, and use of a dose-rate effectiveness factor to further reduce effects at low dose rates is inappropriate. For example, the BEIR V Committee used a linear-quadratic relationship to model leukemia, which predicts greatly reduced numbers of leukemias at low doses and dose rates (NRC 1990).

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2 As noted earlier, the UNSCEAR defines *low dose* as 0–0.2 Gy; *intermediate dose* as 0.2–2.0 Gy; *high dose* as 2.0–10 Gy; and *very high dose* as greater than 10 Gy. The ICRP also defines *low dose* as less than 0.2 Gy and goes on to define *low dose-rate* as less than 0.1 Gy h^{-1}.

3 Although there may be a dose-rate effect for either endpoint, the effect is not necessarily equal.

The BEIR V Committee, UNSCEAR, ICRP, and EPA each considered the evidence for using dose-rate effectiveness factors; their decisions are discussed below.

BEIR V Committee Dose-Rate Effectiveness Factor

The BEIR V Committee chose to fit separate dose-response curves for each cancer (Fabrikant 1990) and therefore did not use a dose-rate effectiveness factor. The factor used in assessing genetic risk, which is based on the ratio of genetic risk from high to low dose-rate irradiation of mice, was approximately 3.

UNSCEAR Dose-Rate Effectiveness Factor

The UNSCEAR chose not to use a dose-rate effectiveness factor for cancer risks; however, the committee recognized the need for a correction factor (probably between 2 and 10) and announced its intent to study the matter in detail. A factor of 3, discussed in the committee's 1977 report (UNSCEAR 1977), was used for genetic risks.

ICRP Dose-Rate Effectiveness Factor

The ICRP applied a dose-rate effectiveness factor of 2 to its cancer risks. The commission made no specific mention of a factor for genetic risks; however, the ICRP's estimate of risk seems to be based on the UNSCEAR's estimate for genetic risk, which used a dose-rate effectiveness factor of 3. Thus we may assume that this factor was incorporated in the ICRP's assessment.

EPA Dose-Rate Effectiveness Factor

The EPA did not apply a dose-rate effectiveness factor to its cancer risk assessment. The EPA planned, however, to reassess this decision in light of the UNSCEAR 1988 and BEIR V reports. For its genetic risk assessment, the EPA followed the lead of the BEIR III Committee (NRC 1980) and used a factor of 3 to extrapolate from high to low dose-rate irradiation.

Summary

Table IV summarizes the dose-rate effectiveness factors used by the BEIR V Committee, UNSCEAR, ICRP, and EPA in their risk assessments, and a discussion of the EPA's choices follows.

Table IV. Dose-Rate Effectiveness Factors

Risk	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Cancer	Not used	Not used	2	Not used
Genetic	3	3	3 (assumed)	3

The EPA's choice of dose-rate effectiveness factors in assessing cancer and genetic risks coincides with the factors chosen by both the BEIR V Committee and UNSCEAR. All of these organizations note, however, that further consideration should be given to applying a dose-rate effectiveness factor in assessing cancer risks. The ICRP is the only organization that has taken this advice and actually applied such a factor to cancer risks.

COMPARISON OF CANCER RISK PROJECTION METHODS

Background

Lifetable analyses using standard mortality tables that have been modified to include an additional incremental risk from radiation were used by the BEIR V Committee, UNSCEAR, ICRP, and EPA to calculate lifetime cancer risks from specific irradiation. Input for lifetable analyses includes radiation doses and parameters used in the assumed dose-response relationship (Bunger et al. 1981).

Consider a lifetime irradiation at a constant annual rate. A lifetable analysis starts with a hypothetical population of 1 million newborns, and the columns of the table provide the following information.

- The first column gives the number of infants expected to survive to each age.
- The second column gives the cancer death rate predicted by the dose-response curve.
- The third column gives the number of cases of cancer deaths (the product of the first and second columns).
- The fourth column gives the number of deaths from causes other than radiation based on mortality rates.

The number of infants surviving to each age (first column) less the number of radiogenic and nonradiogenic cancer deaths (sum of the third and fourth columns) is the number of survivors at the beginning of the next age interval. This process continues until the entire population is dead or until age 100 (NRC 1990).

Quantifying excess cancer deaths from radiation is the key to projecting risks. When the risk to exposed people exceeds the risk to unexposed people by the same amount at all ages, the effect of the radiation is additive, and the mathematical expression for this risk is thus an additive one. This is often called the absolute risk because at all ages the excess risk is constant.

When the risk to exposed people exceeds the risk to unexposed people by a constant fraction, the effect of the radiation is multiplicative. Also known as relative risk (because at all ages after irradiation, the relative risk or risk ratio is constant), the multiplicative relationship is a mathematical expression of this risk (Muirhead and Darby 1987).

Cancer risk projection requires knowledge of several parameters, including

- the relationship between excess cancer risk and baseline risk,
- the latency period (the time from irradiation to the first expression of excess cancer risk),

- the plateau period (the time from the first expression of excess risk until the excess cancer risk disappears),
- the age distribution of the exposed population and the baseline pattern of age-specific mortality rates from all causes and from the cancers under consideration,
- the age at irradiation, and
- the dose-response function.

Other factors include effects of sex, environmental radiation, high- and low-LET radiation, and high and low dose rates (UNSCEAR 1988).

These parameters are brought together in the cancer risk projection methods used by the BEIR V Committee, UNSCEAR, ICRP, and EPA. These organizations used cancer risk projection to provide several measures of risk; for example, the UNSCEAR estimated the probability of radiation-induced cancer death (expressed as a percentage), the number of projected cancer deaths (expressed as deaths per thousand or million exposed people per unit dose), and the number of years of life lost in an exposed population because of radiation-induced cancers. All these estimates, however, derive from a single measure chosen by each organization, as discussed below.

BEIR V Committee Cancer Risk Projection Methods

The BEIR V Committee chose to use only multiplicative methods to project cancer risk. The measure chosen by this committee was excess lifetime cancer risk, which is the increase in the lifetime probability that a person will die from a specific cancer as a result of a specific irradiation. The excess lifetime cancer risk can be represented mathematically as

$$\int_e^\infty \mu_c(a \mid e, D)\, S(a \mid e, D)\, da - \int_e^\infty \mu_c(a)\, S(a \mid e)\, da$$

where

μ is the death rate,

c is the specific cause of death,

a is the age at death,

e is the age at which the experimental population was exposed,

D is the dose received instantaneously (for the control group, $D = 0$), and

S is the probability of survival (Thomas et al. 1992).

The first term in this equation is the lifetime cancer risk for an experimental population, and the second term is the lifetime cancer risk for a control population. (The control population is, of course, always exposed to the same background radiation as

the experimental population.) The excess cancer risk is simply the difference between the two lifetime risks (NRC 1990).

Parameter estimates used for the BEIR V Committee's cancer risk projections were obtained using AMFIT, a program developed for the analysis of survival data. Some of these parameters provide insight into the assumptions made by the BEIR V Committee and are discussed below.

Death Rate

The BEIR V Committee used the U.S. death rate for 1979–1981, assuming that a negligible proportion of cancers in the general population were radiation-induced. Because most of the dose data came from Hiroshima and Nagasaki survivors (DS86 dosimetry system), we must consider whether data obtained from a population of one nationality can be applied to a population of a different nationality (see "Comparison of Population Transfer Coefficients" in the present paper).

The method used by the BEIR V Committee is distinct from other methods because within the death rate, μ, terms that decrease risk with increasing time since irradiation are incorporated. These terms adjust the death rate for sex, age at death, age at irradiation, and time since irradiation and were determined separately for leukemia, lung cancer, and breast cancer (ICRP 1991).

Specific Cause of Death

As noted in the discussion of populations, the BEIR V Committee projected risks separately for leukemia, breast cancer, respiratory tract cancer, digestive tract cancer, and other nonleukemia cancers. For leukemia deaths, the BEIR V Committee assumed a 2-year latency period. For deaths from other cancers, a 10-year latency period was assumed. The BEIR V Committee provided no specific information on plateau values for each type of cancer.

Age of Population

Because some of the cancers used as endpoints depend strongly on age at irradiation (for example, leukemia risks for people exposed before age 20 are much greater than leukemia risks for people exposed later in life [Vaeth and Pierce 1990]) and because risk varies as a complex function of age and time since irradiation (Thomas et al. 1992), the age distribution of a population at the time of irradiation must be specified if we are to predict the effect of that radiation. The BEIR V Committee applied the age structure that would eventually result from a constant birth rate (a stationary population distribution) to estimate the age distribution of the Hiroshima and Nagasaki survivors.

Dose Received

As stated earlier, the BEIR V Committee used doses for the Hiroshima and Nagasaki survivors based on the DS86 dosimetry system (Shimizu et al. 1987). In this reassessment, the Radiation Effects Research Foundation reviewed information on the number of fissions that occurred in the explosions over Hiroshima and Nagasaki and calculated in detail the radiation transport through the weapons materials and the intervening air. They performed Monte Carlo calculations of the radiation fields within homes, taking into account shielding by nearby houses. Organ doses were thus calculated for each survivor by considering shielding circumstances, location, orientation, and size. Instead of using the organ doses calculated for each survivor directly, however, the reviewers used age- and city-specific transmission factors to average the organ dose over survivors of all ages. The neutron contribution to doses in both cities was assumed to be small compared with the gamma contribution (NRC 1990).

Doses to ankylosing spondylitis patients, because radiotherapy was aimed at the spine, were received by a large fraction of the body. Individual doses were not estimated for the entire population; instead a random sample of patients' records (one out of fifteen) were extracted and Monte Carlo simulations were used to estimate individual organ doses to thirty organs or body regions and twelve bone marrow sites (Lewis et al. 1988).

Individual breast tissue doses were estimated for the entire population of women examined by fluoroscopy in Canada for tuberculosis. These estimates were based on the recorded number of fluoroscopies, physician interviews, phantom measurements, and Monte Carlo simulations. Dose per fluoroscopy was averaged for the province (Nova Scotia or other) and the year of irradiation (Sherman et al. 1978). Individual breast tissue doses were also estimated for the women examined by fluoroscopy in Massachusetts. These doses were based on patient and physician interviews, comparable fluoroscopic measurements, and Monte Carlo simulations (Boice et al. 1981). Finally, individual breast tissue doses were estimated from original radiotherapy records for the entire population of women treated with radiotherapy for postpartum mastitis in New York (Shore et al. 1986).

UNSCEAR Cancer Risk Projection Methods

The UNSCEAR used both multiplicative and additive methods to project cancer risk. The measure chosen by this committee was risk of exposure-induced cancer death,

which is the risk over an entire lifetime that a person will die from a cancer that has been caused by a specific irradiation.

The multiplicative method for risk of exposure-induced cancer death can be represented mathematically as

$$\int_{e}^{\infty} \left[\mu_c(a \mid e, D) - \mu_c(a)\right] S(a \mid e, D)\, da$$

where

μ is the death rate,

c is the specific cause of death,

a is the age at which the experimental population was exposed,

e is the age at irradiation,

D is the dose received instantaneously (for the control group, $D = 0$), and

S is the probability of survival (Thomas et al. 1992).

In this equation, the relative excess cancer death rate is calculated by subtracting the cancer death rate for a control population from the cancer death rate for an experimental population. This relative excess cancer death rate from radiation is multiplied by the probability of survival for the experimental population and integrated over all ages.

The additive method for risk of exposure-induced cancer death can be represented mathematically as

$$\int_{e}^{\infty} I(D)\, S(a \mid e, D)\, da$$

where I(D) is the absolute excess cancer death rate, which incorporates the concept that there is a constant number of excess cancer deaths in any given year per unit number of people exposed per unit dose.

Parameter estimates used by the UNSCEAR were computed using an interactive, parametric demographic model developed by the Centre d'Etude sur l'Evaluation de la Protection dans le Domaine Nucleaire in 1985. The assumptions made by the UNSCEAR are contained in some of the parameters used in these equations and discussed in detail below.

Death Rate

The reference populations used by the UNSCEAR were the 1982 general Japanese population for the Hiroshima and Nagasaki survivors, the 1982 adult male population of the United Kingdom for the ankylosing spondylitis patients, and the 1982 adult female population in the United Kingdom for the cervical cancer patients.

Although the UNSCEAR report does not state this directly, these populations' mortality rates were probably used in the projections of exposure-induced cancer death.

Specific Cause of Death

The UNSCEAR applied risk projection methods to cancer sites for which mortality increases both statistically and significantly with increasing dose. These are leukemia and cancers of the bladder, breast, colon, esophagus, ovary, stomach, and lung. The latency period for leukemia was assumed to be 2 years; for all other cancers, the latency period was taken as 10 years. The plateau period for leukemia was assumed to be 40 years; for all other cancers the plateau periods extended the full lifetime.

Age of Population

An alternative to using the stationary population distribution (as the BEIR V Committee did) is to use the current age distribution for a real population of interest. This is the approach taken by the UNSCEAR, which estimated the age distribution of the Japanese population. The actual age distribution of a population reflects trends in birth rates and thus varies considerably from the stationary distribution. Using the actual age distribution results in a cancer risk projection that is geared toward a population of specific nationality; thus its application to a population of a different nationality must be approached cautiously (see "Comparison of Population Transfer Coefficients" in the present paper) (Thomas et al. 1992). It would seem logical that the UNSCEAR would choose to estimate age distribution for each of the reference populations (that is, male and female United Kingdom populations), but the UNSCEAR report does not state that this was the committee's approach.

Dose Received

The UNSCEAR used the DS86 dosimetry system to determine dose to the Hiroshima and Nagasaki survivors (Shimizu et al. 1987). Doses to the ankylosing spondylitis and cervical cancer patients were therapeutic doses, which in general are substantial doses given over a short period of time and administered locally. Dosimetry for the ankylosing spondylitis patients was discussed previously. Doses to most of the cervical cancer patients were from radium implants or external radiotherapy. These procedures resulted in substantial doses to organs near the cervix and moderate doses to other organs (Boice et al. 1988).

ICRP Cancer Risk Projection Methods

The ICRP used a multiplicative method to project risks from all cancers except leukemia; because all leukemias had already been expressed in the Japanese population, the ICRP stated that there was no need to project leukemia risks for that population. The

ICRP did not indicate, however, how it projected leukemia risks for other populations. The multiplicative method chosen by the committee seems to be similar to the UNSCEAR's method, which was expressed as the risk of exposure-induced cancer death.

Death Rate

Death rates were obtained from the U.S. for the years 1980–1985 using the SEER program, which gives 5-year survival rates by cancer site.

Specific Cause of Death

The ICRP projected risks separately for leukemia and cancer of the esophagus, stomach, colon, lung, breast, ovary, bladder, bone marrow, thyroid, bone, skin, liver, and remainder organs. The ICRP assumed an average latency period for all cancers (including leukemia) of 10 years. Although it did not specifically mention the plateau period chosen, the commission cited research that suggests a plateau for leukemia at 20 years and no plateau for other cancers.

Age of Population

The ICRP did not specify which population distribution technique it used, stationary or actual.

Dose Received

As with the BEIR V Committee and UNSCEAR, the ICRP used the DS86 dosimetry system to determine doses to the Hiroshima and Nagasaki survivors, the main population on which it based its risk projections (Shimizu et al. 1987).

EPA Cancer Risk Projection Methods

The EPA chose to use multiplicative methods to project risks from most cancers and additive methods to project risks from leukemia and bone cancer. These are the same methods used by the BEIR III Committee (NRC 1980), which chose a risk measure only slightly different from the risk of exposure-induced cancer death used by the UNSCEAR. The multiplicative method of this measure can be represented mathematically as

$$\int_{e}^{\infty} \left[\mu_c(a \mid e, D) - \mu_c(a)\right] S(a \mid e)\, da$$

where

μ is the death rate,

c is the specific cause of death,

a is the age at death,

e is the age at which the experimental population was exposed,
D is the dose received instantaneously (for the control group, $D = 0$), and
S is the probability of survival (Thomas et al. 1992).

The difference between this method and that used by the UNSCEAR is in the survival term, S(a), which in the BEIR III Committee's method (NRC 1980) is the probability that people in the control group will survive to age *a* and in the UNSCEAR method is the probability that people in the experimental group will survive to age *a*. Thomas et al. (1992) consider the BEIR III Committee's method an approximation of the UNSCEAR's risk of exposure-induced cancer death.

Following this trend, we would expect the additive method used by the EPA to approximate risk of exposure-induced death and to be represented mathematically as

$$\int_{e}^{\infty} I(D)\, S(a \mid e)\, da$$

Again, I(D) is the absolute excess cancer death rate, and the survival term is for a control population.

Parameters used by the EPA were estimated by the CAIRD subroutine of the RADRISK computer program for calculating doses. This program was furnished by the EPA to the BEIR III Committee (NRC 1980); thus the calculations by the EPA and the BEIR III Committee should be the same. Some of the parameters used by the EPA in making these calculations are discussed below.

Death Rate

The EPA used mortality data for the U.S. during 1969–1971. As with the mortality data used by the BEIR V Committee, we must consider the validity of using U.S. population data with dose data obtained primarily from Japanese and British populations (see "Comparison of Population Transfer Coefficients" in the present paper).

Specific Cause of Death

The EPA used the BEIR III Committee's risk projections for deaths caused by solid cancer (lymphoma and cancer of the thyroid, breast, lung, esophagus, stomach, intestine, liver, pancreas, urinary tract, and other organs), by bone cancer, and by leukemia (NRC 1980). A latency period of 10 years and a plateau period of 20 years were assumed for solid cancers. For bone cancer and leukemia, a 2-year latency and a 30-year plateau period were used.

Age of Population

The age distribution used by the EPA was that of a hypothetical population. According to Thomas et al. (1992), this provides an estimate of risk that is similar to that

for a specific population (used by the UNSCEAR); these estimates, however, differ from the estimate of risk obtained using a stationary population distribution (used by the BEIR V Committee).

Dose Received

As stated earlier, the EPA used doses based on the T65DR dosimetry system for the Hiroshima and Nagasaki survivors (Auxier 1977). In this system, described by the BEIR III Committee (NRC 1980), neutron doses (assumed to be a major contributor to doses at Hiroshima but not at Nagasaki) and gamma doses were estimated separately and reported as tissue kerma (rad) in air. Shielding histories were collected and environmental transmission factors were estimated. The kerma dose was multiplied by a conversion ratio to obtain absorbed organ dose (Preston and Pierce 1988).

Summary

Table V summarizes the cancer risk projection methods used by the BEIR V Committee, UNSCEAR, ICRP, and EPA in their risk assessments, and a discussion of the EPA's choices follows.

Table V. Cancer Risk Projection Methods

Projection Method Parameter	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Method type	Multiplicative	Multiplicative Additive	Multiplicative	Multiplicative Additive[a]
Risk measurement	Excess lifetime risk	Risk of exposure-induced death	Risk of exposure-induced death	Approximate risk of exposure-induced death
Computer program	AMFIT	French program	Not specified	RADRISK
Population statistics				
Country	U.S.	Japan, U.K.	U.S.	U.S.
Year	1979–1981	1982	1980–1985	1969–1971

Table V. Cancer Risk Projection Methods (cont)

Projection Method Parameter	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Latency period				
Leukemia	2 years	2 years	10 years	2 years[a]
Other	10 years	10 years	10 years	10 years
Plateau period				
Leukemia	Not specified	40 years	20 years	30 years[a]
Other	Not specified	Lifetime	None	20 years
Age distribution	Stationary	Actual (Japanese)	Not specified	Hypothetical
Dosimetry (Japanese)	DS86	DS86	DS86	T65DR

[a]Leukemia and bone cancer

The EPA made several parameter choices that vary from the BEIR V Committee, ICRP, and UNSCEAR preferences. The EPA's choice of a risk measurement cannot be interpreted as either excess cancer risk or risk of exposure-induced cancer death and has been criticized by Thomas et al. (1992) because it uses a survival function for unexposed, rather than exposed, population. This measure ". . . does not estimate any meaningful population parameter, . . . and [we] do not advocate continued use of this approximation" (D. Thomas et al. 1992, p. 261).

Another concern is with the EPA's choice of population statistics. In accordance with the BEIR III Committee (NRC 1980), the EPA used mortality data that is at least 10 years out of date when compared with the data used by the BEIR V Committee, ICRP, and UNSCEAR. We can postulate many population trends over 10 years that could affect a lifetable analysis: declining birth rates, changing death rates because of improved diagnosis and treatment, and increased life spans.

Finally, we must consider the effect of using old dosimetry data. As discussed earlier, the T65DR data overestimated the dose equivalent to organs. In both of the mathematical relationships used by the EPA, the overestimated dose affects only the cancer death rate. If the observed death rates were due to a lower dose than previously estimated, then the risk must be greater than previously estimated.

COMPARISON OF GENETIC RISK PROJECTION METHODS

Background

Genetic risks from radiation are a result of mutations, which are of special concern when they occur in the mitotically dividing spermatogonia of males and immature oocytes of females. Changes in the genetic material of these cells include dominant and recessive mutations in autosomal chromosomes, mutations in sex-linked chromosomes, chromosome aberrations (physical rearrangement or removal of part of the genetic material on the chromosome or abnormal numbers of chromosomes), and irregularly inherited diseases (such as genetic conditions with complex causes and degenerative diseases). Mutations may be passed on to and expressed in future generations.

Genetic effects of radiation are detected by the study of endpoints such as visible chromosome abnormalities, protein changes, spontaneous abortions, congenital malformations, and premature death. To accumulate sufficient data for statistical analysis of these endpoints, massive epidemiological studies with long-term follow-up are required (see "Comparison of Populations Used in Studies" in the present paper) (NRC 1990).

The major methods used to project genetic risks can be classified broadly as direct or indirect. In the direct method, the frequency in animals of a mutation or heritable defect for a given radiation dose is extrapolated to obtain a frequency in humans. This is done by directly measuring the rate at which radiation at high dose rates induces a specific class of genetic defects in mice (such as skeletal anomalies), and these results are extrapolated to low dose rates. Then, the proportion of serious dominant genetic diseases in humans that involves similar defects is estimated and used as a proportionality factor with the induction rate in mice to estimate the induction rate for all dominant mutations in humans. Direct methods are generally used to estimate genetic effects in the first generation after the irradiation occurs (NRC 1990).

The indirect method (also known as the doubling dose or relative mutation risk method) uses the natural prevalence of genetic diseases caused by radiation in the population as a frame of reference for estimating the additional number of cases of these diseases that will occur. The average radiation-induced mutation rate for an experimental population is divided by the spontaneous mutation rate for all genetic diseases to obtain the relative mutation risk. (The inverse of the relative mutation risk is the doubling dose, which is the amount of radiation that results in as many mutations as occur spontaneously in a generation.) The relative mutation risk is multiplied by the

spontaneous mutation rate for the specific genetic disease, by the dose,[4] and by the mutation component to estimate the induction rate for the specific disease in humans (NRC 1990).

The concept of a mutation component was introduced by the BEIR I Committee (NRC 1972); it is the degree to which the disease is due to radiation rather than other causes, such as genetic predisposition and environmental factors. This component makes allowance for genetic diseases of complex etiology that may be caused by multiple factors. The mutation component is multiplied by the incidence of genetic diseases of complex etiology to estimate the number of these diseases that will result from irradiation. The use of this component was deemed necessary because relative mutation risk considers dominant and recessive diseases but not genetic diseases of complex etiology.

Indirect methods are usually used to estimate genetic effects on all future generations (after a continuously irradiated population has reached equilibrium between mutations that arise spontaneously and mutations that are eliminated by selection in every generation). These methods can also be used to estimate genetic effects on the first few generations, which sustain a certain percentage of the total equilibrium damage (NRC 1990).

A third method, the gene number method, was discussed by the BEIR V Committee but was not used by any of the organizations reviewed.

BEIR V Committee Genetic Risk Projection Methods

The BEIR V Committee considered both direct and indirect methods but chose to use only the indirect method to project genetic risks from radiation. The direct method was considered by the committee to require unreliable assumptions that became even more unreliable as the number of assumptions increased. Thus, the direct method was used only to test the consistency of results obtained using the indirect method. The gene number method was also considered but was not used at all. The difficulties with this method are that it requires the estimation of societal cost and human suffering from genetic death, definition of genetic mutability, and estimation of the number of mutable genes.

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4 For the indirect method, the BEIR V Committee used doses based on T65DR dosimetry because "data based on . . . DS86 were not available to this committee in the detail necessary for doubling dose estimates at the time the [BEIR V] report was being prepared" (p. 96). This is probably true also of the UNSCEAR, ICRP, and EPA, whose risk assessments were published in 1988, 1990, and 1989, respectively, before or concurrent with the BEIR V Committee's risk assessment in 1990.

For autosomal dominant effects, the BEIR V Committee used a mutation component of 1 in its doubling dose calculations; risks of congenital abnormalities were calculated using a mutation component of 0.05–0.35. Other genetic diseases of complex etiology that may be caused by multiple factors were not included in the committee's calculations; the committee suggested that further research was required before these risks could be projected accurately.

Use of the indirect method was confined to low doses, which were defined by the committee in this situation as those "at which the dose-response curve is essentially linear" (NRC 1990, p. 72).[5] Estimates of genetic effects are given for an average population dose equivalent of 1 rem per generation. Applying these estimates to low-LET radiation, a dose equivalent of 1 rem translates to 0.01 Sv, or a dose of 0.01 Gy, which the UNSCEAR and ICRP classify as "low dose" (see "Comparison of Dose-Response Curves" in the present paper).

Other pertinent factors used by the BEIR V Committee to project genetic risk include the following.

- Estimates were made for an average population dose equivalent of 0.01 Sv per 30-year generation. This implies that the significant doses were those received in the first 30 years of life.
- Estimates were provided, for the most part, as a single number.
- The BEIR V Committee gave no indication of its position on sex-related differences in sensitivity to radiation, but it referred to studies that found evidence both for and against a difference.
- Based mainly on data from mouse studies and supported by studies done by others using DS86 dosimetry data from Hiroshima and Nagasaki survivors, the BEIR V Committee assumed a doubling dose of 1 Gy.

UNSCEAR Genetic Risk Projection Methods

The UNSCEAR provided genetic risk projection based on both the indirect and direct method, as estimated in its 1986 report (UNSCEAR 1986). The pertinent factors used by the UNSCEAR to project genetic risk include the following.

- The UNSCEAR did not use a mutation component (or in other words, used a mutation component of 1) because it did not estimate the genetic risk of congenital anomalies and other diseases of complex etiology.

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5 This must refer to the linear portion of a linear-quadratic model, although the committee chose to use a linear dose-response model for genetic risks (see "Comparison of Dose-Response Curves" in the present paper).

- Estimates were based on the assumption that mean age of childbearing is 30 years and the average life expectancy at birth is 70–75 years; thus the dose received by age 30 is about 40% of the total lifetime dose.
- Single estimates were given based on the indirect method; estimated ranges were given based on the direct method.
- Estimates were adjusted for possible sex-related differences; risks for females were assumed to be up to 0.44 times the risk for males.
- Based mainly on data from mouse studies, the UNSCEAR assumed a doubling dose of 1 Gy.

ICRP Genetic Risk Projection Methods

The ICRP projected genetic risk based on the indirect method and the following factors.

- The ICRP used a mutation component of 0.05 to estimate the genetic risk of congenital anomalies and other diseases of complex etiology. The commission further reduced this estimate by one-third to account for the lesser severity of such diseases.
- As with the UNSCEAR, the ICRP assumed that the mean age of childbearing is 30 years and the average life expectancy at birth is 70–75 years; thus the dose received by age 30 is about 40% of the total lifetime dose.
- Single estimates of risk were prepared by the ICRP.
- No indication was given by the ICRP that estimates were adjusted for possible sex-related differences.
- The ICRP assumed a doubling dose of 1 Gy.

EPA Genetic Risk Projection Methods

The EPA based its genetic risk projections on those prepared by the BEIR III Committee (NRC 1980). As with the BEIR V Committee, the EPA considered both indirect and direct methods but chose to use only the indirect method "... because the risk estimated by the direct method is incomplete . . . and does not include the same types of damage estimated by doubling doses" (EPA 1989a, p. 6-65).

Although the EPA adopted the doubling dose calculated by the BEIR III Committee (NRC 1990), its definition of doubling dose is actually based on a method of calculating relative mutation risk proposed by the BEIR I Committee (NRC 1972). In this calculation, the relative mutation risk in humans is the induced mutation rate for mice divided by the spontaneous mutation rate for humans. This mixture of mouse and

human data was rejected by the BEIR III Committee, which based its calculations solely on mouse data.

In agreement with the BEIR V Committee, the EPA used the same mutation components in its indirect method of calculating genetic risk (except that the upper limit of the mutation component for risks of congenital abnormalities was 0.5) and estimated genetic risk for an average population dose equivalent of 0.01 Sv per generation, based on low dose-rate studies in mice.

Other pertinent factors used by the EPA to project genetic risk include the following.

- Estimates used the radiation dose accumulated up to age 30, the median age of childbearing.
- Estimates were provided as a range, to emphasize the uncertainty involved in projecting genetic risk.
- Estimates of the upper limit of risk to males were multiplied by 1.44 to account for possible sex-related differences in sensitivity to radiation. This was based on data suggesting that maturing oocytes in mice are 44% less sensitive to radiation than spermatogonia; hence the combined risk to both sexes is 1.44 times the risk to males.
- Based mainly on data from mouse studies, the EPA assumed a doubling dose of 0.5–2.5 Gy.

Summary

Table VI summarizes the genetic risk projection methods used by the BEIR V Committee, UNSCEAR, ICRP, and EPA in their risk assessments, and a discussion of the EPA's choices follows.

Table VI. Genetic Risk Projection Methods

Projection Method Parameter	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Method	Indirect	Indirect Direct	Indirect	Indirect
Mutation component				
• autosomal dominant diseases	1	1	1	1
• congenital diseases	0.05–0.35	Not evaluated	0.05	0.05–0.50
Length of generation	30 years	30 years	30 years	30 years
Type of estimate	Point	Point (indirect method) Range (direct method)	Point	Range
Adjustment for sex differences	None	1.44	Not specified	1.44
Doubling dose	1 Gy	1 Gy	1 Gy	0.5–2.5 Gy

Most of the parameters chosen by the EPA are similar to those chosen by one or more of the other organizations with the exception of doubling dose. The EPA, based on the work of the BEIR III Committee (NRC 1980), chose to use a range of doubling doses. The other organizations preferred a single estimate, and the BEIR V Committee noted that although a single estimate of 1 Gy is "somewhat arbitrary, the number has the advantage of arithmetic simplicity and is a round number that does not invite an unwarranted assumption of high accuracy" (NRC 1990, p. 77). The BEIR V Committee also pointed out that this value is supported by human data. The EPA, on the other hand, defended the use of a range by asserting that it reflects the uncertainty in our knowledge of mutation rates for specific genes. Although the EPA chose to use a range, the geometric mean of this range is 1.1 Gy, which approximates the single estimate chosen by the other organizations.

COMPARISON OF RISK ESTIMATES

Background

All of the parameters discussed to this point—populations used in studies, population transfer coefficients, dose-response curves, dose-rate effects, and risk projection methods—are used to estimate the probability that radiation effects (whether carcinogenic or genetic) will occur. These probabilities or risk estimates (also called risk coefficients, lifetime risks, and nominal fatality probability coefficients) vary as the parameters vary, and we would expect different values from different organizations.

The terms in which risk estimates are expressed vary as follows: by the units in which the dose or dose equivalent is expressed (rad, gray, rem, or sievert); by the sex of the exposed population; by the duration of irradiation (continuous over a lifetime or single, one-time); and by the extent of irradiation (whole body or specific organ). Thus to compare risk estimates across organizations, we must develop a common method of expression.

For estimates of cancer risk, the task is complex. A technique for expressing these probabilities has been developed by the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC) for two organizations, the BEIR V Committee and UNSCEAR (using data from its 1988 report). In *Use of BEIR V and UNSCEAR 1988 in Radiation Risk Assessment* (CIRRPC 1992), the risk estimates prepared by the two organizations were adjusted for dose-rate effect (as appropriate) using a dose-rate effectiveness factor of 2 (which is the most conservative value; see "Comparison of Dose-Rate Effect" in the present paper) and compared using common terms. The CIRRPC did not try to reconcile the different approaches to risk assessment taken by each organization. This process results in an estimate of the risk of death from leukemia and solid cancers for each gray received by the general population (averaged for both males and females) in a single, whole-body irradiation, and it can be applied to the risk estimates developed by the ICRP and EPA.

For estimates of the risk of genetic effects, comparisons among the various organizations are relatively straightforward. Each organization has considered many of the same issues and so it is simply a matter of converting units to obtain values that can be compared.

BEIR V Committee Risk Estimate

Cancer Risk

The BEIR V Committee estimated the following probabilities of excess cancer deaths in the general population from a single, whole-body irradiation by low-LET radiation. The CIRRPC adjusted these probabilities to allow comparison among organizations.

- For males, the BEIR V Committee estimated 110 excess leukemia deaths and for females, 80 excess leukemia deaths in 100,000 people exposed to 0.1 Gy; the average for both sexes is approximately 1×10^{-2} per Gy. The CIRRPC noted that the use of a dose-rate effectiveness factor is inappropriate in this situation because the risk estimate was based on a linear-quadratic dose-response curve.
- For males, the BEIR V Committee estimated 660 excess deaths and for females, 730 excess deaths from nonleukemia cancers per 100,000 people per 0.1 Gy; the average for both sexes is 695 per 100,000 per 0.1 Gy or 6.95×10^{-2} per Gy. The CIRRPC adjusted this estimate by applying a dose-rate effectiveness factor of 2, thus obtaining a final estimate of 3.5×10^{-2} per Gy.
- Using the CIRRPC method, the overall risk estimate is the sum of the leukemia and nonleukemia cancer estimates; that is, $(1.0 \times 10^{-2}) + (3.5 \times 10^{-2}) = 4.5 \times 10^{-2}$ per Gy.

Genetic Risk

The BEIR V Committee did not provide a direct estimate of the risk of total genetic damage, stating that these estimates were highly uncertain because they did not include allowance for genetic diseases of complex etiology that may be caused by multiple factors. The committee suggested that these diseases make up the largest category of genetically related diseases and that further research was required before these probabilities could be estimated accurately.

The committee did, however, provide estimates of genetic effects for other types of genetic disorders, and the sum of these provides an estimate of 116–206 additional genetic effects in all generations of 1,000,000 people after a parental dose equivalent of 1 rem of low-LET radiation, or an average risk of 1.6×10^{-2} per Gy. It must be remembered that this figure is expected to be low because it does not include diseases of complex etiology.

UNSCEAR Risk Estimate

Cancer Risk

Using its multiplicative risk projection method, the UNSCEAR estimated the following probabilities of exposure-induced cancer deaths in the general population

(age-averaged) from a single, whole-body irradiation by low-LET radiation. The CIRRPC denotes these as *premature* cancer deaths (defined as "the number of excess cancer deaths plus the number of cancer deaths that would occur earlier than expected" [CIRRPC 1992, p. 7]) to distinguish between the cancer risk projection methods used by the EPA and UNSCEAR (see "Comparison of Cancer Risk Projection Methods" in the present paper). The CIRRPC adjusted the UNSCEAR's risk estimates to allow comparison among organizations.

- For males and females averaged, the UNSCEAR estimated 9.7 exposure-induced leukemia deaths in 1,000 people receiving a dose of 1 Gy or approximately 1.0×10^{-2} per Gy. The CIRRPC maintained that application of a dose-rate effectiveness factor of 2 is appropriate (in spite of the fact that the UNSCEAR, like the BEIR V Committee, based its risk estimate for leukemia on a linear-quadratic dose-response curve). The final estimate thus obtained using the CIRRPC method was 0.5×10^{-2} per Gy.
- For males and females averaged, the UNSCEAR estimated 61 exposure-induced nonleukemia cancer deaths in 1,000 people receiving a dose of 1 Gy or 6.1×10^{-2} per Gy. The CIRRPC adjusted this estimate by applying a dose-rate effectiveness factor of 2, thus obtaining a final estimate of 3.1×10^{-2} per Gy.
- Using the CIRRPC method, the overall risk estimate is the sum of the leukemia and nonleukemia cancer estimates; that is, $(0.5 \times 10^{-2}) + (3.1 \times 10^{-2}) = 3.6 \times 10^{-2}$ per Gy.

Genetic Risk

As with the BEIR V Committee, the UNSCEAR chose not to estimate the risk of diseases of complex etiology because of a lack of information. However, the committee noted that even if these diseases were assigned a mutation component of 100% (an extreme assumption), the genetic risks to the first generation would be less than the cancer risks. Thus the UNSCEAR's estimate is unchanged from 1986; that is, 2% per Sv or 2×10^{-2} per Gy. Again, it must be noted that this figure is low because it does not include diseases of complex etiology.

ICRP Risk Estimate

Cancer Risk

The ICRP also estimated probabilities of exposure-induced cancer deaths in the general population from a single, whole-body irradiation by low-LET radiation. The ICRP, however, did not calculate separate probabilities for leukemia and other cancers; instead, all cancers were treated together. The ICRP used an "average" of the BEIR V

Committee and UNSCEAR estimates. Applying the CIRRPC method, the ICRP risk estimate can be adjusted as follows.

- The BEIR V Committee's estimate for leukemia (approximately 1×10^{-2} per Gy), because it was based on a linear-quadratic dose-response curve and thus contained an implied dose-rate effectiveness factor of 2, according to the CIRRPC method is multiplied by 2 to provide an estimate for high-dose, high-dose rate irradiation of 2×10^{-2} per Gy.
- The BEIR V Committee's estimate for overall cancer risk then becomes, by the CIRRPC method, $(2 \times 10^{-2}) + (6.95 \times 10^{-2}) = 9 \times 10^{-2}$ per Gy.
- The UNSCEAR's estimate for age-specific probabilities (approximately 11×10^{-2} per Gy, not corrected for dose-rate effect) was used by the ICRP; however, it seems that the UNSCEAR's estimate for age-averaged probabilities (approximately 7×10^{-2} per Gy, not corrected for dose-rate effect) more closely approximates the parameters used by the BEIR V Committee and hence is a better comparison.
- The "average" of the BEIR V Committee's estimate (modified using the CIRRPC method, as above) and the UNSCEAR's estimate (age-averaged) is approximately 8×10^{-2} per Gy (compared with the ICRP's "average," based on the UNSCEAR's age-specific estimate, of 10×10^{-2} per Gy). Applying a dose-rate effectiveness factor of 2 provides a final estimate, using the CIRRPC method, of 4×10^{-2} per Gy (compared with the ICRP's "average," based on the UNSCEAR's age-specific estimate, of 5×10^{-2} per Gy).

Genetic Risk

The ICRP, in contrast to the BEIR V Committee and UNSCEAR, included diseases of complex etiology in its estimate of genetic risk, as discussed in "Comparison of Genetic Risk Projection Methods" in the present paper. The commission estimated that there would be 1.0×10^{-2} genetic effects in all generations after a parental dose equivalent of 1 Sv of low-LET radiation, or a genetic risk of 1.0×10^{-2} per Gy.

EPA Risk Estimate

Cancer Risk

The approach used by the CIRRPC can be used with the risk estimates adopted by the EPA from the BEIR III Committee (NRC 1980).

- For males and females averaged, the EPA predicted 47.3 leukemia and bone cancers in 100,000 people receiving a dose of 0.01 Gy or approximately 0.5×10^{-2} per Gy. Because the EPA based all of its risk estimates on linear dose-response relationships,

the CIRRPC method suggests that it is appropriate to apply a dose-rate effectiveness factor of 2, which reduces the risk estimate to approximately 0.3×10^{-2} per Gy.

- For males and females averaged, the EPA estimated 400 other cancers in 100,000 people receiving a dose of 0.01 Gy or 4×10^{-2} per Gy. According to the CIRRPC method, a dose-rate effectiveness factor of 2 is appropriate, and the risk estimate is 2×10^{-2} per Gy.
- Using the CIRRPC method, the overall risk estimate is the sum of the leukemia and nonleukemia cancer estimates; that is, $(0.3 \times 10^{-2}) + (2 \times 10^{-2}) = 2.3 \times 10^{-2}$ per Gy.

Genetic Risk

The EPA seems to have included genetic diseases of complex etiology in its risk estimate, having assigned such diseases a mutation component of 0.05–0.5. The EPA estimated that 260 serious heritable disorders will result in all generations of 1,000,000 people from a parental dose of 1 rad of low-LET radiation, which represents a genetic risk of 2.6×10^{-2} per Gy.

Summary

Table VII summarizes the risk estimates developed by the BEIR V Committee, UNSCEAR, ICRP, and EPA in their risk assessments and adjusted using the CIRRPC method to allow comparison. A discussion of the EPA's choices follows.

Table VII. Risk Estimates (per Gy) Adjusted by the CIRRPC Method

Effect	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)	EPA's NESHAP (1989a)
Leukemia	1×10^{-2}	0.5×10^{-2}	Not estimated separately	0.3×10^{-2}[a]
Other Cancers	3.5×10^{-2}	3.1×10^{-2}	Not estimated separately	2×10^{-2}
All Cancers	4.5×10^{-2}	3.6×10^{-2}	4×10^{-2}	2.3×10^{-2}
Genetic	1.6×10^{-2}	2×10^{-2}	1.0×10^{-2}	2.6×10^{-2}

[a]Includes bone cancer

Using the CIRRPC technique, the EPA cancer risk estimates are consistently lower than those of the other organizations; they are nearly half those of the BEIR V Committee. However, the EPA has suggested that a higher estimate of nonleukemia cancer risk, 1200 cancers in 100,000 people who receive 0.01 Gy or 12×10^{-2} per Gy, might be more accurate. This would increase the EPA's overall estimate, using the CIRRPC method, to 6.3×10^{-2} per Gy, which is closer to the CIRRPC-method estimates of the BEIR V Committee, ICRP, and UNSCEAR.

The EPA's estimate of genetic risk is greater than the estimates of the other organizations. This would be expected in the cases of the BEIR V Committee and UNSCEAR, as these estimates did not include estimates of genetic diseases of complex etiology. However, the ICRP estimate, which is the lowest of all, did include these diseases and thus should be comparable to the EPA estimate. All organizations noted the difficulties in estimating genetic risks; perhaps these uncertainties are responsible for this discrepancy.

CONCLUSION

The most important ways in which the BEIR V Committee, UNSCEAR, and ICRP risk assessments differ from the EPA's NESHAP risk assessment are displayed in the shaded sections of Table VIII. It can be seen in this table that some of the EPA's parameters coincide with those chosen by at least one other organization. Other parameters (risk projection methods and probability estimates) do not match well at all. It should be noted that many parameters chosen by the BEIR V Committee, UNSCEAR, and ICRP differ not only from EPA's parameters but also from each other's. While the differences emphasize the controversy surrounding many of these parameters, it is nonetheless useful to identify those parameters chosen by EPA that differ from all three of the organizations.

Table VIII. BEIR V, UNSCEAR, and ICRP Parameters Compared with those of EPA NESHAP

Parameter	BEIR V Committee (NRC 1990)	UNSCEAR (1988)	ICRP (1991)
Populations	Same	Same	Same
Population Transfer Coefficient	Different	Same	Different
Dose-Response Curve	Different	Different	Same
Dose-Rate Effect	Same	Same	Different
Cancer Risk Projection Method	Different	Different	Different
Genetic Risk Projection Method	Different	Different	Different
Cancer Risk Estimate[a]	Different	Different	Different
Genetic Risk Estimate	Different	Different	Different

[a] Adjusted using the CIRRPC method

The cancer risk projection method used by the EPA differs from the other organizations' methods in several important ways. The EPA's unique choice of a risk measurement has been criticized for being difficult to interpret (Thomas et al. 1992). In

addition, the EPA relied on outdated population statistics and dosimetry data. Because population statistics are the basis for the lifetable technique, this is a serious shortcoming. The use of outdated population information affects the results in ways that cannot be predicted or compensated for. Finally, the T65DR dosimetry system used by the EPA for most parameters overestimated the dose equivalent to organs. When this error is carried through the projection method and into the final estimate of cancer risk, it is possible that the risk is underestimated (Mettler et al. 1990). Complicating this analysis, however, is the EPA's decision to use DS86 dosimetry data to choose a linear dose-response curve. This inconsistency affects the EPA's entire risk assessment method.

The use of outdated or inconsistent information was acknowledged by the EPA, which suggested that " . . . a detailed reevaluation of EPA's current risk estimates is indicated when this [the BEIR V Committee's] report is issued" (EPA 1989a, p. 6-4). However, current information was available to the EPA in 1989, just as it was available to the UNSCEAR (UNSCEAR 1988), and indeed, the EPA used data from the DS86 dosimetry system to choose a linear dose-response curve. Thus it is difficult to justify the EPA's reliance on outdated information.

The EPA also differs from the other organizations in its calculation of doubling dose used to project genetic risks. The EPA chose to use a range established by the BEIR III Committee, 0.5–2.5 Gy, while the others settled on a single doubling dose of 1 Gy (NRC 1980). This range was chosen because of the uncertainties in genetic risk: we do not know mutation rates for all gene loci that are affected by ionizing radiation, and we have not identified all gene loci associated with serious genetic diseases. These same uncertainties were shared by the BEIR V Committee, UNSCEAR, and ICRP, yet these organizations all agreed on a single doubling dose of 1 Gy. Judging from the BEIR V Committee's assertion that a doubling dose of 1 Gy is supported by the DS86 dosimetry data from the Hiroshima and Nagasaki survivors, this may be another situation in which the EPA used outdated information.

The EPA's estimate of the probability of genetic disease may also have been affected by the EPA's choice of a mutation component for congenital diseases, for which the EPA also chose a range. It is the upper bound of this component that varies from the values chosen by the other organizations. This range was first proposed by the BEIR I Committee in 1972 but was narrowed by the BEIR V Committee. This may be yet another situation in which the EPA used outdated information.

Finally, as modified for comparison using the CIRRPC method, the EPA's estimate of fatal cancer probability from a single, whole-body irradiation by low-LET

radiation was much lower than the estimates of the other organizations. Perhaps this is a result of the projection method discrepancies discussed earlier. More likely this is a complex combination of several differences in parameter choices. Either explanation suggests the importance of choosing risk assessment parameters carefully.

Discrepancies between the risk assessment methods established by internationally respected organizations and the method applied by the EPA in preparing the NESHAP suggest a simple question: Why didn't the EPA adopt one of the methods used by the BEIR V Committee, UNSCEAR, or ICRP? One answer might be that the EPA's document predates the BEIR V Committee and ICRP documents; yet the data were available for use by the UNSCEAR in its 1988 document.

The methods used by the BEIR V Committee, UNSCEAR, and ICRP have much in common with each other and are based on the most current data. The EPA could benefit from the research done by these prestigious organizations and would no doubt improve its own credibility by employing one (or a combination) of these methods. In the EPA's own words, "radiation risk assessment is a process that continues to evolve as new scientific information becomes available" (EPA 1989a, p. 6-2). Perhaps it is time for the EPA to reconsider its choice of a risk assessment method in setting NESHAP limits.

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