

**REPORT OF
THE NATIONAL INSTITUTES OF HEALTH
AD HOC WORKING GROUP
TO DEVELOP
RADIOEPIDEMIOLOGICAL TABLES**

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
Public Health Service National Institutes of Health

DAVID G. WELLS, CHAIR

REPORT OF THE NATIONAL INSTITUTES OF HEALTH
AD HOC WORKING GROUP TO DEVELOP RADIOEPIDEMIOLOGICAL TABLES

Responding to the Congressional Mandate under Section 7(b) of the
Orphan Drug Act of January 4, 1983 (PL 97-414)

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EXECUTIVE SUMMARY

Public Law 97-414, the Orphan Drug Act, passed by the Congress and enacted on January 4, 1983, directed the Secretary of Health and Human Services to construct radioepidemiological tables showing the probability that certain cancers could result from prior exposure to radiation.

To ensure as far as possible that the radioepidemiological tables would represent the best possible scientific judgment, the Secretary of Health and Human Services established the NIH Ad Hoc Working Group to Develop Radioepidemiological Tables. To assist the Working Group, the NIH and the Assistant Secretary for Health requested the National Academy of Sciences to form an advisory committee (the National Academy of Sciences Oversight Committee on Radioepidemiologic Tables). The Working Group would like to thank Dr. C. Frederick Mosteller and the other members of the Oversight Committee for their constructive criticisms, which have been of great benefit during the preparation of the report. The Working Group also benefited greatly from the groundwork laid by the National Council on Radiation Protection and Measurements (NCRP) Committee No. 71, which already was addressing the question of probability of causation (PC) for radiogenic cancers. Finally, the Working Group has had an opportunity to interact with the Science Panel of the Committee on Interagency Radiation Research and Policy Coordination, Office of Science and Technology Policy, Executive Office of the President, during the course of the Panel's evaluation of the tables, and has its report dated November, 1984.

In constructing the tables, the NIH Working Group and the Oversight Committee identified the same set of problems involved in the calculation of probability of causation for cancer following exposure to ionizing radiation. Additionally, the Oversight Committee has made several important suggestions that a future committee, whose task is to update this report, should find useful.

The Working Group determined that it could not attempt a new analysis of the epidemiologic data but should base many of its calculations on the report issued in 1980 by the National Academy of Sciences Committee on the Biological Effects of Ionizing Radiation (BEIR III) (1) that itself had required more than three years to complete. The Working Group, however, did depart from the BEIR III report in several important details because of the availability of new data. These include adoption of a new "wave function" time-response model for leukemia and bone cancer, different coefficients for leukemia and cancers of the lung, thyroid and breast, addition of cancer of the salivary gland, omission of lymphoma as a radiation-induced cancer, and avoidance of PC calculations for certain cancers following exposure at younger ages. Overall, of the 78 age-, sex-, and site-specific risk coefficients employed in the present report, 40 were taken directly from the BEIR III report and 38 were obtained from more recent sources.

The problems recognized by both groups can be resolved more accurately in the future through the accumulation of more human data, and especially by new insights into the mechanisms of carcinogenesis, and perhaps, rather less by mathematical ingenuity or further in-depth analysis of existing

data, although more refined analysis of newer data will be useful. The Working Group interpreted its mandate from the Orphan Drug Act as requiring assessment of currently available data and the exercise of its best judgment regarding the handling of the scientific uncertainties that are at present unresolved.

Historically, not long after ionizing radiation was discovered in 1895 and methods for producing and utilizing various types of radiation became available, it was demonstrated that such radiation could be seriously damaging. First came the recognition that radiation to the skin could cause a serious, sunburnlike effect. By 1904 it was learned that radiation could cause skin cancers, and somewhat later (1911) it was shown that the incidence of leukemia was elevated in radiologists.

In 1928 the International Congress of Radiology adopted the first international recommendation for radiation protection. At that time, it was believed that there was a threshold for the deleterious effects of radiation, that is, a dose below which there would be no damage. Work on the genetic effects of radiation in the 1930's suggested that any dose of radiation had a certain likelihood of producing a damaging effect on germ cells. Concern over the genetic effects of radiation (2), so prevalent in the 1950's, has lessened in the last two decades, whereas the carcinogenic effects of radiation have become much more evident.

Radiation acts to cause cancers in a largely random manner. In a situation in which a large number of people have received a moderate-to-large amount of radiation, the numbers of cancers of specific sites (e.g., breast cancer, leukemia, etc.) produced by that amount of radiation can be estimated. We cannot, however, predict which individuals will develop cancer. Even after the cancer has developed, we cannot state with certainty whether it was caused by radiation, since it is usually impossible to differentiate cancers induced by irradiation from those which occur "normally" in the population.

Cancers appear to be associated with a large number of environmental factors and genetic susceptibilities although, in any individual case, it is usually not possible to be sure of the exact cause of the cancer. The events that may cause or predispose to cancer interact in several ways, but only a few of these interactions are known and understood. Moreover, different individuals are exposed differently, and to a greater or lesser extent, to various carcinogenic factors as the result of cigarette smoking, alcohol consumption, viral infection, dietary habits, occupation, heredity, etc. If detailed knowledge were available about the effects of all these exposures and interactions, it would be possible theoretically to classify individuals into a large number of groups among which the probability of causation of a particular cancer by a given agent could be calculated more accurately. For any carcinogen, however, including radiation, the number of such groups is severely limited at present; i.e., from available data we can, with some assurance, partition populations into categories based only on a few factors, including age at diagnosis, sex, smoking history and age at exposure to radiation. Except for these subdivisions we calculate probabilities of causation only for aggregate groups in which unknown variations among individuals may be appreciable. However, probabilities of causation based on even the most minimal partitioning are valid probabilities for these groups.

Attempts to estimate the probability that an observed effect resulted from one of several possible causes are not uncommon, even in the more exact physical sciences. Decay of short-lived subatomic particles, where only a small number of events can be observed and several potential mechanisms exist, is in some respects analogous to the problems involved in constructing radioepidemiological tables. In both cases, probabilities are calculated from a small number of events. There is, however, an important difference. In physics a large number of well-tested and comprehensive theories exists to guide calculations, whereas in biology and medicine there are few well-established general and predictive theories and the systems are immeasurably more complex. This becomes particularly important for calculation of the probability that radiation caused a certain cancer when the dose of radiation was small. Such calculations are therefore subject to great uncertainty (see Chapter VII).

In order to construct the radioepidemiological tables, several fundamental decisions were made, which are explained in the remainder of this Summary.

I. The Working Group first had to decide what data should be used to develop the numbers in the tables. In general, epidemiologic data derived from radiation exposure to humans were utilized. However, effects in experimental animals, largely rodents, and additional data from in vitro studies of effects of radiation on cell cultures, which can provide useful information on principles, were also considered. The animal data on low levels of ionizing radiation are constrained by the same limitations as the data on humans--the difficulty that the small effects require very large numbers of animals. Furthermore, the studies on rodents have been restricted almost entirely to highly inbred strains of animals and to types of tumors that occur with high frequency. Hence their relevance to the carcinogenic effects of low-level irradiation in the human population is uncertain. The in vitro experiments suffer because the cells are studied under conditions that differ profoundly from those in vivo, and are of uncertain relevance to the carcinogenic effects of irradiation in man (3).

II. Secondly, the Working Group had to resolve how to estimate the risks from low doses of radiation. Although effects of moderate-to-high doses on large populations can be estimated reasonably well, several government reports, such as the 1979 Report of the Work Group on Science of the Interagency Task Force on the Health Effects of Ionizing Radiation (4), the 1981 report of the Comptroller General to the U.S. Congress (5), and the 1981 report of the Interagency Radiation Research Committee (6), as well as such authoritative reports as the 1980 (BEIR III) report of the National Academy of Sciences (1) and the 1977 report of the United Nations Scientific Committee on the Effects of Atomic Radiation (7), testify to the uncertainty of the carcinogenic effects of very low doses of radiation. Thus, the BEIR III committee was unwilling to make estimates of the carcinogenic effects of radiation for acute doses below 10 rad or for continuing exposure to doses below 1 rad per year. Although the non-threshold hypothesis is accepted for radiation protection purposes, empirical evidence as to the existence of a threshold is lacking.

Some environmental and occupational doses are quite small, on the order of those resulting from natural background radiation to which we are all exposed (about 0.08 to 0.2 rem per year in the United States). It might be supposed, therefore, that studies of populations living in regions where background levels vary greatly would yield estimates of carcinogenic risks associated with such differences. Several such studies have been attempted, but the risks are so low that any effect of variation in background radiation is overshadowed by the natural variations in cancer incidence (1,7-9). At the present time, estimations of effects at low doses are based upon assumptions as to the mathematical form governing the dependence of effect upon dose, since we must extrapolate from the dose region where we have evidence of effects, to lower doses where effects have not been observed or may not be large enough to be detectible.

In general, the Working Group has sought to use the dose-effect model for each cancer which is most consistent with both the human epidemiologic data and the radiobiological data. For leukemia, the data are consistent with a so-called linear-quadratic model; hence this model is the basis for the PC tables calculated for leukemia. This model utilizes two constants and, in general, predicts that small doses of radiation have a lesser effect per rad than do higher doses. There are radiobiological reasons for assuming that a linear-quadratic dose-effect model is generally applicable to other cancers, which are discussed both in the BEIR III report and in Chapter III of the present report. Accordingly, we have used this approach for all cancers except those of the thyroid and breast. For carcinoma of the breast and thyroid, the data appear to be best described by a simple linear relationship in which the carcinogenic effect of radiation is directly proportional to the dose; again, the tables are based on this interpretation.

III. The Working Group also had to consider the relative effectiveness of radiation delivered at different dose rates. Although there are no conclusive human data on the carcinogenic effect of radiation delivered at a very low dose rate relative to that delivered at a high dose rate (atom bomb survivors, therapeutic radiation), several national and international bodies have suggested that radiation of low linear energy transfer (low LET) is considerably less carcinogenic at a low dose rate than at a high dose rate (6,7,10). If a linear-quadratic model is used, no separate dose-rate correction is necessary for protracted radiation exposures, given a certain partitioning of the dose (see Chapters III-I and V-B). In the case of carcinoma of the breast and thyroid, the use of the linear dose-effect model implies that there should be no dose-rate effect; data available for both of these cancers are consistent with this prediction.

IV. An additional assumption required for calculation of PC values concerns the relationship between the number of cancers produced at any given time after radiation and the number normally occurring in a similar population of the same age and sex not exposed to radiation. The BEIR III report utilized both a relative risk time projection model and an absolute risk time-independent model. The absolute risk model assumes that the radiation-induced risk of developing cancer is constant after a suitable latent period following irradiation. The relative risk time projection model states that, at any time after a latent period, a given

dose of radiation increases the probability of developing cancer by a constant fraction of the baseline risk. Available data, particularly on breast and lung cancer in Japanese atomic bomb survivors, which have appeared since the preparation of the BEIR III report, support the relative risk time-projection model more convincingly. Therefore, the Ad Hoc Group has adopted this model, as discussed in Chapter III.

There is a substantial body of data on the risk of developing leukemia (both acute leukemia and chronic granulocytic leukemia) after radiation. Hence, it is possible to develop a model that accurately follows the observed data. This model is basically wave-like in form, following neither the constant absolute risk nor the constant relative risk time-projection model. Accordingly, we have used the wave-like model to describe the risk of developing leukemia as a function of time after radiation.

V. A problem awaiting resolution is the relative carcinogenicity of high-LET radiation. This is the type of radiation delivered by large, highly energetic particles such as neutrons or alpha particles. For the same absorbed dose this kind of radiation appears to be more effective in causing cancers than low-LET radiation, such as that delivered by X rays or gamma rays. All the tables except for bone cancer, and for lung cancer after exposure to radon (which occurs principally in uranium miners), deal with the more commonly occurring low-LET radiation. Several committees are currently investigating the carcinogenic effects of high-LET radiation. Pending their conclusions, it is not possible to use these tables relevant to low-LET radiation for the calculation of PC estimates for high-LET radiation unless a biologically equivalent dose can be determined for the individual case.

Other estimates of probability of causation, or their equivalent, have been prepared by British Nuclear Fuels, Limited (BNFL), by Gofman (11), and by Stewart (12). The BNFL procedure is not available to the public, and certain objections have been raised to the Gofman calculations (13). Stewart's analysis was based on data from the Hanford workers (14), which are much too limited to provide any basis for a compensation system (15,16). The present report represents a consensus of the Working Group, aided by its interaction with the Oversight Committee of the National Academy of Sciences and the Science Panel of the Committee on Interagency Radiation Research and Policy Coordination.

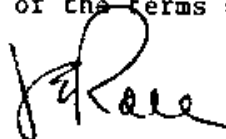
Chapter I of the report outlines the Congressional actions that mandated its preparation; Chapter II describes briefly what is known about human cancer. Chapter III describes relations between radiation and cancer, including a listing of those cancers which may be caused by radiation and for which adequate data are available to calculate PC, and those for which an association with radiation is not proved. Chapter IV describes concepts involved in calculating the probability that any given amount of radiation was the cause of any particular cancer. Chapter V lists data sources and assumptions that are required for calculations of PC values and justifies these choices. Chapter VI describes how the calculations have been performed. Uncertainties in the basic data and assumptions which are necessary ingredients in the calculation of probabilities of causation are reflected in uncertainties in the final PC values themselves. An attempt has been made in Chapter VII to identify

and assess the various sources of uncertainty and to combine these uncertainties into single measures for individual cancers. The combined uncertainties, while not small, are not so large as to negate the usefulness of the PC's, especially at the low and high ends of the scale. Chapter VIII discusses how the present PC estimates may be updated and describes what new information may become available, and how it might be handled. Chapter IX describes how to calculate the probability of causation for any radiation dose and any cancer using only a few tables, which appear in Chapter X. In Chapter X each cancer for which a probability of causation can be calculated is discussed and specific examples of calculations are presented, together with tables of the constants necessary for these calculations. This arrangement has necessarily given rise to some redundancy, but the Working Group believes that the present format permits anyone to obtain all the basic information for calculation of PC for a specific cancer in any specific case from just one of the subsections of Chapter X.

In Appendix I, tables of the probability of causation for individual cancers are presented for radiation doses of 1, 10 and 100 rad. For any specific case, the reader is encouraged to use the simple formulae in Chapter X for calculation of a probability of causation.

In Appendix II, the Working Group has reproduced the specific recommendations of the NAS Oversight Committee with respect to the July, 1984 draft of the present report and its future revisions (17). Since this final version of the Tables incorporates most of the recommendations made by the Oversight Committee, each recommendation is annotated as to its status in the final report presented here.

Appendix III is a glossary of some of the terms used in this report.



J. E. Rall, M.D., Ph.D., Chairman,
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Radioepidemiological Tables

January 4, 1985

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Chapter I: LEGISLATIVE AUTHORITY

A. Background

On January 4, 1983 the President of the United States signed Public Law 97-414 (known as the "Orphan Drug Act"), an act to amend the Federal Food, Drug and Cosmetic Act to facilitate the development of drugs for rare diseases and conditions, and for other purposes. This legislation includes a provision (Section 7 (b) of the bill) directing the Secretary of Health and Human Services to "devise and publish radioepidemiological tables that estimate the likelihood that persons who have or have had any of the radiation-related cancers and who have received specific doses prior to the onset of such disease developed cancer as a result of these doses." The complete text of section 7 (b) of the bill and an excerpt from President Reagan's statement, on the occasion of his signing the Orphan Drug Act, are included in section B of this chapter.

On February 25, Dr. Edward N. Brandt, Jr., Assistant Secretary for Health, Department of Health and Human Services, assigned lead responsibility for the implementation of this charge to the National Institutes of Health. An Ad Hoc Working Group, chaired by Dr. J. E. Rall, Deputy Director for Intramural Research, NIH, was established; this group has met regularly since April 5, 1983. Subsequently (August 4, 1983), the Secretary of Health and Human Services approved the Charter for an "Ad Hoc Working Group to Develop Radioepidemiological Tables" to carry out this mandate. The text of the Charter is included as section C.

It may be noted that the section of P.L. 97-414 pertaining to the development of radioepidemiological tables originally was introduced by Senator Orrin Hatch (Utah) as a part of Senate bill S 1483: "Radiation Exposure Compensation Act" to provide for damages due to radiation exposure from nuclear weapons tests in Nevada. Since neither this bill nor the companion House bill (H.R. 6052) was reported out of the respective committees, the section relating to radioepidemiological tables was attached as an amendment to the "Orphan Drug Act" which was passed by both houses and signed into law on January 4, 1983. On March 23, 1983, Senator Hatch introduced the "Radiogenic Cancer Compensation Act" which intends to use as the basis for award of compensation the tables of probability of causation of cancer from radiation exposures, prepared in response to the requirements of the "Orphan Drug Act."

B. Public Law 97-414 - January 4, 1983

"7(b)(1) Within one year after the date of enactment of this Act, the Secretary of Health and Human Services shall devise and publish radioepidemiological tables that estimate the likelihood that persons who have or have had any of the radiation-related cancers and who have received specific doses prior to the onset of such disease developed cancer as a result of these doses. These tables shall show a probability of causation of developing each radiation related cancer associated with receipt of doses ranging from 1 millirad to 1,000 rads in terms of sex, age at time of exposure, time from exposure to the onset of the cancer in question,

and such other categories as the Secretary, after consulting with appropriate scientific experts, determines to be relevant. Each probability of causation shall be calculated and displayed as a single percentage figure.

(2) At the time the Secretary of Health and Human Services publishes the tables pursuant to paragraph (1), such Secretary shall also publish--

- (A) for the tables of each radiation related cancer, an evaluation which will assess the credibility, validity, and degree of certainty associated with such tables; and
- (B) a compilation of the formulas that yielded the probabilities of causation listed in such tables. Such formulas shall be published in such a manner and together with information necessary to determine the probability of causation of any individual who has or has had a radiation related cancer and has received any given dose.

(3) The tables specified in paragraph (1) and the formulas specified in paragraph (2) shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise. The Secretary of Health and Human Services shall update these tables and formulas every four years, or whenever he deems it necessary to insure that they continue to represent the best available scientific data and expertise."

Excerpt from President Reagan's statement on the occasion of his signing the Orphan Drug Act

"... there is as yet no consensus among radiation experts in relating human cancers and exposure to low levels of radiation. Yet, Section 7 mandates that probability of causation tables be calculated for even very small dose levels. Accordingly, I am directing the Secretary of Health and Human Services to complete the tables to the extent that may be possible and scientifically responsible, in light of the analysis also mandated by Section 7, which requires him to 'assess the credibility, validity, and degree of uncertainty associated with such tables.'"

C. Charter - Ad Hoc Working Group to Develop Radioepidemiological Tables

"Purpose

Section 7(b) of Public Law 97-414 directs the Secretary of Health and Human Services to devise and publish radioepidemiological tables that estimate the likelihood that persons with any radiation-related cancer who received specific radiation doses before the onset of the cancer developed the disease as a result of such exposure. The tables must show the probability of causation for each cancer associated with receipt of doses ranging from 1 millirad to 1,000 rads in terms of sex, age at time

of exposure, time from exposure to disease onset, and such other categories as the Secretary, after consultation with appropriate scientific experts, determines to be relevant.

In carrying out this mandate, the Secretary deems it necessary to establish an Ad Hoc Working Group to Develop Radioepidemiological Tables comprised of scientific experts whose qualifications will insure a thorough, competent, and timely completion of the task.

"Authority

42 U.S. Code 217a, Section 222 of the Public Health Service Act, as amended.

This Ad Hoc Working Group to Develop Radioepidemiological Tables is governed by the provisions of Public Law 902-463, which sets forth standards for the formation and use of advisory committees.

"Function

In addition to developing radioepidemiological tables, the Ad Hoc Working Group shall:

1. Assess the credibility, validity, and degree of certainty associated with such tables; and
2. Compile the formulas that yielded the probabilities of causation listed in such tables. Such formulas shall be published in such a manner and together with information necessary to determine the probability of causation of any individual who has or has had a radiation-related cancer and has received any given dose.

The tables specified in paragraph (1) and the formulas specified in paragraph (2) shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise. The Secretary of Health and Human Services shall update these tables and formulas every four years, or whenever necessary, to insure that they continue to represent the best available scientific data and expertise.

"Structure

The Ad Hoc Working Group to Develop Radioepidemiological Tables shall consist of eight members, including the chairperson. Members and chairperson shall be selected by the Secretary, or designee, from outstanding authorities in the fields of endocrinology, radiation biology and pathology, radioepidemiology, biostatistics, and radiobiology. Members shall be invited to serve for a period of one year. Management and support services shall be provided by the Office of the Director, National Institutes of Health.

"Meetings

Approximately eight meetings shall be held at the call of the chairperson who shall also approve the agenda. A government official shall be present

at all meetings. Meetings shall be conducted and records of proceedings kept as required by applicable laws and Department regulations. Meetings shall be open to the public, except as determined otherwise by the Secretary; notice of all meetings shall be given to the public.

"Compensation

Members who are not full-time Federal employees shall be paid at the rate of \$100 per day, plus per-diem and travel expenses in accordance with Standard Government Travel Regulations.

"Annual Cost Estimate

Estimated annual cost for operating the Ad Hoc Working Group, including compensation and travel expenses for members but excluding staff support, is \$36,700. Estimated annual man years of staff support required is one at an estimated annual cost of \$49,213.

"Reports

Section 7(b) of Public Law 97-414 directs that within one year after the date of enactment of this Act (January 4, 1983), the Secretary of Health and Human Services shall publish the radioepidemiological tables. The Ad Hoc Working Group will complete its task as outlined in the Function section of this document and submit these findings to the Director, National Institutes of Health, by October 15, 1983.

"Termination Date

Unless renewed by appropriate action prior to its expiration, the Ad Hoc Working Group to Develop Radioepidemiological Tables will terminate on May 15, 1984.

Approved:

8-4-83

Date

(signed) Margaret M. Heckler "
Secretary

Chapter II: THE ETIOLOGY OF CANCER

A. Introduction

Cancer is the second leading cause of death in the United States and has recently become one of the most intensively studied of diseases. Many forms of human cancer are now recognized to have multiple causes. In addition, a number of theories have been proposed to explain the biological mechanisms of carcinogenesis. While our understanding of such mechanisms is still very limited, it is apparent that the overall incidence of cancer is related in large measure to cancer-causing factors in the "environment" defined broadly to encompass air, water, food, and such other factors as individual lifestyle, occupation, smoking habits, sexual activity, etc.

This chapter surveys briefly some of the current theories of cancer. It also summarizes what is known about the more important risk factors that determine the likelihood of cancer in an individual.

B. Current Theories of Carcinogenesis

For many carcinogens the process of tumor development is postulated to involve successive phases, three of which have traditionally been designated the initiation phase, the promotion phase, and the progression phase. During the initiation phase, the DNA of the target cell, which contains the genetic code, is presumed to be damaged or structurally altered as the result of exposure to radiation, a carcinogenic chemical, or some other initiating agent. A variety of molecular mechanisms has been hypothesized to explain the alteration of cellular DNA, including random point mutation, gene rearrangement, chromosomal translocation, and altered DNA methylation (1,2).

The promotional phase of cancer development is concerned with the subsequent changes in the initiated cell that lead to development of an overt tumor. It differs from initiation in a number of respects, being a much slower process, which may cover a major portion of the human lifespan. While a single exposure to an initiating substance can suffice to alter DNA, promoting effects typically are induced only by prolonged contact with the agent in question (2). Promotion may thus be based on different mechanisms; for example, interference with normal regulation of cell growth or with the body's natural defense mechanisms, including repair of DNA damage, conjugation and detoxification of toxicants, immunological resistance, hormone balance, etc. The progressive phase involves the outgrowth of progressively more malignant variants of the original neoplasm.

Together, the promotion and progression of neoplasia are envisioned to involve a series of changes in the regulation of cell growth, with variations in the malignancy of the resulting tumors by the time they become detectable clinically. Some forms of cancer, for example, are known to grow rapidly and metastasize early, while others grow slowly and remain localized indefinitely. These differences, which remain to be fully explained, affect the probability of ascertainment of the cancers in question.

Although much of the research on carcinogenesis has been focused on the initiation phase, promotion may ultimately be of greater importance in determining the incidence of cancer (3). It is noteworthy moreover, that the distinction between initiating and promoting agents is not always clear-cut (2). Radiation and certain chemicals appear to be capable of acting both as initiators and promoters; i.e., as complete carcinogens (4).

Genetic effects leading to cancer may involve germ cells as well as somatic cells. Evidence for the influence of germ cell mutations on human carcinogenesis comes primarily from studies of single-gene defects associated with cancer, family aggregations of neoplasia, and cytogenetic studies showing some cancers to be associated with inherited chromosomal abnormalities. Every form of cancer probably has a heritable component of some magnitude. For some forms it can be large.

It is difficult to estimate the carcinogenic risks of radiation by extrapolation without further knowledge of the precise mechanisms involved in radiation carcinogenesis. Advances in the molecular biology of cancer should eventually lead to new understanding of how radiation induces malignancy and to refinement in our approaches to risk assessment. Significant advances in cancer biology have already come from studies of the genes involved in malignant transformation, some of which are called "oncogenes" (5). Oncogenes discovered originally in tumor viruses have since been found to have homologues in normal cells (6), where they can be "activated" to produce malignant transformation by (a) linking them to powerful retroviral promoters, (b) mutations which may be produced by chemical carcinogens like nitrosomethylurea (7,8), or (c) chromosomal translocations (6-9). Since ionizing radiation is known to cause both point mutations and chromosomal aberrations, it is conceivable that radiation carcinogenesis may, in some instances at least, involve activation of cellular oncogenes. Recently, direct evidence for activation of the c-K-ras oncogene by gamma radiation, through a single base mutation, has been reported (10).

Recent studies of malignant transformation by viral oncogenes and activated cellular oncogenes suggest that the transformation of cells to malignancy may require activation of more than one cellular oncogene. It is thus possible that the long "latent" period that characteristically elapses between radiation and the clinical appearance of a cancer may result from the need for successive oncogenes to be activated or for other types of sequential changes to take place.

C. Environmental and Life Style Risk Factors

It has been inferred that as much as 75-80% (3) of fatal cancers in the United States results from the influence of life style and other non-hereditary, or environmental, factors. Epidemiological studies imply that the largest effects are related to smoking, alcohol consumption, diet and other factors related to life style. Occupational exposures and the effects of radiation, chemical pollution, medical therapy, sexual activity, and infections are thought to contribute to a lesser extent. In some instances, heredity may render an individual more vulnerable to the effects of an

environmental carcinogen, as is illustrated by the heightened susceptibility of individuals suffering from xeroderma pigmentosum to the development of skin cancer as a result of exposure to the ultraviolet radiation in sunlight. In evaluating the importance of the various environmental risk factors, one should consider the potential influence of host-related characteristics as well as the possibility that a cancer may have multiple causes.

1. Smoking

Smoking of tobacco, particularly in the form of cigarettes, is generally recognized as the single most important external risk factor for human cancer, being estimated to cause 25-40% of all cancer deaths in the U.S. (3,11,12). It is the primary cause of lung cancer in both men and women, and is also associated with an increased risk of cancer of the larynx, oral cavity, esophagus, bladder, kidney, and pancreas. Although the percentage of the smokers in the population has declined from 42% in 1965 to a current level of approximately 33%, the number of active smokers in the United States is estimated to be about 53 million (12), and there is concern about the potential risks from "passive" smoking in non-smokers (13-15). Although the specific mechanism(s) by which tobacco smoke contributes to an increased risk of various types of cancer is not yet known, a variety of carcinogenic chemicals are known to be components of tobacco smoke (12).

2. Alcohol consumption

Alcohol consumption is thought to play a role in the onset of cancer at a variety of sites, including the mouth, pharynx, larynx, esophagus, liver, and lung; and some investigators have associated 3-5% of all cancer deaths with the drinking of alcoholic beverages (3). Although approximately one-third of the adult U.S. population drinks alcoholic beverages at least once a week, and about 10 million members of the population are estimated to be problem drinkers (4), the specific impact of alcohol per se on human cancer risk is difficult to assess since, among the complexities, reliable quantitative data on consumption are difficult to obtain. Furthermore, many investigators believe that alcohol acts chiefly by enhancing the effects of other primary carcinogens such as those in tobacco smoke (4).

3. Diet

Although there is a growing recognition that diet can influence the risks of specific types of cancer, the mechanisms and magnitudes of dietary effects are poorly understood. Doll and Peto infer that diet may be involved in 10-70% of all cancers in this country (3). Humans are exposed to a multitude of agents that can enhance or inhibit the onset of cancer, through the dietary intake of meats and fats, fibers, vitamins, and naturally occurring carcinogens and their precursors (16). Carcinogens in the diet also arise as by-products of food preparation (polycyclic aromatic hydrocarbons), or may be introduced as natural contaminants

(aflatoxin), environmental contaminants (pesticide residues, heavy metals, PCBs, etc.), and additives for coloring, flavor (cyclamates and saccharin), and food preservation. Dietary carcinogens may act as tumor initiators or promoters, may facilitate the formation of carcinogens in the body, or may affect the transport, activation, or deactivation of carcinogens already present in the body (4).

4. Occupational exposures

Exposure to various occupational risk factors can increase the likelihood of cancer. Carcinogens that have been identified in the workplace include arsenic, asbestos, benzene, coal tar pitch volatiles, 2-naphthylamine, vinyl chloride, nickel and radiation. Moreover, there are a number of industries such as the petrochemical industry, the rubber industry, and coal mining, in which workers seem to have an excess risk of developing cancer, even though the specific risk factor or agent has yet to be identified. Because of the relatively long latencies associated with most forms of occupationally related cancers, current incidences of, or deaths from, occupationally related cancers are typically the result of exposures that occurred one or more decades in the past, when exposure levels were usually much less well-controlled and not as well-documented as are present-day levels. Furthermore, since workers frequently change jobs, both within and between industries, they may be exposed to a variety of potentially carcinogenic agents, the individual effects of which are not easily isolated.

5. Pollution

Manmade pollution of air and water is another source of potential cancer risk for humans. The frequently observed increase in lung cancer death rates among inhabitants of the more urban areas of the United States has been interpreted as evidence that air pollution, primarily polycyclic aromatic hydrocarbons from auto exhaust contributes to the risk of cancer. This argument is confounded, however, by the fact that the typical urban dweller is more likely to smoke than his rural counterpart and more likely to come into contact with a variety of occupational/ industrial risk factors as well. Although it is extremely hard to separate the impact of polluted air from the effects of these other risk factors, most researchers seem to believe that the actual percentage of all cancers specifically attributable to air pollution, while perhaps not negligible, is likely to be small (4).

The carcinogenic effects of water contamination, which may arise as a result of industrial pollution, agricultural runoff, waste dump seepage, and as a byproduct of drinking water purification (17), are even more difficult to assess than those associated with air pollution (4). Even in the few instances where case-control studies have been conducted, results have not always been consistent (4).

6. Medical therapy and diagnosis

Some agents used in the past to diagnose or treat various diseases have subsequently been shown to increase the risk of cancer, and their use has been curtailed. Examples include inorganic trivalent arsenic (skin cancer), chloronaphazine (bladder cancer), the radioactive contrast agent, thorostrast (cancer at the organ of concentration), and diethylstilbestrol (vaginal adenocarcinoma) (4). Ionizing radiation and some of the drugs that have been found to possess carcinogenic potential, such as certain alkylating agents used to treat different types of cancer and various immunosuppressive drugs employed in organ transplantation, continue to be used with discretion, insofar as their expected benefits are considered to outweigh their known risks.

7. Sexual development and behavior

Hormonal stimulation associated with normal sexual development influences the risk of cancer in humans. For example, the risk of breast cancer in women is affected by age at menarche, age at first childbirth, and age at menopause. The incidence of testicular cancer is elevated in men born with cryptorchidism or undescended testes. The likelihood of developing cancer of the uterine cervix increases with the number of different sexual partners that a woman has had (4).

8. Viral infections

Viral infections are a known cause of various cancers in animal species and have been regarded as potential risk factors in the development of human tumors. The Epstein-Barr virus is thought to act as a causative cofactor in the onset of Burkitt's lymphoma (in Central Africa and New Guinea) and nasopharyngeal carcinoma (in the Far East, especially South China). Hepatitis B virus evidently plays a role in the development of hepatocellular carcinoma, particularly in Asia and Africa (3,4).

Other viruses of possible importance in human reproductive tract cancer development include herpes simplex virus (4) and cytomegalovirus (4). Human T-cell leukemia virus (18) has been isolated and sequenced and is clearly the etiologic agent in this type of leukemia. At the present time, the role of retroviruses or oncogenes in other cancers is unclear, but it could well be that activation or mutation of oncogenes are important factors in the genesis of many cancers.

9. Interactive effects

The preceding discussion of carcinogenic risk factors concerned primarily the effects of individual agents, whereas humans are ordinarily exposed to a variety of agents. The potential for interactions among the effects of different risk factors should also thus be considered. The interaction of two factors can be expressed in a variety of ways. For example, one may act as a vector that carries the other to a critical target site; the first may promote or enhance the carcinogenic activity of the second; the two may act independently; or they may produce a joint effect which markedly exceeds the sum of their separate effects.

Although epidemiology has not focused to any great extent on interactive effects between suspected or known carcinogenic risk factors, there are a few well-known examples of such phenomena. It has already been noted that alcohol consumption is generally regarded as a co-factor that combines with cigarette smoking to elevate the risk of esophageal cancer. Similarly, the joint action of infection with hepatitis B virus and dietary intake of aflatoxin has been cited as a cause of liver cancer in certain African and Far Eastern populations. Dietary zinc deficiency may also interact with alcohol consumption to increase the likelihood of developing esophageal cancer (4). Furthermore, some investigators have suggested that air pollutants combine with carcinogens in cigarette smoke to enhance the production of lung cancer (4). However, the most striking example of an enhanced response resulting from the joint action of two environmental carcinogens is the combined effect of asbestos and cigarettes. The mortality ratios for workers exposed to either asbestos or cigarettes individually were observed in one industrial study to be approximately 5- and 10-fold, respectively, whereas the corresponding ratio for workers exposed to both (i.e., asbestos-exposed workers who smoked) was in excess of 50-fold (4). Cigarette smoking also appears capable of altering the carcinogenic effects of ionizing radiation in certain circumstances, as is discussed in a later section of this report (Chapter IV-H).

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Chapter III: RADIATION AS A CAUSE OF CANCER

A. Introduction

Although ionizing radiation has been a part of the natural environment since the world began, only within the past century has man begun to study and use radiation as a tool in industry, biology, medicine, and warfare. The study of ionizing radiation as a cause of cancer has been particularly productive, with the result that we probably know more about its carcinogenic effects than about those of any other environmental carcinogen (1). This knowledge has been gained because it has been possible to identify study populations with documented exposures to fairly high radiation levels, and because ionizing radiation has proved to be a precisely controllable means of inducing cancer experimentally in laboratory animals. As a public health problem, ionizing radiation ranks well down the list of carcinogens: less than 3% of the U.S. cancer burden can be plausibly attributed to ionizing radiation from natural sources and human activities (2), compared to around 30% for tobacco smoking (3). We also know, however, that large doses of ionizing radiation can noticeably increase the cancer risk, and we are able to quantify these effects with some confidence (4). For example, among 6,035 atom bomb survivors in the Life Span Sample who were exposed to 100 or more rad, there were 498 deaths from cancer in the period 1950-1978, when only 323 such deaths would have been expected on the basis of the experience of survivors exposed to less than one rad, an increase of 54 per cent (5). Among the 23,073 exposed to 1-9 rad, however, the observed 1,248 cancer deaths are no higher (even slightly less) than expected on the same basis.

B. Characteristics of Ionizing Radiation

Ionizing radiation includes electromagnetic radiation (such as X rays and gamma rays), and energetic subatomic particles (such as protons, neutrons and alpha particles). These radiations have the capacity to produce ions from atoms or molecules in their paths by adding or removing electrons. A mechanism by which ionizing radiation induces cancer is thought to begin with the absorption of energy within cells, leading to alterations in the genome of the cell (1; see also Chapter II). Some other forms of radiant energy, like ultraviolet light, can affect cellular DNA directly and induce cancer, but not by ionization.

The energy absorbed per unit mass from the radiation traversing a tissue is termed the absorbed dose. Absorbed dose (or, for simplicity, dose) is measured in rad (1 rad = 100 erg per gram) or gray (1 gray (Gy) = 1 joule per kg = 100 rad). In general, the greater the dose, the greater the likelihood of an observable biological effect. Different biological effects can interfere with one another, however; e.g., it is possible for the likelihood of cancer to decrease with increasing dose at very high dose levels if cells that might otherwise give rise to cancer are so severely damaged that they lose the ability to multiply (1,4,6).

Different types of ionizing radiation have been compared experimentally with respect to various biological effects, including cell killing, mutagenesis, and carcinogenesis (6). In general, the relative biological effectiveness (RBE) of a given absorbed dose of charged particle radiation depends on the spatial density of the ionizations (linear energy transfer, or LET) produced along the tracks of the radiation, the heavy particle radiations tending to produce very closely spaced ionizations (high LET), while electrons, X rays and gamma rays tend to have fewer ionizations per unit length of track (low LET). In dealing with different types of radiation, the practice in radiation protection has been to relate the doses and effects of a given high-LET radiation to those of 250 kVp X rays as a standard, by introducing the quantity "dose equivalent." For a given end point, e.g., 50% acute mortality, the RBE of a certain type of radiation, say, neutron radiation of a given energy, is defined as the ratio of the required dose of X rays to the required dose of neutrons for that end point. For other end points, for different energies and for different dose rates or total doses, the RBE will have different values. A variable RBE is difficult to use for radiation protection purposes, and therefore practical reliance for assessing the impact of occupational or environmental exposures to high-LET radiation has been placed on a "quality factor", Q, which varies in relation to LET and is assumed to remain constant in the low-dose range (7,8). By multiplying the absorbed dose (in rad) by the quality factor (Q) for a given radiation, one obtains the "dose equivalent" for that type of radiation (expressed in rem = "rad equivalent in man"). The use of the Q factor is unsatisfactory, however, for the purpose of estimating cancer risk from high-LET radiation, in view of the aforementioned variations in RBE. In general, data are not available for estimating the site-specific RBE for each particular set of circumstances;¹ the necessary information includes the LET of the radiation at the target tissues. For internal emitters (deposited radionuclides), knowledge of the spatial and temporal distribution within the target tissue will also be required. These are factors that must be determined on a case-by-case basis. For this reason, the Working Group has refrained from making tables for high-LET radiation except in the limited case of alpha particle radiation from radium-224 in bone and exposure to radon daughters in the case of lung, for which epidemiological data exist from direct observations.

C. Sources of Radiation Exposure

Each of us is continually exposed to ionizing radiation from cosmic rays, disintegrating radioactive elements in the earth, and radioactive elements occurring naturally in our bodies (4). People living at sea level in the United States receive about 80 millirem (1,000 millirem = 1 rem) average dose (strictly speaking, average dose equivalent) to their internal organs per year (Fig. III-1); but at higher elevations, where cosmic rays are more intense, or in regions where the natural radioactivity of the soil is fairly high, the dose can be twice that size, or greater. Natural background radiation is increased by building materials

¹The NCRP and ICRP-ICRU currently have task groups working on high-LET radiation.

containing radioactive minerals. People in poorly ventilated buildings are exposed to elevated levels of the radioactive gas radon, given off by building material and by the natural radioactivity in the underlying soil (9,10). The average dose equivalent to the bronchial epithelium, which reflects exposure to radon, is now thought to be 3 rem annually (11). This represents an increase of the previous estimate of 0.5 rem and reflects (a) a decision to employ a quality factor of 20 in place of the factor of 10 previously used, and (b) recent measurements of the indoor exposure to radon daughters inhalation, which has increased because of reduced exchange with the outside air.

Average radiation doses from man-made sources are of the same order of magnitude as from natural background, about 100 millirem per year (4). By far the largest contribution is from medical diagnosis. Individuals receiving radiation therapy for benign or malignant disease can get very large doses to certain parts of the body, up to several thousand rad, but relatively few people get such treatment. Similarly, the number of people occupationally exposed to ionizing radiation is not large and, because the average exposures are within a few hundred millirem per year, the contribution to the population average is quite small (4). The dose from global fallout produced by nuclear weapon tests and from radiation-emitting components of consumer products like television sets and smoke detectors is negligibly small (4,6,12).

D. The Evidence for Radiation Carcinogenesis in Man

We know that ionizing radiation can cause cancer in man because studies of different populations with documented exposures to high radiation levels (hundreds or thousands of times natural background) have consistently found higher cancer rates than those seen in comparable, non-exposed populations (13). Ionizing radiation was used in diagnosis and to cure or alleviate the symptoms of disease long before its carcinogenic potential was fully appreciated, and is the treatment of choice for some diseases (including cancer) for which the potential benefit outweighs the risk of subsequent cancer.

Studies of patient populations highly exposed to X radiation during diagnostic or therapeutic procedures constitute much of the epidemiologic basis for our knowledge of radiation carcinogenesis (14). Information on the effects of alpha-particle radiation comes from studies of workers who ingested radium while painting instrument dials with luminous paint (15) and from studies of uranium and other hard-rock miners working in atmospheres heavily contaminated with radon (16-17). There have been intensive studies of the survivors of the atomic bombings of Hiroshima and Nagasaki in 1945 (5), and of natives of the Marshall Islands, who in 1954 were exposed to radioactive fallout from a nuclear weapons test in the Pacific (18). The largest number of persons studied who were exposed to low-LET radiation at low dose and dose rate were patients who received oral iodine-131 for the treatment of hyperthyroidism (19).

From many studies it appears that, at some level of exposure, ionizing radiation can increase the risk for many, and perhaps most, of the types of cancer that occur in man. In general, it is clear that

radiation does not create unique forms of cancer, but increases the risk of some cancers that occur naturally. For the acute forms of leukemia, chronic granulocytic leukemia, and female breast cancer, the association is so strong as to appear certain (4). There is fairly strong evidence that ionizing radiation does not cause chronic lymphatic leukemia (4,6). For most other forms of cancer, the evidence lies somewhere between these two extremes, although for many the position on this scale is uncertain because there is very little information.

The credibility of a presumed causal association between risk and radiation exposure depends upon several factors, which must be considered in evaluating the evidence that radiation exposure affects risk for a particular cancer site:

- 1) Statistical significance - This depends on the total number of cancer cases observed and the apparent size of the excess relative to the baseline risk. For a fixed number of cases, the strength of the association is greater if the excess risk is relatively large and, for a fixed relative excess, the association is more credible if the evidence is based on many cases.
- 2) Specificity - How certain is it that the association was not due to something else? Credibility is helped by comparison with a non-exposed population, otherwise similar to the exposed population. It is especially important to satisfy this requirement in studies of medically exposed populations, for which the conditions leading to exposure may themselves be related to the risk of subsequent cancer. Since population groups that have been exposed to radiation actually differ in many ways from the general population, differences in rates of disease from general population rates may be difficult to interpret or to attribute to the radiation exposure.
- 3) Dose response - The level of risk should appear to increase with increasing radiation dose to the tissue of interest. Each of us is exposed to natural background radiation at the very least, and so the concept of increased risk from additional exposure involves the assumption of a gradient of risk with increasing exposure. As already mentioned, it is always possible that an increased risk among medically exposed persons may be attributable to the reasons for exposure rather than to the exposure itself. This possibility is less likely if there is an association of risk with level of exposure among the exposed persons.
- 4) Consistency - Is the association seen in a number of exposed populations, and are the apparent excesses similar when such factors as dose, age, and period of observation have been taken into account? "Statistically significant" associations will occur as a consequence of mere chance in a small proportion of studies - and in the field of radiation carcinogenesis the number of studies is large. Further, spur-

ious associations can arise by chance between cancer risk and practically anything, or exposure can be fortuitously related to a true risk factor. But such spurious associations are very unlikely to arise in many different populations, exposed under different circumstances. We therefore tend to place most credence in associations that turn up frequently and under diverse circumstances of exposure, while distrusting isolated reports not verified by other experience.

E. Quantification of Risk

Partly because we cannot tell for certain whether or not a person will develop cancer, even when we have the most detailed information possible about that person's physical condition, genetic background and life experiences, and partly because, in our present state of knowledge, carcinogenesis seems to be largely a random process, it is useful to think in terms of probabilities. In other words, whether or not a person develops cancer, and the time when that cancer becomes detectable, are matters of chance. Most of what we know about cause-effect relationships and cancer rates in different population subgroups is useful to the extent that it tells us how the probability of cancer diagnosis in a given person at a given time depends upon certain observable facts. Thus, information that ionizing radiation is associated with a particular type of cancer should, if it is to be of any help to us, lead to improved estimates of the probability that cancer will occur following radiation exposure.

It is not possible to tell whether or not a particular cancer observed in a given individual following exposure to ionizing radiation was caused by that exposure. Cancers occur in nonexposed people and are in general indistinguishable from radiation-induced cancers. We often can tell, however, if the number of cancers observed in a group of exposed people is greater than the number that would have been observed in the absence of exposure and, if so, we can estimate roughly how many of the observed cancers were induced by radiation. Thus we can estimate the excess risk, in an average sense, that pertains to any similar group of exposed people. Such an estimate pertains to a single individual only to the extent that that person can be considered "typical" of the group from which the estimate was obtained. In a particular case of radiation exposure, one must consider a number of relevant factors, including radiation dose; sex; age at exposure; time following exposure; and additional risk factors or modifiers.

F. Sex

For some organ sites, baseline cancer rates vary markedly by sex, while for others there is no real difference. Sensitivity to the carcinogenic effects of ionizing radiation also varies by sex and not always according to the pattern of natural rates. Sex differences in sensitivity seem to mirror differences in natural rates for leukemia and for thyroid and breast cancer. For cancers that vary between sexes because of differing exposures to carcinogens other than ionizing radiation (e.g., cigarette smoking in the case of lung cancer) sex differences in sensitivity to radiation otherwise may be small or nonexistent (4). Although many

populations studied for radiogenic cancer risk are wholly or predominantly male or female, the roughly equal sex distribution of the Japanese A-bomb survivor population allows sex-specific risk estimation for most cancer sites for which a radiation related risk has been established (4).

G. Age at Exposure

One of the most interesting observations to come out of the Japanese A-bomb survivor studies, which are based on a large population of all ages in 1945, is that the risk of radiation-induced cancer depends strongly on age at exposure (5,20). This dependence is complicated by a strong relationship between age and the time from exposure to cancer diagnosis but, in general, children appear to be more sensitive to radiation than are adults. This pattern has long been recognized for leukemia, for which we appear to have a more or less complete picture of the excess risk among A-bomb survivors (21,22). All age groups experienced a temporary increase in leukemia risk, which was higher relative to the baseline risk among the very young. In terms of the absolute number of leukemias per capita, however, the excess among the oldest group was fully as high as that in the youngest group (Fig. III-2).

The pattern of age dependence has emerged only gradually for the solid tumors, as A-bomb survivors exposed as children have reached ages at which cancer is ordinarily an important contributor to mortality. Relative to baseline cancer rates, radiogenic cancer risk appears to decline with increasing age at exposure. This pattern is very clear for cancer of the female breast (Fig. III-3) and for the thyroid, but it also seems to hold for all solid cancers as a group (Fig. III-4). There is clear evidence of an excess risk following exposure after age 50 for leukemia and for digestive and other cancers (5), but not for cancers of the female breast and thyroid (23,24). In general, observations on other exposed populations are consistent with those obtained from the A-bomb survivors, but do not have a similar breadth of coverage with respect to age (4).

The bulk of epidemiological data on cancer risk in populations exposed to ionizing radiation is based on follow-up of 35 years or less. For many cancer sites, no excess risk is discernible until ages at which baseline population rates are appreciable, and as a result, risk estimation for persons exposed at very young ages can be difficult because, so far, observations are few. For example, it was not until very recently, when follow-up of the Japanese A-bomb survivors and thymically-irradiated children in the United States was extended to 35 years or so, that it became clear that there was an excess risk of breast cancer associated with radiation exposure in early childhood (25,26). Age-specific risk estimates for cancers of the esophagus, intestine, and pancreas were formulated by the BEIR III Committee through the expedient of assuming that radiogenic digestive cancers as a group share a common pattern of variation by age at exposure (4). Without such an assumption, it is difficult to justify estimates for these cancer sites following exposures at young ages. Reasonable estimates can be calculated, however, for leukemia and cancers of the thyroid, breast, bone and salivary glands.

Although an association appears to be well established between prenatal X irradiation and childhood cancer, the extent to which the association may be causal is highly controversial (4,27-29). More precisely, it is difficult to reconcile an order-of-magnitude difference between risk estimates derived from studies of the frequency of X-ray pelvimetry, usually carried out shortly before birth (4, page 452) and estimates derived from studies of patients given therapeutic X-radiation during infancy (30), or A-bomb survivors exposed in utero (31) or in early childhood (5). It is not readily apparent that the association is explainable in terms of a medical indication for pelvimetry that itself confers an increased risk of childhood cancer; analyses adjusting for variables such as birth weight, maternal age, and a few others, have not greatly affected risk estimates (29,32). Furthermore, analyses restricted to twin births, for which medical indication for pelvimetry should be less important, have yielded estimates similar to those not restricted to twins (33,34).

Experimental studies do not support a greater cancer risk from prenatal as opposed to postnatal exposure to ionizing radiation (4,35,36). A particularly thorough experimental investigation of the influence of age at exposure on cancer risk has been carried out by Sasaki *et al.* at the National Institute of Radiological Sciences in Japan (37-40). These studies indicate that mice irradiated with X or gamma rays at fetal, perinatal, neonatal, pubertal, and young adult stages of development vary with respect to the type and frequency of tumors developing after irradiation. The observed differences suggest, however, a smooth variation by exposure age and, in particular, little if any difference between exposure at the late fetal, neonatal, and suckling stages. Irradiation during the middle intrauterine stage, on the other hand, was followed by significantly lower cancer risk than that observed among non-irradiated controls, especially for tumors of lymphoreticular tissue, the lung, and, in females, the uterus (38).

H. Time to Response

The plausibility of a causal association between a cancer and a prior exposure of the patient to ionizing radiation depends partly upon the length of time by which diagnosis follows exposure. Detection is unlikely until hundreds of millions of cancer cells have been replicated from what probably begins as a single transformed cell. Moreover, for many, but not all, types of cancer the epidemiological evidence suggests that events subsequent to irradiation may be required before any cellular changes initiated by ionization can result in a transformed cell capable of uncontrolled proliferation. Thus, for example, in irradiated populations no excess risk of breast cancer or lung cancer has been seen until the exposed individuals have reached ages at which these cancers usually are observed in non-irradiated populations, which suggests that cancers of these sites require other time-dependent etiologic factors whether or not exposure to ionizing radiation plays a role in their causation. Bone cancer and leukemia, on the other hand, have appeared in excess within a very few years after exposure in heavily irradiated populations, suggesting that subsequent events follow rapidly, or may not be required to complete

the carcinogenic process. Another marked contrast that distinguishes leukemia and bone cancer from most other cancers that have been identified as radiation-related is that leukemia and bone cancer risk appears to return to near-normal levels within a period of 30 years or less after irradiation, whereas for other types of cancer, the period of increased risk is much longer and may extend to the end of life.

Reports of expert committees concerned with cancer risk from ionizing radiation have dealt with response time mainly in relation to lifetime estimates of risk, a purpose for which sophisticated modelling is not always necessary. For example, in the 1980 BEIR report, radiation-induced leukemia and bone cancer were judged to have limited expression periods following an exposure of brief duration and lifetime risk was calculated as if excess risk were constant during the third to 29th years after exposure and zero before and after (4). This "plateau" model gave about the same lifetime risk as would have been obtained from a biologically more reasonable model. We know, however, as did the BEIR Committee, that leukemia and bone cancer risk increase over time to a peak followed by a more gradual decline, and that (for example) a radiation-induced bone cancer is much more likely to be diagnosed during the 10th year after exposure than during (say) the 4th or 28th years. The plateau model is thus unsuitable for calculating probability of causation, and should be replaced by models that more closely reflect observed temporal patterns.

The BEIR Committee rejected a plateau model of finite length for cancers other than leukemia and bone cancer, because after approximately 30 years of follow-up in the major exposed populations, excess risk has shown no sign of declining. It was noted that evidence of an excess risk was much slower to develop than for leukemia and bone cancer, however, and the first 10 years after exposure were ignored in the risk calculations. Alternative models were used to project estimated risk beyond the period of follow-up to the end of life. The "absolute risk" model is a plateau model that extends to the end of life; in other words, given that an exposure of brief duration has caused a cancer, the time to diagnosis in different members of the population is assumed to be uniformly distributed over the remainder of life following the minimum response time, assumed by the BEIR Committee to be 10 years. This projection model was used in parallel with the "relative risk" model, so called because the ratio between the risk of a radiation-induced cancer and the average risk in the absence of exposure, as determined from population rates, is assumed to be the same for each year of life following the minimal response time. Under the relative risk model, therefore, the distribution of response time is non-uniform, varying in proportion to baseline rates which depend upon age at observation.

Depending upon age at exposure, lifetime risk projections according to the absolute and relative risk models can vary markedly, with the greatest deviation corresponding to young exposure ages. Averaged over all exposure ages, the relative risk model lifetime projection on the basis of follow-up data now available tends to be about 3 times as high as the absolute risk model lifetime projection (4), because population rates for the most important cancers tend to increase steeply with increasing age. Even during the first 30 years or so after exposure, for which the total excess risk estimated by the two models must agree because this

is the length of the follow-up period on which the risk estimates were based, the models differ with respect to the likelihood that a radiation-induced cancer will occur in any given year. For example, the 1980 BEIR report estimated that, for a 100-rad exposure at age 15, the average excess breast cancer risk during years 11-30 following exposure (i.e., from age 25 through age 44) is 730 cancers per year per million women exposed (4, page 198). Ignoring intercurrent mortality, about 14,600 extra breast cancers would be predicted during this period under either projection model, compared to about 10,000 which would be expected according to population rates. But the distribution of the excess cases differs markedly by model. The U.S. incidence of breast cancer per million women (i.e., the number expected to develop breast cancer at a given age) is about 64 at age 26, 435 at age 35, and 1,314 at age 44 (41). The absolute risk model would predict 730 excess cancers at each of these ages following a 100-rad exposure at age 15, while the relative risk model would predict 93 at age 26, 635 at age 35, and 1918 at age 44. Looked at in another way, in a population exposed to 100 rad to breast tissue, 92% of the total breast cancer risk at age 26, or 730 out of 794 cases predicted according to the absolute risk model, would be radiation-related compared to 63% of those at age 35 and 36% of those at age 44, while according to the relative risk model, 59% of all breast cancers observed at each of these ages would be considered radiation-related.

Probability of causation calculations, which pertain to a particular cancer diagnosed at a particular time following a particular radiation exposure, clearly require an approach to response time that is more refined, and less ambiguous, than that of the BEIR Committee. A number of authors (42-44) have suggested that the lognormal model applied by Sartwell (45) to the incubation period for infectious disease may be appropriate for radiation-induced cancer. This suggestion seems reasonable for those cancers, like bone cancer (46) and leukemia (47), that have been observed to follow a wave-like pattern of an increase in risk followed by a decline; it seems less plausible, or less practicable, for cancers of sites like the lung, female breast, and digestive tract, for which radiation-related excess risks were slow to become apparent and showed no signs of declining at last follow-up (5).

Epidemiological data permit response-time analyses for only a few cancer sites; the crucial considerations are (a) a high excess relative to background, i.e., so high that most of the cancers diagnosed following exposure can be assumed to be radiation-related; (b) an exposure of brief duration; and (c) a lengthy follow-up period. These criteria are satisfied best for bone cancer data from a German population given therapeutic injections of radium-224, a bone seeker with a half-life of 3.6 days. Fifty-three bone sarcomas were observed compared with only 0.2 expected, so that essentially all the cases can be considered to be radiation-induced, and treatments lasted less than one year (46). Less pure, but nevertheless useful, data pertain to leukemia (21) and breast cancer (48,49) among A-bomb survivors. The criteria are satisfied to a lesser extent by lung cancer mortality among A-bomb survivors (5,49) and breast cancer incidence in patients treated by X rays for acute postpartum mastitis and in tuberculosis patients given multiple chest fluoroscopies (50), and marginally by stomach cancer among A-bomb survivors (5,51). Thyroid cancer presents special difficulties because it is usually an indolent disease which may

go undetected for a long time unless special efforts have been made at detection, as has been the case for A-bomb survivors and practically every other irradiated group in which an excess has been demonstrated. Thus the somewhat anomalous finding of a continuing observation of an excess among A-bomb survivors who were under 20 years old in 1945, and an apparent disappearance of excess risk over time among older survivors (24), could conceivably be an artifact of screening in which cancers that might otherwise have been discovered in recent years had been picked up earlier through improved surveillance.

Schematic representations of leukemia risk as a function of time after exposure based on A-bomb survivor data resemble lognormal or gamma distributions. These distributions, moreover, may differ by histological type and age at exposure (47). Formal statistical comparisons of dates of diagnosis among heavily exposed A-bomb survivors with those among lightly exposed survivors or non-exposed residents of Hiroshima and Nagasaki are consistent with this interpretation (48).

Comparisons of response time distributions between cancers of the breast, lung and stomach among heavily exposed persons and otherwise similar persons with little or no exposure are remarkable for the similarity they reveal (5,49,51). That is, heavily exposed persons have more cancers of the breast, lung, and stomach than they would otherwise have, but the temporal distributions of the excess cancers are not distinguishable from those of non-radiogenic cancers. This finding is plausible in terms of a multi-stage model for carcinogenesis, in which radiation produces an early-stage change that can also be produced by other common agents, and in which late-stage changes are caused by events that are highly age-dependent. If, in fact, the likelihood of early-stage changes for these sites declines with increasing age in about the same way that the relative risk of radiation-induced cancer declines with increasing age at exposure, and if the likelihood of late-stage changes increases with increasing age in about the same way as population cancer rates increase with age, the observed temporal patterns of radiation-induced and baseline cancer rates following a radiation exposure should be very similar (52).

Congruence between radiation-induced and baseline cancer rates of the same site, in persons of similar ages at observation, with respect to temporal distribution of risk, is equivalent to the relative risk projection model used by the BEIR III Committee. The relative risk projection model asserts that, for a cohort of persons of given age, after the passage of a necessary latent period, the relative risk of radiation-induced cancer is essentially constant. It is inconsistent with the absolute risk model, according to which the relative frequency of radiation-induced cancers compared to baseline cancers should decline over time for those sites for which baseline cancer rates increase with age, and it is also inconsistent with another model, proposed by Gofman (53), in which this relative frequency is assumed to increase for about 40 years after exposure, and then decline. The justification given by Gofman for this model is unconvincing: the increase with time in relative risk that he noted depended upon an analysis that ignored age; the increase was a consequence of cohort effects, in which increasing numbers of younger (and more radiation-sensitive) women entered upon the ages at which breast cancers occur. The decrease in relative risk postulated by Gofman is entirely speculative.

The hypothesis is inconsistent with available data within 35 years after exposure, and beyond that point there are no data with which to test it. When age-specific analyses are done on the data used by Gofman to support his model, no increase in relative risk with increasing follow-up is found (5,49,50).

Finally, minimal response time is an essential element of temporal distribution of risk, and one that is extremely difficult to estimate. If cancers are of monoclonal origin, as seems likely, the development of a radiation-induced cancer can be considered sequentially in terms of the transformation of an affected cell which then becomes capable of unrestrained proliferation, followed by a growth period involving 30 or so generations of replication resulting in hundreds of millions of cancer cells, at which point detection becomes likely (54). Observed doubling times for radiographically-monitored primary and metastatic tumors of various sites in human patients appear to be lognormally distributed, with considerable variation by type (metastatic vs. primary) and site (54). These observations, especially those of primary tumors, necessarily occurred after many generations of replication had already taken place, and it does not necessarily follow that the time required for the entire growth phase can be determined by extrapolation. Doubling time may well depend upon attained tumor size, the degree of vascularization, or upon variable factors not influenced by the existence of a tumor. Also, lognormality of the doubling time at any stage of tumor growth does not necessarily imply lognormality for the total time necessary for growth; for example, if the process were characterized by some degree of statistical independence between growth rates at different times, a more nearly symmetric temporal distribution would result.

Tumor doubling-time data are intriguing in their implications for radiation carcinogenesis as a multi-stage process. If tumor growth tended to begin quite soon after irradiation, a wave-like temporal pattern of excess risk might be expected on the basis of growth kinetics alone. If, on the other hand, the beginnings of tumor growth were distributed over time in such a way as to produce a constant ratio between excess and background risk, there should be an initial period of several years during which, due to growth kinetics, the relative excess slowly increases from an initial value of zero to its eventual value.

I. Models for Dose Response and Dose Rate

To predict the risk of cancer at a given radiation dose from empirical observations of effects at other doses, one must use a mathematical model relating cancer incidence to dose. Various mathematical models have been proposed for the purpose (4,6,55); however, the empirical data are so imprecise in most instances as to be compatible with any of the available theoretical models. Hence, the choice of the most appropriate model is a matter of expert judgement.

For carcinogenesis, in general, and radiation carcinogenesis in particular, there are strong grounds for questioning the assumption that the dose-response relationship has a threshold (4,6,56-59). The evidence that many, if not most, cancers arise from a single cell (60), the putative

role of DNA or chromosomal damage in carcinogenesis (61-66), the heritable nature of the neoplastic transformation in somatic cell lines, and the linear-nonthreshold nature of the dose-effect relationship for radiation-mutagenesis and chromosome aberration induction in the low-dose region (6,67) imply that radiation-induced damage to the DNA or to the chromosomes of a single somatic cell may, under certain conditions, exert a potentially carcinogenic stimulus, even at the lowest radiation exposure level.

The extent to which host factors such as immune surveillance can introduce a practical threshold by delaying the onset of detectable cancer beyond the life span cannot be calculated at present. The existence of a complicated series of enzymes that repair DNA does not favor any particular model for interpolation of cancer incidence at low doses of radiation, since repair does not operate with total effectiveness. In addition, unless other carcinogenic agents act through unrelated mechanisms, the heterogeneity of the human population and the baseline incidence of cancer are high enough so that any dose of radiation may be conceived to increase the risk of cancer in the most sensitive members of the population (68-70). For these and other reasons, the assumption of a threshold for radiation carcinogenesis is currently not considered to be tenable for purposes of risk assessment.

If we are interested in the risk from lower-dose exposures, it is necessary to have an extrapolation rule or dose-response model by which the estimated high-dose risk determines lower-dose risk estimates. A fairly simple rule is to assume that excess risk is proportional to the number of ionizations produced in the tissue at risk, that is, proportional to absorbed dose. This rule is equivalent to drawing a straight line from a point representing zero excess risk at zero dose (natural background radiation levels) to the point representing the excess risk estimated at whatever dose was received by the population studied (the so-called linear model). Other rules, not based on a simple proportionality between dose and risk, correspond to curved lines. A general model widely accepted in experimental and theoretical radiobiology for stochastic effects (mutagenesis and carcinogenesis) of low-LET radiation allows for an unspecified degree of positive curvature corresponding to interactions between two radiation tracks, and negative curvature, influential mainly at high dose levels, corresponding to the competing effect of cell inactivation (4). The model assumes that two ionizing events are more likely to produce a biological effect if they occur very close together than if they are separated; because ionizing events tend to be widely spaced along low-LET tracks, closely-spaced events are likely to be at the intersections of different tracks and their probabilities are approximately proportional to the square of dose. A frequently observed, and related, phenomenon is that acute exposures to low-LET radiation tend to be more effective than the same amount of radiation delivered continuously over time or delivered in several fractions separated by periods of time. This, too, is thought to reflect variations in the likelihood that two ionizing events will occur close together in time and space. Such an occurrence is less likely if the events are not simultaneous, because the damage caused by the first ionizing event may be repaired before it can interact with the damage from the second event.

The above considerations do not apply to high-LET radiation, for which close spacing of the ionizing events along the radiation tracks is the rule, rather than the exception. Both theoretical and experimental studies suggest that, for high-LET radiation, the dose-response tends to be linear but is modified by negative curvature, mainly at high dose levels, due to cell inactivation. The data also indicate that fractionated or protracted exposures to high-LET radiation tend to be no less effective than acute exposures for the induction of stochastic effects (4).

Data on laboratory animals can provide principles to guide extrapolation from effects at high radiation doses to predict effects at low doses. For measuring small effects, however, such large numbers of animals are required that no experiment has been performed on a scale that suffices to define the dose-incidence relationship for carcinogenesis in different organs at doses below 10 rad. Furthermore, in most species of laboratory animals that are convenient to use (mice, rats), the "natural" incidence of cancers differs markedly among strains, as do the shapes and slopes of the dose-incidence curves for radiation-induced cancers (6). In some strains of mice, for example, breast cancers occur spontaneously in nearly 100% of females, whereas the incidence is 1% or less in the females of other strains; the effects of radiation on the incidence of such cancers vary similarly. These differences among strains appear to depend on genetic variations which are magnified by the highly inbred character of laboratory mice. Because of the highly outbred character of the human population--in which the incidence of cancer appears to be influenced more by differences in the environment, diet, and lifestyle than by genetic factors--animal-to-human extrapolations are fraught with uncertainty. For this reason, quantitative risk estimates for man have generally relied primarily on human epidemiological data (4,6).

Epidemiological data are not very informative about the choice of a dose-response model, for the same reasons that low-dose data tend not to be informative about excess risk (71). This is true even when the possibility of high-dose cell inactivation is ignored. The two cancer sites for which linearity with low-LET radiation is strongly suggested, the thyroid and the female breast, are in fact the only two for which there is much direct evidence for an excess risk from external exposures under 50 rad (24,72,73). For other cancers, including leukemia, dose-response analyses using general models, in which details of curvature are not fixed in advance, tend to yield risk estimates with very wide confidence limits. Also, less general models with specified curvature, which may be located anywhere in the range from linear to pure quadratic, tend to fit the available data more or less equally but produce a great variation in the estimated risk at low dose levels (4,71).

The related phenomena of variable increases in risk per rad depending on dose or dose rate can be handled crudely by the use of a dose-rate reduction factor, according to which the effectiveness of a high radiation dose delivered at a low dose rate or in many fractions is assumed to be several times smaller than that of the same dose delivered acutely. A more refined method uses a linear-quadratic dose-response model in which the quadratic coefficient is assumed to depend on dose rate - that is, the model as given corresponds to acute exposures and the quadratic coefficient is reduced for protracted exposures. Various official bodies

have used different approaches. The United Nations Scientific Committee on the Effects of Atomic Radiation (6) used a dose-rate reduction factor of 2.5, while the National Council on Radiation Protection and Measurements (55) gave a range of 2-10 for this factor and recommended the use of a linear-quadratic dose-response function. The 1980 BEIR Committee chose a linear-quadratic model for low-LET radiation in which the excess risk is proportional to $D + 0.0086D^2$, where D is the dose in rad (4). The linear term (proportional to dose) dominates below a so-called crossover dose of 116 (= $1/0.0086$) rad and the quadratic term (proportional to dose-squared) dominates above that dose. This crossover dose, which was obtained by curve-fitting to A-bomb survivor leukemia data, is consistent with those obtained for chromosome aberrations in circulating human lymphocytes and in a number of studies involving chromosome aberrations and mutations in experimental animals or mammalian cells in culture (74).

It is generally agreed (4,55) that the linear term of the linear-quadratic dose-response model is unaffected by dose fractionation and by variations in dose rate, and that the quadratic term should become smaller as fractionation increases or the dose rate decreases. Thus, the BEIR committee used only the linear term of the linear-quadratic model to estimate risk from continuous exposures to 1 rad per year (4). Based on the data for mutation production in *Tradescantia* by gamma radiation (55), it appears that one may reasonably apply the linear term alone to continuous exposures to low LET radiation at dose rates several orders of magnitude higher (e.g., 0.01 rad per hour which corresponds to about 90 rad per year continuous exposure).

For cancers of the breast and thyroid gland, linearity of the dose-incidence relationship is suggested by the available data. For example, the risk coefficients derived from the carcinogenic effects of high thyroid doses in infants treated for thymic enlargement (30) are similar to those derived from average thyroid doses of 9 rad in Israeli children treated with X rays for tinea capitis (73). Similarly, risk coefficients for breast cancer in A-bomb survivors are essentially the same whether derived from the effects of doses below 30 rad or from the entire range of doses (72); furthermore, the incidence of breast cancer per unit dose in women who received their irradiation in daily occupational exposures as dial painters (75) or in many small, widely spaced exposures during multiple fluoroscopic examinations of the chest appears to be essentially the same as in women who received their irradiation in a single instantaneous exposure to atomic bomb radiation or in a few brief exposures during radiation therapy (50).

The BEIR III Committee did not incorporate the competing effect of cell inactivation, mainly at high dose levels, into its risk calculations, although it did consider the problem theoretically (4, p. 182). There appear to have been three reasons for this: First, the Committee had great difficulty obtaining useful information by fitting even a linear-quadratic dose-response model to the available data, and better results could not be expected from a more complex model. Second, the Committee relied heavily on data from the studies of Japanese A-bomb survivors, for whom exposures were fairly uniform over the entire body. Doses high enough to reduce the carcinogenic response appreciably through the competing effect of cell inactivation might well be in the lethal range for

man when delivered to the whole body. Moreover, the A-bomb survivor data gave no clear evidence of a high-dose downturn in the carcinogenic response. Finally, the BEIR Committee was concerned mainly with applications to low-dose exposures, for which the competing effect of cell inactivation is not a serious consideration. Nevertheless, cell inactivation at high dose levels is a likely explanation for increases in leukemia risk that have been lower than would be predicted among patient populations given partial-body exposures, and partial-organ exposures in terms of active bone marrow, at therapeutic dose levels for the treatment of ankylosing spondylitis (76) and cervical cancer (77).

J. Modifying Effects of Other Exposures

The literature of experimental carcinogenesis abounds with examples in which a co-carcinogen or promoting agent has been found to modify the level of effect, or even the shape of the dose-response curve, for radiation carcinogenesis. Examples in the epidemiological literature are rare, but not unknown. Increased skin cancer risk was found among persons given epilating doses of X rays as children for treatment of tinea capitis, but the cancers occurred more commonly in those irradiated areas with high levels of exposure to sunlight, did not occur in blacks, and among whites occurred preferentially in persons with light complexions (78). Smoking and radon exposure were found to interact multiplicatively among U.S. uranium miners in the causation of lung cancer (79); that is, increased risk per unit radiation dose was many times higher among smokers than among nonsmokers. On the other hand, an additive rather than multiplicative interaction was found among Swedish iron miners (80) and Japanese A-bomb survivors (81). The similar excess breast cancer risks among Japanese A-bomb survivors and medically irradiated U.S. women (50) suggest that whatever causes American women to have about 5 times the lifetime breast cancer risk of Japanese women does not interact synergistically with ionizing radiation.

In summary, little is known about the influence of other physical and chemical agents on radiation-induced cancer risk in man, and what little is known is generally consistent with additive interactions, at least for low-LET radiation. The experimental literature suggests that synergistic relationships exist, but they are yet to be discovered in humans, and we do not know how important they are relative to other determinants of risk.

K. Extrapolation from One Population to Another

As mentioned above, epidemiological data relating cancer risk to radiation exposure come from a variety of exposed populations but predominantly from patients given diagnostic or therapeutic X radiation and the Japanese A-bomb survivors whose exposures were chiefly to hard gamma radiation. Basing risk estimates on these data requires assumptions about the comparability of the irradiated populations on which the estimates were based with the population to which the estimates are to be applied.

For example, the population rates not influenced by radiation exposure among the Japanese A-bomb survivors and their non-exposed, local comparison group are similar to the USA population rates for leukemia but far lower for breast cancer and far higher for stomach cancer (82). The question arises: Should the absolute excess risk attributable to radiation exposure, that is, the difference between total risk and that expected according to population rates, be assumed to be the same for an irradiated USA population as for a similarly exposed group of Japanese A-bomb survivors, or should the excess be scaled proportionally to the underlying population rates? Both these extrapolation rules are very simple, even crude, and there is little information to support more complicated rules.

In general, absolute excess leukemia risk appears comparable between Japanese A-bomb survivors and medically irradiated Western populations with similar doses at similar ages (4). Comparisons between the A-bomb survivors and two medically irradiated USA populations with respect to breast cancer risk suggest that the absolute excess risk is about the same in all three populations, for similar ages at exposure, in spite of a five-fold difference in the underlying population rates (50). At high dose levels, the excess stomach cancer risk among British patients given X ray therapy for ankylosing spondylitis was not much different from that in A-bomb survivors of similar ages at exposure (5,83,84).

Radiation is believed to affect an early stage of the multi-stage process that results in cancer at least for breast cancer and perhaps for other cancers as well. If that is so, then the effect of other agents which act at an early stage would be simply to add to the effect which results from radiation. That the causes of excess stomach cancer in Japan act on early stages is implied by the fact that among Japanese migrants to the United States, although stomach cancer rates do decline from the Japanese levels to those which characterize the host country, they do so only after a very long delay--several decades (85). The implication is that the initial events had already occurred before the migrant left Japan.

A possible contradiction between the constant relative risk model for time to response and the absolute risk model for projection from one population to another has been pointed out by Land et al. (50) and by the National Academy of Sciences Oversight Committee on Radioepidemiologic Tables (86). Briefly, if the ratios of baseline rates in the two populations vary markedly by age at diagnosis, it seems unlikely that both models can hold. In the case of breast cancer, baseline risk is about 4 times higher in the United States than in Japan, based on age-adjusted rates from the Connecticut, Miyagi Prefecture, and Nagasaki City tumor registries (82). On an age-specific basis, however, this ratio varies from less than 3 at ages under 50 to more than 6 at ages over 70. Thus, if the variation of baseline risk over time following some event, like a radiation exposure, is truly represented in both populations by the published population rates, and if within both populations the constant relative risk model holds, then, for an exposure at age 20 (say), estimates of average yearly absolute excess risk should not agree between Japanese and Americans both for the period 10-30 years after exposure and the period 40-60 years after exposure. Conversely, if measures of absolute risk agreed between the two populations for any similar follow-up period,

the distribution of excess risk over time should not follow the constant relative risk model in both populations. Yet the evidence which suggests that both models hold, or rather, that the two models are simultaneously consistent with epidemiological experience, was obtained largely from extensive follow-up data on breast cancer among Japanese atomic bomb survivors and North American populations exposed to medical X ray (49,50).

The apparent contradiction in the case of breast cancer would appear to have been resolved by Moolgavkar and Lee (87), who point out that published age-specific population cancer rates of the type cited above (e.g., from reference 82) are based on relatively short observation periods, and that rates for different ages at observation correspond to different birth cohorts. Moreover, they offer evidence that, within cohorts, the distribution of baseline breast cancer risk among Japanese women follows a common pattern, similar to that seen in western societies, but that the overall level of risk, at similar ages at observation, varies considerably by birth cohort. Breast cancer risk has steadily increased in Japan, and women born within the last 50 years or so are at higher risk than women born earlier. This trend is reflected in published population rates, which show proportionally lower risks at older ages because the women whose experience contributes to these rates are members of cohorts whose overall breast cancer risk is low. In the United States, on the other hand, breast cancer risk has been remarkably stable over at least the past 30 years (88), and therefore published age-specific rates are a better indication of the temporal distribution of baseline risk within a birth cohort. It should be noted that the analyses of Japanese atomic bomb survivor data, on which the inference of a constant relative risk over time after exposure is largely based, involved comparisons of cancer risk between heavily exposed and lightly exposed or nonexposed members of the same birth cohorts (5,48,49,50).

The above discussion demonstrates that no contradiction exists between the constant relative risk model for distribution in time and the constant absolute risk model for projection of risk from one population to another in the case of breast cancer. It does not demonstrate a similar lack of contradiction for all other cancers to which the models might be applied. In general, however, patterns of age-specific cancer risk do not differ between Japan and the United States to the same extent for such other cancers as they do for breast cancer (82), and it is therefore less likely for a contradiction between the two models to become apparent. To the extent that risk variation by age in the United States may reflect cohort effects, it would of course be preferable to apply the constant relative risk model, if appropriate, to cohort-specific baseline rates. That may be possible decades from now, when extensive cancer incidence data have been accumulated over many years, but it is not practicable at the present time.

Overall, the evidence favors absolute, as opposed to proportional transport of risk from one irradiated population to another. It should be noted, however, that the choice of the absolute model is based on data for only a few cancers and populations. For example, some population differences in cancer risk conceivably might depend upon differential exposure to an agent that interacts synergistically, or antagonistically, with radiation, and in such cases, the absolute model would not hold. As

with models for low-dose extrapolation of risk, the unresolved issues for extrapolation from one population to another involve questions fundamental to the nature of carcinogenesis.

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Natural Sources :

- Environmental**
 - Cosmic Radiation
 - Terrestrial Radiation
 - Internal Radioactive Isotopes

Manmade Sources :

- Environmental**
 - Technologically Enhanced Global Fallout
 - Nuclear Power
- Medical**
 - Diagnostic Radiopharmaceuticals
- Occupational**
 - Consumer Products and Miscellaneous

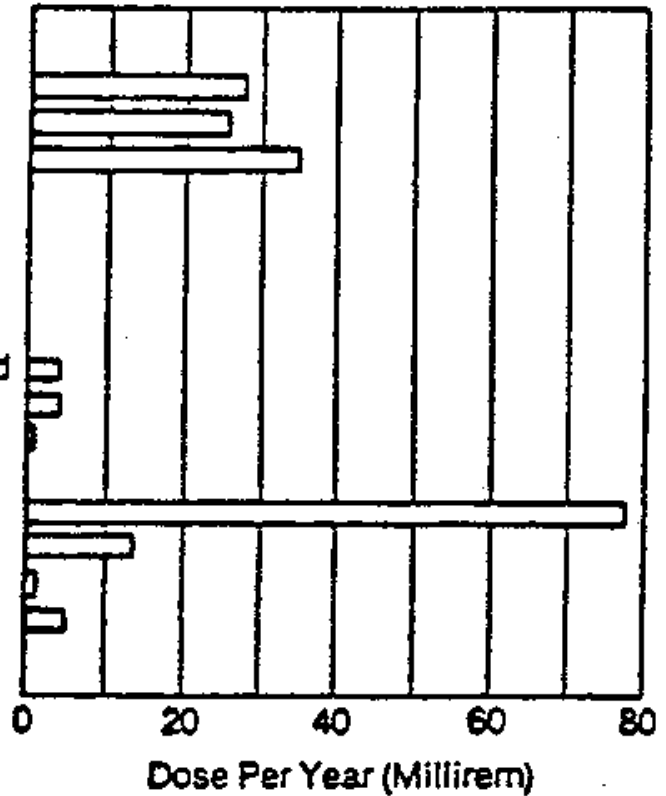


Figure III-1. Radiation exposure of a typical person in the U.S. from natural and man-made sources. [Redrawn from ref. 1.]

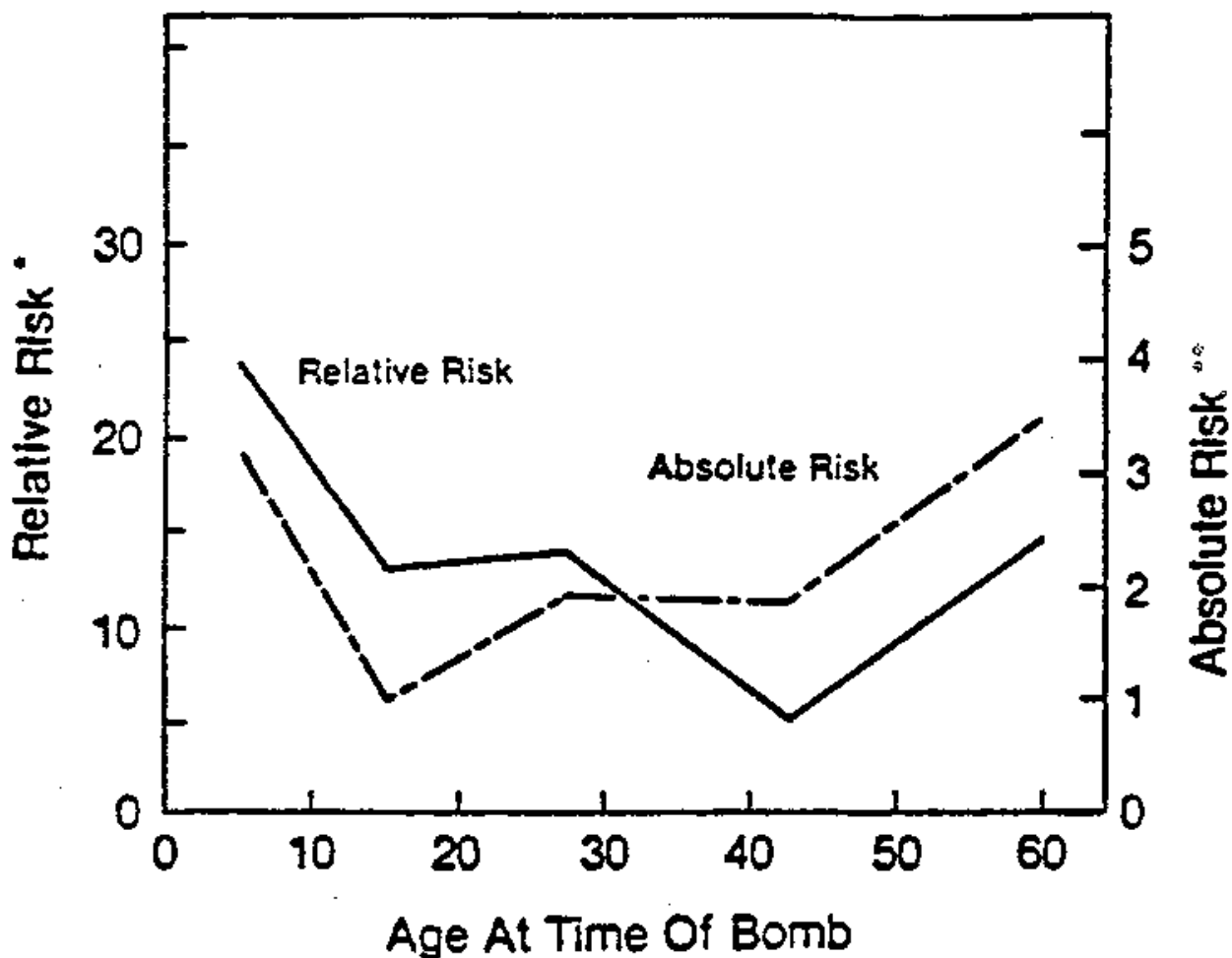


Figure III-2. Measures of leukemogenic effect among A-bomb survivors, by age at the time of the bomb, average for both cities.

The footnotes explaining the two ordinate scales are:

*Risk of 100+ versus 0-9 rad.

**Excess cancers per million persons per year per rad.

[Redrawn from Beebe, G. W., Kato, H., and Land, C. E., Radiat. Res. 75: 138-201 (1978), Fig. 1.]

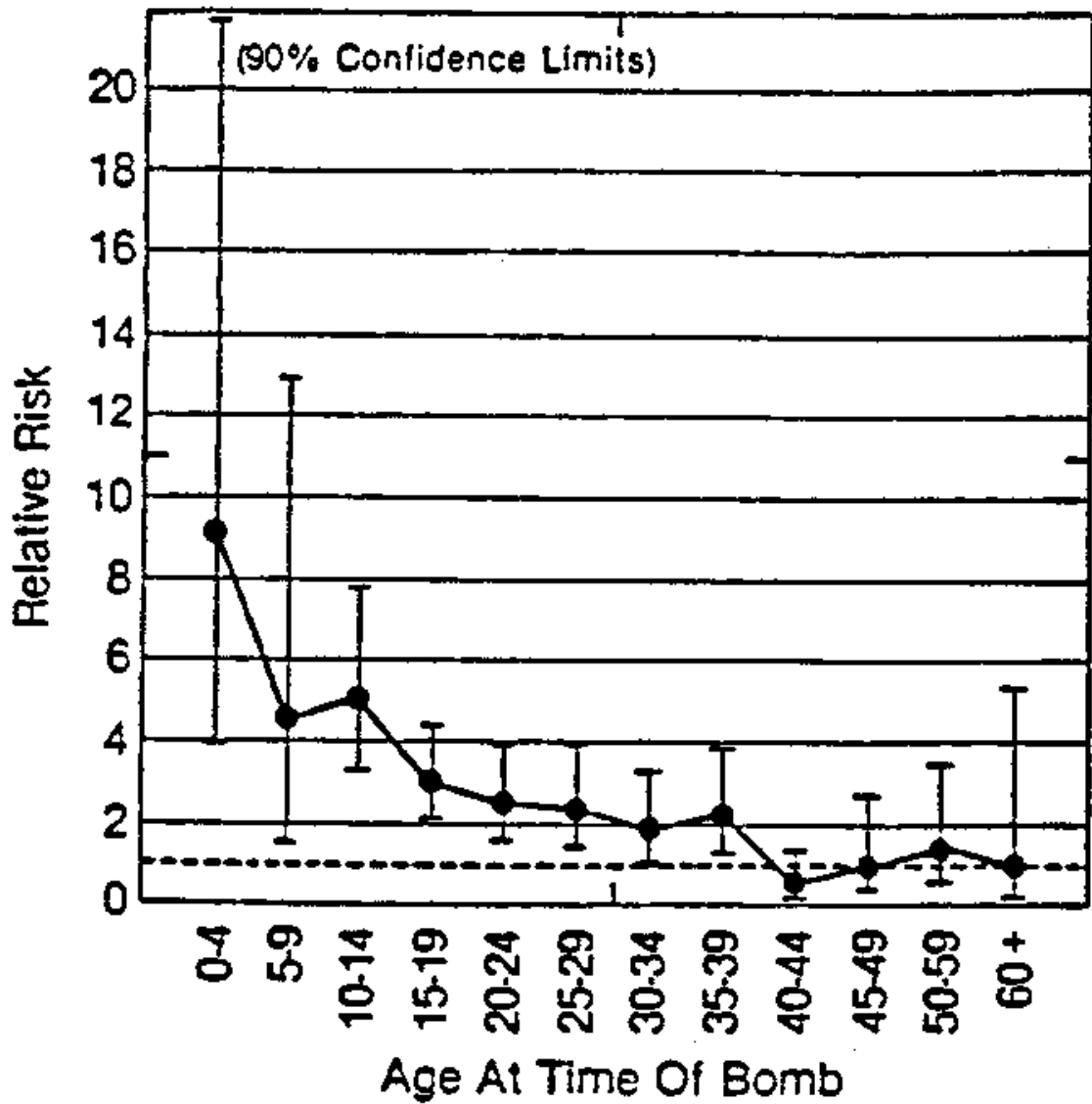


Figure III-3. Relative risk of breast cancer among female Japanese A-bomb survivors, incidence 1950-1980, 50+ rad versus 0-9 rad and non-exposed, by age at the time of the bombings, both cities combined. [Land, C. E., unpublished data.]

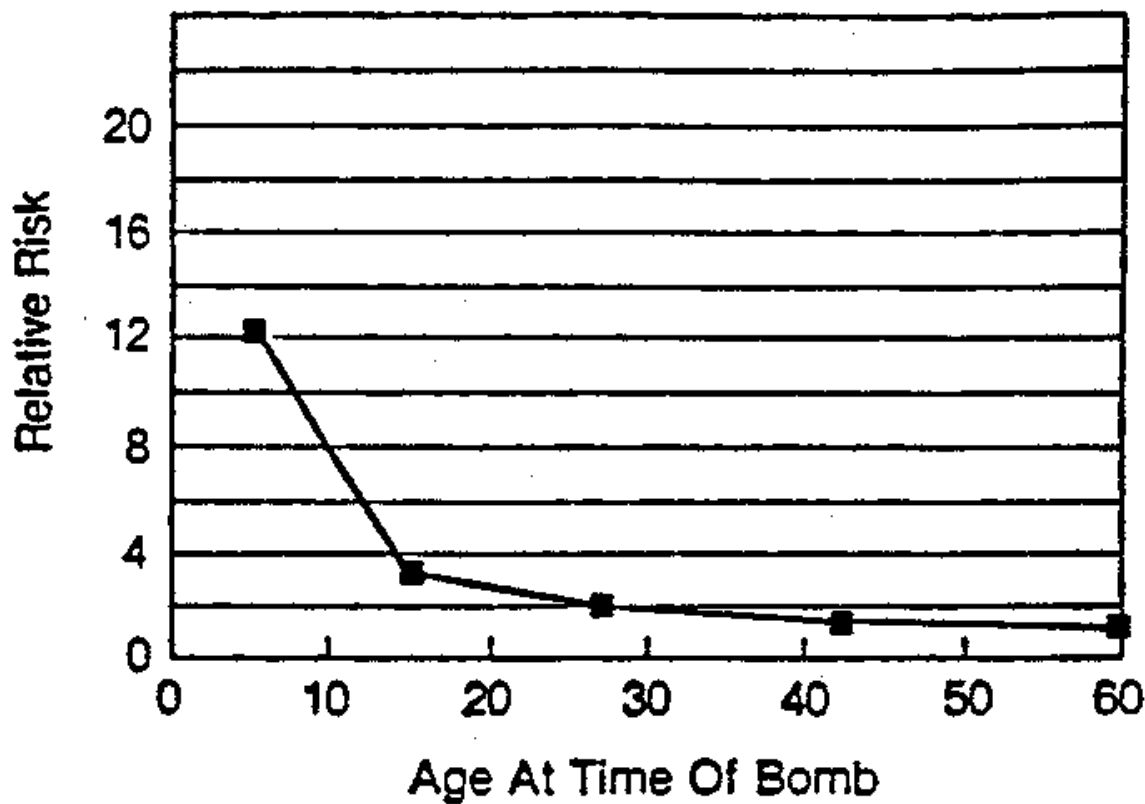


Figure III-4. Relative risk of all forms of cancer except leukemia among Japanese A-bomb survivors, mortality 1950-1978, 200+ rad versus under 1 rad, by age at the time of the bombings, both cities combined. [Redrawn from Kato, H., and Schull, W. J., Radiat. Res. 90: 395-432 (1982), Fig. 4.]

Chapter IV: THE PROBABILITY OF CAUSATION

A. General

The word "probability" has a number of definitions, but even more protean is "cause" or "causation." We are satisfied that the "cause" of the light going on is the closing of the electric circuit. But what is the "cause" of a case of tuberculosis? The answer is usually "infection with the tubercle bacillus, of course." But the inhalation of a modest number of tubercle bacilli will be followed by clinical disease in only a minority of persons or experimental animals. Some individuals are more susceptible than others. Is the "cause" of clinical disease in a given person the bacillus or the susceptibility, or both? Those who consider this example strained might reflect that, 100 years ago, virtually everyone who lived in a crowded, poor, urban environment was infected by tubercle bacilli, yet only a minority contracted clinical disease. In some sense, in that situation, the "cause" of tuberculosis was susceptibility.

The above is preliminary to a definition of what we mean here by "probability of causation." We must define the term not only precisely, but so that it leads to a unique mathematical formulation that will govern the calculations required for the radioepidemiological tables. The definition that we give below is the operational definition for this expression. The definition carries with it certain implications, some of which reflect important policy decisions.

B. Definition

Let a particular possible outcome event be denoted C. Let X (a vector) denote the particular set of individual characteristics. Denote the presence of a possible cause by D and its absence by \bar{D} .

Then $P(C, D; X)$ is the probability of outcome C if D is present, conditional on the characteristics X. Similarly, $P(C, \bar{D}; X)$ is the probability of outcome C if D is not present. Then D is a possible "cause" of C only if

$$P(C, D; X) > P(C, \bar{D}; X).$$

$$\text{Define } Ex(C, D; X) = P(C, D; X) - P(C, \bar{D}; X).$$

as the increase in the probability of C due to the presence of D. Then, the probability of causation of C by D, the PC, is defined as:

$$PC(C, D; X) = Ex(C, D; X) / P(C, D; X). \quad (IV-1)$$

In words, the PC is defined as the increase in the probability of C due to D as a proportion of the probability of C given D, everything conditional on the characteristics X.

Note that the PC does not allocate causation as between characteristics X and Y. If, for example, the event C is the occurrence of lung

cancer, and if D is exposure of the lung to 20 rad of gamma radiation, while X and Y represent, respectively, being a regular cigarette smoker, or a non-smoker, then according to our definition, $PC(C, D;X)$ measures the probability of causation of lung cancer from 20 rad among smokers and $PC(C, D;Y)$ that among non-smokers.

Although it can be argued that cigarette smoking is a far more important cause of lung cancer than is ionizing radiation, our work addresses the radiation risk exclusively: Given a person, with whatever risk factors may apply to him, what is the probability that the documented radiation dose that he received was the "cause" of his cancer? This may be interpreted as: what proportion of his total risk resulted from the radiation? Although the question might be asked (and answered), we do not address "What proportion of the risk resulted from smoking?" or "What proportion arose from the combination of smoking and radiation?"

The phrase "Probability of Causation" is intuitively appealing, but the ratios so designated are not probabilities in a mathematically rigorous sense. It must be recognized that different persons vary as to their (prospective) chances of having cancer. Besides age and sex, other characteristics such as diet, exposures to carcinogenic chemicals, genetic factors and a host of others, some of which can only be guessed at, all combine to increase or decrease from the average value the chance that a specific person will contract a particular kind of cancer. For present purposes it is possible to take account of only a limited number of such characteristics, principally age, sex and cigarette smoking habit. The probabilities of cancer, then, are average values for all persons in a given class, for example, male non-smokers aged 35 years. The Probability of Causation that is calculated for an individual in that class will be more or less correct as his personal characteristics match or vary from the average in the class. Nevertheless, our procedure assigns the same PC to all members of the class.

Evidently, were the classes defined differently - for example, by specification of residence in Utah, the calculated PC might well change. In effect, our procedure partitions the population of the United States into a set of mutually exclusive classes, by sex, age and smoking characteristics. These characteristics were chosen because 1) they affect cancer rates in important ways which can be specified from available data, and 2) every person can be assigned unequivocally to one of the classes.

It has been suggested that the term "Assigned Share" would more accurately describe the ratios that are calculated (1). We are, however, constrained by the legislative mandate embodied in Public Law 97-414 wherein the specific term "Probability of Causation" is employed.

Although the PC as defined can be calculated prospectively, it would have little meaning for any person because of its specificity as to type of cancer and date of diagnosis, as well as tissue dose and age at exposure. Following the imposition of cause D, an individual may be interested in $P(C, D;X)$ - "What is the probability that C will occur?" or in $P(C, D;X) - P(C, D;Y)$ - "By how much has the probability that C will occur been increased?", but $PC(C, D;X)$ tells him that if the event C does

occur, then $PC(C, D;X)$ is the probability that D is the "cause" in the sense described above. In short, $PC(C, D;X)$ will usually be of interest only retrospectively; supposing event C (a cancer) has occurred, what is the probability that D was the cause?

C. Specifics

The discussion above is purposely quite general. To be more specific:

The event C will be the occurrence (clinical detection) of a particular cancer that is known to be inducible by ionizing radiation and for which specific estimates of the risk from particular radiation doses can be made.

The cause D will be the receipt, by the organ in which the cancer has arisen, of a specified radiation dose.

The characteristics X of the person under consideration will include, at a minimum, the age at which the radiation was received, the number of years after radiation when the cancer was diagnosed and the sex of the individual.

We shall usually be concerned with annual rates of occurrence, the rate representing the yearly number of cases of C per 100,000 or per million persons.

The values $P(C, \bar{D};X)$ will be identified with the incidence rates provided by the SEER Program (2) for the years 1973-1981 for all areas, excluding Puerto Rico. Although, formally, an incidence rate is not a probability, the numerical difference is trivial over any interval for which the probability of death from all causes is small. We shall refer to these rates as the "Baseline Rates."

D. Calculational Formulas

There is a calculational advantage in expressing the PC in terms of the relative excess risk $R = R(C, D;X)$, defined as the increase due to D as a proportion of the probability of C in the absence of D:

$$R(C, D;X) = Ex(C,D;X)/P(C, \bar{D};X).$$

Writing $P(C,D;X)$ as the sum of $Ex(C,D;X)$ and $P(C, \bar{D};X)$ and dividing both the numerator and denominator in (IV-1) by $P(C, \bar{D};X)$, we obtain

$$PC(C,D;X) = R(C,D;X)/(1 + R(C,D;X)). \quad (IV-2)$$

The advantage of expressing the PC in terms of R is that R is the simple product of several quantities that are naturally thought of separately, and that can be either calculated using simple formulae or presented in tables. For example, in Chapter X, Section 10, we find that the relative excess of breast cancer following exposure to radiation

is proportional to dose and that, for a single exposure to low-LET radiation at age 15, the relative excess for a typical American woman is .0107 times dose in rad, at any time more than 10 years after exposure (Table X-10). If a cancer should be diagnosed at age 37, for example, following exposure at age 15 to 30 rad, the relative excess would be $R(\text{breast cancer, 30 rad; age 15, 22 years}) = (30)(.0107) = 0.321$, and the PC would be $0.321/1.321 = .243$ or 24%.

E. Cases in which US Baseline Incidence Does not Apply

PC calculations based on SEER values for baseline cancer incidence require the assumption that the individual in whom cancer was diagnosed following a documented radiation exposure would have been, in the absence of that exposure, "typical" of the US population for his or her age and sex with respect to cancer risk. But the subject may have had an atypical history of exposure (or nonexposure) to known carcinogens or may have experienced other life events associated with a higher or lower cancer risk than average. Or the subject may be a member, perhaps even a "typical" member, of an ethnic, religious, or other population subgroup known to have cancer rates higher or lower than the U.S. population as a whole. Should the PC calculations be modified in such cases, and if so, how?

Having introduced the problem, we should also make it clear that it is a problem about which very little is known. Although experimental studies have demonstrated that levels of carcinogenic response to ionizing radiation can be modified drastically through the use of certain so-called "promoters", agents that do not in themselves appear to initiate the carcinogenic process, we do not know whether or not similar agents contribute to human cancer risk associated with radiation. It is by no means clear, at this time, whether people who are at high risk of cancer in the absence of radiation exposure are more sensitive than other people to the carcinogenic effects of radiation. Epidemiological research in the area of combined effects of different risk factors is difficult because combinations that might be of interest are relatively rare, and in the case of radiation and other factors, such epidemiological study is just beginning.

The estimates of cancer risk from radiation exposure presented by the BEIR III Committee were based on syntheses of data from various exposed populations, some of which, like the Japanese A-bomb survivors, have cancer incidence levels for certain cancer sites that are very different from U.S. rates. Making the estimates involved the implicit assumption that the carcinogenic effects of radiation are additive with respect to whatever factors are responsible for differences between population cancer rates. This assumption appears to hold for breast cancer in the case of Japanese and American women (3), for whom population rates differ by a factor of 4 or 5, and it is not inconsistent with data on radiation-induced stomach cancer in A-bomb survivors and British patients treated with X radiation for ankylosing spondylitis (4). There may be other sites for which the assumption does not hold, but we have no way of knowing at present.

Clearly, the problem of calculating PC values in the presence of differences in total cancer incidence because of exposure to other carcinogenic

agents, personal history with respect to factors related to cancer risk, or membership in a particular population subgroup, is fraught with uncertainty. The problem is not difficult given certain assumptions, as illustrated in subsequent sections, but with very few exceptions the informational basis for such assumptions is lacking. Without such information, any rule for making use of additional cancer data is necessarily arbitrary, and it may be preferable simply to proceed as if the subject were a typical member of the U.S. population.

F. Multiple Radiation Exposures

If two radiation exposures to doses D_1 and D_2 , respectively, would, if given alone, result in excess risks $E(D_1)$ and $E(D_2)$ at an age for which the baseline risk is I , and if they are separated in time by a day or more so that they do not interact, it is assumed that the excess from the two exposures is the sum of the respective excesses, $E(D_1, D_2) = E(D_1) + E(D_2)$. The relative excess for the two exposures, $R(D_1, D_2) = E(D_1, D_2)/I$, is therefore the sum of the separate relative excesses, each computed as if only one had occurred:

$$R(D_1, D_2) = E(D_1, D_2)/I = E(D_1)/I + E(D_2)/I = R(D_1) + R(D_2).$$

Clearly, a PC calculation should be based on both the exposures or, if only one is of interest (perhaps one was voluntary and the other involuntary), the calculation should take account of the fact that the total risk was altered by the other exposure. If the first exposure is the one of interest, the calculated relative excess should take account of that by replacing I with

$$I' = I \times (1 + R(D_2)).$$

It will be convenient to write $W(D_2) = 1/(1 + R(D_2))$, so that $I/I' = W(D_2)$. The relative excess for the first exposure given the second then is

$$R(D_1; D_2) = (E(D_1, D_2) - E(D_2))/I' = E(D_1)/I' = R(D_1) \times W(D_2). \quad (IV-2)$$

The role of $W(D_2)$, therefore, is to put the relative excess due to D_1 in the context of the baseline risk as altered by D_2 . The PC value for the first exposure given the second is

$$PC(D_1; D_2) = R(D_1; D_2)/(1 + R(D_1; D_2)) = (R(D_1)W(D_2))/(1 + R(D_1)W(D_2)),$$

a number different from and, in this example, smaller than the value $PC(D_1)$ which would have resulted if the second exposure had not taken place.

G. Modification of the PC Formula To Take Account of the Effects of Exposure to Carcinogens Other Than Radiation

A person with a malignant neoplasm of a kind that can be induced by radiation may have a history not only of radiation exposure, but also of exposure to other carcinogens that may be significant with respect to that particular cancer. Cigarette smoking or benzene exposure are examples. The PC has been defined as being conditional upon individual characteristics,

among which are included other carcinogenic exposures, but it may vary depending on the presence (or absence) of exposure to other carcinogens.

It is not possible to modify the PC formula to account for every possible exposure that can be listed. For example, prolonged exposure to inhaled asbestos fibers is a risk factor for lung cancer and for mesothelioma. Although mesothelioma has not been shown definitely to be induced by ionizing radiation, lung cancer has. If possible, therefore, it would be desirable to take explicit account of the possible role of asbestos exposure in the causation of a lung cancer in, for example, a shipyard worker who had radiation exposures while working as a radiographer examining welds, who also had spent several years installing asbestos insulation, and who smoked two packs of cigarettes daily. It is impossible to undertake so complete an analysis at this time, because data concerning such combined exposures are not available, and further because we are not yet able to classify asbestos exposures adequately with respect to lung cancer risk in relation to duration and intensity of exposure or exact type or fiber size of mineral.

Models

The way in which exposure to another carcinogen affects the PC depends upon the magnitude of the carcinogenic effect of that factor in the presence or absence of radiation. Although the interaction between the two factors might, theoretically, be extremely complex (even antagonism might occur), two interaction modes are especially simple and natural, and we confine our further attention to them. Those modes are the multiplicative and the additive. We avoid using the term "synergism" because it has been used by different writers with somewhat different meanings, although some have defined it to mean what we call multiplicative interaction and others as more than additive interaction.

(1) The Additive Interaction Model (AIM)

If the total excess risk from a radiation exposure and from another risk factor is assumed to be the sum of the excess risks from each of the two taken separately, we say that they interact additively. This is what was assumed (on the basis of extensive information) for two radiation exposures in section F above. As in that section, if $R(D)$ denotes the relative excess for radiation at dose D and $R(Z)$, the relative excess for another factor at level Z , the relative excess for both factors combined is

$$R(D,Z) = R(D) + R(Z).$$

Defining, in continuing analogy with section F, the altered baseline due to Z as

$$I' = I \times (1+R(Z)) = I/W(Z),$$

the relative excess for radiation given the other factor is

$$R(D;Z) = (E(D,Z)-E(Z))/I' = (R(D,Z)-R(Z)) \times W(Z) = R(D) \times W(Z). \quad (IV-3)$$

The PC for radiation given the other factor is

$$PC(D;Z) = R(D;Z)/(1+R(D;Z)) = (R(D) \times W(Z))/(1 + R(D) \times W(Z)).$$

(2) The Multiplicative Interaction Model (MIM)

If the relative risk (the relative excess plus one) due to two risk factors is the product of the relative risks for the two factors taken separately, we say the two factors interact multiplicatively. Thus, if radiation interacts multiplicatively with another factor, the relative excess for radiation at dose D and the other factor at level Z is

$$R(D,Z) = (1 + R(D)) \times (1 + R(Z)) - 1,$$

and the relative excess for D given Z is

$$\begin{aligned} R(D;Z) &= (E(D,Z)-E(Z))/I' = (R(D,Z)-R(Z)) \times W(Z) \\ &= R(D) \times (1+R(Z)) \times W(Z) = R(D), \end{aligned}$$

$$\text{and } PC(D;Z) = PC(D).$$

H. Cigarette Smoking and Lung Cancer

The most important risk factor which may be confounded with radiation in the causation of cancer is cigarette smoking, especially in relation to cancer of the lung and bronchus.

As has been shown, if a multiplicative interaction holds then the PC's for radiation causation do not vary according to the smoking history (nor would the PC's for smoking history vary according to the radiation history). Whittemore and McMillen (5) concluded that in a group of nearly 3,400 uranium miners, an MIM appeared to hold as between exposure to radon measured in cumulative Working Level Months and cigarette smoking measured as accumulated pack-years (one pack-year is one year's experience smoking one pack daily).

On the other hand, Prentice *et al.* (6) found that in a group of more than 40,000 residents of Hiroshima and Nagasaki, some of whom were exposed to a wide range of acute doses of radiation from the atomic bombs in those cities, the MIM definitely did not hold for death from all non-hematologic cancers and, specifically for lung cancer, the AIM fit the data better than the MIM.

Further, Blot *et al.* (7), in a case-control study of lung cancer in Hiroshima and Nagasaki have demonstrated that radiation and smoking interact in an additive way in the causation of lung cancer.

It is possible that the difference in results obtained by the several groups stems from an intrinsic difference between a radiation dose of sparsely ionizing radiation (gamma rays) received in a matter of seconds (A-bomb) and a dose of densely ionizing radiation (alpha-particle-

emitting radon daughters) received over a period of years. In any case, we will illustrate the calculations appropriate to the AIM.

(1) The Additive Interaction Model for Cigarette Smoking and Lung Cancer.

The AIM formula (see Chapter IV-G) for a given level s of smoking is:

$$R(D;s) = R(D) \times W(s)$$

where

$$W(s) = 1/(1 + R(s)), \quad (IV-4)$$

and where $R(s)$ represents the relative excess for smoking levels as compared to baseline lung cancer incidence.

Baseline incidence depends upon age; however, from Kahn's data (8), it is evident that $R(s)$ can be treated as independent of age. Because baseline incidence corresponds to the general population of smokers and nonsmokers, $R(s)$ is negative for smoking levels s corresponding to lung cancer risks less than average, such as nonsmoking, and the average over all levels of $R(s)$ is zero. Thus, if $p(0), p(1), \dots, p(k)$ is the distribution of the general population over integer values of s from $s = 0$ for nonsmokers to $s = k$ for heavy smokers,

$$p(0)(1+R(0))+\dots+p(k)(1+R(k)) = 1. \quad (IV-5)$$

Published values of the relative risk $RR(s)$ of lung cancer at various smoking levels compare the rate at each level to that among nonsmokers, and can therefore be written as

$$RR(s) = (1+R(s))/(1+R(0)). \quad (IV-6)$$

Therefore equation (IV-5) can be rewritten as

$$p(0) + p(1)RR(1)+\dots+p(k)RR(k) = 1/(1+R(0)) = W(0). \quad (IV-7)$$

If the values $p(s)$ and $RR(s)$ are known then $W(0)$ can be calculated from IV-7 and $W(s)$ can be calculated from $W(0)$, IV-6, and IV-4 for $s = 1, 2, \dots, k$ as $W(s) = W(0)/RR(s)$. (IV-8)

The data on incidence of lung cancer used here refer to the period 1973-1981; we use data concerning smoking habits for the year July, 1964 - June, 1965 published by the National Center for Health Statistics (9). Since the SEER incidence data for the years 1973-1981 center on the year 1977, we apply the smoking percentages obtained in 1964-1965 to the incidence rates at ages ten years later; that is, for example, we apply the percentages obtained in 1964-1965 at ages 25-44 to incidence data for ages 35-54.

We copy the values of RR(s) from Rogot and Murray (10).

Text Table A

	RR(s)	p(s)*	
		Males	Females
Nonsmokers	1.00	29.82	59.01
Former smokers**	3.97	19.23	7.81
Present cigarette smokers - all	11.28	50.95	33.18
Present amount***			
<10/day	3.89	13.56	13.50
10-20/day	9.63	24.72	15.02
21-39/day	16.70	11.24	4.37
40+/day	23.70	1.43	0.30

*NCHS 10-34 shows a small number (3.3 percent of male smokers and 1.6 percent of female smokers) of unknown present amount; we have distributed these proportionately to the categories of known amount.

**The value of W for former smokers applies to persons who stopped smoking cigarettes at least five years prior to onset of lung cancer. The data of Rogot and Murray (10) show that during the first five years after cessation of smoking, the risk of death from lung cancer is actually more than one and one-half times that of current smokers, implying that some stop smoking because of early symptoms of what eventually will prove to be lung cancer. It seems most appropriate to treat such persons as if they were current cigarette smokers.

***The class intervals shown here are those used by Rogot and Murray (10); the NCHS 10-34 intervals are slightly different; less than 11; 11-20; 21-40; 41 and over.

From equation IV-7 we obtain:

$$\text{Males } .2982 + 3.97 \times .1923 + 11.28 \times .5095 = 1/(1+R(0))$$

$$\text{Females } .5901 + 3.97 \times .0781 + 11.28 \times .3318 = 1/(1+R(0))$$

so that

$$\text{Males } W(0) = 1/0.1469$$

$$\text{Females } W(0) = 1/0.2154,$$

whence, from equation IV-8 we obtain the values of W(s).

<u>Values of W(s) - Lung Cancer</u>		
<u>Smoking Category</u>	<u>Males</u>	<u>Females</u>
Total	1.00	1.00
Nonsmokers	6.81	4.64
Former smokers	1.71	1.17
Present cigarette smokers - all	0.604	0.411
<10/day	1.75	1.19
10-20/day	.707	.482
21-39/day	.408	.278
40+/day	.287	.196

(2) Probability of Causation for Lung Cancer - Additive Interaction Model.

Referring back to equation IV-2, it is evident that the smoking characteristic can be accounted for in calculating the PC merely by multiplying R(D) by the appropriate value of W(s). This process is exemplified, and illustrative examples are given, in Chapter X-9.

I. Subpopulations with Non-standard Cancer Risks

From a reading of SEER rates for the different reporting areas, it is easy to select examples in which cancer incidence for a particular reporting region, and especially a particular ethnic group within a particular reporting region, is markedly higher or lower than the rates used for this report, which were based on all reporting regions except

Puerto Rico. Presumably, these differences are due to differential exposures, and an individual case probably should be evaluated in terms of that individual's exposure history rather than in terms of regional or ethnic classification. For example, male lung cancer rates in Utah are about half as high as those in the United States as a whole, but this is ascribable to the fact that the proportion of smokers in Utah is smaller than that in the rest of the country, due to the predominance of the Mormon Church, which proscribes tobacco use among its members. As we have seen above, nonsmokers have less than one sixth the lung cancer rate among males generally. Clearly, for lung cancer, information about smoking is more useful than information about area of residence and, presumably, about other factors as well (i.e., a member of the Mormon Church who smokes is unlikely to have a lung cancer risk much different from that of a non-Mormon with the same smoking history).

As a purely calculational exercise, it is a simple matter to define a factor W for membership in a certain subpopulation, as the ratio of the appropriate SEER rate to the corresponding subpopulation rate. Whether this should, or can, be done, however, is another matter. Differences between subpopulations with respect to cancer rates may depend mainly upon differences in exposure histories, and except for exposure to tobacco smoke, in the case of lung cancer, and radiation exposures other than the one(s) of interest, there appears to be no basis for a model by which other exposures may interact with a radiation exposure of interest. Simply ignoring information about a possibly altered cancer rate, on the other hand, amounts to treating the factors responsible as if they were known to interact multiplicatively with radiation.

Although in the abstract it would be desirable to take account of factors that interact additively in the appropriate way, we are ignorant of the nature of interactions except for smoking and lung cancer. Moreover, even if one wished to take account of a particular interaction as if it were additive, the necessary data that would enable the calculations are not available. However, the relative risk time-response model for radiation is consistent with existing data, and also with the idea that many, if not all, other risk factors do interact multiplicatively with radiation. It should be recognized, however, that to use the tables ignoring the influence of any particular other factor, is equivalent to treating that factor as one that interacts multiplicatively with radiation.

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CHAPTER V: DATA SOURCES, ASSUMPTIONS, AND MODELS

A. Data Sources

The calculation of probabilities of causation for radiogenic cancers requires baseline data for individual cancers and parallel quantitative risk estimates for cancer arising from exposure to ionizing radiation. Although the bulk of the data on the risk of cancer is in the form of mortality rates, in the late 1930s the National Cancer Institute began periodic surveys of cancer incidence and survival. As the Surveillance, Epidemiology, and End Results (SEER) program, this effort, covering about 10 percent of the U.S. population, now provides systematic, national incidence data for the period beginning with 1973 that are unequivocally the best source of data on cancer incidence for the U.S. Data for 1973-77 are published (1); the Working Group has had access to the unpublished tabulations through 1981 (Table V-1). Site-specific baseline incidence data by age and sex have been used here as the basis for PC calculations without regard to ethnic or geographic sources of variation that often are considerable. PC estimates are necessarily sensitive to the baseline incidence used in the calculation of relative excess risk, and choices must be made whenever incidence is known to vary with characteristics of individuals for whom such estimates are required. Although the SEER data extend to geographic and ethnic variation, there is some uncertainty about the statistical stability of much of this variation, and the extent to which it may reflect the influences of factors whose interaction with radiation in the causation of cancer is simply unknown. With the single exception of smoking related to lung cancer, the methods and calculations presented here are appropriate to "average" Americans whose baseline risk levels are represented by the combined SEER registries.

The use of a single set of rates also takes no account of changes in population incidence over time, but these have been considerable only for stomach cancer and lung cancer.

The PC calculations have been limited to sites and types of cancer for which radiation is known to be a cause and for which reasonable data exist for purposes of calculation. (See chapters VII and X for further discussion). Site-specific estimates of radiation-induced cancer risk in terms of incidence have been taken from Tables V-14 and V-16 of the 1980 BEIR report (2) with updating for several sites and with deletions appropriate to the calculation of PC values (Table V-2). The BEIR report is the only comprehensive source of human, site-specific incidence data relating radiation exposure to cancer risk and the time constraints placed upon the Working Group have precluded any systematic reworking of the relevant literature, much less the original data upon which it is based.

The A-bomb survivor data for leukemia (3) were subdivided by type to develop separate sets of risk estimates for acute leukemia and chronic granulocytic leukemia. The BEIR leukemia coefficients themselves were modified to achieve a more stable, and plausible, dependence of risk on age at exposure (see Section D, below). The lung cancer coefficients were revised on the basis of new data from the A-bomb survivor series (4) (see Chapter X-9). Recent reports of thyroid cancer and breast cancer

incidence among A-bomb survivors (5,6) provided new information on the dependence of risk on age at exposure, an issue that had not been resolved satisfactorily by the BEIR III Committee (see Section D). A recent review of studies of salivary gland cancer following childhood irradiation (7) provided a numerical risk estimate for exposure ages 0-14, and the site was included in the calculations. Finally, BEIR estimates for certain sites and exposure ages were evaluated and rejected as uncertain, and corresponding PC calculations were not performed. Of the 78 age, sex, and site-specific risk coefficients employed in the present report, 40 were taken directly from the BEIR report and 38 were taken from more recent sources; also other coefficients presented in the BEIR report for the lymphomas and "miscellaneous other" sites were not used (see Chapter VII-F).

B. Dose-Response and Dose-Rate-Effect Models

As discussed in Chapter III-E, the weight of radiobiological evidence favors a linear-quadratic dose response to low-LET radiation for most cancers, with a "crossover" dose, at which the components of risk proportional to dose and dose-squared are equal, somewhere between 50 and 200 rad (8). In general, the epidemiological evidence discriminates poorly among competing dose-response models (9). Thyroid cancer and female breast cancer are exceptional in that the epidemiological data strongly favor linearity (2,5,6). Accordingly, the Working Group has adopted linearity for breast and thyroid cancer and the BEIR III linear-quadratic model for all other sites, for PC calculations involving exposure to low-LET radiation. The BEIR III linear-quadratic model estimates excess cancer risk, following a radiation exposure of short duration, as

$$\text{Excess} = e_{LQ} \times (D + D^2/116),$$

where e_{LQ} is a site-specific coefficient depending upon age at exposure and sex, and D is radiation dose in rad (see Chapter III-H). The linear model, of course, expresses excess risk as

$$\text{Excess} = e_L \times D.$$

The so-called crossover dose of 116 rad in the formulation of the BEIR linear-quadratic model, which specifies the degree of curvature in the graph of risk as a function of dose, was originally determined from the Japanese leukemia data (2,3), but is also consistent with a number of other radiobiologic end points (see Chapter III-I). Since no other human cancer data are adequate for calculating crossover doses for individual sites other than the thyroid gland and female breast, the value of 116 rad has been assumed to apply to all sites for which a linear-quadratic dose-response model for low-LET radiation is considered appropriate for low-LET radiation (i.e., all cancers other than those of the thyroid and female breast).

Although the BEIR Committee's site-specific incidence risk coefficients, except for leukemia, corresponded to the linear dose-response model, the Committee provided numerical coefficients for both linear and

linear-quadratic models with respect to total mortality from all types of cancer other than leukemia, considered as a group (reference 2, Tables V-19 and V-20). The ratio of these coefficients,

$$e_1/e_{LQ} = 3.470/1.397 = 2.48 = 2.5,$$

and the crossover dose of 116 rad were used by the Working Group to convert the BEIR III linear-model coefficients to the corresponding linear-quadratic coefficients for the appropriate sites.

The present radioepidemiological tables have been prepared primarily for low-LET radiation exposures. The tables and algorithms may, however, be applied to high-LET radiation exposures by substituting for dose the "biologically equivalent dose" (BED) determined for the particular exposure. This calculation involves the assumption that for high-LET radiation the dose-response relationship is approximately linear, which may be justified for doses below 10 rad. In its simplest form, the BED is the product of the dose in rad and a "relative biological effectiveness" (RBE) factor for the given radiation (see Chapter III-B). The RBE factor depends on the end point selected and varies with the dose and with the LET of the radiation, which is a function not only of the energy of the incident radiation but also of the attenuation and scatter in the tissues surrounding the target tissue. For internally deposited radionuclides, estimates of equivalent doses are further complicated by spatial and temporal variations in the distribution of the sources of radiation. Therefore for a best estimate of the cancer risk from a given exposure to high-LET radiation, biologically equivalent doses must be calculated on a case-by-case basis, and it clearly would make little sense to produce separate PC tables for any given high-LET radiation. Exposure of bone to high-LET radiation from internally deposited radium-224 and lung exposures from radon daughters are a special case since there is a direct observational basis for risk estimation (see Chapter X-2 and X-9).

The calculation of BED is a complicated process, and particularly so for radiation from internally deposited radionuclides. The Ad Hoc Working Group has made no attempt to pursue the issue beyond this point.

Considerations of dose rate and dose-fractionation effects influenced the Working Group's choice of the linear-quadratic model for cancer sites other than the breast and thyroid (see Chapter III-I). By treating exposures widely separated in time as independent, and therefore additive in effect, a model-dependent approach to dose rate was obtained. The scientific basis for this procedure is that repair of DNA sublesions is rapid, generally occurring within hours following irradiation. Consider a case in which exposures to D_1 and D_2 rad occurred during successive months. Under the linear model, the effects of the two exposures are proportional to D_1 and D_2 , respectively, and their combined effect is therefore proportional to $D_1 + D_2$, just as if the two exposures had occurred simultaneously. Thus for fast neutrons and alpha particles in the lower-dose range (below 10 rad), and for low-LET radiation in the case of breast cancer or thyroid cancer, there is no reduction in effect due to fractionation or protraction of exposure. Under the linear-quadratic model, on the other hand, the effects of the two exposures are proportional to $D_1 + D_1^2/116$ and $D_2 + D_2^2/116$, respectively. The combined effect is proportional to the sum of these two numbers, and is less than the effect

of a single exposure to $D_1 + D_2$ rad, which is proportional to $(D_1 + D_2) + (D_1 + D_2)^2/116$. Thus for low-LET radiation there is a reduction in effect for fractionation and protraction of exposure, for all cancers except those of the thyroid gland and the female breast.

In practice, the reduction in effect due to fractionation of exposure in the above example is slight unless the sum of D_1 and D_2 is greater than 5 rad or so. (If $D_1 + D_2$ is less than 5 rad, then $(D_1 + D_2) + (D_1 + D_2)^2/116$ exceeds $D_1 + D_1^2/116 + D_2 + D_2^2/116$ by 2% or less.) Accordingly, for cancer sites for which the linear-quadratic model is appropriate, the Working Group suggests the following approach for calculating PCs for low-LET exposures separated in time or protracted over time: Generally, exposures occurring within a few months of each other can be combined (i.e., treated as a single exposure, with dose equal to the sum of the separate doses), provided that the sum of their doses is less than 5 rad. Consecutive acute exposures should not be combined if the total combined dose is greater than 5 rad. For protracted exposures, accumulations of 5 rad or less need not be subdivided unless the exposure extended over more than one year. Independence of effect cannot be assumed for exposures separated by less than 24 hours or so. In the absence of a detailed and reliable model, the Working Group recommends that cumulative exposures of 5 rad or more within a period of 24 hours or less be treated as if from a single acute exposure. This rule may result in the overestimation of the effects of exposures separated by a few hours. For very low dose rates the above approach gives results that are virtually the same (within 4%) as would be obtained if the quadratic (dose-squared) term were ignored. For a detailed example, see Chapter IX, Example 5. Also, see site-specific examples in Chapter X.

C. Time after Exposure

Clearly, time is required for a single transformed cell to develop into a clinically detectable cancer, and for that reason alone, a cancer detected within a few weeks or months after a particular radiation exposure would not be considered a possible consequence of that exposure. More generally, assumptions about the distribution of excess risk over time following exposure can strongly influence the PC calculations. There are two issues: how long does it take before there is a non-negligible excess risk, and how does the risk vary over time subsequently?

The BEIR III Committee used a plateau model for leukemia and bone cancer and both a constant absolute risk projection model and a constant relative risk projection model for other cancers, in order to extend their estimates of average excess risk, obtained from follow-up periods of 30 years or so, to estimated lifetime cancer risks. The Working Group faced a much more difficult problem, for two reasons: First, a PC calculation pertains to a specific cancer diagnosis at a particular time following one or more exposures to radiation, and not to risk averaged over a lifetime. Second, the charge to the Working Group was to provide a single "best" estimate and not an array of more or less plausible ones. Thus it was necessary to use specific time-to-response models which could, however, depend upon cancer site and upon individual characteristics such as age at exposure, sex, and radiation dose. Fortunately, research subsequent to the 1980 BEIR report, made possible mainly by the increased duration

of follow-up on the Japanese A-bomb survivors and other irradiated groups (see Chapter III-H), helped the Working Group to arrive at a number of assumptions needed for its calculations.

The 1980 BEIR report, as well as the published analyses reviewed in Chapter III-H, suggested that time from an acute exposure until diagnosis for radiation-induced bone cancer and leukemia follows wave-like distributions like the lognormal. Accordingly, the Working Group conducted analyses of data on time to diagnosis from a German series of patients treated by radium-224 injections for ankylosing spondylitis, and who later developed bone cancer at a rate more than 250 times that expected from baseline population rates (10), and leukemia data from A-bomb survivors with high radiation doses (11), supplemented by leukemia data from a British series of patients treated with X radiation for ankylosing spondylitis (12). Lognormal time-response models were fitted to these data, for all exposure ages combined and as partitioned by age at exposure.

The bone cancer data were found to conform closely to a lognormal distribution for time to response, with minimum 1.52 years, and for which the mean and variance on the logarithmic scale, after subtraction of the minimum, were 2.12 and 0.48, respectively (Figure V-1). The minimum value was the least precise of the three estimated quantities; virtually the same fitted probability distribution was obtained when the BEIR III minimum of 2 years was assumed a priori. There was no evidence that the distribution of time to response depended on age at exposure or on radiation dose.

The leukemia data were less easy to work with, partly because the possibility that a given high-dose case was not radiogenic could not be ruled out with as much confidence as with the bone cancer data, but mainly because the cancer data for the A-bomb survivors for the first 5 years after exposure lacked suitable denominators (11). The BEIR III minimum of 2 years for the latent period was assumed. Based on the British ankylosing spondylitis data (12), it was estimated that the average annual excess leukemia rate during the period 2-5 years after exposure was about half that during the next five years. From published analyses of the A-bomb survivor data (3,13) it was determined that acute leukemia (AL) and chronic granulocytic leukemia (CGL) have different temporal distributions following exposure, and that for AL, but not CGL, time to diagnosis depends on age at exposure. (Very few of the leukemias in the series are of types other than AL or CGL.) According to the Working Group's analysis, the fitted lognormal distribution for CGL had mean 2.68 and variance 1.51 on the logarithmic scale of time in years minus the assumed 2-year minimum (Figure V-2), while that for AL required an adjustment for age at exposure. The estimated mean on the logarithmic scale was $1.61 + .015 A_1 + .0005 A_1^2$, where A_1 denotes age at exposure, and the variance was 0.65. For AL, therefore, the fitted distribution predicts that with increasing age at exposure, radiation-induced cases tend to occur longer after exposure and to be more widely dispersed in time (Figure V-3). For leukemia in general, excluding the chronic lymphocytic form that apparently is not caused by radiation, the Working Group used a mixture of the estimated time-to-response curves for CGL and AL, weighted by .32 and .68, respectively (Figure V-4).

For leukemia and bone cancer the temporal distributions of risk imply that the plausibility of a causal connection between a particular cancer and a prior radiation exposure may depend strongly upon the length of the intervening time interval. For example, according to the time-to-response model described above, a radiation-induced bone cancer is about 6 times more likely to be diagnosed 5 years after exposure than 20 years after exposure; therefore, all other things being equal, the plausibility of a causal connection between a diagnosed bone cancer and a prior radiation exposure is greater for a 5-year interval from exposure to diagnosis than for a 20-year interval.

For cancers other than leukemia and bone cancer, the estimated probability of causation is independent of time from radiation exposure until cancer diagnosis, if that time is greater than 10 years. This is a consequence of the constant relative risk model for time to response which the Working Group adopted on the basis of published studies discussed in Chapter III-H. Because these studies pertained mainly to breast and lung cancer, the Working Group carried out a comparable analysis of stomach cancer among high-dose A-bomb survivors, and obtained results similar to those obtained for breast cancer and lung cancer.

The constant relative risk model applies only after some initial period, which the BEIR III Committee fixed at 10 years. The Working Group felt that this value was consistent with epidemiological findings for persons exposed at ages at which baseline incidence was already high enough for an appreciable number of excess cancers to be expected under the model, and that for younger exposure ages the practical importance of the initial period was small because few cancers, radiation-induced or otherwise, would be expected until much later than 10 years after exposure. On the other hand, the radiation-related excess risk is zero at the time of exposure, and assumes its eventual full value relative to baseline incidence after about 10 years. The Working Group felt that not enough is known about tumor growth kinetics to justify a distributional model for the time required for a single transformed cell to develop into a clinically detectable tumor; what is known, however, suggests that the risk of radiation-induced cancer (other than bone cancer and leukemia) is negligible for the first 5 years after exposure (see Chapter III-H). A discontinuity is biologically unlikely, and the Working Group therefore decided upon a cubic function of time to provide a smooth transition from an assumed zero excess for the first 5 years after exposure to the eventual constant relative excess after 10 years (Figure V-5), to be applied on the basis of time in whole numbers of years. In the table below, Y represents the integer part of time in years from exposure until diagnosis (e.g., 11 years, 10 months corresponds to $Y = 11$) and $T(Y)$ is the corresponding proportion of the eventual relative excess applying at time Y :

Y:	0-4	5	6	7	8	9	10+
T(Y):	0	.074	.259	.500	.741	.926	1.000

PC estimates are most reliable, of course, when they are based altogether on observational data. Unfortunately, there are no series that provide followup data beyond 40 years after exposure, and most of the available longterm data pertain to the interval from exposure to

30-35 years. Use of the constant relative risk model of time-response for most solid tumors makes the dependence on the present PC tables for estimates beyond this interval less hazardous than would be the case if the constant risk model were to have been used. This is because absolute risks within each age-at-exposure cohort of A-bomb survivors have continued to rise steadily, tracking baseline mortality, well beyond the 1974 cut-off that was the basis for many of the BEIR coefficients. The constant relative risks resulting from these observations have been published through 1978 (4) and are seen in preliminary drafts of the current analysis that extend through 1982. For leukemia and bone cancer, the wave-like functions fall so precipitously after attaining their respective peaks that the Working Group has extended the tables beyond the period of observation to 49 years.

D. Age at Exposure

A rule that appears to hold for all radiation-induced cancers as a group, and for many cancer sites individually, is that excess risk declines relative to baseline risk with increasing age at exposure. Also, however, because excess risk tends to increase over time proportionally with baseline risk and because available data are limited to the period 30 years or so after exposure, absolute measures of risk tend to increase with increasing age at exposure. For cancers of the lung, digestive tract, and urinary system, which comprise a large part of both the excess and baseline cancer risk in exposed populations, this increase appears to be smooth (2,4). For some cancer sites, like the liver, bone, and, until recently, the thyroid gland, there was insufficient evidence on which to base estimates of variation by exposure age, and the BEIR age-specific risk coefficients for these sites are flat. Three important sites, however, are exceptions to the general rule.

A recent study of thyroid cancer incidence among A-bomb survivors indicates strongly that absolute, as well as relative, measures of risk are markedly reduced for adult compared to childhood exposures (5). Breast cancer, however, for which the existence of a risk following exposure during the first decade of life was only recently established (14,15), shows an increase in absolute risk with increasing age at exposure over the first two decades of life, but a marked decrease thereafter (6,16,17). To the 1980 BEIR Committee, which relied mainly on Japanese A-bomb survivor data for exposures after the age of 40, it seemed possible that the apparent absence of an excess might reflect a hormonal influence due to ovarian irradiation, or perhaps a difference between Japanese and western populations (2). More recently, however, a large survey of breast cancer mortality among Canadian women given multiple chest fluoroscopies during treatment for tuberculosis revealed the same pattern of greatly reduced risk for exposure after age 40 (17). Accordingly, the Working Group computed new age-specific breast cancer risk estimates from the most recent A-bomb survivor data (6), relying on a study of Swedish women given therapeutic X radiation for benign breast disease (16) to provide a smooth downward transition in risk from age 40 down to 75, at which age a zero excess was assumed.

For leukemia, there is a high absolute excess risk for exposures during the first decade of life, with a much lower excess for exposure at ages 10-19, and a steady increase for exposures at older ages (4). The BEIR report estimates, which were based on A-bomb survivor incidence data (3), do not vary smoothly with age, in that the coefficient for exposure ages 20-34 is higher than those for ages 10-19 and 35-49. The difference is far from significant statistically, however, and a similar pattern is not seen in data based on the British spondylitis series (18). Accordingly, the Working Group replaced the BEIR coefficients for exposure age intervals 10-19, 20-34, 35-49, and 50+ by values corresponding to a quadratic function of age, fitted by least squares using weights based on the variances of the BEIR estimates. No adjustment was made to the BEIR coefficient for exposure ages 0-9, about which the spondylitis data are uninformative.

Epidemiological data linking fetal radiation exposure to increased cancer risk largely pertain to exposure from pelvimetry examinations shortly before birth. The 1980 BEIR report presented an estimate of this risk based on the results of the Oxford Survey (19), as 25 excess leukemia deaths and 28 excess deaths from other cancers per million persons per year per rad for the first 12 and 10 years of life, respectively. The Committee did not, however, explicitly include these estimates in its tabulated estimates of lifetime risk following acute and chronic exposures to radiation. Even after allowing for the difference in follow-up (5-26 years for the A-bomb survivors vs. 0-12 years for the Oxford Survey) in the light of the calculated lognormal time-to-diagnosis distribution for exposure at age 0 (Table X.1.H), and allowing, with Stewart (20), for the possibility that estimated radiation doses in the Oxford Survey may have been too small by a factor of 2, the above estimate for leukemia is three times as high as an extrapolated estimate based on the leukemia coefficients used for the present report (Table VI-1). Experimental studies, in fact, suggest that there is little or no cancer risk associated with exposure during the middle uterine period, and that exposure during the late uterine stage is comparable in effect to exposure during infancy and early childhood (21-24). Given the uncertainties that remain about the magnitude of radiogenic risk of leukemia and other childhood cancers following fetal irradiation (see Chapter III-G), the Working Group is unpersuaded that cancer risk depends strongly upon whether or not the exposed person was in utero or postnatal, and suggests that in-utero exposures be treated no differently than postnatal exposures at age 0.

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Table V-1. SEER Baseline Cancer Incidence Rates (Cases per 100,000 per Year), 1973-1980, by Sex, Cancer Site, and Age at Diagnosis

Cancer Site: Males

Age	COL	AL	LEUK	BONE	SALIV	ESOPH	STOM	COLON	LIVER	PANCR	LUNG	BRST	URIN	THYR
0-4	1.1	6.9	7.0	1.1	.02	0	0	0	.4	0	0	---	1.7	0
5-9	1.1	3.2	3.3	.3	.01	0	0	0	.1	0	0	---	.4	.1
10-14	1.1	2.4	2.5	1.3	.05	0	0	0	.1	0	0	---	.1	.2
15-19	2.2	2.5	2.7	1.5	.09	0	0	.2	.1	0	0	---	.3	.6
20-24	4.6	1.8	2.2	.9	.28	0	0	.4	.2	.1	.3	---	.8	1.2
25-29	9.9	2.0	2.9	.7	.41	.1	.3	3.2	.3	.5	.6	---	1.4	1.9
30-34	18.8	2.2	3.0	.5	.39	.1	.7	2.4	.3	1.2	2.3	---	3.0	3.7
35-39	1.0	2.4	3.4	.5	.57	.4	2.1	5.2	.5	2.9	8.5	---	5.5	3.7
40-44	1.1	2.9	4.0	.6	1.08	.8	6.1	9.3	.9	3.1	24.0	---	7.2	3.5
45-49	1.2	4.4	5.6	.8	1.01	4.8	6.1	16.8	2.3	6.9	61.4	---	12.8	3.7
50-54	1.9	5.8	7.9	1.0	1.74	9.1	8.8	34.5	3.6	16.0	116.7	---	23.5	3.8
55-59	3.0	6.2	11.4	1.2	2.23	15.4	24.1	61.9	6.4	21.3	192.2	---	42.2	4.8
60-64	6.4	13.4	17.9	1.7	2.54	22.7	42.0	104.4	10.4	38.2	295.0	---	69.3	4.4
65-69	5.5	18.2	24.1	1.7	3.46	30.2	58.9	166.3	15.2	53.0	409.1	---	106.0	5.4
70-74	7.7	31.2	39.2	2.1	4.48	34.9	74.8	243.3	18.1	74.0	491.6	---	156.1	5.9
75-79	12.2	65.5	58.0	3.2	7.10	33.6	113.7	328.4	23.0	91.5	527.0	---	216.6	6.3
80-84	19.0	58.6	74.4	1.9	8.15	32.9	142.9	399.5	22.1	98.0	462.5	---	272.0	6.7
85-98	18.9	44.8	66.4	2.7	8.19	35.5	157.0	448.1	21.2	115.4	373.0	---	335.3	6.1

Cancer Site: Females

Age	COL	AL	LEUK	BONE	SALIV	ESOPH	STOM	COLON	LIVER	PANCR	LUNG	BRST	URIN	THYR
0-4	0	5.7	5.7	1.4	0	0	0	0	.3	0	0	0	2.1	0
5-9	1	1.7	2.0	1.4	.03	0	0	0	.1	0	0	0	.8	.2
10-14	1	1.7	1.8	1.2	.13	0	0	.2	.1	0	0	0	.2	.4
15-19	2	1.2	1.4	1.1	.19	0	0	.6	.1	0	.2	0	.2	.2
20-24	4	1.6	1.6	.6	.25	0	0	1.6	.1	0	.2	1.2	.8	5.1
25-29	4	1.5	1.8	.4	.36	0	.2	1.2	.2	.3	.6	1.2	.6	6.4
30-34	8	1.9	2.1	.4	.58	0	.6	2.9	.5	.8	1.0	27.2	1.3	9.7
35-39	8	3.9	3.3	.2	.84	.2	1.4	5.3	.5	1.0	3.8	57.6	2.7	9.7
40-44	1.0	2.3	4.4	.3	1.08	.7	2.5	10.3	.7	1.8	15.7	106.3	5.3	10.2
45-49	1.5	4.0	5.4	.5	1.98	3.6	6.1	20.5	.8	4.1	31.9	166.2	9.0	9.1
50-54	1.6	5.6	7.4	.8	1.35	5.0	6.2	34.2	1.5	0.8	51.4	192.6	14.2	9.1
55-59	2.4	8.5	10.7	1.1	1.61	7.5	11.8	58.2	2.3	1.6	77.1	225.8	22.9	7.9
60-64	3.4	11.1	14.4	1.0	2.68	9.0	24.7	83.8	3.4	2.2	99.8	259.7	35.4	7.9
65-69	3.5	16.4	20.1	1.3	2.91	8.5	34.1	131.7	7.0	3.9	112.8	290.6	49.5	8.9
70-74	5.9	22.6	28.8	1.7	3.52	9.5	52.7	266.4	8.3	6.4	108.7	312.5	60.4	9.1
75-79	8.7	32.6	41.9	1.6	3.44	10.3	68.7	313.1	10.9	7.0	101.7	344.3	75.8	9.5
80-84	8.7	32.6	41.9	1.6	3.44	10.3	68.7	313.1	10.9	7.0	101.7	344.3	75.8	9.5
85-98	11.0	35.4	47.0	3.0	4.04	13.4	89.3	347.8	11.4	79.0	77.7	374.2	100.3	8.6

TABLE V-2. Individual Types of Cancer for Which the BEIR III Report Provides Incidence Risk Coefficients and Those for Which the Working Group Has Calculated the Probability of Causation

BEIR III	Working Group
Leukemia (all except CLL) + bone cancer	Leukemia, all except CLL acute forms chronic granulocytic
Bone	Bone and joint*
Thyroid	Thyroid
Breast	Breast
Lung	Lung
Esophagus	Esophagus
Stomach	Stomach
Intestine (colon)	Colon
Liver	Liver
Pancreas	Pancreas
Urinary organs	Kidney and urinary bladder
Lymphoma	Salivary gland

*Alpha radiation from radium-224 only.

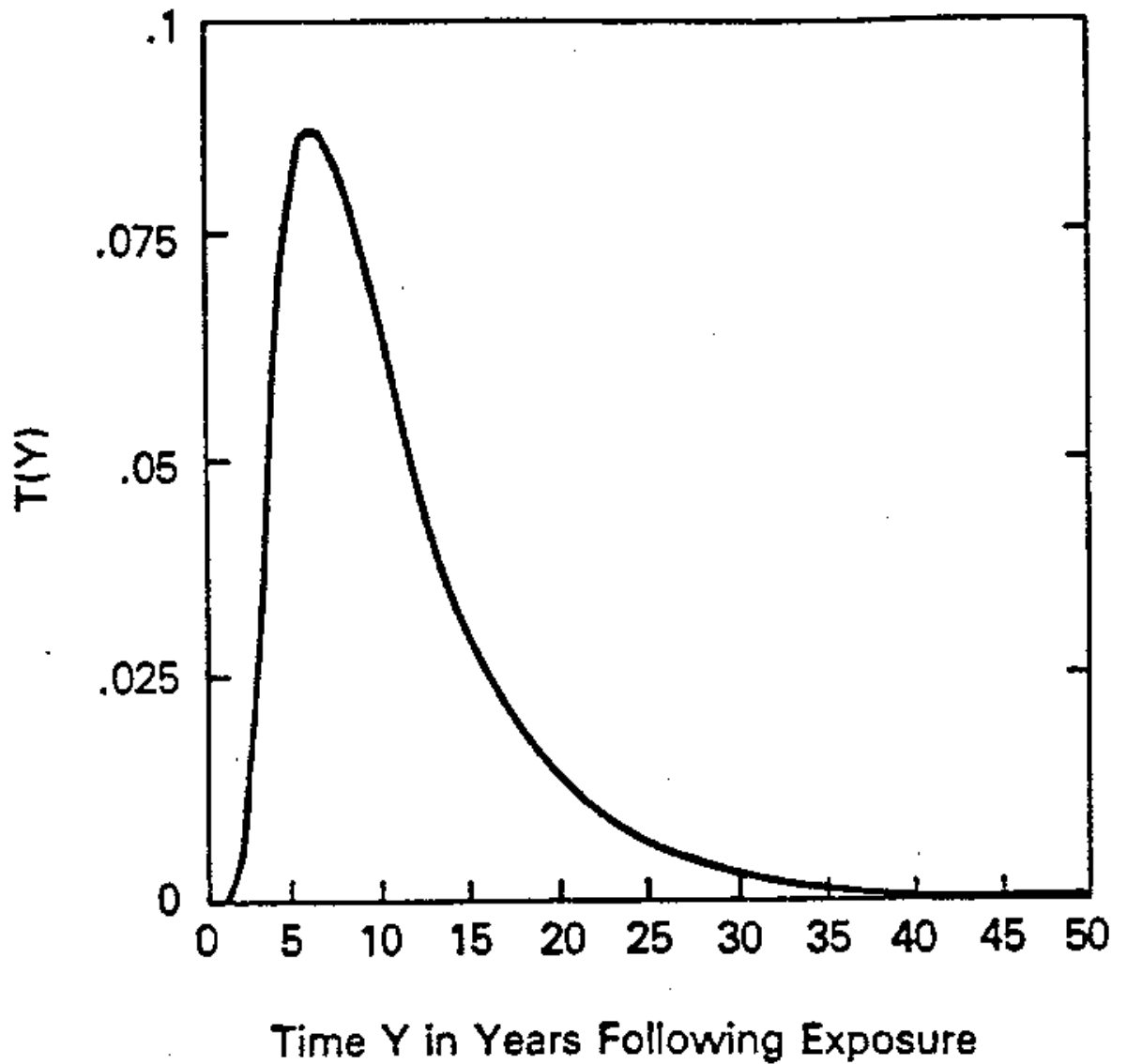


Figure V-1. Fitted time-to-tumor model for bone sarcoma induced by a brief exposure to radium-224. $T(Y)$ is the probability of diagnosis within one year after time Y . (Data from reference 10.)

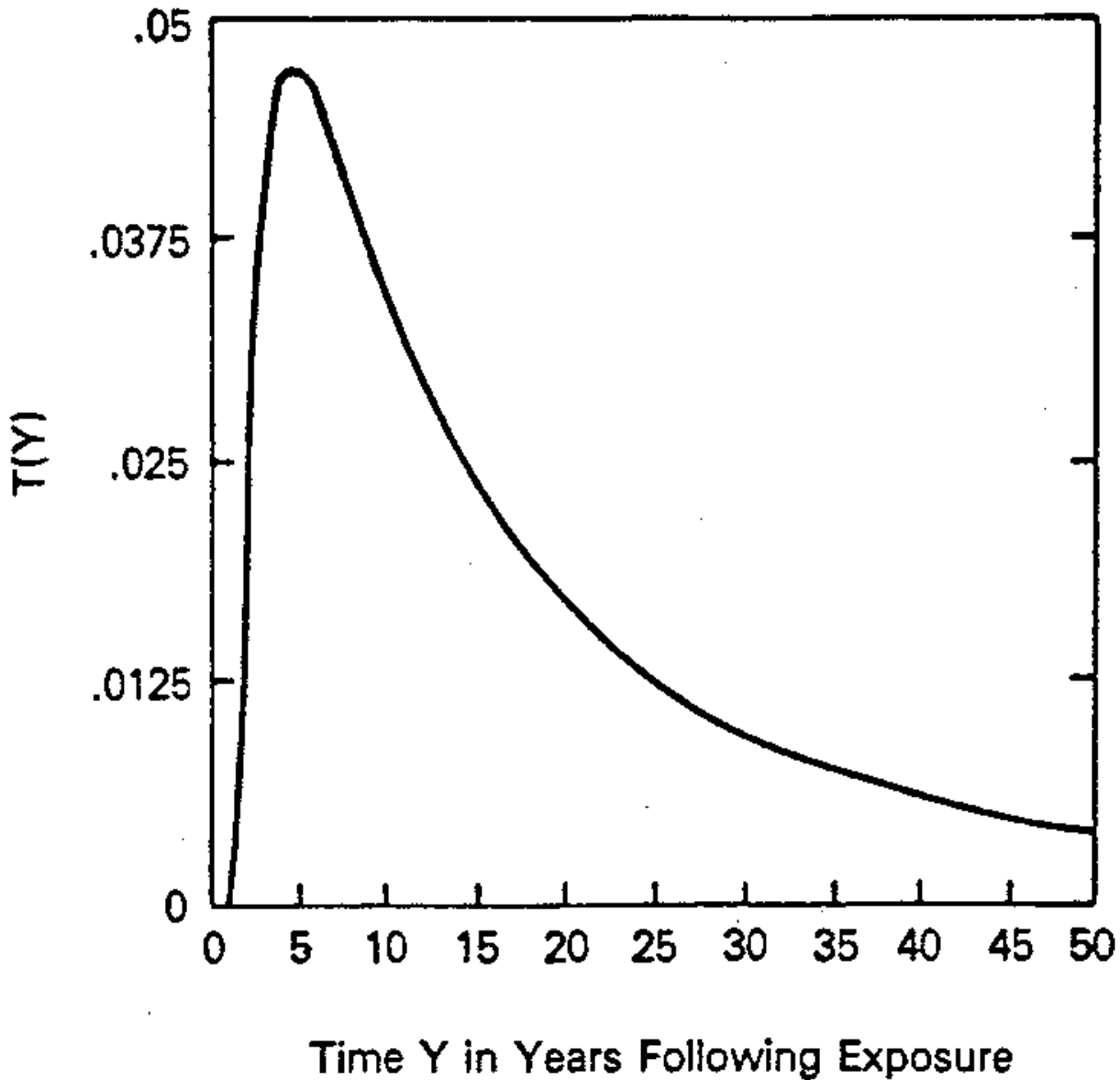


Figure V-2. Fitted time-to-tumor model for chronic granulocytic leukemia induced by a brief exposure to ionizing radiation. $T(Y)$ is the probability of diagnosis within one year after time Y . (Data from refs. 11 and 12.)

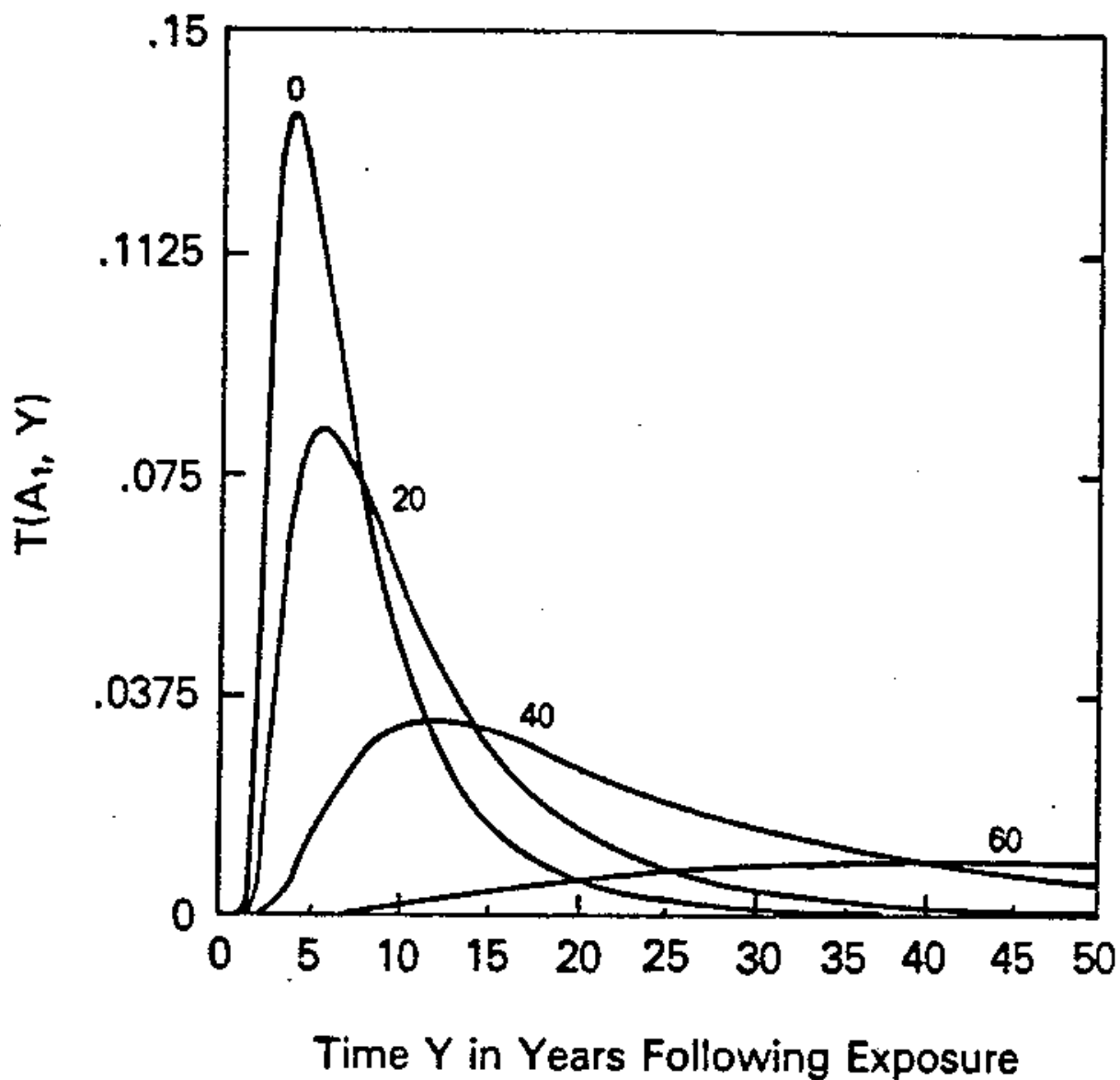


Figure V-3. Fitted time-to-tumor model for acute leukemia induced by a brief exposure to ionizing radiation at age A_1 . $T(A_1, Y)$ is the probability of diagnosis within one year after time Y. Numbers within the graph indicate age at exposure. (Data from refs. 11 and 12.)

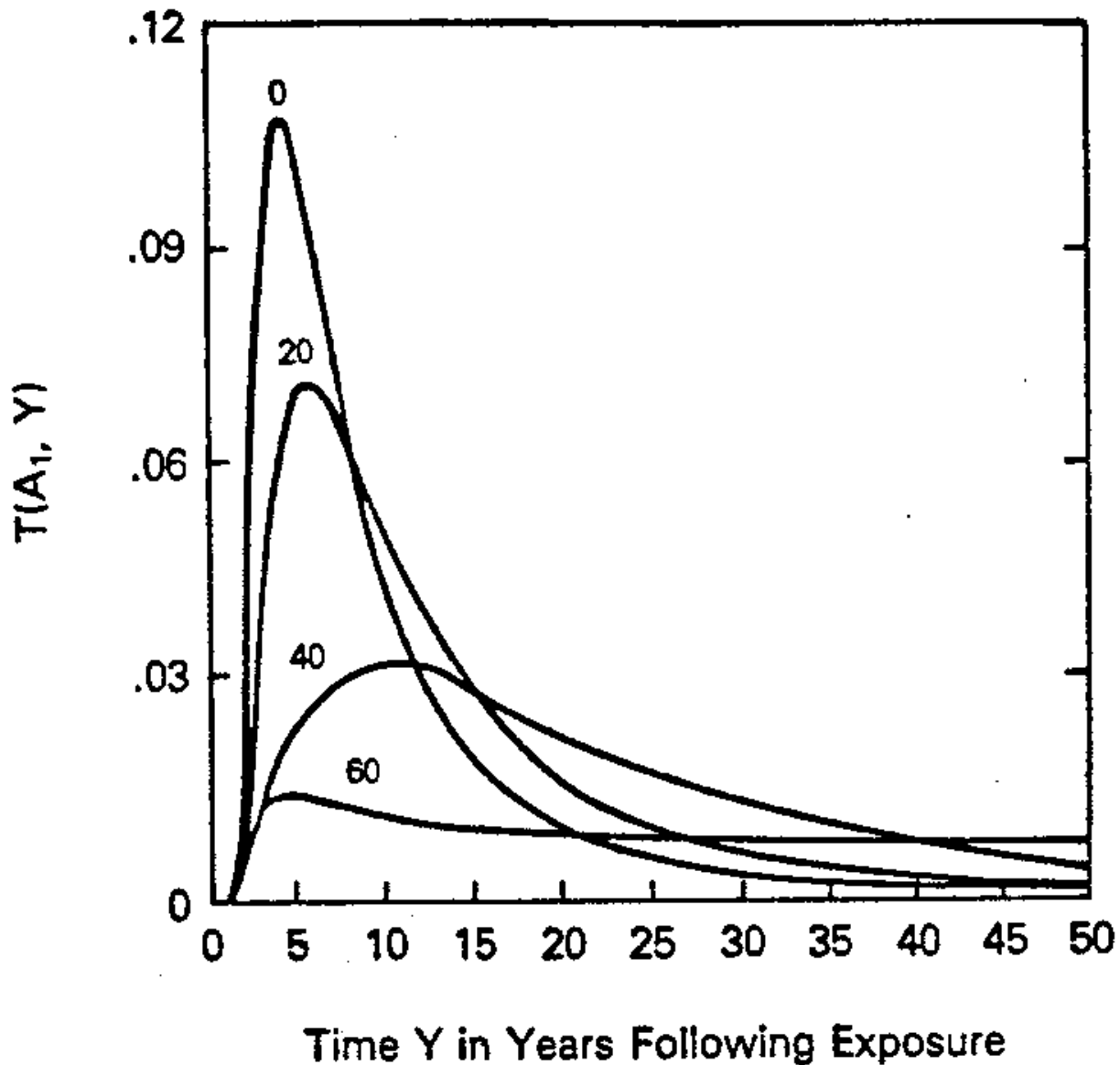


Figure V-4. Time-to-tumor model for leukemia (all types except chronic lymphocytic leukemia) induced by a brief exposure to ionizing radiation at age A_1 . $T(A_1, Y)$ is the probability of diagnosis within one year after time Y . Numbers within the graph indicate age at exposure. (Data from refs. 11 and 12.)

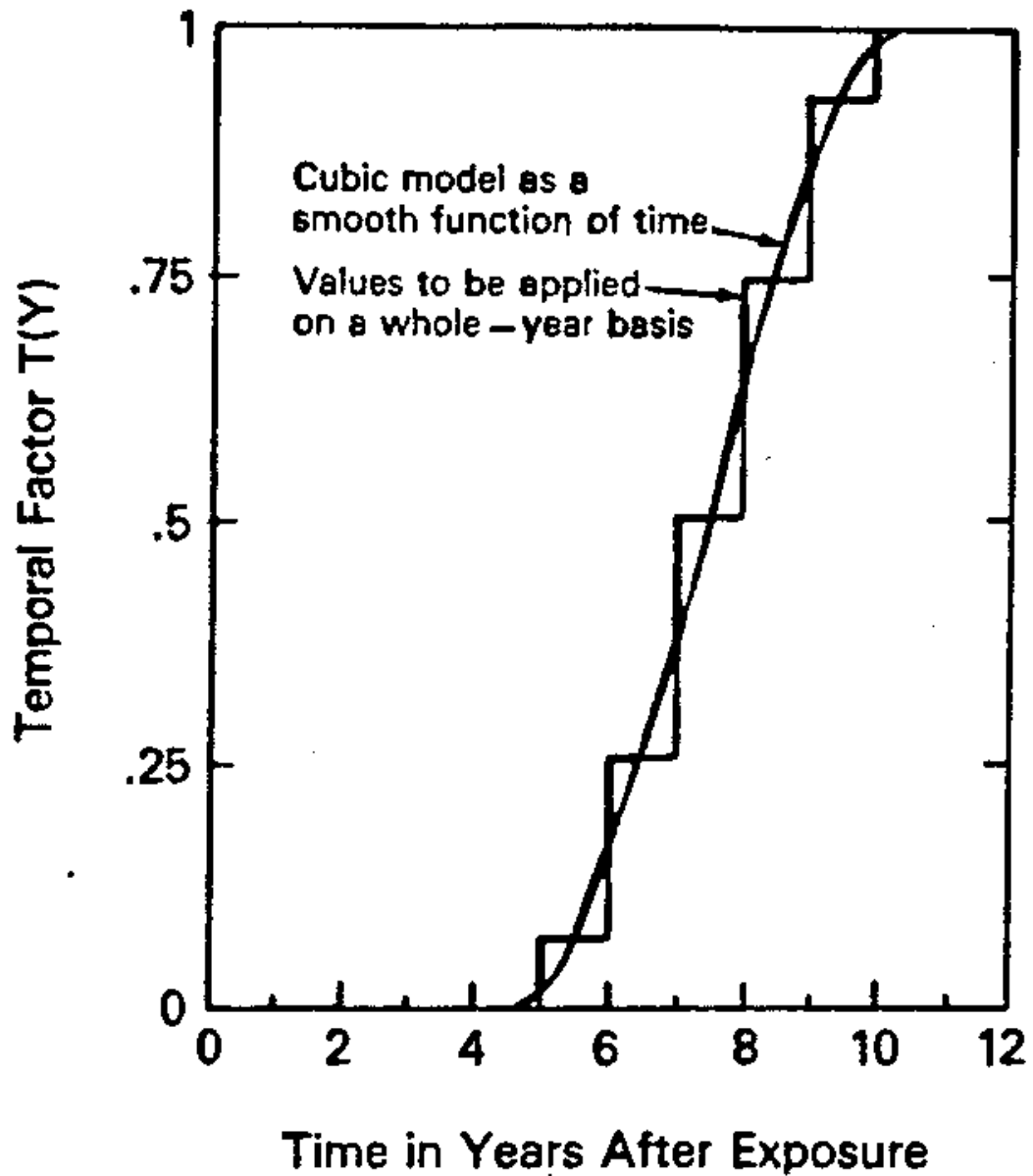


Figure V-5. Temporal factor $T(Y)$ to be applied to relative excess risk for cancers other than leukemia or bone sarcoma.

CHAPTER VI: METHOD FOR ESTIMATING RELATIVE EXCESS RISK

AND CALCULATION OF PROBABILITY OF CAUSATION

A. Coefficients of Absolute Excess Risk

The model assumed here for breast and thyroid cancer, for low-LET radiation, is that of risk as a linear function of organ dose, without threshold. For all other cancers considered, the linear-quadratic model is used for low-LET radiation (see Chapter V-B).

Table VI-1-A shows linear and linear-quadratic model risk coefficients for the incidence of excess cancers for specified periods after radiation exposure, by site, sex, and age at exposure, and for low-LET exposure, as adapted from the 1980 BEIR Report or from more recent data (see Chapter V, sections, A, B, and D). The tabulated coefficients represent the average absolute excess risks per 100,000 per year per unit increment in D or $D + D^2/116$, depending upon the dose-response model, where D is given in rad, over the specified follow-up periods for persons in the given ranges of age at exposure. Type-specific coefficients for acute and chronic granulocytic leukemia were derived from coefficients for leukemia of all types as follows: From A-bomb survivor data (1) it was determined that acute leukemias (AL) accounted for 68% of the excess leukemia risk due to radiation and chronic granulocytic leukemia (CGL) for the remaining 32%. Because this proportion did not appear to vary by age, the tabulated coefficients for leukemia were distributed accordingly. Tables VI-1-B and VI-1-C are for high-LET radiation and are only applicable to cancers of bone and joint and to lung cancer associated with exposure to radon.

PC calculations pertain to situations in which exposure age may be given for a single year of age, rather than an interval of 10 or more years, and smoothness of transition from one year of age to another is a desirable property of any calculational method that might be devised. Although the variation by age at exposure of the coefficients in Table VI-1 and in the BEIR report surely has a large random component, the Working Group did not, except in the cases of leukemia (see Chapter V-D) and lung cancer (see Chapter X-9), feel justified in smoothing this variation by assuming a parametric model for risk as a function of exposure age.

Accordingly, the tabulated coefficients were made specific to single years of age at exposure by an interpolation procedure. Each tabulated value was treated as if it pertained to the mean age of the corresponding interval, weighted by the expected length of follow-up, assuming a lifetable distribution (2) (see Table VI-2) of ages at exposure within the interval. Coefficients for single years of age were obtained by a cubic spline interpolation algorithm (3). For ages outside the range of interpolation (e.g., less than 5 for breast cancer or less than 25 for colon cancer, and greater than 58 for most sites), for which interpolation methods are notoriously unreliable, the following methods were used to minimize the effects of minor variations in the tabulated coefficients: BEIR coefficients for ages 0-9 or 10-19 deemed by the Working Group to have insufficient evidential basis for PC calculations were used as interpolation points to extend risk estimates to age 10 (stomach) or 20 (esophagus, colon, and

others). For lung cancer, the trend was linear over all ages (see Chapter X-9). For breast and thyroid cancers the trend in Table VI-1 from 10-19 to 0-9 was extended linearly to age 0, while for leukemia the interpolation routine produced an approximately linear extension which appeared to require no correction. For extrapolation to older ages an interpolation endpoint of zero risk at age 75 was used for breast cancer (see Chapter V-D), but for other sites the interpolation algorithm continued a smooth trend with increasing age at exposure which seemed to require no correction in view of the extremely limited information available on cancer risk from radiation exposures at age 60 or older.

B. Derivation of Coefficients for Calculating Relative Excess Risk

The interpolated absolute risk coefficients $e(A,S)$, where A denotes age at exposure and S denotes sex, were used to calculate coefficients from which the relative excess pertaining to a given year after exposure could be computed. For any given cancer site, age at exposure, and sex, let $P(Y)$ denote the absolute excess risk coefficient for Y years after exposure. The coefficient e was based upon observed cancer risk over a period of years after exposure, $y_1 \leq Y \leq y_2$ (see Table VI-1). The observed population was subject to attrition, mainly from the usual age-dependent force of mortality. Therefore, to an acceptable level of approximation, e is defined as the lifetable average of $P(Y)$ over the period $y_1 \leq Y \leq y_2$. Depending upon the way in which $P(Y)$ varies with time and with the age-specific baseline rate, the needed coefficients can be defined in terms of e . Two algorithms were used, one for leukemia and bone cancer, and the second for all other cancers.

1. Leukemia and bone cancer

For leukemia (AL and CGL) and bone cancer following brief irradiation type-specific lognormal distributions were obtained by fitting to data, and made specific to each age at exposure (see Chapter V-C). The distribution for all types of leukemia, from which chronic lymphocytic leukemia (CLL) was specifically excluded, was defined as a mixture of the distributions for AL and CGL, weighted by .68 and .32, respectively. The distribution, denoted by $T(A_1, Y)$ or $T(Y)$, depended upon age at exposure (A_1) for AL and therefore also for all leukemia except CLL, considered as a group, but T did not depend upon A_1 for CGL or bone cancer.

For each cancer type, for given (A_1, S) , the time-specific coefficient $P(Y)$ can be written as

$$P(Y) = E \times T(Y),$$

where $E = E(A_1, S)$ denotes the probability that a radiation-induced cancer will be observed at some time after exposure, provided that no other cause of death intervenes. Therefore the coefficient e , which is the lifetable average of P over $y_1 \leq Y \leq y_2$, can be written as the product E , times the lifetable average of T . Solving for E , we obtain

$$E = e \times \{L(y_1) + \dots + L(y_2)\} / \{T(y_1)L(y_1) + \dots + T(y_2)L(y_2)\}.$$

In the above formulation, $L(y)$ denotes the lifetable value for the expected number of person-years at age $A_1 + y$ (the average of the lifetable probabilities of reaching ages $A_1 + y$ and $A_1 + y + 1$), using the 1970 U.S. lifetables (2) (see Table VI-2). The relative excess at age A_2 , Y years after an exposure at age A_1 , is given by

$$R(A_1, A_2, Y, S) = F \times T(A_1, Y) \times E(A_1, S) / I(A_2, S),$$

where F denotes an appropriate function of dose. $I(A_2, S)$ denotes the baseline incidence of cancer of the given site and type for a person of age A and sex S , as determined from the SEER values in Table VI-3 by an interpolation process analogous to that used to obtain the values $e(A_1, S)$. In the above formulation Y assumes only integer values, being the integer part of the time in years from exposure to diagnosis (e.g. if that time is 12 years and 11 months, $Y = 12$).

Although the 1980 BEIR Committee presented risk coefficients for bone sarcoma resulting from exposure to low-LET radiation, these coefficients were derived by the use of conventional quality factors from coefficients appropriate for exposure to alpha radiation (4, pp. 411-418). Bone sarcomas were seen above 67 rad alpha dose to the endosteal layer, which corresponds, using a constant quality factor of 20, to 1300+ rem dose equivalent. Bone sarcoma has not been observed in excess among the Japanese atomic bomb survivors (4, p. 416), and in patients treated by X radiation for ankylosing spondylitis cases have been seen only in association with bone doses well above 1000 rad (4, p. 413). The Working Group, while convinced of the validity of the BEIR estimate for bone sarcoma following brief irradiation from radium 224, did not feel that there was a sufficient basis for extending it to low-LET radiation at doses below 1000 rad or to other forms of high-LET radiation. Accordingly, estimates for bone cancer are presented only for high-LET radiation, from radium-224 (see Table VI-1-B).

2. Cancers other than leukemia and bone cancer, following exposures to low-LET radiation

For other cancers, the temporal distribution of excess risk over time after exposure was assumed to be proportional to the variation of baseline incidence by age, at least beyond 10 years after exposure. In other words, for given (A_1, S) , the ratio

$$K = P(Y) / I(A_2, S),$$

where (roughly) $A_2 = A_1 + Y$, was assumed to be constant for $Y > 10$. It was enough, therefore, to calculate, and tabulate, this ratio. Because the absolute risk coefficient $e = e(A_1, S)$ is the lifetable average of $P(Y)$ over the follow-up period $y_1 \leq Y \leq y_2$ given in Table VI-1, it can also be expressed as the lifetable average over that period of $K \times I'(Y)$, where $I'(Y) = I(A_2, S)$ for $A_2 = A_1 + Y$. Because K does not depend upon Y for $Y > 10$, the relationship can be inverted to solve for $K = K(A_1, S)$:

$$K = e \times [L(y_1) + \dots + L(y_2)] / [I'(y_1)L(y_1) + \dots + I'(y_2)L(y_2)].$$

For $Y > 10$ years, the relative excess risk is simply $K(A_1, S)$ multiplied by an appropriate function F of radiation dose. There was, therefore, no requirement to tabulate the temporal distribution of risk or the baseline risk, as was done for leukemia and bone cancer. But because the relative excess must begin at zero and reach its full value after 10 years, and because biological considerations demand a smooth transition (see Chapter III-H), we have represented this transition by T , as given below and in Chapter V-C, in the case of cancers other than leukemia or bone cancer.

Y:	0-4	5	6	7	8	9	10+
T(Y):	0	.074	.259	.500	.741	.926	1.000

As before, Y denotes the integer part of time in years from exposure until cancer diagnosis. Thus, the relative excess Y years following radiation exposure at age A_1 , for a person of sex S , is

$$R(A_1, Y, S) = F \times T(Y) \times K(A_1, S).$$

3. The special case of lung cancer following exposure to inhaled radon daughters

The 1980 BEIR report (4) gave a single set of linear-model coefficients to be applied to low-LET radiation and, with a suitable Q factor, to high-LET radiation from inhaled radon daughter products. The Working Group found the BEIR coefficients to be difficult to use, as discussed in Chapter X-9, and calculated separate absolute risk coefficients for exposures from external, low-LET radiation based on A-bomb survivor data. For inhaled radon daughter products, the Working Group adopted relative risk coefficients based on a review by Jacobi (5) of data from various studies of uranium miner populations. These estimates, as discussed in Chapter X-9, pertain to cumulative exposure in Working Level Months (WLM), and express excess risk as a percentage of underlying risk per WLM. The estimates do not depend upon sex or age at exposure, but take account of a possible difference in the method of measuring radon levels in U.S. mines before about 1961 as compared to after that time and in other countries (Table VI-1-C).

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Table VI-1-A. Absolute Risk Coefficients: Absolute Excess Cancer Incidence per 100,000 Persons per Year per Rad (Organ Dose) at Low Levels of Low-LET Radiation, by Site, Sex, and Exposure Age, Averaged over the Specified Follow-up Period

Site	Exposure Age	Years ¹ Follow-up	Dose-response Model	Sex	
				M	F
Leukemia ² (all types except CLL)	0-9	5-26	Linear-Quadratic	.173	.110
	10-19	5-26		.0854	.0543
	20-34	5-26		.0846	.0538
	35-49	5-26		.105	.0670
	50+	5-26		.156	.0990
Salivary ²	0-14	10-30	Linear-Quadratic	.00104	.00104
Esophagus ³	20-34	10-30	Linear-Quadratic	.0052	.0052
	35-39	10-30		.0084	.0084
	50+	10-30		.0224	.0224
Stomach ³	10-19	10-30	Linear-Quadratic	.0160	.0160
	20-34	10-30		.0308	.0308
	35-49	10-30		.0508	.0508
	50+	10-30		.134	.134
Colon ³	20-34	10-30	Linear-Quadratic	.0208	.0208
	35-49	10-30		.0336	.0336
	50+	10-30		.0892	.0892
Liver ³	20-34	10-30	Linear-Quadratic	.028	.028
	35-49	10-30		.028	.028
	50+	10-30		.028	.028
Pancreas ³	20-34	10-30	Linear-Quadratic	.018	.018
	35-49	10-30		.030	.030
	50+	10-30		.0788	.0788
Lung ²	10-19	10-33	Linear-Quadratic	.030	.030
	20-34	10-33		.056	.056
	35-49	10-33		.086	.086
	50+	10-33		.120	.120
Breast ²	0-9	10-35	Linear	-	.38
	10-19	10-35		-	.76
	20-29	10-35		-	.49
	30-39	10-35		-	.49
	40-49	10-35		-	.13
	50+	10-35		-	.08
Urinary ³	20-34	10-30	Linear-Quadratic	.0200	.0200
	35-49	10-30		.0368	.0368
	50+	10-30		.0648	.0648
Thyroid ²	0-9	10-34	Linear	.15	.50
	10-19	10-34		.15	.50
	20-34	10-34		.05	.15
	35-49	10-34		.05	.15
	50+	10-34		.05	.15

Table VI-1-B. Linear-model BEIR Absolute Risk Coefficients by Sex for Bone and Joint Cancer Following Exposure to Alpha Particle Radiation from Injected Radium-224: Absolute Excess Incidence per 100,000 Persons per Year per Rad to the Endosteal Layer

Exposure Age	Years Follow-up ¹	Sex	
		M	F
All	0-30	.10	.10

Table VI-1-C. Linear-Model Relative Risk Coefficient R for Lung Cancer Following Exposure to Alpha Particle Radiation from Inhaled Radon Daughters: Percent Excess Incidence per Working Level Month, by Source of Data (Reference 5)

Exposure Age	Source of Data	Estimate (R)
All	Combined Uranium Miner Data	1.2
All	U.S. Miners, Exposed Before 1961	0.7
All	U.S. Miners, Exposed 1961 or Later	1.5

¹Observed years of expression over which excess risk was averaged to produce the risk coefficients shown. PC estimates for events beyond the intervals shown lack a direct observational basis.

²Coefficients derived by Working Group; see Chapter X for details.

³Coefficients derived from BEIR (reference 4, p. 198, Table V-14). Conversion of the linear-model BEIR coefficients to linear coefficients in a linear-quadratic model involved dividing them by 2.5. Note that the original BEIR coefficients were given per 10⁶ person-year-rad.

TABLE VI-2 - U S 1970 LIFETABLE, BY SEX AND AGE, ALL RACES COMBINED¹

Age	Sex		Age	Sex		Age	Sex	
	Male	Female		Male	Female		Male	Female
0	1.000000	1.000000	37	.9261400	.9574150	74	.4293750	.6473600
1	.9887750	.9912700	38	.9233600	.9557600	75	.4019100	.6234450
2	.9769000	.9819650	39	.9203600	.9539600	76	.3738800	.5978550
3	.9757900	.9810150	40	.9171050	.9519750	77	.3456600	.5706400
4	.9749550	.9803450	41	.9157500	.9498650	78	.3175000	.5419050
5	.9742650	.9798000	42	.9097600	.9475650	79	.2897100	.5117750
6	.9736700	.9793400	43	.9056300	.9450800	80	.2625800	.4804150
7	.9731250	.9789650	44	.9011400	.9423850	81	.2362950	.4479700
8	.9726100	.9785900	45	.8962450	.9394550	82	.2109550	.4145900
9	.9721150	.9782700	46	.8909050	.9362700	83	.1866850	.3805650
10	.9717100	.9779800	47	.8850950	.9328100	84	.1636800	.3463250
11	.9713400	.9777150	48	.8787900	.9290750	85	.1421000	.3122950
12	.9710000	.9774650	49	.8719550	.9250650	86	.1219800	.2787200
13	.9706300	.9772050	50	.8645500	.9207550	87	.1033100	.2457300
14	.9701450	.9769150	51	.8565350	.9161200	88	.0861900	.2137050
15	.9694500	.9765600	52	.8478550	.9111350	89	.0708100	.1832950
16	.9684900	.9761200	53	.8384450	.9057750	90	.0573250	.1550900
17	.9672550	.9755950	54	.8282350	.9000200	91	.0457500	.1293750
18	.9657600	.9749900	55	.8171550	.8938500	92	.0359550	.1061900
19	.9640600	.9743350	56	.8051700	.8872400	93	.0277800	.0855900
20	.9622150	.9736550	57	.7922550	.8801550	94	.0210700	.0676900
21	.9602450	.9729600	58	.7783850	.8725700	95	.0156600	.0525400
22	.9581450	.9722550	59	.7635500	.8644750	96	.0114050	.0400400
23	.9559350	.9715350	60	.7477350	.8558450	97	.0081600	.0299800
24	.9536850	.9707950	61	.7309300	.8466500	98	.0057500	.0220850
25	.9514800	.9700400	62	.7131350	.8368600	99	.0039950	.0160300
26	.9493700	.9692700	63	.6943500	.8264100	100	.0027400	.0114800
27	.9473600	.9684750	64	.6745800	.8152200	101	.0018550	.0081150
28	.9454400	.9676550	65	.6538150	.8032050	102	.0012400	.0056650
29	.9435650	.9668000	66	.6320450	.7902950	103	.0008200	.0039100
30	.9416750	.9659000	67	.6092800	.7764350	104	.0005350	.0026700
31	.9397300	.9649450	68	.5855700	.7615500	105	.0003450	.0018050
32	.9377150	.9639200	69	.5610150	.7455700	106	.0002200	.0012100
33	.9356250	.9628150	70	.5357500	.7284250	107	.0001400	.0008098
34	.9334600	.9616250	71	.5099050	.7100800	108	.0000900	.0005360
35	.9311450	.9603350	72	.4835750	.6905250	109	.0000550	.0003502
36	.9287250	.9589350	73	.4568800	.6696700	110	.0000200	.0001370

¹ U.S. Decennial Life Tables for 1969-71, Vol. 1, No. 1, DHEW Publication No. (HRA) 75-1150, U.S. Department of Health, Education and Welfare, Public Health Service, Health Resources Administration, National Center for Health Statistics, Rockville, MD (May, 1975).

Chapter VII: SOURCES OF UNCERTAINTY

A. Introduction

P.L 97-414 requires that the tables on probability of causation "shall be devised from the best available data that are most applicable to the United States, and shall be devised in accordance with the best available scientific procedures and expertise."

The statement by the President, on the occasion of his signing the Orphan Drug Act, expresses the Administration's reservations in regard to the preparation of the tables:

"...there is as yet no consensus among radiation experts in relating human cancers and exposure to low levels of radiation. Yet, Section 7 mandates that probability of causation tables be calculated for even very small dose levels. Accordingly, I am directing the Secretary of Health and Human Services to complete the tables to the extent that may be possible and scientifically responsible, in light of the analysis also mandated by Section 7, which requires him to 'assess the credibility, validity, and degree of uncertainty associated with such tables.'"

What follows is a discussion of the many sources of uncertainty that should be recognized in connection with the use of the tables.

The probability-of-causation (PC) tables bring to bear on the adjudication of claims the very extensive information available on the risk of radiogenic cancer. Although we know more about the effects of ionizing radiation than any other carcinogen, and much of the knowledge is quantitative in form, our present knowledge is far from complete, and the tables can be regarded as no more than a guide to causation in the particular case. However, even an imperfect guide that summarizes the relevant literature in such a way that it can be brought to bear on the individual case should be helpful in determining whether a prior exposure to radiation was a significant factor.

Each element of the PC calculation has its own uncertainties, some of which are interdependent: choice of sites and cell-types for which tables can be prepared, baseline incidence, absorbed radiation dose, dose rate, minimum latent period, time to tumor recognition, choice of dose-response function, radiation risk coefficient, choice of time-response function, and the influence of individual host factors and competing etiologic influences. In Section VII-0 an effort has been made to integrate most of these sources of uncertainties into an overall assessment of the accuracy that can be ascribed to any value of PC.

B. Sites of Cancer and Cell-Types

Although ionizing radiation has been shown to produce a very wide array of human cancers, for certain cell-types, e.g., chronic lymphocytic leukemia, radiation seems not to be detectably carcinogenic. For many

sites and cell-types, the empirical evidence is simply inadequate to establish or deny carcinogenicity, and for some, e.g., multiple myeloma, the evidence seems rather controversial (see Chapter X, Section 13). Authoritative lists of cancers considered to be radiogenic (1-4) are based on judgment as to the sufficiency of the human data available and the cogency of the evidence involving radiation as a cause. As a practical matter, however, even if a particular tissue is considered to be sensitive to the carcinogenic force of ionizing radiation, useful PC tables cannot be calculated in the absence of reasonably good estimates of risk coefficients. It is this requirement, for example, that limits the preparation of tables by cell-type to the leukemias. There are recent reports, for example, linking brain cancer with exposure to ionizing radiation (5,6) but none provides the kind of information that would be required for PC calculations. Further, as has been noted for the various types of leukemia, it remains possible that differentials may ultimately be established for the risks of certain cell-types among the solid tumors. If there are large probabilities of causation that involve sites of cancer other than those selected for the PC tables, those cancer sites must be quite rare.

The Working Group accepted the BEIR III list of radiogenic cancers with the following modifications: (a) lymphomas (including multiple myeloma) were deleted; (b) salivary gland cancers were added; and (c) "other" sites, needed by the BEIR III Committee in order to estimate the totality of radiogenic cancer, and for which no real data exist, were excluded. Of these changes, the first is discussed in Chapter X, Sec. 13, the second in Chapter X, Sec. 3. Sites of cancer for which PC estimates can be made, but for which the quantitative data are least reliable, are salivary glands, esophagus, pancreas, liver, urinary bladder and kidney.

C. Source Tables of Cancer Incidence in the U.S. Population

Age- and sex-specific SEER rates for the U.S.A are averages for the period 1973-1981 and for 10 areas containing about 10 percent of the U.S. population. Although the SEER sample is not a probability sample, it is reasonably representative of the U.S. population as judged by mortality rates. The quality of the data is very high, only 1.4 percent of reported cases depending on death certificates alone, and 92 percent being microscopically confirmed (7). Geographic and ethnic variations are very real, of course, especially for certain anatomical sites (7). In addition, over the period of interest there have been important changes in the incidence of cancer for certain sites, especially stomach and lung (7-9). Although incidence data are not available systematically over time in the U.S., there are bench-mark data for 1947 and 1969-1971, and for some sites, especially lung and stomach, mortality data adequately reflect incidence. Incidence and mortality from stomach cancer have been moving down steadily for some time. For example, the death rate for white males that was 16 per 100,000 per year in 1960 had fallen to 8.2 by 1977. Conversely, death rates for lung cancer have been increasing rapidly over this period, the comparable rates for white males being 38 in 1960 and 68 in 1977. Changes in rates for other sites are less dramatic or seem less certain at the level of incidence. For example, mortality from thyroid cancer has been falling but there are indications of a 10 percent increase in incidence from 1970 to the average for 1973-1981. There are also some changes for non-whites of

which the most significant is for the esophagus: the mortality rate for non-white males that was 10 in 1960 had risen to 14 by 1977.

Among the ten SEER regions, there is a fair amount of variability for some cancer sites (Table VII-1). For example, the incidence of lung cancer may vary by as much as a factor of three between the SEER regions with the lowest and highest rates. Table VII-2 exhibits for each kind of cancer the largest and smallest ratios for any area to the All Areas incidence rate. Although a few of the extreme ratios are based on small numbers of incident cases, and hence are subject to large sampling variability (e.g., the ratio of 0.26 for esophageal cancer in females in Utah is based on only nine cases) most of the ratios are fairly stable with respect to sampling variability: the very high ratio of 2.14 for stomach cancer in Hawaii males is based upon 442 cases. Most of the variability exemplified in Table VII-2 must be considered real.

Explanations for some of the variation come readily to mind: Hawaii has a very diverse ethnic mix, and the high ratios for thyroid and stomach cancer, and the low ratio for breast cancer, result from that fact, as an examination of ethnicity-specific rates in Hawaii makes clear (7). The low ratios in Utah for cancers of the lung and bronchus, esophagus, and colon presumably result from the well-known differences in life style of the Mormon populations of that state. To the extent that the low ratios for lung and bronchus reflect a high proportion of non-smokers, that effect will be accounted for if smoking history is considered by the method explained in Chapters IV and IX.

D. Minimal Latent Period

Time to tumor recognition is approximated by the interval from exposure to date of diagnosis. This approximation may be subject to "error," in that diagnosis may be delayed beyond the time when it might have been made, but it would be unusual if the delay were more than a year or two, except in the case of thyroid cancer. Most incidence rates for cancer do not change rapidly over such short age intervals. An "error" of this kind could be significant only if it affected whether or where the interval from exposure to tumor detection fell within the period over which the minimum latent period is smoothed as described in Chapter V-C; e.g., 5.0-9.9 years for most solid tumors.

The minimum latent period assumed in the calculation of PC tables is empirically based, but can be only roughly estimated for solid tumors. The BEIR III report (1) gives a minimal latent period of 2-4 years between exposure and tumor detection for leukemia and bone cancer, and this range seems well established. The BEIR III value of 10 years given as the minimal latent period for solid tumors is very approximate, as it is not site-specific and all indications are that the interval varies greatly with age at exposure, being longer for younger than for older individuals. For younger individuals especially, the uncertainties are appreciable, but of little practical effect when the constant relative risk model of time-response is used.

Although the Working Group starts from the assumption of minimum

latent periods of two years for leukemia and bone (brief irradiation only) and 10 years for the other cancers, to avoid the sharp step-up from 0 to full effect at these points, it has "smoothed" the minimum latent period as described in Chapter V-C. For leukemia and bone cancer, for which a fitted "wave" function represents the distribution of excess cases over time, no such additional smoothing was necessary. For the other forms of cancer, however, the process of smoothing is rather arbitrary as empirical data are lacking. The interval 5.0-9.9 years after exposure may not be the optimal choice, and the cubic function used to graduate the effect of time to diagnosis within this interval may not be the best function to use.

For bone cancer and leukemia the minimal latent periods, 1.5 and 2 years, respectively, have a range of uncertainty from about 1 to 4 years. For the solid tumors the Working Group has assumed that the full expression of the increased relative risk occurs as early as ten years after exposure, and that the increased risk builds up in the interval 5 to 9 years after exposure. It is thought that these assumptions, in all probability, under-estimate the required period of latency. It is only with respect to intervals of 5-14 years between exposure and diagnosis that this source of uncertainty is meaningful.

E. Dose-Response Function

In general, it has not been possible to show that doses of a few rad have any influence on the likelihood of cancer since the risk, if any, is lost in the background of natural incidence. It should be noted that the BEIR committee was unwilling to make estimates for acute doses below 10 rad or for continuous exposure to less than 1 rad per year. Although it has been suggested that a dose as low as 2-3 rad during fetal life may be leukemogenic (10,11), these studies have been questioned by some because exposure generally occurred on a selective basis associated with the medical indications for X-ray pelvimetry. Comparable studies in which radiation exposure occurred on a non-selective basis from routine pelvimetry (12) or atomic bomb radiation (13) do not suggest that doses of 2-3 rad have any effect, but these series are small (see Chapter III-G).

In the very low dose region useful estimates cannot be made without interpolation between the risk at 0 rad and the demonstrable and measurable risk in the relatively high dose region, generally at or beyond 100 rad. In the absence of a satisfactory theory of radiation carcinogenesis to guide the choice of mathematical function with which to perform the interpolation, considerable uncertainty attaches to interpolated risk coefficients in the low-dose range. In the BEIR III report, for example, the calculated linear coefficients (i.e., the limiting slopes of the dose-response curves at very low doses) for the risk of leukemia from low-LET radiation are 0.99 ± 0.93 excess cases per 10^6 persons per year per rad under the so-called linear-quadratic model and 2.24 ± 0.60 under the linear model. In the "pure" quadratic model, of course, the linear term vanishes entirely. At 2 rad the risk of leukemia under these three models is 2.0 per million persons per year for the linear-quadratic, 4.5 for the linear, and 0.056 for the "pure" quadratic. Corresponding values for all forms of cancer, other than leukemia, considered as a group, are

2.8, 6.94, and 0.074. The linear model is generally considered to over-estimate the risk in the low dose range, although it is possible to postulate a distribution of susceptible individuals in the population such that a power curve might better describe the dose-response relationship (14). In this latter case, low-dose risk estimates might exceed those based on the linear model, but the applicability of such estimates to the calculation of PC values would be questionable.

Animal experiments in which a wide range of dose is employed often show a turn-down in the dose-effect curve at high doses, an observation attributed to cell-inactivation. The BEIR III committee did not employ a model with a term that brings down the curve at high doses since it was concerned with low dose estimation and, since the LD₅₀ for acute whole-body doses to man is in the range of 350-450 rad, the turn-down is not as definite in the data on the A-bomb survivors. But for partial-body irradiation this aspect of dose-response may have considerable importance when organ doses are very high, as is suggested by the low incidence of second cancers in patients treated with therapeutic doses of radium and X radiation for cervical cancer. Failure or inability to correct for this phenomenon has the effect of over-estimating the PC values at very high doses.

As indicated in Chapter V-B, for exposure to low-LET radiation the Working Group has chosen the linear-quadratic dose-response model for all forms of cancer except cancers of the breast and thyroid. Since the coefficient of the linear term of the linear-quadratic dose-response function was generally derived from the corresponding coefficient of the linear function employed in the BEIR report for cancer incidence, and the procedure was merely to divide the latter by 2.5 to create the coefficients used here, this factor provides one measure of the uncertainty associated with the choice of the dose-response function, at least in the range of 20 rad or less. Above 20 rad the $D^2/116$ term becomes increasingly important; the risk on the linear model would be less than 2.13 times that on the linear-quadratic model, not 2.5. In addition, there is an uncertainty in the factor 2.5 that rests on the choice of the cross-over dose, estimated in Section VII-0 below to range from about 1.0 to 6.3.

F. Influence of Age at Exposure

Although the BEIR III risk estimates (1) in Table VI-I here represented a consensus of informed scientific opinion at the time, there were few human data to substantiate some of the risk estimates for exposures below age 10 or, in some cases, below age 20. Although for a few cancers (thyroid, breast, lung, leukemia) the Working Group has modified the BEIR 1980 risk values on the basis of later data not available to the BEIR Committee, for most of the cancer types the BEIR risk estimates have been adopted.

The accuracy of a risk estimate is limited by the number of cases of a particular cancer observed among persons whose doses were at least 10 rad. Even when that number is reasonably large, the risk estimate may be subject to considerable uncertainty but, when the number is small, the uncertainty may be so large that the risk estimate is unusable for the

present purpose. The most recent mortality data concerning the Japanese A-bomb survivors that were available to the BEIR Committee apply to the period from five to thirty years following the radiation exposures (15).

Age 0-9 in 1945. For the digestive organs and peritoneum, there evidently were barely enough data to support an estimate of risk for the class as a whole; risk estimates for pancreas, liver, etc are supported by no data. For these cancers in children, no data were available to the BEIR Committee except those from the Japanese survivors. Table VII-4 provides no basis for calculating PC's for exposures at ages under 10 years for cancers of any of the digestive or respiratory organs. PC's cannot be calculated because the underlying BEIR risk coefficients are not supported by adequate data.

Age 10-19 in 1945. The data in Table VII-5 may be sturdy enough to support PC's for stomach cancer, but not for any other individual digestive organ. The number of deaths from respiratory cancer is also very small, but the coefficients in Table VI-1 were based on the later 1950-1978 report (10), with 15 deaths in this age group from lung cancer. The tables in Chapter X, therefore, provide the basis for calculating PC's for this age group at exposure only for the stomach among the digestive organs, as well as for lung cancer, bone cancer, leukemia, thyroid cancer, breast cancer, and cancer of the salivary gland.

The next BEIR report will be able to take advantage of extensive data compiled since the BEIR 1980 report (1) was prepared, including eight additional years of follow-up of the Japanese A-bomb survivors. Risk estimates for young persons, and knowledge of latent periods applicable to them, will be much improved, and future versions of these tables can then provide PC's for ages and cancer types for which presently available data are inadequate.

In addition to the extreme uncertainties that make it inadvisable to attempt estimates of risk at the younger ages, the statistical uncertainties in age-specific risk coefficients arising from sampling error, and the possibly atypical character of some of the populations whose experience has been drawn upon for epidemiologic studies, there is the technical problem of interpolation among the risk coefficients calculated for age intervals to produce estimates for single years of age, as well as the problem of extrapolation in the age range beyond the given data points. Knowledge of age at exposure as a determinant of risk is too limited to provide sure guidance for the choice of a fitting procedure for each site, and different methods naturally give somewhat different results, especially at the oldest ages. The BEIR coefficients are given in age-at-exposure intervals of 0-9, 10-19, 20-34, 35-49, and 50+. For some sites it makes a great deal of difference, particularly at ages 65 and older, how the fitting is performed. Linear interpolation between the midpoints of adjacent age intervals would produce a sequence of irregular changes with age and leave undefined the regions under age 5 and over age 65. A cubic spline interpolation provides a smoother sequence of values within the range bounded by the midpoints of the extreme age groups, e.g., 4.5 to 58 or 59 in the case of leukemia, and 24.5 to 58 or 59 in the case of colon cancer, but the behavior of the spline function outside this range can be difficult to predict. These problems have been

handled as described in Chapter V-D, by a method that seems reasonable and satisfactory to the Working Group. It must be admitted, however, that other plausible approaches might have yielded different estimates for very young and very old exposure ages.

G. Sex

Sex differences in the absolute risk of radiogenic cancer are apparently small (1), except for breast cancer, thyroid cancer, and leukemia, but the topic is not fully developed in the radiation literature. In the BEIR III report the age-specific absolute risk coefficients are identical for the two sexes, except for the 3 sites named, but when, as here, these coefficients are employed to derive relative risk factors by sex, such factors differ considerably between the sexes, most notably for lung cancer, but also for major gastrointestinal and urinary organs for which SEER baseline rates for males are well in excess of those for females. There is uncertainty here, but it cannot be quantified.

H. Dosimetry

The organ dose from external low-LET radiation can usually be estimated within a factor of 2 in individuals who wear film badges or other quantitative detection devices or who work in carefully monitored areas. The absorbed radiation dose is even more uncertain for any unbadged individual whose dose estimate depends on an environmental reading that may not be in his immediate vicinity, and is subject to attenuation by environmental shielding as well as body shielding and thus may vary over time. Exposure from ingestion or from sources absorbed within the body, such as iodine-131, thorostrast, radium, and radon daughters, is characterized not only by uncertainties as to level of dose, but also by the lack of precise information on their relative biological effectiveness. If the absorbed radioisotope is long-lived and can be measured in an individual and in specific organs, dose estimation may be much more accurate. The determination of iodine-131 doses to the thyroid after the fact, e.g., from weapons tests, will always be difficult in view of the indirectness of the exposure through the food chain and the physiological variables affecting the uptake of the radioisotope by the gland. A major effort, also mandated by PL 97-414, is currently in progress to address the radiiodine problem. The Working Group early determined that it should extend its PC estimation to internal emitters only where adequate epidemiological data were available, i.e., for radium-224 in relation to bone cancer.

The absorbed dose to the relevant tissue, generally an average over the target organ in the case of external radiation, is the quantity employed in these tables because this is the form in which BEIR III presented its risk estimates. These, in turn, were based on reports on the effects of diagnostic and therapeutic irradiation that generally state dose-specific risk estimates in terms of the tissue dose, and on reports on the A-bomb survivors whose external (kerma) doses were converted to tissue doses by means of Kerr's table (1). The relevant dose to a particular organ will, however, in many instances be difficult

to determine for such reasons as the following: (a) attenuation by overlying tissues will in general vary with photon energy; and (b) in the case of partial-body exposure, or whole-body exposure to highly directional radiation fields, calculation of a mean organ dose may be very uncertain. In the case of partial-body irradiation, the dose to an organ may be markedly non-uniform; this is especially true for an organ like the active bone marrow, which is widely distributed in the body. If the dose-response function were truly linear, it would be appropriate to utilize the average dose over the entire organ and, for small doses--of the order of 10 rad or less--linearity can be assumed. If, however, the maximum and minimum doses to different parts of the organ are very different, serious errors can result--in either direction. If the maximum dose is not too large, and the response function is linear-quadratic, then the "effective" dose will be under-estimated by the averaging process, but if the maximum dose is large enough to cause substantial cell sterilization, the "effective" dose can be over-estimated.

The quality of the dosimetry on which risk coefficients are based is best for series derived from therapeutic irradiation. Treatment plans are carefully made and usually recorded in a fashion that permits the calculation of doses, even to organs outside the primary radiation field. The dose estimates for diagnostic irradiation are more uncertain and can be difficult to reconstruct and describe with precision, e.g., in the case of fluoroscopy used to monitor artificial pneumothorax therapy for tuberculosis (16). Average values may be fairly accurate, but individual doses highly variable.

Because the dosimetry for the A-bomb survivors is now being revised (17,18), the age- and sex-specific risk estimates which depend on their experience are now uncertain. Various attempts have been made (19-21) to predict the extent to which the next generation of dose estimates will change previously calculated risk coefficients, and it appears that certain low-LET risk coefficients may be increased, but probably by no more than a factor of 2 (20). The types of cancer for which the coefficients depend essentially on the A-bomb data are: leukemia and cancers of the esophagus, stomach, colon, lung, breast, bladder, and kidney. Sites for which the risk coefficients are relatively independent of the A-bomb data, at least as to level of risk, are: bone, salivary gland, liver, pancreas, and thyroid. Charles et al (22) recently reviewed the 1977 UNSCEAR report (2) to estimate the overall risk of radiogenic cancer based on all sources of human data except the experience of the A-bomb survivors. Their estimate also differs from current risk estimates by a factor of about 2.

The dosimetry for the British ankylosing spondylitis series (23), a major source of data for the calculation of risk coefficients, has been under investigation by a British team for some time but, except for leukemia, the only published estimates are the preliminary figures given in the BEIR III report (1).

A particularly difficult dose-reconstruction has been that for the thyroids of patients with tinea capitis treated with epilating doses of X rays in Israel (24). The attribution of excess thyroid cancer to an average tissue dose of about 9 rad has important implications for the

shape of the dose-response curve, but even a careful reconstruction with phantom simulation may not take full account of the influence of movement on the part of the patient during the therapeutic procedure, movement that might have led to higher doses to the thyroid than those estimated.

I. Coefficients Describing the Dependence of Risk on Dose

Although the risk coefficients are the most complex element in the PC calculation, it is doubtful whether they are subject to errors as large as those of most dose estimates for persons exposed to fallout, for example. Standard statistical measures of uncertainty calculated for specific data sets are meaningful when data are reasonably numerous, as is true for some sites in the case of A-bomb survivors, but such instances are few, and sampling variation is only one part of the uncertainty surrounding risk coefficients. As an example, Table VII-3 reproduces the linear regression estimates and 90 percent confidence intervals for many types of cancer mortality associated with ionizing radiation among A-bomb survivors (25). Only for leukemia, lung cancer, and breast cancer do the 90 percent limits differ from the mean by a factor less than 2. These coefficients are for all ages at exposure. When one confronts the task of calculating PC tables over the entire age range, one finds that it is only for leukemia, and cancers of the breast, bone, salivary glands, and thyroid, that there is enough experience upon which to base risk coefficients for those exposed under age 10. Most recorded series pertain to exposure during adult life, and even the A-bomb survivors exposed before age 10 provide very little information on the risk of radiogenic cancers of gastrointestinal, urinary, and respiratory organs. This is discussed more fully above in Section F.

It should be borne in mind that the site-specific risk coefficients for cancer incidence in the BEIR III report are, except for leukemia and bone cancer, linear coefficients. They were derived by the BEIR III committee as an adjunct to the mortality estimates, and represent the Committee's summary of the evidence from the medical and the environmental exposures reported in the literature as of 1979. In some instances incidence risk estimates were obtained by transforming mortality risk estimates as explained in the BEIR report (1). The technique employed the lifetime expectations of (a) developing, and (b) dying of, cancer of a specific site.

The conversion of BEIR linear-model risk coefficients to coefficients for the BEIR linear-quadratic model, in which the excess risk from an exposure to D rad is proportional to $D + D^2/116$, was accomplished by dividing the linear coefficients by 2.5 (see Chapter V-B). The results obtained by this procedure are not necessarily identical to those that would have been obtained by reanalyses of the original data using the new model, but this source of uncertainty is unimportant relative to that involved in the choice of the crossover dose of 116 rad. The statistical uncertainties underlying this procedure are appreciable. The reliability of the crossover value depends more on its agreement with experimental results obtained over a wide range of biologic systems than on its statistical stability (See Chapter V-B).

Finally, a question has been raised as to the source of the BEIR III coefficients, especially their considerable dependence upon the experience of the Japanese A-bomb survivors and their applicability to the U.S. population. The only available test here is one of consistency among sources, and in general the absolute risk coefficients obtained in Japan are very much like those obtained in the U.S. and U.K. except that their variances are smaller because the experience is larger. This subject is discussed more fully in Chapter III-K.

J. Dose Rate

The linear-quadratic model used for the risk estimates with low-LET radiation for all cancer other than breast and thyroid, having a "cross-over" point at 116 rad, is based on acute (i.e., fairly high dose rate) exposures to radiation. As has already been discussed in Chapter III, at low dose rates the quadratic term becomes less important, and at very low dose rates it is assumed that the dose-response function is reduced to the linear term only. The exact dose rate below which the quadratic term can be ignored is not precisely determined, but experimental studies indicate that it might be on the order of 0.001 rad/min or 1 rad/day, or perhaps somewhat greater (see Chapter III-I). For acute exposures below 5 rad, the contribution of the quadratic term is on the order of 4 percent or less of that of the linear term alone. The approach being suggested for the calculation of protracted or fractionated radiation (see Chapter V) will reduce any dose-rate effect to well within these limits of error. For thyroid and female breast the available data suggest a linear dose-response model which implies that there should be no influence from variation in dose rate. The latter inference is borne out in the case of the breast.

In human cells in vitro the greatest change in effect (cell inactivation) with dose rate occurs in the range 100 rad/min to 10 rad/hr (26); one may, therefore, as a first approximation, assume no variation in effect with dose rates in the LQ model at dose rates greater than 100 rad/min. For dose rates in the transition range (10 rad/hr to 100 rad/min), if one were to treat large exposures as acute doses, the margin of error would be the contribution of the quadratic term of the linear-quadratic model. Below the cross-over point (116 rad) that would imply a factor less than 2.0. It is reasonable to assume that not many exposures will fall in this dose-rate range, but such exposures should be treated on an ad hoc basis.

The uncertainty associated with the dose rate is essentially incorporated in the factor estimated for the choice of dose-response model, especially when account is taken of the uncertainty in the crossover dose.

K. Time-Response Models

Risk coefficients are either absolute, i.e., calculated as an excess over and above baseline incidence, or relative, i.e., expressed in multiples of the natural incidence. Absolute risks are frequently expressed as excess cases per million persons per year and per rad (or rem), whereas a

relative risk estimate may be some (generally constant) fraction of the baseline incidence corresponding to the effect of a fixed dose, e.g., a rad (or rem). When a constant absolute risk is used as a time-response model it suggests that the risk of radiogenic cancer is viewed as independent of the underlying baseline risk. A constant relative risk model for time-response is suggestive of mechanisms by which radiation interacts with other causes to multiply the baseline risk by some constant (see Chapter IV-H). These models, and the measures they generate, have very different implications for the calculation of excess cancers following exposure to radiation. Under the constant absolute risk model for distributing radiogenic cancers over time, once expression has been established, the excess per unit of population, dose, and time, is constant. Under the constant relative risk time-response model, the number of excess cases during the period of expression is a fixed multiple of baseline incidence and, therefore, for most solid tumors, increases with age. For the interval observation from which the risk estimates are generated, both measures must, of course, yield the same total excess, but the excess will be distributed differently over time. For the period beyond the interval of observation, the predicted excess will frequently be very different for the two measures and greater with the relative risk model since baseline rates of cancer generally increase markedly with age.

Although the absolute risk time-response model has dominated the literature and has been the choice of such groups as the ICRP (4) and UNSCEAR (2), in the NAS BEIR I (27) and BEIR III (1) reports it has been used in parallel with the constant relative risk time-response model. Recent data on the experience of the A-bomb survivors (25,28) have provided a strong basis for employing the relative risk model in preference to the absolute risk model, especially for breast cancer and lung cancer, and the working group has adopted the relative risk approach in calculating this first edition of the PC tables (see Chapter V-C). The use that is made of the constant relative risk approach, however, is not based on the assumption that the relative excess per rad is invariant with respect to age, sex, tumor site, geographic or cultural region, etc. Rather, it is limited to the assumption of a relative risk that is constant over the period 10-35 years after exposure for a particular tumor, a particular age-group at exposure, a particular sex, and a particular population level of baseline incidence.

Within the period of observation, generally up to 35 years after exposure, the uncertainty introduced by the choice between the two models is not large, but it does increase thereafter. In the life-time projections of the BEIR III report, where risks are extrapolated beyond the present range of the available human data, constant relative risk estimates of the total burden of radiogenic cancer from a continuous exposure of 1 rad/year beginning at birth are about 3 times those based on constant absolute risk estimates (1). With continuous exposure beginning at age 20, however, the differential in risk is only about two-fold.

The constant relative risk model is definitely superior to the constant absolute risk model which simply does not fit the data. But with additional observations, beyond the 35-year interval for which data are presently available, the constant relative risk model may fit less well than it does for the earlier period. For example, the multiple of baseline incidence may decline

after 40 or 50 years. Thus, PC estimates calculated for intervals of more than about 35 years after exposure have an additional element of uncertainty.

L. Interaction with Other Carcinogens

The prevalence of carcinogenic influences in one's environment and life-style suggests that any individual with cancer following exposure to ionizing radiation will also have been exposed to other carcinogens. The only competing risk factor for which the Working Group has been able to find adequately quantitative data is smoking in relation to lung cancer. Smoking is a very potent risk factor for lung cancer. The relative risk of lung cancer for heavy smokers versus non-smokers, about 24, is exceeded for very few risk factors. Unfortunately the literature is unclear as to the nature of the interaction between smoking and ionizing radiation in this case: a recent analysis of the experience of the U.S. uranium miners suggests a multiplicative relationship (29), another on Swedish iron miners suggests an additive relationship (30), and finally, the data on the A-bomb survivors suggest additivity (31). In the present report, additivity has been assumed for low-LET radiation and a multiplicative relationship for exposures to radon daughters. The range of uncertainty surrounding the choice of model in this case is roughly indicated by the values of "W" in Chapter IV-H that vary from 6.8 for non-smoking males to 0.29 for males with a two-pack-a-day habit. That is, these are the multipliers that are considered appropriate for the additive model, while under the multiplicative model "W" is one.

For many sites of cancer there are factors that seem able to increase the risk of cancer by a factor of two or more, and for all of these it has been assumed that the multiplicative model is more appropriate. This assumption, it should be noted, is not based, as is the choice of model for smoking, on empirical studies of radiation and other specific carcinogens, but on the fact that, in the few series with relevant observations, the distribution of the radiogenic excess over time appears to be proportional to baseline incidence. If another carcinogenic factor is present in addition to the radiation, and to a degree greater than average for the baseline population, and the two factors are additive in effect, the normal cancer incidence assumed for the PC calculation is too low and the resulting PC value, too high. If, on the other hand, they interact multiplicatively, no adjustment is required. The problem is discussed further in Chapter IV.

M. Other Sources of Uncertainty

In addition to the above sources of uncertainty, for which there is some information, others can be named for which information is completely lacking: hormonal status, genetic or other differences in DNA repair capability, and other host factors, particularly immune status. It is extremely difficult to establish the etiology of an individual tumor, but epidemiologic and toxicologic studies have identified a number of specific carcinogens for man, and any instance of a cancer following exposure to ionizing radiation should ideally be reviewed in the context of exposures to other carcinogens that may, in fact, have been responsible for initiating

the tumor. Assigning to each known carcinogen its share of responsibility in the process, however, requires far more information than is presently available in quantitative form, and the Working Group has been able to go no farther in this direction than to account for the influence of smoking status in instances of lung cancer (see Chapter VI-H). The PC calculations are unaffected, however, by exposure to carcinogens which interact multiplicatively with ionizing radiation. Finally, if completeness of ascertainment for slowly progressing tumors, like thyroid cancer, has been greater for exposed subjects than for the general population, an upward bias is introduced into any PC calculation.

N. Effects of Variation in Density of Energy Deposition (LET)

The above discussion has dealt largely with low-LET radiation. There are, however, two exceptions: the tables for bone cancer apply only to alpha radiation from radium-224, and tentative estimates have been provided for lung cancer following exposure to alpha particles from inhaled radon daughters. Data on the induction of bone cancer by low-LET radiation are inadequate as a basis for PC estimation and the Working Group, following the BEIR III report, has used the medical experience with radium-224 as a basis for PC estimation, but with no intention that it be applied to the long-lived isotopes of radium much less to low-LET radiation. This means that the bone tables are of very restricted applicability.

Although the Working Group has assumed, throughout, that X and gamma radiation are equivalent in terms of RBE, this is not strictly so since the LET and, therefore, generally the RBE for any given type of radiation, will diminish as the energy is increased. For this reason, energetic gamma radiation is less effective than 250kVp X rays. The difference is relatively small at higher doses and dose rates, but may be quite significant at low doses and dose rates. For example, for mutations in *Tradescantia* and chromosome aberrations in animal cells, cobalt-60 gamma radiation at low doses was observed to be between 1/3 to 1/2 as effective as the reference 250kVp X radiation (32,33). This implies that at low doses and dose rates exposures to energetic gamma radiation is less damaging than exposure to so-called ortho-voltage X rays and that the tables will yield PC's in excess of the true values. It also implies that, insofar as some of the site-specific risk factors derive in part from the Hiroshima-Nagasaki experience, these risk factors may be somewhat lower than they would for kVp X rays. The Working Group does not have the data that would allow it to address this issue at the computational level.

O. Propagation of Uncertainties and Their Effect upon the Probability of Causation

Table VII-6 summarizes the various sources of uncertainty, how they were handled, their estimated magnitude and how their resolution by the Working Group may have influenced the PC values that can be calculated from the procedures detailed here. It is desirable to estimate the effect that these uncertainties, acting jointly, may have on the calculated value of the PC.

The excess relative risks are considered to be subject to uncertainties that have lognormal distributions. The logarithms of the "best estimates" which are tabulated then correspond to the mean values of normal distributions.

A normal distribution is symmetric about its mean, and deviations from that mean are expressible in standard form as multiples of the standard deviation of the distribution. Thus, for example, 95% of a normal distribution with mean μ and standard deviation σ lies between $\mu - 1.96\sigma$ and $\mu + 1.96\sigma$. A lognormal distribution also is symmetric about its geometric mean G , but in a multiplicative sense. G is the exponential of the arithmetic mean on the logarithmic scale. Defining the "geometric standard deviation" (G.S.D.), S , as the exponential of the standard deviation on the logarithmic scale, it follows, for example, that 95% of the distribution lies between

$$L = G \times S^{-1.96} = \exp(\ln G - 1.96 \ln S)$$

and

$$U = G \times S^{1.96} = \exp(\ln G + 1.96 \ln S).$$

In the above formulation, if G and S are estimated, then the interval (L,U) corresponds approximately to a 95% confidence interval for the true geometric mean. In some applications no value of S may be obtainable directly from data, but if a 95% "credibility interval" of the form (L,U) can be constructed for the true geometric mean, a subjective estimate for S can be calculated by solving the relationship

$$L/U = S^{3.92}.$$

The G.S.D. for a lognormally distributed estimate G , which is itself the product of K independent estimates, each with G.S.D. S_1 , can be calculated as

$$\ln^2 S = \ln^2 S_1 + \dots + \ln^2 S_K,$$

and a credibility interval for the true value can be calculated in terms of G and S .

Where G.S.D.s could be calculated from available data, as for variation in baseline rates, the values S_1 were estimated as the exponentials of the standard deviations of the logarithms of the rates. In other instances the values of S_1 were estimated as described above, relying on estimates of U and L .

The uncertainties are of two kinds: Those which may equally well be in either direction and those, like that which derives from the reassessment of the A-bomb dosimetry, which are considered more likely to be in one direction than the other. We refer to them briefly as unbiased and biased uncertainties.

1. Unbiased uncertainties

o Baseline values. The All Areas SEER incidence rates are appropriate for an average member of the population of the United

States; a different baseline rate may, however, apply to a particular individual, based on geography of residence. Table VII-1 shows, for each of the ten SEER areas, the age-adjusted incidence rate for each cancer. Geometric standard deviations (G.S.D.s) of the rates have been calculated for each cancer for males and females separately; they ranged from a low of 1.076 for acute leukemia in males to a high of 1.636 for liver cancer in males. In general, the G.S.D.s for particular cancers were of similar magnitude for males and females. Upon pooling the G.S.D.s for cancers for which the values were similar, the following values were obtained:

Kind of Cancer	Geometric Standard Deviation among SEER Registries S_i
All leukemia except chronic lymphatic	1.10
Acute or chronic granulocytic leukemia, bone, breast, pancreas, colon and kidney and bladder	1.17
Salivary glands, thyroid, lung and stomach	1.36
Esophagus and liver	1.53

o Influence of Age at Exposure. Risk estimates have been provided for only those ages at exposure for which adequate data are available. From Table VI-1 it can be seen that for most cancers excess risk per rad varies by a factor of about 4 as between ages 20-34 and 50+. Exceptions are leukemia, liver, breast and thyroid cancer. Taking account of the stepwise nature of the age variations shown in Table VI-1, a total uncertainty of about 50 percent is suggested. If U and L are estimated as 1.5 and 0.667 times the stated values, then $U/L = 2.25$, and the G.S.D. is calculated as $S_1 = 1.23$.

o Time Response. As explained in Chapter V, a wave-like, lognormal functional form has been used to express the time course following exposure for radiation-induced leukemia or bone cancer. For all other cancers, following an initial latent period, relative risks per rad are assumed to be constant. It is unlikely that the time course for leukemia is in error by more than about two years - that is, the peak year for chronic granulocytic leukemia is estimated to be five years after exposure; the body of data concerning human radiation leukemogenesis is sufficiently large and consistent that an error of more than two years in the timing of that peak is most unlikely. The temporal distribution curve following exposure (Table X-1-A) shows that an error of two years in the placement of the curve seldom changes the value of the curve by much more than 10 percent, and amounts to about 20 percent as between three

and five years after exposure. The G.S.D. can be estimated, then, to be no more than 1.10.

With respect to the solid cancers, the Working Group has adopted the constant relative risk time projection model. Available data indicate that this model is at least an excellent first approximation; there may, however, be some variation with time in the relative risk, especially for persons young at the time of exposure, and after intervals of twenty-five to thirty years. Such uncertainty is assessed to be no more than a factor of about 1.3; the G.S.D. is estimated as 1.15.

o Ratio of the Linear Coefficients in the Linear (L) and Linear-Quadratic (LQ) Dose-Response Models.

As explained in Chapter V, the 1980 BEIR regression analyses of mortality from all forms of cancer except leukemia yielded coefficients in the ratio of 2.5. That is,

$$E_L/E_{LQ} = 2.5.$$

This ratio depended on the assumed crossover dose of 116 rad, an estimate derived from the data on mortality from leukemia. Had a different cross-over value been selected, a different ratio would have resulted. The ratio depends on the cross-over dose, C, as follows:

$$E_L/E_{LQ} = 1 + 174/C.$$

The consequences of assuming that C is as small as 33 rad, or as large as infinity, in alternative fits to the original data of the BEIR Committee, are shown below:

Cross-over Value C (rad)	Ratio E_L/E_{LQ}
33	6.3
50	4.5
75	3.3
116	2.5
200	1.9
Infinity	1.0

The formula for the "effective" dose is $D + D^2/C$ and thus effective dose varies little with the value C if the dose is less than 5 rad, but uncertainty in the linear term, 2.5, illustrated above, strongly affects the PC.

It is thought that the true value of the cross-over dose

is almost certainly in the range from 33 rad to infinity. The ratios which correspond to those values are 6.3 and 1, with a geometric mean of 2.5. If the probability that the stated range does cover the true value is assessed at 99%, then the G.S.D. for the ratio is $1.43 = 6.3^{1/5.12}$. This value applies to all cancers except breast cancer and thyroid cancer, for which a linear dose response model has been used.

An infinite cross-over value, which corresponds to the value of 1.0 for the ratio E_L/E_{L0} , characterizes the linear dose-response model. The pure quadratic dose response model would correspond to a cross-over value of zero rad, and an infinite ratio. Even for a cross-over value as low as 33 rad, the dose-squared term adds no more than 15 percent to the effective dose for an organ dose of 5 rad.

2. Biased Uncertainties

o Latent Period. There seems little doubt that beyond 15 years from exposure, the full radiation risk applies for all cancers except leukemia and bone cancer and that at least five years is required for a radiation exposure to result in an overt cancer. The Working Group has chosen to calculate PC's on the assumption that full expression occurs as early as 10 years after exposure and has assumed that risk rises in a smooth way from the fifth to the tenth year. While there is little reason to question the estimates on the basis of latent period except in the interval 5 to 14 years, within that interval uncertainty does exist. This uncertainty is biased, in the sense that the estimates, if erroneous, are likely to be erroneously high. If it be supposed that, in the interval 5 to 15 years, the risk estimate is, with credibility 95 percent, between one-half of that embodied in the Working Group's formula, and the full value, then the range .50 to 1.00, with geometric mean 0.71 (bias correction factor) has a G.S.D. of 1.19.

o Risk Coefficients. Many, but not all, of the risk coefficients used here are based mainly upon the experience of the Japanese A-bomb survivors; the exceptions are for cancers of bone, salivary glands, liver, pancreas, and thyroid gland. Recently it has become apparent that the dosimetry system, designated T-65, upon which the Japanese data are based, was seriously in error (34-36). An intensive effort to provide a new and better dosimetry system is under way (37,38) but has not yet been completed at this time (December, 1984). Estimates have been provided, however, of the changes that may result in the dose-effect coefficients for gamma rays, by Fujita as increases by a factor of 1.2 to 1.7 (39) and by Jablon as 1.6 to 2.2 (40). If it is assumed that a 95 percent credibility interval on the factor ranges from 1.2 to 2.2, the geometric mean would be 1.62, with a G.S.D. of 1.17. These values would apply only to those cancers for which the BEIR III risk estimates were based, in large part, upon the A-bomb survivor experience: the leukemias and cancers

of the esophagus, stomach, colon, lung, breast and kidney and bladder.

In addition to the uncertainty which results from prospective revision of the A-bomb dosimetry, additional uncertainty follows from the fact that the low-LET radiations in that situation were high-energy gamma rays, while 250kVp X rays, in experimental situations, have been reported to be more effective by a factor of 2 or 3 at doses on the order of two or three rad (32,41,42). This will not affect the use of the tables in cases where the radiations in question are hard gamma rays, as for workers in nuclear power plants or persons present at tests of nuclear weapons.

3. Combined Uncertainty

Recapitulating the uncertainties, and combining them, we have:

Source	G.S.D. (S ₁)
Baseline values	
Esophagus and liver cancer	1.53
Salivary glands, thyroid, lung & stomach cancers	1.36
All leukemia except chronic lymphatic	1.10
All other cancers	1.17
Effect of age at exposure	1.23
Time responses	
Leukemia & bone cancer	1.10
Other cancers	1.15
Ratio of the L to LQ linear coefficient (Except breast & thyroid cancer)	1.43
Latent period (years 5-14 after exposure only) (Except leukemia and bone cancer) with bias correction factor = 0.71	1.19
Risk coefficients derived from A-bomb survivors Leukemia, cancers of esophagus, stomach, colon, lung, breast, kidney & bladder with bias correction factor = 1.62	1.17
<u>Risk coefficients for other tabulated cancers</u>	<u>1.17</u>

The combined uncertainties for each form of cancer are shown in Table VII-7.

4. Effect of Uncertainty of Risk upon the Probability of Causation

To obtain a 90 percent "credibility interval" for the PC

we first obtain limits for the value of R in the formula:

$$PC = R/(1 + R).$$

If upper and lower limits on R are substituted in this formula corresponding limits on the PC are obtained.

Suppose R is multiplied by some factor, V, giving

$$R' = R \times V.$$

If PC' is the "true" value of the PC which corresponds to R', then

$$PC' = R \times V / (1 + R \times V).$$

The value of PC' can be expressed directly in terms of PC and V as:

$$PC' = V \times PC / (1 + PC \times (V - 1)). \quad \text{Eq. (1)}$$

Note that in Eq. (1) the PC is expressed as a fraction, rather than a percent.

The upper limit of the 90 percent "credibility" interval for R is obtained by multiplying the value of R by $S^{1.645}$; the corresponding lower limit is obtained by multiplying by the reciprocal of that value. Both limits must then be multiplied by the "bias factor" if it is different from 1.0.

For example, for bone cancer the value of S is 1.57 (Table VII-7). Raising this to the power 1.645 gives the result 2.10. The 90 percent credibility limits on R, for bone cancer, are obtained by multiplying by 2.10 and its reciprocal, 0.48. For All Leukemia the value of S is 1.59 which, when raised to the power 1.645 yields 2.14. For leukemia, however, the bias factor 1.62 applies, so the upper and lower limit factors must be multiplied by 1.62, yielding 3.47 and 0.76. These values can be used for V in Eq. (1) to obtain the 90% limits that correspond to any calculated PC. For bone cancer and All Leukemia, respectively, the 90% limits for a PC calculated as 5% would be

Bone cancer	2% to 10%
All leukemia except CLL	4% to 15%

The bounds for leukemia are quite asymmetrical because of the bias correction factor.

Table VII-8 shows, for each cancer, the factors V to be used to obtain lower and upper limits for the 90% credibility interval on any PC.

Table VII-9 shows for certain PC values and factor V values the corresponding lower and upper limits for the 90% credibility interval on the PC. As examples:

Acute leukemia - PC is calculated as 10%. From Table VII-8 the lower and upper factors are 0.74 and 3.55. From Table VII-9 the bounds on the credibility interval are 7% to 29%.

Breast cancer - PC at 15 or more years post-exposure is calculated as 5%. The factor bounds (Table VII-8) are 0.93 and 2.82. The bounds on the credibility interval (Table VII-9) are 5% to 13%.

Table VII-10 shows the calculated PC for which (with 95% credibility) the "true" PC is more than 50%. For example, from Table VII-8 it is found that for acute leukemia, the factor for the lower limit is 0.74. From Table VII-10 it is found that the value of the calculated PC, for which the "true" PC is at least 50%, with credibility 0.95, is between 56% and 59%. Exact calculation inverting Eq. (1) shows the value to be 57%.

In summary, although the effect of uncertainty is somewhat variable depending upon the particular cancer and the latent period, certain generalizations can be made:

1. If the PC as calculated here is 2% or less, the "true" PC almost surely would be 7% at most (upper limit) even if we had sure knowledge concerning all the unknowns which contribute to the uncertainties.
2. If the PC is in the range of 5 to 10% the "true" PC might be quite small (1%), but might be as large as 30%.
3. If the PC is calculated to be at least 20%, the "true" PC is most unlikely to be less than 5% and may be as large as 40%.

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Table VII-1

Age-Adjusted Annual Incidence Rates per 100,000
All Races Combined, SEER Data for 1973-1977

Males

	Leukemia												
	Acute	Chronic Granulo- cytic	All*	Salt- vary	Thy- roid	Lung & Bronchus	Bones & Joints	Esophag- us	Pan- creas	Stom- ach	Colon	Liver	Kidney & Bladder
All Areas, except Puerto Rico	5.3	1.8	9.0	3.0	2.5	78.3	1.0	5.9	12.2	14.1	36.9	3.2	35.0
Connecticut	5.3	1.7	9.1	4.1	2.0	78.1	0.8	6.8	12.6	14.7	44.2	2.4	39.3
Detroit	4.4	2.1	12.0	3.1	2.3	86.6	0.8	7.8	12.0	15.1	37.6	3.4	35.3
Iowa	5.6	2.2	10.0	1.6	1.7	73.5	0.9	3.9	11.6	10.1	35.5	2.2	34.7
Atlanta	5.6	2.1	9.6	3.9	2.3	88.1	1.3	7.6	15.1	9.8	33.3	3.6	33.4
New Orleans	5.3	1.6	8.5	4.8	2.2	113.2	0.9	7.7	14.3	15.0	36.7	4.3	37.8
New Mexico	5.1	1.7	8.1	1.8	3.5	58.6	1.0	2.8	13.9	15.9	24.0	2.9	28.2
Utah	5.2	1.4	9.0	2.0	2.1	41.8	1.0	3.0	9.3	10.4	26.8	1.2	29.1
Seattle- Puget Sound	5.1	1.8	6.7	2.8	2.1	80.3	1.2	4.2	11.3	12.1	35.5	2.3	38.4
San Francisco- Oakland	5.8	1.4	9.0	3.6	3.1	83.2	1.1	6.2	13.1	15.7	39.9	4.2	34.6
Hawaii	5.5	1.8	8.3	2.1	6.2	62.4	1.2	7.4	10.9	30.2	32.6	8.5	24.6

* Excluding chronic lymphocytic leukemia.

** Non-Hodgkin's lymphoma plus multiple myeloma.

Table VIII-1

Age-Adjusted Annual Incidence Rates per 100,000
All Races Combined, SEER Data for 1973-1977

	Females																		
	Leukemia		Salivary Glands		Lung & Bronchus		Esophagus		Pancreas		Stomach		Colon & Rectum		Liver		Bladder		Breast
	Acute	Chronic	All*	Salivary	Thyroid	Lung & Bronchus	Esophagus	Esophagus	Pancreas	Pancreas	Stomach	Stomach	Colon & Rectum	Colon & Rectum	Liver	Bladder	Bladder	Breast	Breast
All Areas, except Puerto Rico	3.7	1.1	5.7	1.2	5.5	22.2	0.6	1.9	8.0	6.4	6.4	31.3	1.3	11.4	85.4				
Connecticut	4.0	0.9	6.1	1.1	4.4	21.8	0.6	2.2	8.7	7.0	35.8	1.2	12.7	91.8					
Detroit	3.1	1.2	5.5	1.1	5.3	22.7	0.5	2.3	7.8	6.5	29.0	1.5	12.0	81.7					
Iowa	3.5	1.3	5.8	0.9	4.2	14.6	0.7	1.1	6.9	4.2	34.5	1.1	10.8	80.6					
Atlanta	3.9	1.1	5.7	1.2	6.3	21.5	0.8	1.7	8.2	5.1	29.6	1.1	10.0	87.3					
New Orleans	3.1	1.3	5.0	1.2	4.6	27.5	0.6	1.5	9.3	6.8	29.1	1.4	12.3	76.2					
New Mexico	2.8	1.0	4.9	1.0	6.6	21.3	0.6	1.4	10.3	7.6	...	2.2	10.5	75.6					
Utah	3.2	1.5	5.7	0.9	6.5	8.5	0.9	0.5	5.9	4.8	22.8	1.1	9.4	74.7					
Seattle-Puget Sound	4.0	0.7	5.6	1.6	4.6	26.5	0.7	1.6	7.2	5.3	31.2	1.0	11.8	89.3					
San Francisco-Oakland	4.2	0.8	5.9	1.7	6.9	29.8	0.6	2.6	8.9	7.5	32.6	1.3	11.1	96.0					
Hawaii	4.5	0.8	6.1	1.4	10.5	25.1	0.4	1.6	7.0	14.8	21.0	3.2	8.5	70.6					

* Excluding chronic lymphocytic leukemia.

** Non-Hodgkin's lymphoma plus multiple myeloma.

Table VII-2

Largest and Smallest Ratios of Individual Registry Age-Adjusted
Cancer Incidence Rates to All Areas Rate

Site	Males		Females	
	Largest Ratio	Smallest Ratio	Largest Ratio	Smallest Ratio
Leukemia				
Acute	1.09 (San Francisco)	0.83 (Detroit)	1.22 (Hawaii)	0.76 (New Mexico)
Chronic Granulocytic	1.22 (Iowa)	0.78 (Utah)	1.36 (Utah)	0.64 (Seattle and Puget Sound)
All Forms*	1.33 (Detroit)	0.90 (New Mexico)	1.07 (Hawaii)	0.86 (New Mexico)
Bones & Joints	1.3 (Atlanta)	0.8 (CT & Detroit)	1.5 (Utah)	0.7 (Hawaii)
Salivary	1.60 (New Orleans)	0.53 (Iowa)	1.42 (San Francisco)	0.75 (Iowa and Utah)
Esophagus	1.32 (Detroit)	0.47 (New Mexico)	1.37 (San Francisco)	0.26 (Utah)
Stomach	2.14 (Hawaii)	0.70 (Atlanta)	2.31 (Hawaii)	0.66 (Iowa)
Colon	1.20 (Connecticut)	0.65 (New Mexico)	1.14 (Connecticut)	0.73 (Utah)
Liver	2.7 (Hawaii)	0.4 (Utah)	2.5 (Hawaii)	0.8 (Seattle and Puget Sound)
Pancreas	1.24 (Atlanta)	0.76 (Utah)	1.29 (New Mexico)	0.74 (Utah)
Lung & Bronchus	1.45 (New Orleans)	0.53 (Utah)	1.34 (San Francisco)	0.38 (Utah)
Breast	—	—	1.12 (San Francisco)	0.83 (Utah)
Thyroid	2.48 (Hawaii)	0.68 (Iowa)	1.91 (Hawaii)	0.76 (Iowa)

* Excluding chronic lymphocytic leukemia.

Table VII-3

Absolute Risk Coefficients for Fatal Radiogenic Cancers
Among A-Bomb Survivors by Site or Type of Cancer

Site or Type of Cancer	Risk Coefficient ^a
Leukemia	1.72 (1.57, 1.87)
Esophagus	0.16 (0.02, 0.30)
Stomach	0.79 (0.34, 1.24)
Colon	0.30 (0.16, 0.43)
Lung	0.61 (0.37, 0.86)
Breast ^b	0.50 (0.29, 0.72)
Urinary tract	0.15 (0.04, 0.26)

^aExcess deaths/10⁶ person-year-rad; linear coefficients with 90% confidence intervals.

^bFemales only

From Kato and Schull, 1982 (25)

Table VII-4

Numbers of Deaths from Cancers of Various Organ Systems, 1950-1974, in A-bomb Survivors under Age 10 in 1945.

	Number of Deaths	
	Total	With 10+ Rad
All malignant neoplasms except leukemia	26	11
Digestive organs and peritoneum	16	5
Stomach	12	4
All other digestive organs combined	4	1
Trachea, bronchus and lung	0	0
Lymphatic and hematopoietic	3	1

Table VII-5

Numbers of Deaths from Cancers of Various Organ Systems, 1950-1974, in A-bomb Survivors Aged 10-19 in 1945.

	Number of Deaths	
	Total	With 10+ Rad
All malignant neoplasms except leukemia	128	45
Digestive organs and peritoneum	70	21
Stomach	44	11
Colon	3	2
Esophagus, rectum and pancreas	7	3
Other digestive organs	16	5
Trachea, bronchus and lung	5	2
Breast	14	11
Lymphatic and hematopoietic	7	3
All other combined	32	8

Table VII-6

Summary of Uncertainties and the Effect of Their
Resolution on PC Values

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
Dose to individual	Outside purview of Working Group	Highly variable, especially if unbadged
Source tables on cancer incidence	SEER tables for all races and regions combined, but specific by age and sex; only 1973-1981 data used	Without further adjustment for ethnic and regional differences, PC values may be high, or low; ignoring changes in incidence over time affects some PC's for early onset of certain cancers
Influence of age at exposure	Many coefficients for younger ages omitted; interpolation is necessary to obtain values for single years	Fewer PC values obtainable for younger ages; PC's for exposure after age 65 especially uncertain
Sex differences	The few known sex differentials are used	Unknown
Sites and cell-types	Lymphomas and multiple myeloma excluded; liver, pancreas, salivary gland included	Exclusion makes PC approach inapplicable; inclusion may provide wrong guidance
Minimal latent period	Minimum of 2 years for leukemia and bone; smoothed 5-10 for solid	There will be fewer zero PC values within 10 years of exposure
Risk coefficients	BEIR III linear coefficients for solid tumors adapted to linear-quadratic model, except breast and thyroid	Essential statistical uncertainty carried forward into PC calculations
Dosimetry in epidemiologic studies	As reflected in the BEIR III coefficients	A-bomb revision may increase many risk coefficients by factor of 1.2-2.2 and PC values somewhat less

Table VII-6 (continued)

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
Dose-response function	Linear-quadratic (LQ) model assumed for low-LET exposure, linear (L) for thyroid and breast	The true PC may be greater or less, depending on the actual form of the dose-response function. PC's calculated at less than 2% may be too large or too small by not more than a factor of 2.5, PC's of 5-20%, by not more than a factor of 2, and larger PC's, by lesser amounts
Dose-rate	Fractionated or continuous exposures within a 24-hour period are treated as single exposures. Other exposures separated in time are treated individually, not summed. Accumulations over longer periods are treated as separate exposures occurring on different days	Ignoring fractionation within a 24-hour period probably overestimates risk by an amount no greater than the quadratic coefficient multiplied by dose-squared. Under the linear model fractionation does not affect estimated risk
Time-response model	Constant relative risk model for solid tumors except bone; wave function for leukemia and bone	For leukemia and bone cancer, for which a wave function is clearly indicated, any uncertainty relates not to the choice of the model but to its precise form. For other tumors the effect on PC values depends on the interval between exposure and diagnosis and whether it falls outside the period of observation. Within the period of observation PC's will be lower toward the beginning of expression, and higher thereafter,

(continued)

Table VII-6 (continued)

Source of Uncertainty	Resolution by the Working Group	Practical Effect on PC Calculations
Other risk factors	No adjustment made, except for smoking	<p>than if based on the constant absolute risk model; after the period of observation PC's will be generally higher. Relative risk models incorporating some variation over time might increase or decrease particular PC estimates</p> <p>Unknown, and depending on any interaction with radiation.</p>

Table VII-7

Combined Uncertainties and Bias Correction Factors

Kind of Cancer	Years after Exposure	Combined Uncertainty (S)	Bias Correction Factor
All leukemia except CLL	Any	1.59	1.62
Acute or chronic granulocytic leukemia	Any	1.61	1.62
Bone	Any	1.57	1.00
Salivary gland	5-14	1.75	0.71
	15+	1.71	1.00
Esophagus	5-14	1.92	1.15
	15+	1.88	1.62
Stomach, lung	5-14	1.79	1.15
	15+	1.74	1.62
Colon, kidney and bladder	5-14	1.68	1.15
	15+	1.63	1.62
Liver	5-14	1.88	0.71
	15+	1.84	1.00
Pancreas	5-14	1.64	0.71
	15+	1.59	1.00
Breast	5-14	1.46	1.15
	15+	1.40	1.62
Thyroid	5-14	1.54	0.71
	15+	1.49	1.00

Table VII-8

Factors to be Used for Limits of a 90 Percent Credibility Interval

Kind of Cancer	Years after Exposure	Factor for	
		Lower	Upper
		Limit	
All leukemia except CLL	Any	0.76	3.47
Acute or chronic granulocytic leukemia	Any	0.74	3.55
Bone	Any	0.48	2.10
Salivary gland	5-14	0.28	1.78
	15+	0.41	2.42
Esophagus	5-14	0.39	3.36
	15+	0.57	4.58
Stomach, lung	5-14	0.44	3.00
	15+	0.65	4.03
Colon, kidney and bladder	5-14	0.49	2.70
	15+	0.73	3.62
Liver	5-14	0.25	2.01
	15+	0.37	2.73
Pancreas	5-14	0.31	1.60
	15+	0.47	2.14
Breast	5-14	0.62	2.14
	15+	0.93	2.82
Thyroid	5-14	0.35	1.44
	15+	0.52	1.93

Table VII-9

Limits for 90 Percent Credibility Intervals on Probabilities of Causation

Factor	PC =	(A) Lower Limits (95 percent)				
		5%	10%	20%	30%	50%
Percent						
0.2		1	2	5	8	17
0.3		2	3	7	11	23
0.4		2	4	9	15	29
0.5		3	5	11	18	33
0.6		3	6	13	20	38
0.7		4	7	15	23	41
0.8		4	8	17	26	44
0.9		5	9	18	28	47

Factor	PC =	(B) Upper Limits (95 percent)				
		2%	5%	10%	20%	30%
Percent						
1.4		3	7	13	26	38
1.6		3	8	15	29	41
1.8		4	9	17	31	44
2.0		4	10	18	33	46
2.2		4	10	20	35	49
2.4		5	11	21	38	51
2.6		5	12	22	39	53
2.8		5	13	24	41	55
3.0		6	14	25	43	56
3.2		6	14	26	44	58
3.4		6	15	27	46	59
3.6		7	16	29	47	61
3.8		7	17	30	49	62

Table VII-10

Values of the PC for which a 95 Percent
Lower Credibility Limit is 50 Percent

Factor for Lower Limit	PC for which 50% is the Lower Limit Percent
0.2	83
0.3	77
0.4	71
0.5	67
0.6	62
0.7	59
0.8	56
0.9	53

CHAPTER VIII - FUTURE REVISION OF THE TABLES

The tables cannot now provide precise measures of the probability that certain cancers have resulted from previous exposures to known doses of ionizing radiation. The tables represent, however, a first and important step in the direction of a rational basis for assigning to radiation exposure a measure of the likelihood of its role in the causation of individual cancers.

The PC tables will have to be revised periodically as new information and new insights become available. The Orphan Drug Act provides a criterion for the frequency of revision: every 4 years or whenever the Secretary of Health and Human Services "deems it necessary to ensure that they continue to represent the best available scientific data and expertise." The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) has in preparation another of its periodic reports that is scheduled to include a section on carcinogenesis, the last such section having been published in the 1977 report. The National Academy of Sciences is forming a new committee that will first study the effects of high-LET radiation and then move on to low-LET radiation. In perhaps two years the revision of the dosimetry of the Japanese A-bomb survivors may have begun to yield revised risk estimates based on that experience. The BEIR III report was based on the world literature as it existed in 1979, and the mortality data on the A-bomb survivors at that time had been reported only through 1974. Their mortality through 1978 has now been reported and within a year or two there should be an update through 1982. These several efforts, at least, ought to be completed before any overall revision of the tables would seem useful, unless the effort to revise the tables were to duplicate those efforts.

On the other hand, it would be well to keep in mind the possibility that some portion of the data on which this first version of the tables rests may become obsolete before a general revision is indicated. In that event, a supplement might well be issued with respect to a particular site for which greatly improved estimates could be provided, or for a site excluded from the present report. Or, perhaps as a result of the initial deliberations of the new NAS Committee, it may be evident that estimates could be made for certain exposures to high-LET radiation. Another possible candidate for a supplement is a revision of the material on thyroid cancer to include the effects of exposure to internally deposited iodine-131 for which the Working Group concluded that PC estimates could not be made at this time. Section 7a of the Orphan Drug Act also provided for a study of the effect of iodine-131 on the likelihood of thyroid cancer, and an Ad Hoc Working Group on Thyroid/Iodine-131 Assessments has been formed to address this task.

The BEIR III report was not created with the needs of the radioepidemiologic tables in view and the Working Group has found that some of the factors developed in that report to enable estimates to be made for the effect of continuous exposure of the entire population from birth to the end of life lack the reliability needed for the present purpose (cf Chapter VII). The BEIR Report also provided no systematic basis for estimating the effects of exposure to internal emitters, a difficult subject at best and one for which few data adequate for PC estimation

exist. Internal emitters are important sources of exposure, especially plutonium and radon daughters, and a comprehensive set of procedures for PC calculations ideally should make provision for them. The NAS committee preparing the next BEIR report should be sensitive to the need for PC estimates and provide the kind of statistical information that is required for their calculation. If the Department of Health and Human Services were to maintain a standing group charged with responsibility for the tables, liaison between this group and the NAS committee will also be necessary if supplements to the tables are to be issued as updates on particular sites of cancer prior to any full-scale revision. A standing committee might also observe the use of the PC tables in compensation cases by the courts or by administrative boards and consider how the tables might be improved for judicial use.

In brief, four or five years hence, authoritative information concerning the radiation induction of solid tumors will be much improved from its present state; not only will the data be more robust statistically in consequence of larger numbers, but the data on A-bomb survivors, now available only through 1978, will have been extended to 1982 or 1986. Thus, it should be possible either to verify that the relative risk time-response model applies to follow-up periods as long as 40 years, or to learn what modifications are required; additional evidence concerning the shape of the necessary dose-response curves should help to clarify this controversial subject and data from other human studies may cast additional light on the general applicability of risk estimates generated from particular populations. Further, greater confidence in the appropriateness and reliability of some of the key assumptions, especially those relating to dose-rate effect, dose-response model, and time-response model, will depend on a better understanding of the mechanisms of malignant transformation at the molecular and cellular levels where research is presently very active.

CHAPTER IX: THE GENERAL FORM OF THE PC CALCULATION

The probability of causation (PC) for a cancer diagnosed after one or more exposures to ionizing radiation has the general form, simplified from formula IV-2,

$$PC = R / (1 + R).$$

The relative excess, R, in the case of a single exposure of short duration to a subject typical of the US population, is given by the product of three quantities:

$$R = F \times T \times K.$$

In the above expression F quantifies the dependence of R on the radiation dose to the relevant tissue, and its quality. The use of a mere badge or environmental reading would lead to erroneous PC values; absorbed tissue dose must be used in the procedures described here. T gives the dependence of R on time after exposure. K indicates the dependence of R on age at exposure, sex, and, for some cancers, age at diagnosis.

For low-LET radiation, the exposure factor F depends only upon radiation dose D and whether the assumed dose-response function is linear or linear-quadratic. The value of F is presented below as a function of absorbed tissue dose (D), measured in rad, by cancer site and radiation quality:

Radiation Quality	Cancer Site		
	Bone	Thyroid or Breast	Other
Low LET	---	D	$D + D^2/116$
High LET	D	---	---

The above procedures are not intended to be used for cases involving exposure from internal emitters, with the exception of radium-224 in relation to bone cancer.

The factor $T = T(A_1, Y)$ represents the relative likelihood that a cancer induced by an exposure at age A_1 will be diagnosed after Y years (i.e., at least Y years but less than Y + 1 years). In this report both age and Y are integer-valued variables: a person exposed 17 years and 4 months after birth is considered to be 17 years old at exposure, and if a cancer is diagnosed 12 years, 11 months after exposure Y is considered to be 12 years.

Under the constant relative risk model, which has been used here for cancers other than leukemia and bone cancer, T depends only on Y, and this dependence is extremely simple (see Chapter V):

Y	0-4	5	6	7	8	9	10+
T(Y)	0	.074	.259	.500	.741	.926	1.000

The constant relative risk model has not been assumed to hold for leukemia and bone cancer. For these cancers T denotes the conditional probability, assuming that a cancer has been caused by an exposure at age A_1 , that it will be diagnosed Y years later. T is calculated as the lognormal probability that a radiation-induced cancer is diagnosed between Y and Y + 1 years after exposure at age A_1 . For bone cancer and chronic granulocytic leukemia, T depends only upon Y, while for acute leukemia and for leukemia generally, without regard to type, T depends upon exposure age A_1 as well as Y. T is tabulated separately in Chapter X for each of these sites, for integer values of Y between 0 and 49 and, where required, for A_1 between 0 and 75.

As noted in Table VI-1, the observational base for the risk coefficients is generally no more than 30 or 35 years after exposure. The various specifications of T(Y) or $T(A_1, Y)$ for specific cancer sites invite application beyond the period of 30-35 years or so of follow-up that form the observational basis for the risk coefficients used in this report, and indeed this seems the most reasonable course to take if estimates must be made for cancer cases occurring long after exposure. But it should be recognized that we do not in fact have much information on the risk of radiation-induced cancer for periods beyond 35 years or so after exposure. Unpublished data on cancer mortality among A-bomb survivors through 1982 (H. Kato, personal communication) appear to be supportive of a continued increase in risk in absolute terms, a finding consistent with the constant relative risk model, and excess leukemia risk, which already had fallen to a level difficult to detect, remains low, as would be predicted according to a lognormal model for temporal distribution of risk. The fact remains, however, that making probability of causation estimates for cancers diagnosed more than 35 years or so after exposure involves projections in time beyond our present observational basis, and that there is more uncertainty involved in such projections as they are removed farther and farther in time from that observational basis.

The factor $K = K(A_1, A_2, S)$ is the relative excess at age A_2 for a person of sex S exposed at age A_1 , when $F = 1$ and $T = 1$. For cancers other than leukemia and bone cancer K does not depend upon A_2 and is tabulated by site. For leukemia and bone cancer

$$K = E/I.$$

In this formulation $E = E(A_1, S)$ has the following theoretical interpretation: it is the estimated probability, for $F=1$, that a radiation-induced cancer will be diagnosed at some time after an exposure at age A_1 , provided that no other cause of death intervenes. A quantity of more practical importance is $T(Y) \times E$, which is the probability of cancer Y years after exposure, assuming survival to that year. $I(A_2, S)$ is the (site-specific) baseline cancer incidence for persons of age A_2 and sex S. E and I are tabulated separately for bone cancer and for each leukemia type considered.

It must be emphasized here, following the discussion in Chapter IV-E to G, that the use of the SEER values for baseline incidence presupposes that the calculation is being made for an individual who, apart from the particular radiation exposure of interest, is "typical" of the US population for his age and sex with respect to cancer risk. The only exceptions that are made here pertain to the smoking history of an individual with lung cancer (see Chapter IV-H) and to prior and unrelated exposure to ionizing radiation itself (see Chapter IV-E). It has not been possible to take into account atypical exposure to other carcinogens such as asbestos, for example, for which quantitative data adequate for the present purpose do not exist. Given an atypically high exposure to a known carcinogen other than ionizing radiation or cigarette smoking (in the case of lung cancer), which interacts additively with radiation exposure, it is clear that the bias in the calculated PC value would be upward. That is, if it were possible to take into account the influence of the other carcinogen, as is done for smoking in the case of lung cancer, the adjustment would increase the baseline incidence above the average SEER rate and thus reduce the PC value below that found by means of the tables presented in this report. The opposite would be true for an atypically low exposure. On the other hand, the other carcinogen might well interact multiplicatively with radiation, for example if the other agent acted by promotion, that is, by increasing the likelihood that a radiation-induced cancer would develop. In that case the PC would have no bias (see Chapter IV-G). Conceivably, other interaction models might also apply, which would affect bias differently.

Example 1 (Breast Cancer):

A woman diagnosed with a breast cancer at age 45, 19.7 years after an X-ray exposure at age 25 that delivered 10 rad to breast tissue.

$$F(D) = F(10) = 10$$

$$T(Y) = T(19) = 1$$

$$K(A_1, S) = K(25, f) = .00329 \text{ (Table X-10)}$$

$$R = F \times T \times K = 10 \times 1 \times .00329 = .0329$$

$$PC = R/(1+R) = .0329/1.0329 = .0319 = 3\%.$$

* * *

Example 2 (Bone Cancer):

A man diagnosed with bone cancer at age 20, 5.4 years after an exposure of 70 rad dose to the endosteal layer from alpha particle radiation at age 15.

$$F(D) = F(70) = 70$$

$$T(Y) = T(5) = .0814 \text{ (Table X-2-A)}$$

$$E(A_1, S) = E(15, m) = 2.79 \text{ (Table X-2-B)}$$

$$I(A_2, S) = I(20, m) = 1.12 \text{ (Table X-2-C)}$$

$$K = E/I = 2.79/1.12 = 2.49$$

$$R = F \times T \times K = 70 \times .0814 \times 2.49 = 14.19$$

$$PC = R/(1+R) = 14.19/15.19 = .934 = 93\%$$

* * *

The calculation of the relative excess where diagnosis occurred following several radiation exposures should be made by adding the relative excesses for each exposure. If doses $D(1)$, $D(2)$, and $D(3)$ occurred at ages $A(1)$, $A(2)$, and $A(3)$, respectively, the relative excess for the combined exposures is given by

$$R = R(1) + R(2) + R(3).$$

The PC of all these exposures is

$$PC = R/(1+R).$$

The PC for any one of them (say the first), given the change in risk caused by the others, is

$$PC(1) = R(1)/(1+R).$$

* * *

Example 3 (Thyroid Cancer):

A man diagnosed with thyroid cancer at age 25, following a 30-rad X ray exposure to the thyroid at age 17, 8.2 years previously. As an infant (age 0, 24.7 years prior to diagnosis of thyroid cancer) the man was successfully treated by high-voltage X radiation for Wilms' tumor and it is estimated that his thyroid gland received 100 rad because of X-ray scatter. The PC for the combined exposures is calculated as follows:

For the first exposure, completely ignoring the second,

$$F(D) = F(100) = 100$$

$$T(Y) = T(24) = 1$$

$$K(A_1, S) = K(0, m) = .106 \text{ (Table X-12)}$$

$$R(1) = F \times T \times K = 100 \times 1 \times .106 = 10.6$$

For the second, ignoring the first,

$$F(D) = F(30) = 30$$

$$T(Y) = T(8) = .741$$

$$K(A,S) = K(17,m) = .0397 \text{ (Table X-12)}$$

$$R(2) = F \times T \times K = 30 \times .741 \times .0397 = .883$$

The relative excess R and the PC for the combined exposures are

$$R = R(1) + R(2) = 10.6 + .883 = 11.5$$

$$PC = R/(1 + R) = 11.5 / 12.5 = .920 = 92\%$$

* * *

Wilms' tumor is nearly always fatal unless treated, and it is highly likely that in the preceding example the high-voltage X ray therapy saved the patient's life. Thus the calculation of greatest interest might well concern the extent to which the patient's cancer is attributable to his second exposure alone. Simply ignoring the first exposure gives $R = R(2)$ and

$$PC(2) = R(2)/(1 + R(2)) = .883/1.883 = 0.468 = 47\%.$$

This calculation treats the patient as if he were a member of the general population; it is clear, however, that he is not. The radiation that saved the subject's life from Wilms' tumor also, as a side effect, increased his chances of getting thyroid later in life. Therefore he is a member of a subpopulation with a baseline rate that is different from the general population. As a group, men given a 100-rad thyroid dose in infancy have a thyroid cancer risk, in the absence of other exposure, $1 + R(1)$ times as large as that of the general population. Therefore the relative excess, in the context of that subpopulation, is

$$R'(2) = R(2)/(1 + R(1)) = .883/11.6 = .0761.$$

The PC calculated from $R'(2)$ is

$$PC'(2) = R'(2)/(1 + R'(2)) = .0761/1.0761 = .0707 = 7\%.$$

The Ad Hoc Working Group considers the last calculation the most appropriate in this case.

In Chapter IV-F the quantity W is introduced as the ratio of baseline rates in the general population and the subpopulation. In the above example $W = 1/(1 + R(1))$, and $R'(2) = R(2) \times W$. This method allows the computation of a PC for a member of a population having a baseline risk different from the general population by means of the formula

$$R = F \times T \times K \times W,$$

provided that the factors causing the subpopulation to have a baseline risk

different from that of the general population are additive in effect with respect to radiation exposure.

Example 4 (Lung Cancer):

A lung cancer has been diagnosed in a 55-year-old man who was exposed to gamma rays at age 28 resulting in a 40-rad dose to the bronchial area of the lungs. He is a lifelong nonsmoker. If the PC calculation were carried out without regard to smoking history, it would be as follows:

$$F(D) = F(40) = 40 + 40/116 = 53.8$$

$$T(Y) = T(27) = 1$$

$$K(A_1, S) = K(28, m) = .000619 \text{ (Table X-9-A)}$$

$$R = F \times T \times K = 53.8 \times 1 \times .000619 = .0333$$

$$PC = R/(1+R) = .0333/1.0333 = .0322 = 3\%.$$

From Table X-9-A, however, the lung cancer rate of male nonsmokers is smaller than that of the general population by a factor of 6.81, and it appears that smoking and radiation interact additively in the causation of lung cancer (see Chapter IV-H). Thus $W = 6.81$, and the revised relative excess is

$$R = F \times T \times K \times W = 53.8 \times 1 \times .000619 \times 6.81 = .206,$$

from which

$$PC = R/(1+R) = .206/1.206 = .171 = 17\%.$$

* * *

Age at exposure, age at diagnosis, and time from exposure to diagnosis are tabulated in annual increments. For multiple, fractionated, or protracted exposures taking place at a single year of age A_1 and corresponding to the same value of Y , the doses can be summed provided that a linear dose-response model is appropriate for each exposure. If the linear-quadratic model applies, however, doses should be given for discrete 24-hour periods and treated as pertaining to separate exposures. In practice, however, there is little purpose to subdivide accumulated doses of less than 5 rad.

Example 5 (Acute Leukemia):

An acute leukemia was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, to one rad average bone-marrow dose, occurred at age 20, 24 years and 2 months before diagnosis ($Y=24$). The second, to 2 rad, occurred 4 months later, at the same age ($A=20$) but 23 years and 10 months before diagnosis ($Y=23$). At age 21, 23 years and 3 months before diagnosis, 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour. Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad,

respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis.

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The partition giving the maximum risk estimate assigns 3 rad to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(A_1, Y) = T(20, 24) = .0101 \text{ (Table X-1-D)}$$

$$E(A_1, S) = E(20, f) = .914 \text{ (Table X-1-E)}$$

$$I(A_2, S) = I(44, f) = 2.73 \text{ (Table X-1-F)}$$

$$K = E/I = .914/2.73 = 0.335$$

$$R_1 = F \times T \times K = 1.01 \times .0101 \times .335 = .00342.$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(20, 23) = .0114$$

$$E(20, f) = .914$$

$$I(44, f) = 2.73$$

$$K = E/I = .914/2.73 = 0.335$$

$$R_2 = F \times T \times K = 2.03 \times .0114 \times .335 = .00775$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(21, 23) = .0120$$

$$E(21, f) = .912$$

$$I(44, f) = 2.73$$

$$K = E/I = .912/2.73 = 0.334$$

$$R_{3a} = F \times T \times K = 3.08 \times .0120 \times .334 = .0123$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(21,23) = .0120$$

$$E(21,f) = .912$$

$$I(44,f) = 2.73$$

$$K = E/I = .912/2.73 = 0.334$$

$$R_{3b} = F \times T \times K = 6.31 \times .0120 \times .334 = .0253$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(35,9) = .0436$$

$$E(35,f) = 1.24$$

$$I(44,f) = 2.73$$

$$K = E/I = 1.24/2.73 = 0.454$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .0436 \times .454 = .0485$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00342 + .00775 + .0123 + .0253 + .0485 = .0973$$

$$PC = R/(1+R) = .0973/1.0973 = .0887 = 9\%$$

* * *

CHAPTER X: THE CALCULATION OF PROBABILITIES OF CAUSATION FOR CANCERS
OF SPECIFIC TISSUES

1. Leukemia (204-207, except 204.1, in 8th International Classification of Diseases Adapted for Use in the United States [ICDA])

The derivation of PC values, described in Chapters IV-VI and IX, is more complex for the leukemias than for the solid tumors. The leukemogenic effect of ionizing radiation does not extend to all forms of leukemia, chronic lymphocytic leukemia (CLL) being the notable exception and there being possibly others of lesser importance, such as hairy-cell leukemia. The major forms of leukemia known to be caused by radiation, the acute forms (AL) and chronic granulocytic leukemia (CGL), differ in the likelihood of their occurrence following exposure to radiation, in their dependence upon age at exposure, and in their distribution over time following exposure.

The only series of radiation-induced leukemias that even approaches the size needed to describe the leukemogenic effect of radiation derives from the studies of A-bomb survivors (1), and for the present purpose it was necessary to analyze those data in greater depth than was required for the BEIR III report in which the risk coefficients for leukemia were derived from the same source. Other human data on radiation leukemogenesis are in reasonable agreement as to the general magnitude of the risk per rad, the role of age at exposure, and the distribution of the radiogenic excess over time (2-4). There is, however, a question as to the comparability of risk coefficients based on partial-body irradiation with those based on whole-body exposure. As a working hypothesis for radiation protection purposes it has generally been assumed that a dose to a portion of the marrow can be averaged over the entire marrow so that, e.g., a dose of 800 rad to 40 percent of the marrow would average 320 over the whole body. This hypothesis, while consistent with a linear dose response, clearly is inconsistent with a model incorporating terms that are quadratic or otherwise nonlinear in dose. For example, if partial-body doses are high enough to kill or otherwise render ineffective a significant number of cells, as seems to be the case, e.g., with X-ray therapy for cervical cancer (5), the hypothesis is surely invalid.

The Working Group has employed the linear-quadratic dose-response function preferred by the BEIR committee for low-LET radiation, but the present tables for calculating PC values distinguish between acute forms and chronic granulocytic leukemia, while providing coefficients for all forms considered as a group but excluding CLL. The material for all forms except CLL may be used in those instances where the precise type cannot be established and for chronic leukemias other than CLL and CGL. The A-bomb survivor material on which the BEIR estimates were based reflects diagnoses that generally were the latest and most definitive obtainable. Leukemia that is neither acute nor chronic at initial diagnosis eventually becomes acute. Therefore, the acute leukemia coefficients

probably should be used for such cases in preference to the all-types coefficients in the PC calculation. Death certificates may not specify histologic type, but are generally reliable for leukemia. The present report also differs from the BEIR report in its use of a "wave" function to distribute the radiogenic leukemia over time, the BEIR report having employed a plateau.

Data from the A-bomb survivor series (1) and the British ankylosing spondylitis series (3) were used to derive lognormal time-to-response models (see Chapter V-C). Time from exposure to response was assumed to be log-normally distributed with a two-year minimum. For chronic granulocytic leukemia (CGL) the fitted distribution of $\log(\text{time in years} - 2)$ was independent of age at exposure and sex, with mean 2.68 and variance 1.51, while for acute leukemia the variance was 0.65 and the mean $1.61 + .015A_1 + .0005A_1^2$, where A_1 denotes age at exposure.

The age-specific linear-quadratic risk coefficients in the BEIR III report for all types of leukemia except chronic lymphocytic leukemia (CLL) in fact pertained to only AL plus CGL. These were made specific to AL and CGL in the ratio 68:32, based on a reanalysis of the A-bomb survivor data (1). Coefficients for single years of age at exposure were derived by the procedure described in Chapter V-D.

Several studies (6,7) have reported excess childhood leukemias following fetal irradiation. Given the well-established association of leukemia with childhood exposure, the causality is less in doubt than the magnitude of the effect. The Working Group has made no distinction between fetal exposure and exposure during the first year of life.

The SEER data on the incidence of leukemia for the period 1973-1981 have been used as the source of age-, sex-, and type-specific incidence of leukemia in the general United States population (see Chapter VII-C). The ICDA-8 code equivalents used were:

chronic granulocytic - 205.1
acute - 204.0, 204.9, 205.0, 205.9, 206.0
206.9, 207.0, 207.2, 207.9
all except CLL - 204.0, 204.9, 205.1, 205.9, 206.0,
206.1, 206.9, 207.0, 207.2, 207.9

The reporting areas for the SEER program (8) are relatively homogeneous as to their incidence of leukemia (see Tables VII-1, and VII-2).

Although the leukemogenic potential of a variety of chemicals is much discussed, it is only for benzene that reasonably cogent evidence is in hand (9). Thus, it is not often that risk factors other than radiation will be identified and appear to compete with radiation. The influence of risk factors other than ionizing radiation is discussed in Chapter IV, Sections E to G and in Chapter IX.

For leukemia, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(A_1, Y) \times K(A_1, A_2, S)$$

where D is the tissue dose in rad for low-LET radiation; $T(A_1, Y)$ represents the conditioning influence of age at exposure A_1 and time to diagnosis (Y); and $K(A_1, A_2, S)$ represents the relative excess of leukemia for a person of sex S, age at exposure A_1 , and age at diagnosis A_2 , when both F and T = 1. The standardized relative excess $K = K(A_1, A_2, S)$ for an exposure at age A_1 and diagnosis at age A_2 is the ratio of the estimated lifetime absolute excess $E = E(A_1, S)$ and the background incidence $I = I(A_2, S)$:

$$K(A_1, A_2, S) = E(A_1, S)/I(A_2, S).$$

The coefficient E was derived from the BEIR III coefficients, fitted to a quadratic function in age A_1 (see Chapter V-D), and is an estimate of the probability that a radiation-induced leukemia of the specified type will be diagnosed at some time after exposure given $F(D) = 1$. For each exposure age A_1 and sex S, $E(A_1, S)$ was determined such that the average of $E(A_1, S) \times T(A_1, Y)$ over the period $Y = 2$ through 28 was equal to the interpolated BEIR coefficient for age A_1 and sex S.

The following look-up tables are provided below:

for CGL: $T(Y)$, Table X-1-A;

$E(A_1, S)$, Table X-1-B;

$I(A_1, S)$, Table X-1-C;

for all acute forms of leukemia: $T(A_1, Y)$, Table X-1-D;

$E(A_1, S)$, Table X-1-E;

$I(A_2, S)$, Table X-1-F;

for all forms of leukemia except CLL: $T(A_1, Y)$, Table X-1-G;

$E(A_1, S)$, Table X-1-H;

$I(A_2, S)$, Table X-1-I.

Under the linear-quadratic model assumed for leukemia when exposure is to low-LET radiation, and the dose, D, is expressed in rad,

$$F = D + D^2/116.$$

The constant relative risk model for time to response does not hold for leukemia, which appears to follow a "wave" function. The factor T is the probability that a cancer caused by an exposure to radiation at age A_1 will be diagnosed Y years later. T depends only on Y for CGL, but on both Y and A_1 for AL and for all types considered as a group.

Several examples are provided to illustrate the procedures for calculating individual PC values:

Example #1 A typical female aged 5 at exposure to 5 rad of low-LET radiation to the bone marrow, with a diagnosis of acute leukemia at age 9, 4.2 years after exposure. Here, $D = 5$, $A_1 = 5$, $A_2 = 9$, and $Y = 4$.

$$F(D) = 5 + 5^2/116 = 5.22;$$

$$T(A_1, Y) = T(5, 4) = .122, \text{ Table X-1-D};$$

$$E(A_1, S) = E(5, f) = 2.04, \text{ Table X-1-E};$$

$$I(A_2, S) = I(9, f) = 2.22, \text{ Table X-1-F};$$

$$K(A_1, A_2, S) = K(5, 9, f) = E/I = 2.04/2.22 = .919;$$

$$\text{then } R = F \times T \times K = 5.22 \times .122 \times .919 = .585;$$

$$\text{and, finally, } PC = R/(1 + R) = .369 \text{ or } 37\%.$$

Example #2 A typical female, exposed at age 45 to 5 rad of low-LET radiation to the marrow, with a diagnosis of leukemia at age 53, 8 years after exposure, the leukemia not being well-established as to chronicity. In this case, one would use the acute leukemia tables: $D = 5$, $A_1 = 45$, $A_2 = 53$, and $Y = 8$;

$$F(D) = 5 + 5^2/116 = 5.22;$$

$$T(A_1) = T(45, 8) = .0159, \text{ Table X-1-G};$$

$$E(A_1, S) = E(45, f) = 2.37, \text{ Table X-1-H};$$

$$I(A_1, S) = I(53, f) = 4.21, \text{ Table X-1-I};$$

$$\text{and } K = E/I = 2.37/4.21 = .563$$

$$\text{then } R = F \times T \times K = 5.22 \times .0159 \times .563 = .0467$$

$$\text{and } PC = R/(1 + R) = .0446 \text{ or } 4\%.$$

Example #3 A typical male, exposed at age 35 to 10 rad of low-LET radiation, with a diagnosis of CLL at age 60. In this case, no calculation would be made as CLL is not an eligible diagnosis.

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide a general orientation to the magnitude of the PC values that result from the procedures described here, Fig. X-1-A, B, and C have been prepared for CGL, acute forms, and all forms respectively. They give PC values for 1, 10, and 100 rad of low-LET radiation to the bone marrow by age at diagnosis, separately for males and females, and each has 8 parts corresponding to ages 0, 10, 20, 30, 40, 50, 60, and 70 at exposure. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig X-1-A-1

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 0

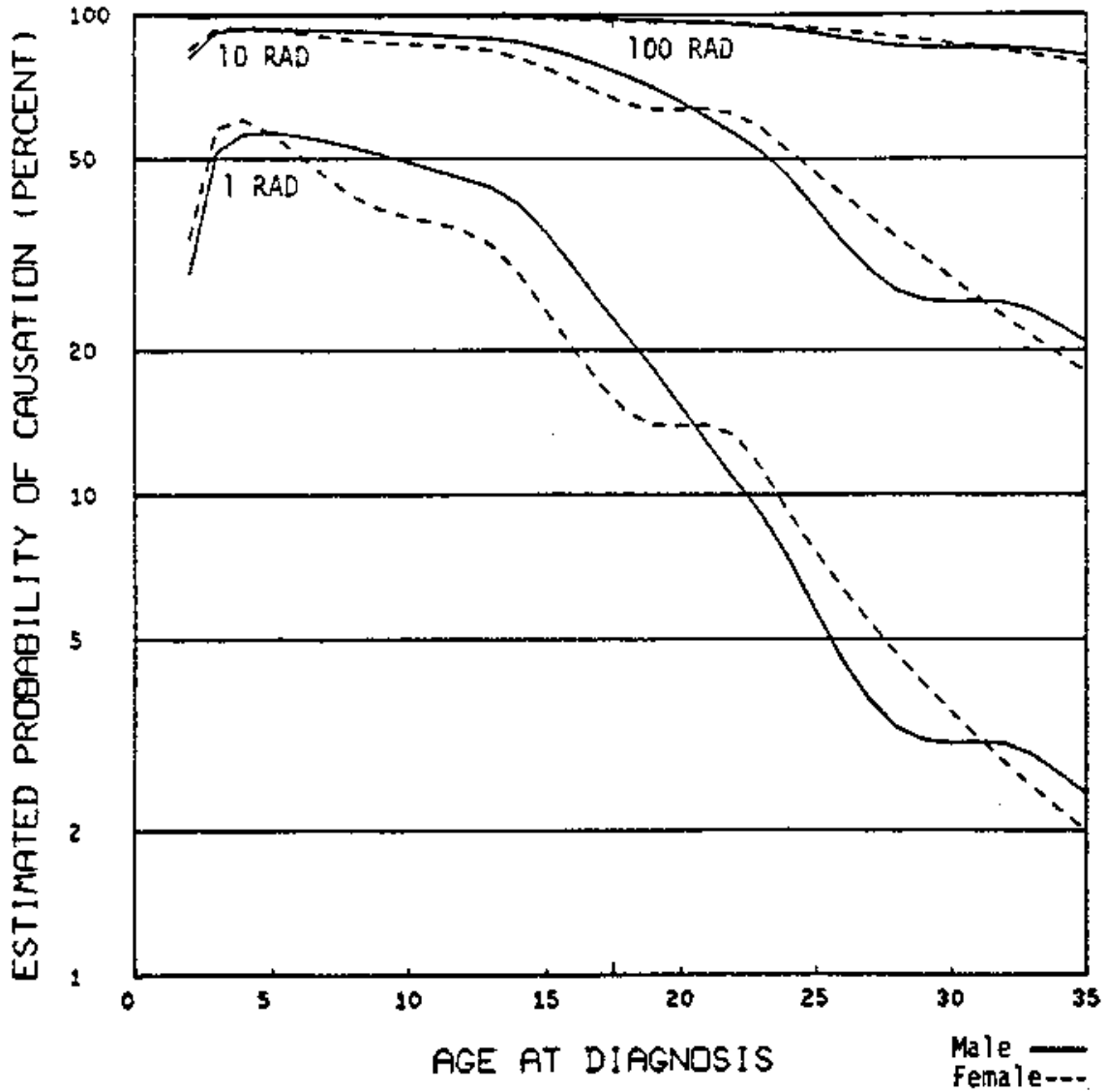


Fig X-1-A-2

CHRONIC GRANULOCYTTIC LEUKEMIA
EXPOSURE AGE 10

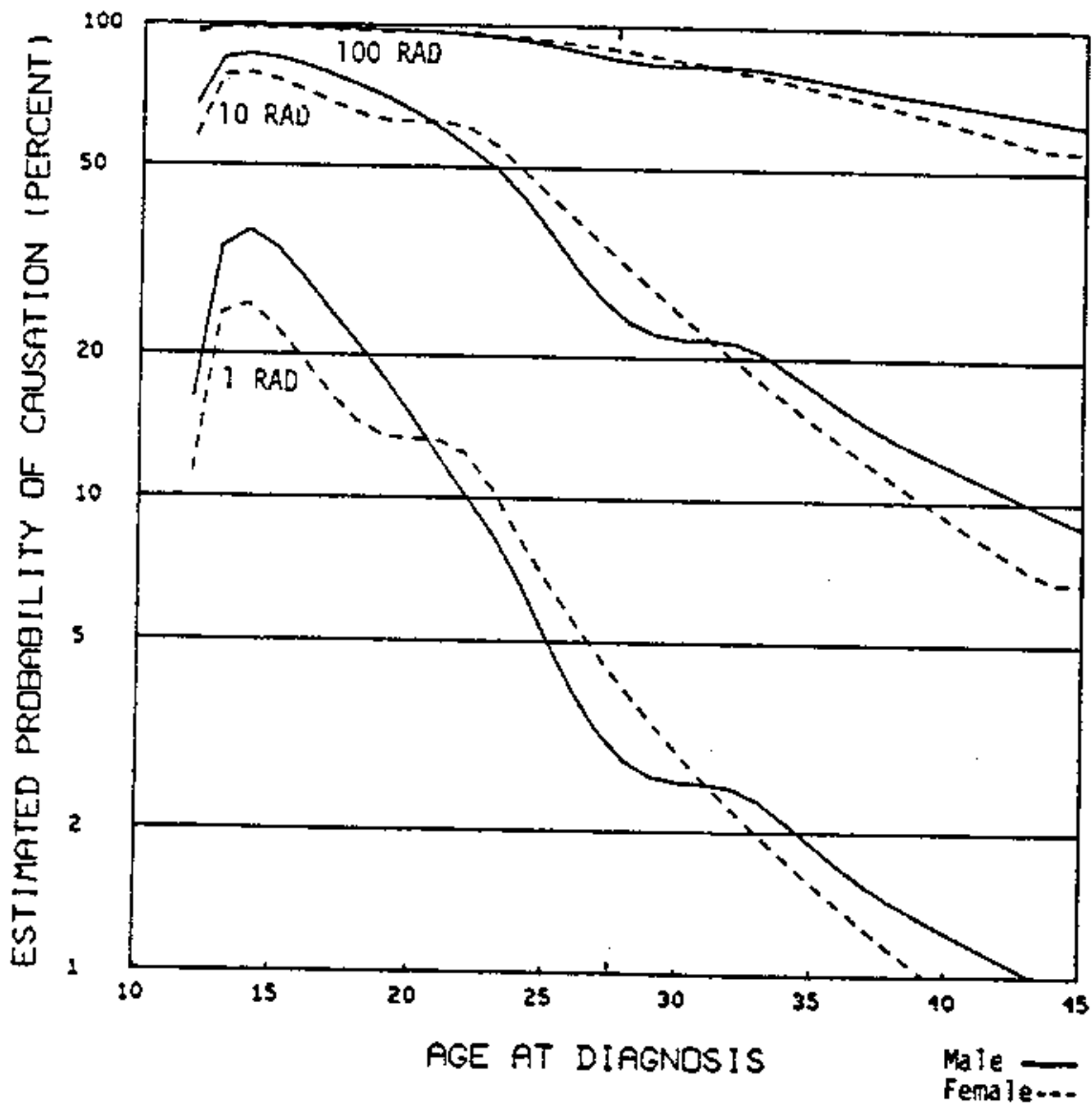


Fig X-1-A-3

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 20

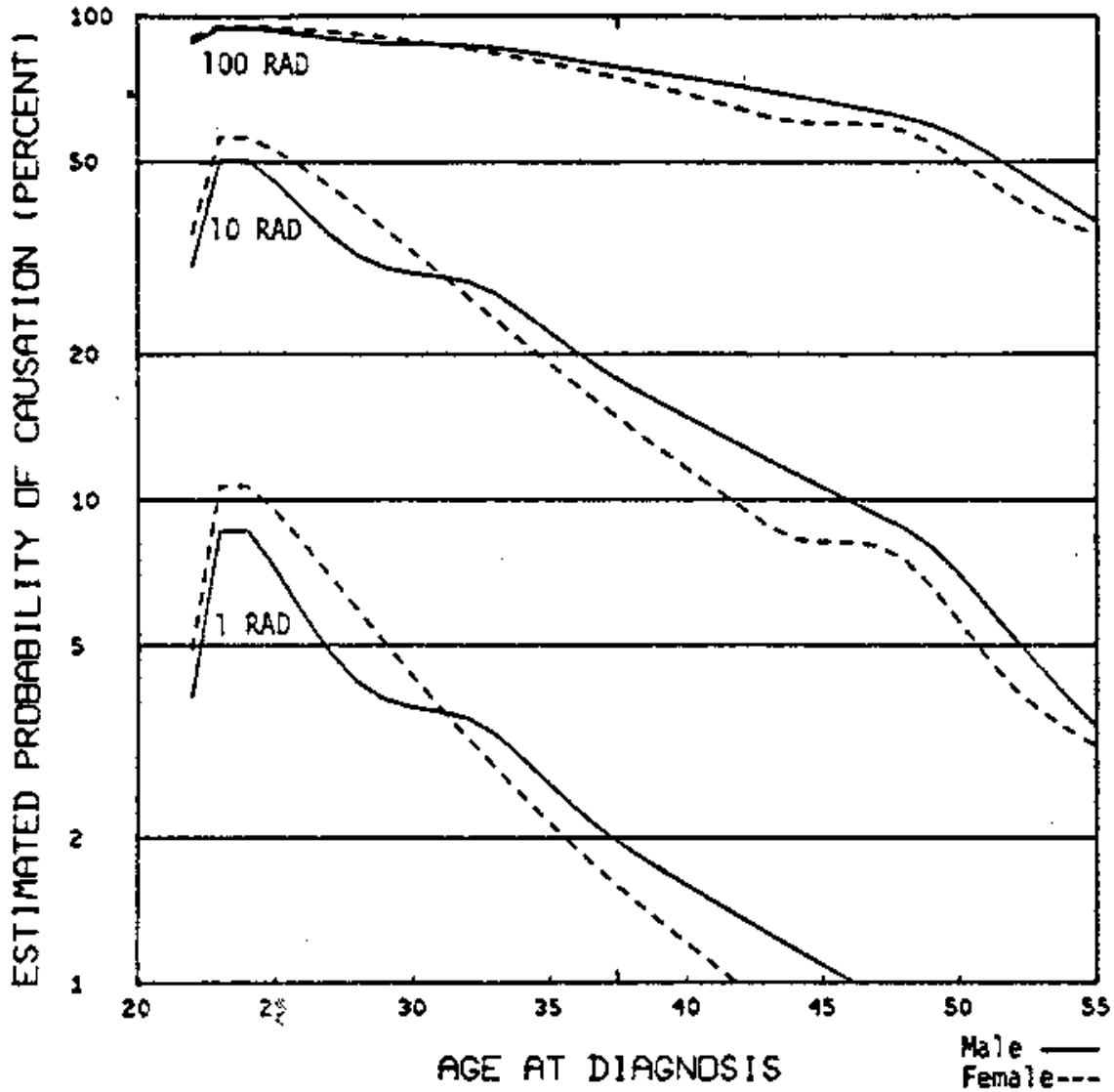


Fig X-1-A-4

CHRONIC GRANULOCYTTIC LEUKEMIA
EXPOSURE AGE 30

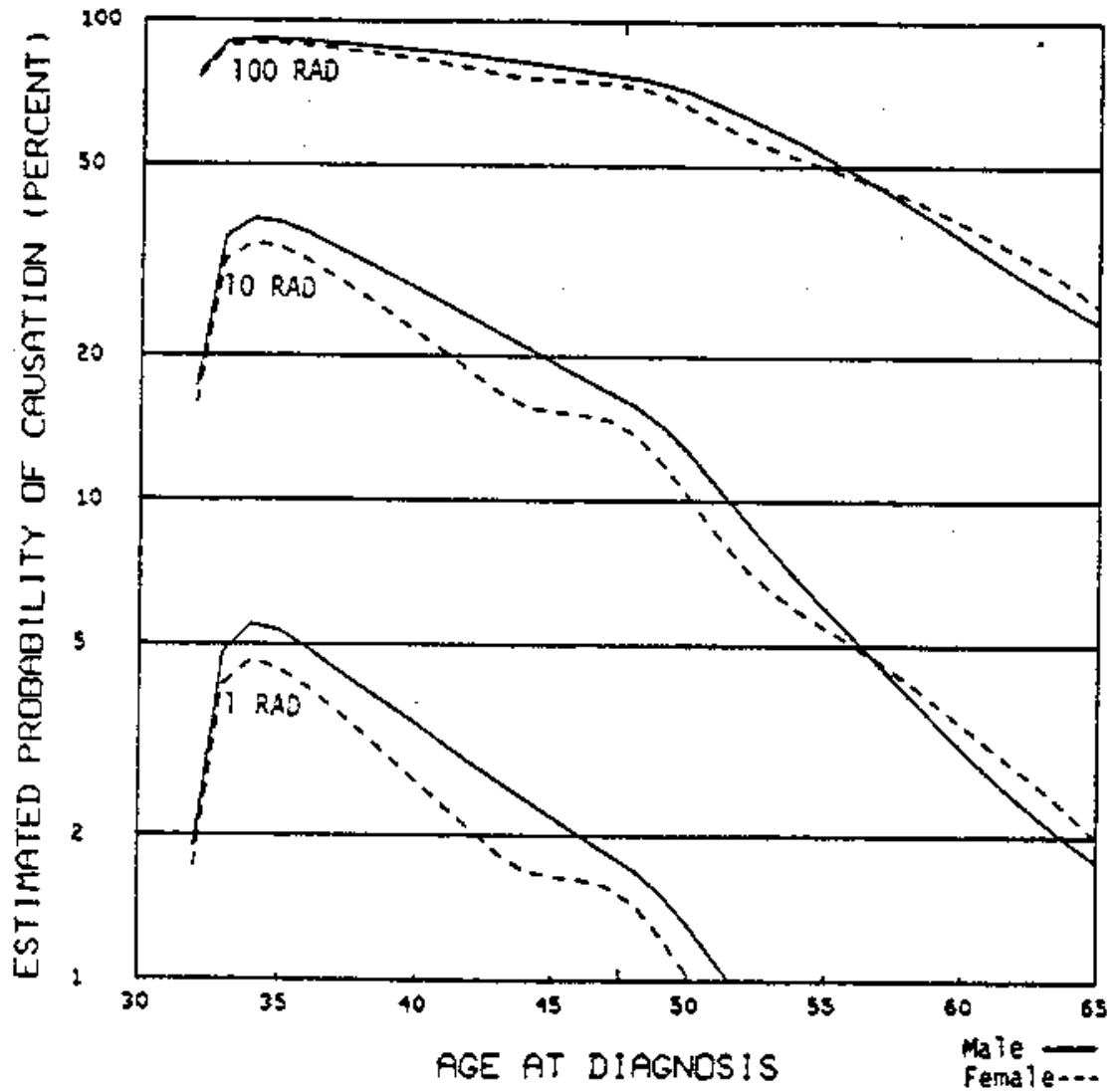


Fig X-1-A-5

CHRONIC GRANULOCYTTIC LEUKEMIA
EXPOSURE AGE 40

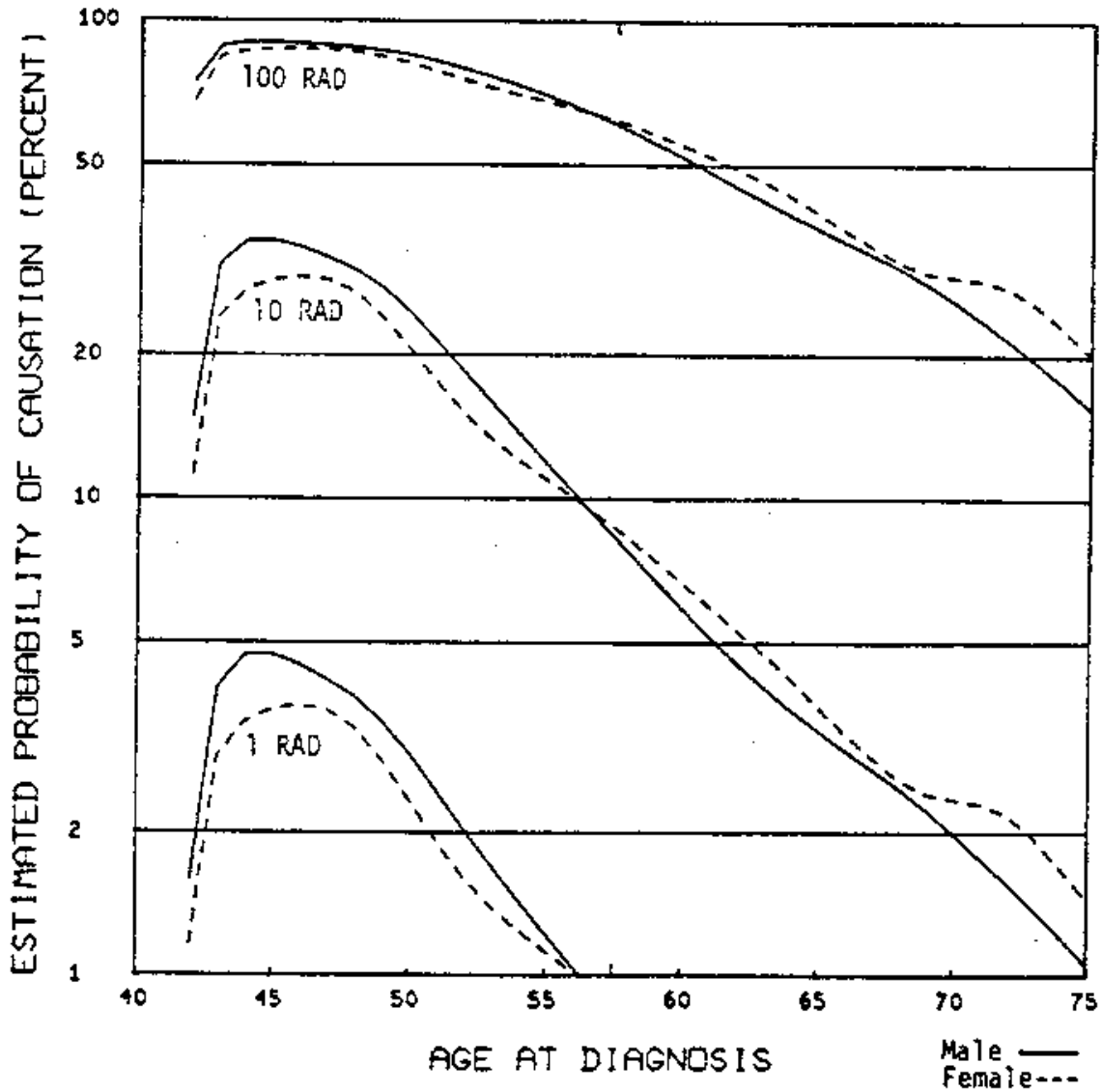


Fig X-1-A-6

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 50

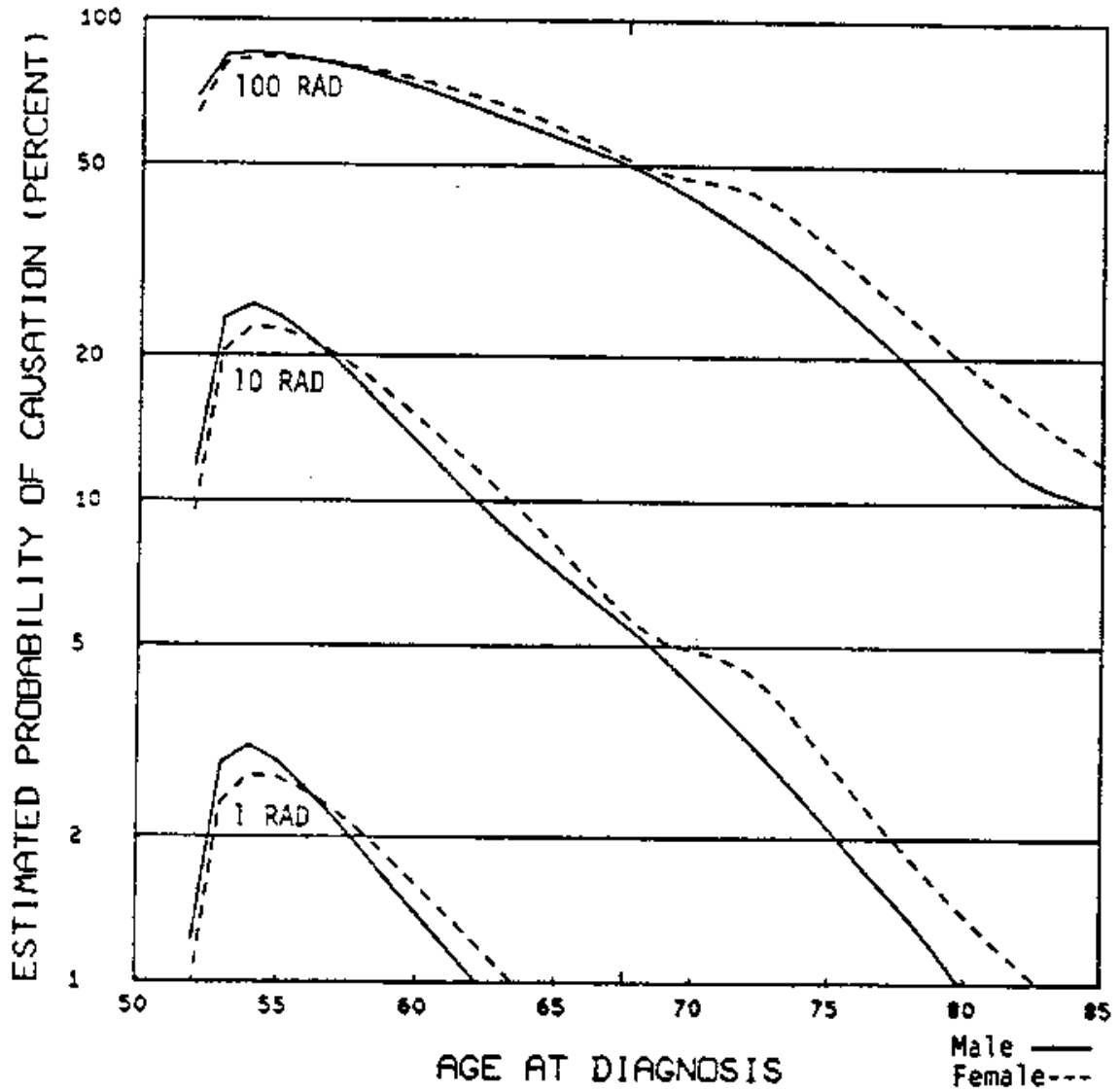


Fig X-1-A-7

CHRONIC GRANULOCYTTIC LEUKEMIA
EXPOSURE AGE 60

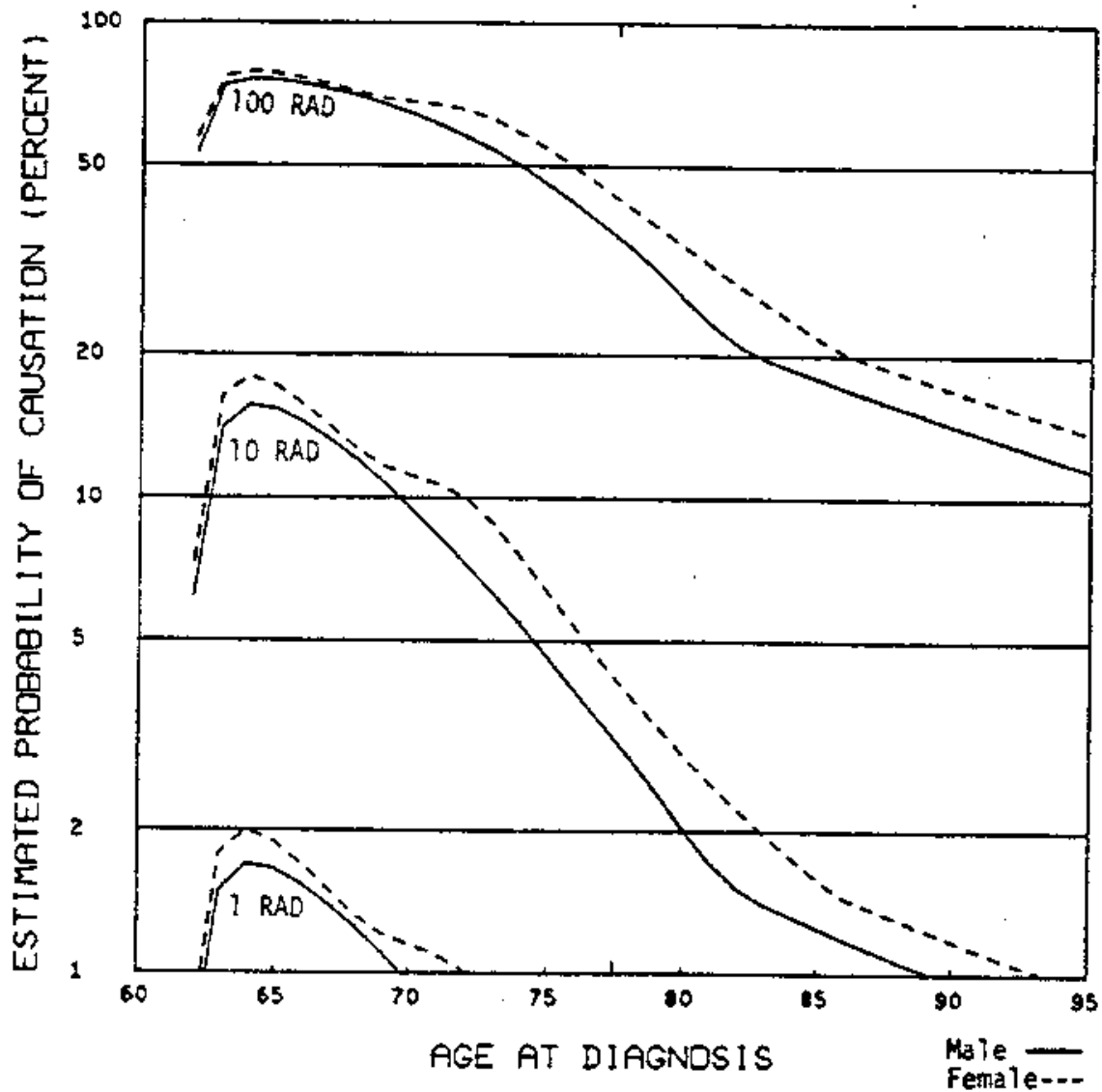


Fig X-1-A-8

CHRONIC GRANULOCYTIC LEUKEMIA
EXPOSURE AGE 70

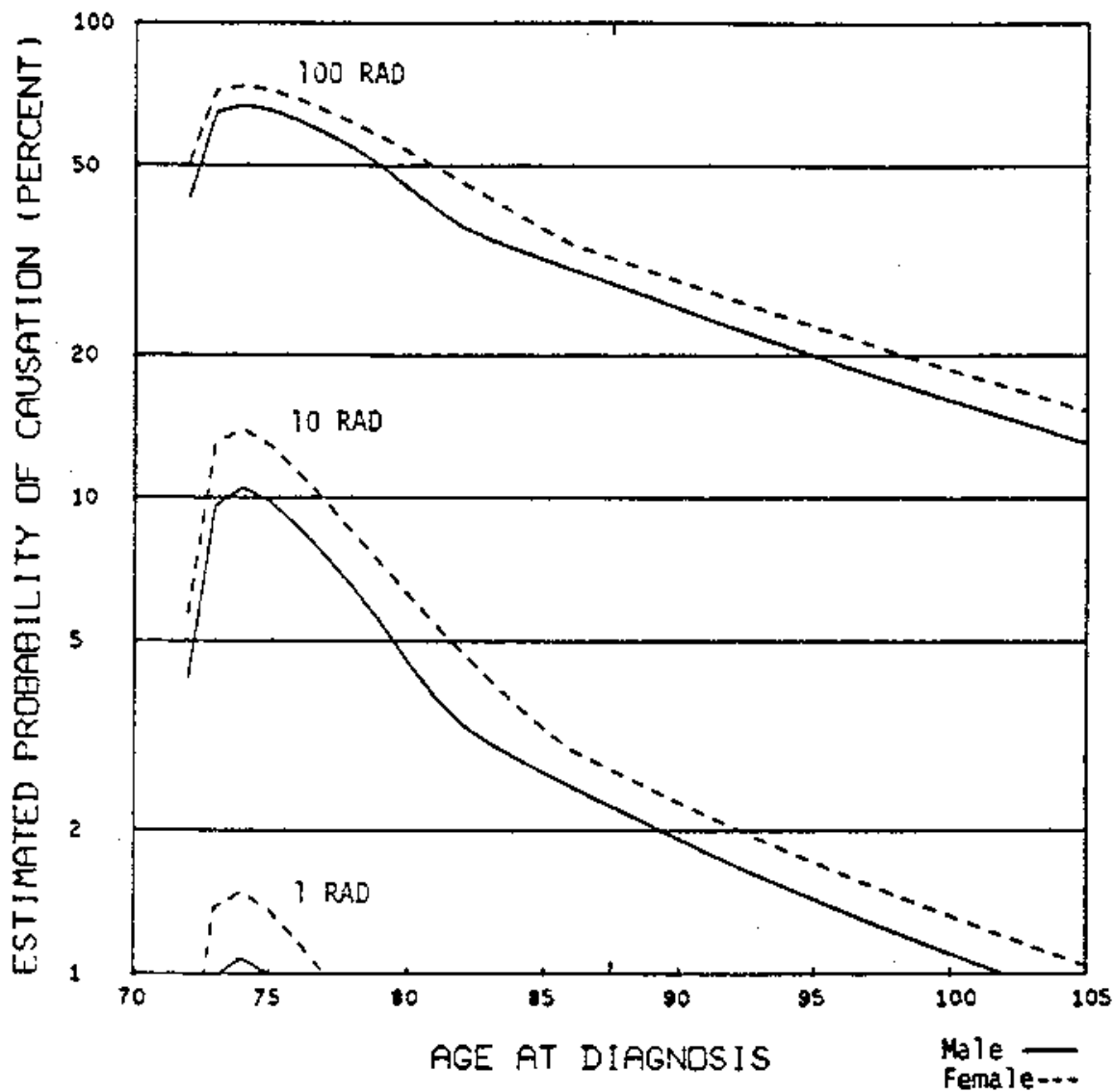


Fig X-1-B-1

ACUTE LEUKEMIA
EXPOSURE AGE 0

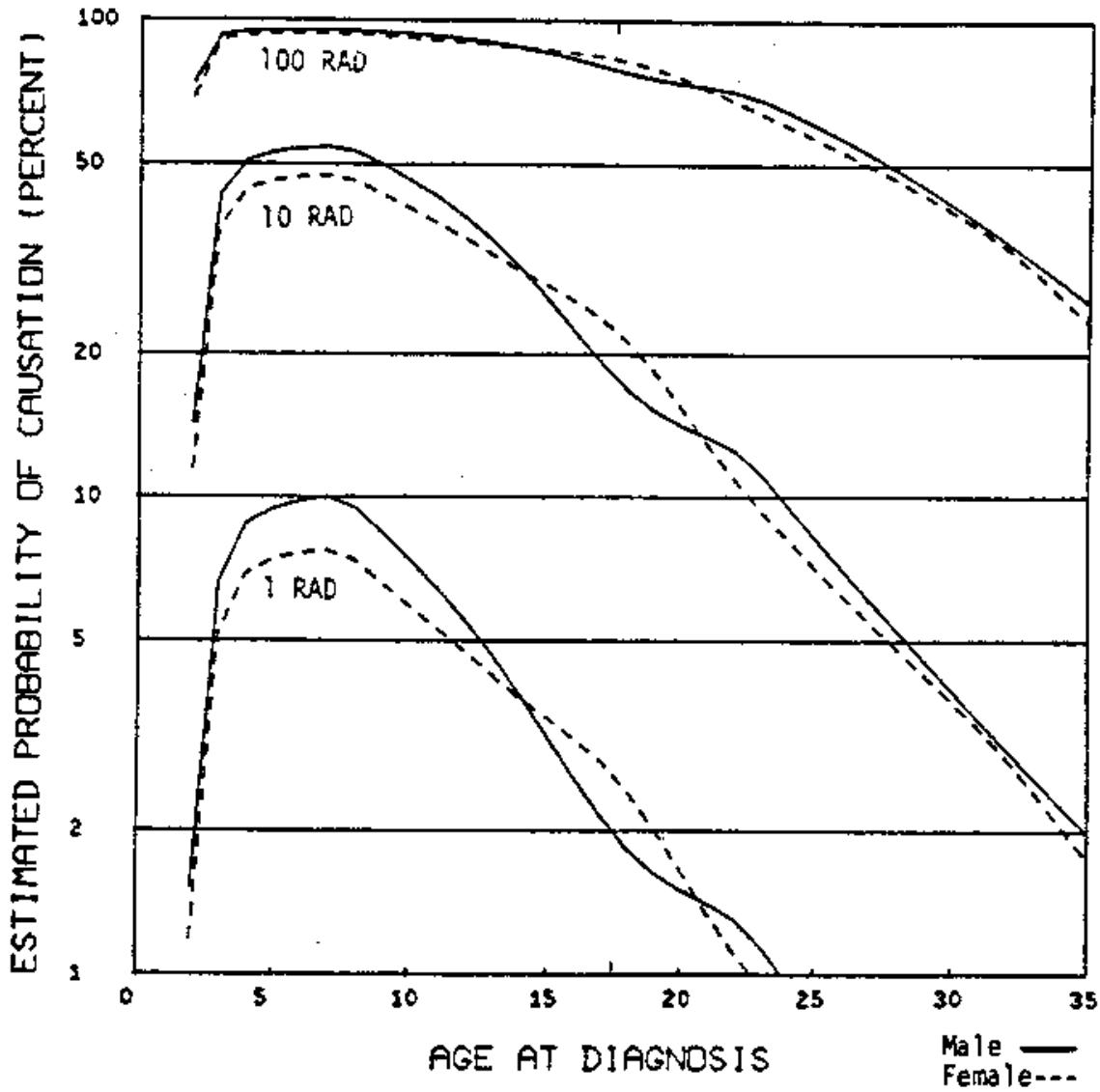


Fig X-1-B-2

ACUTE LEUKEMIA
EXPOSURE AGE 10

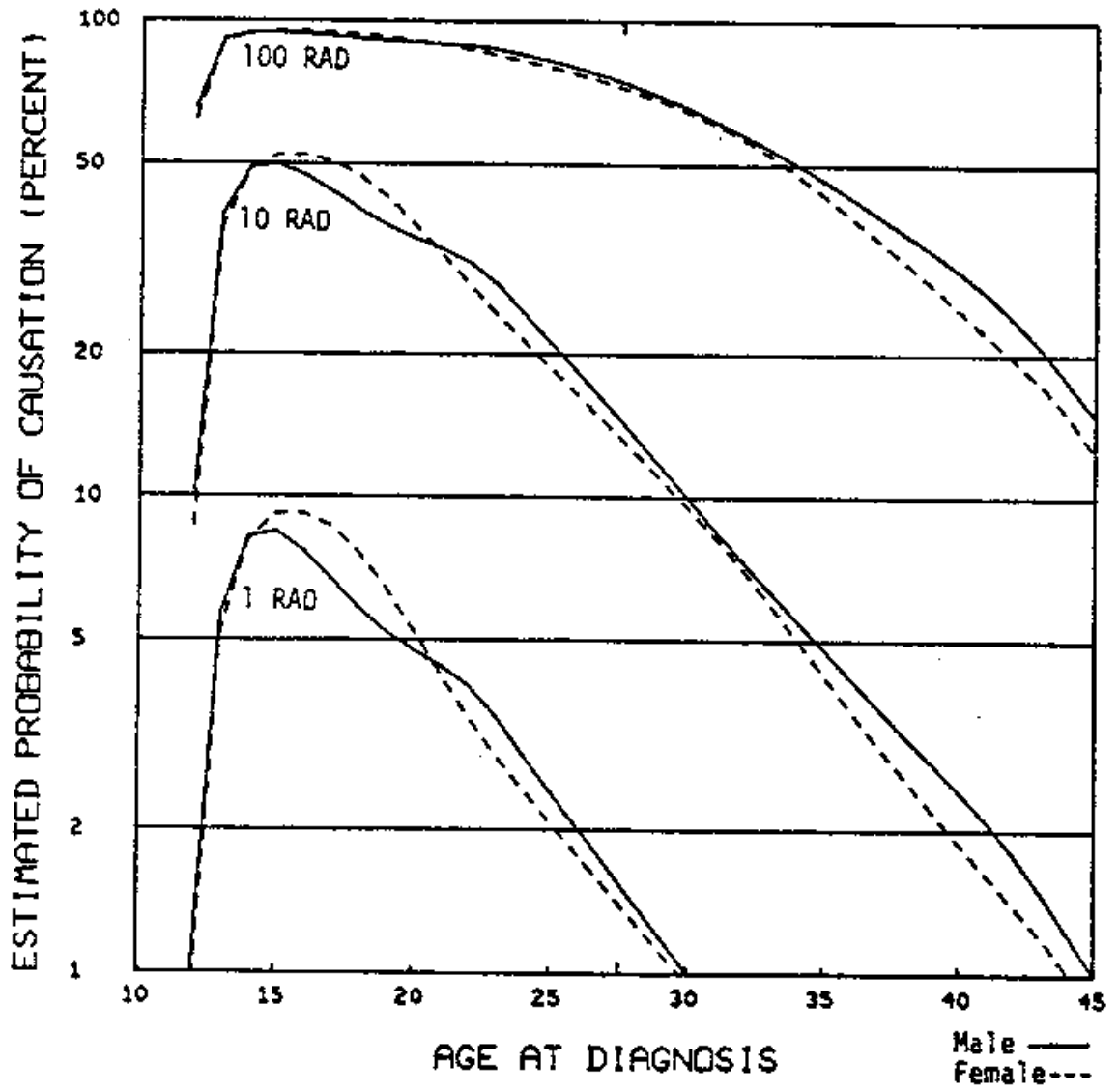


Fig X-1-B-3

ACUTE LEUKEMIA
EXPOSURE AGE 20

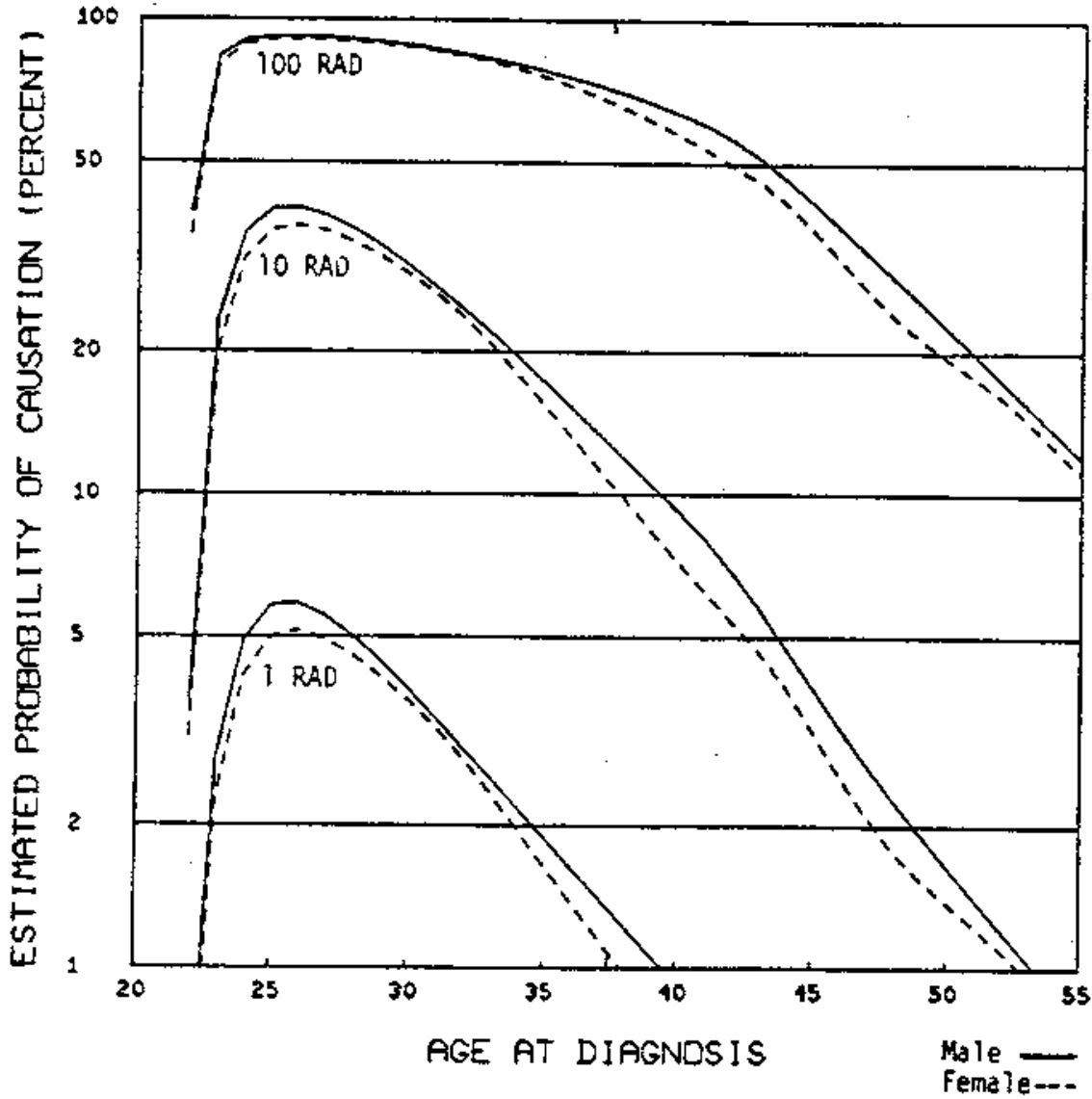


Fig X-1-B-4

ACUTE LEUKEMIA
EXPOSURE AGE 30

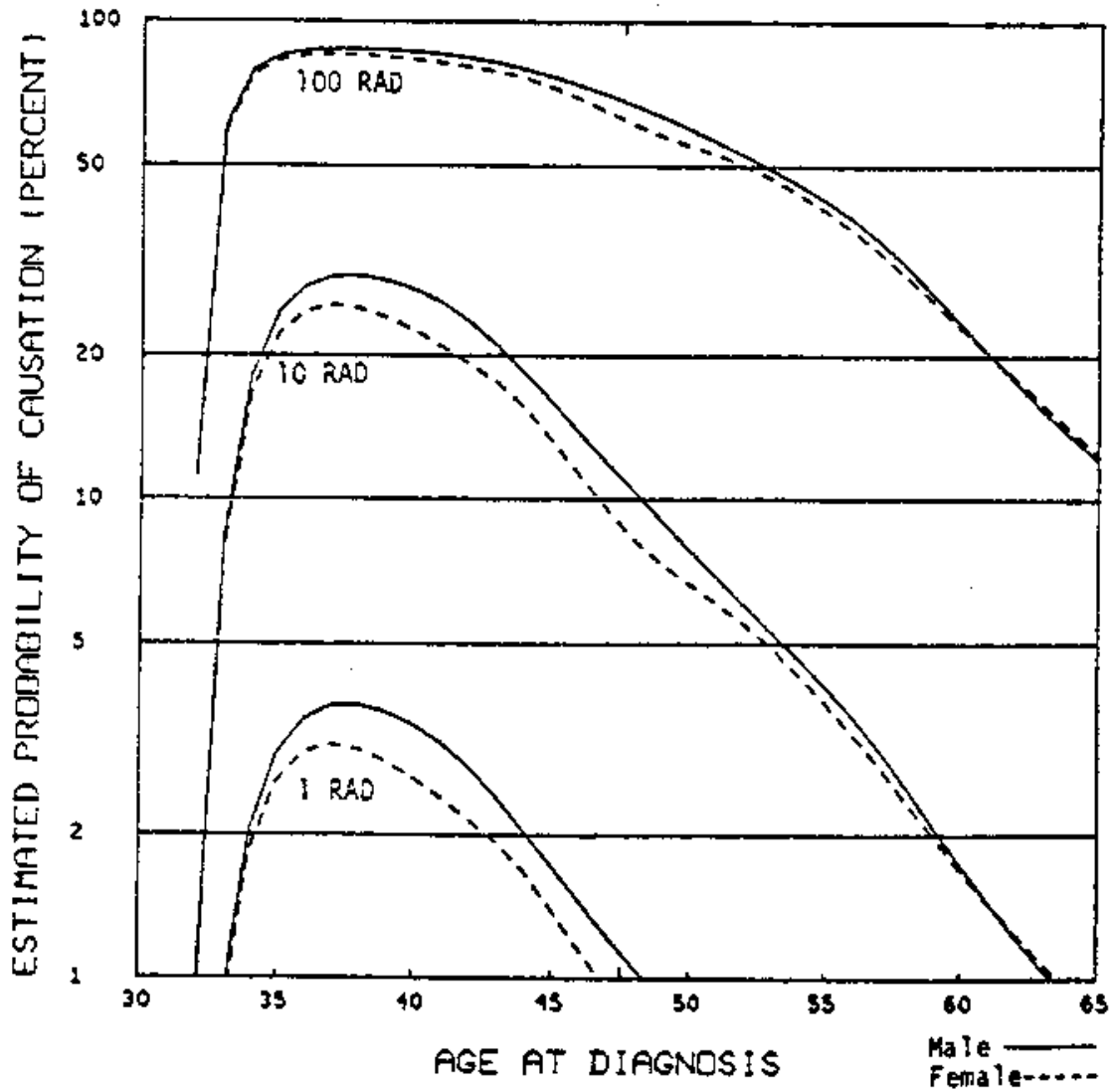


Fig X-1-B-5

ACUTE LEUKEMIA
EXPOSURE AGE 40

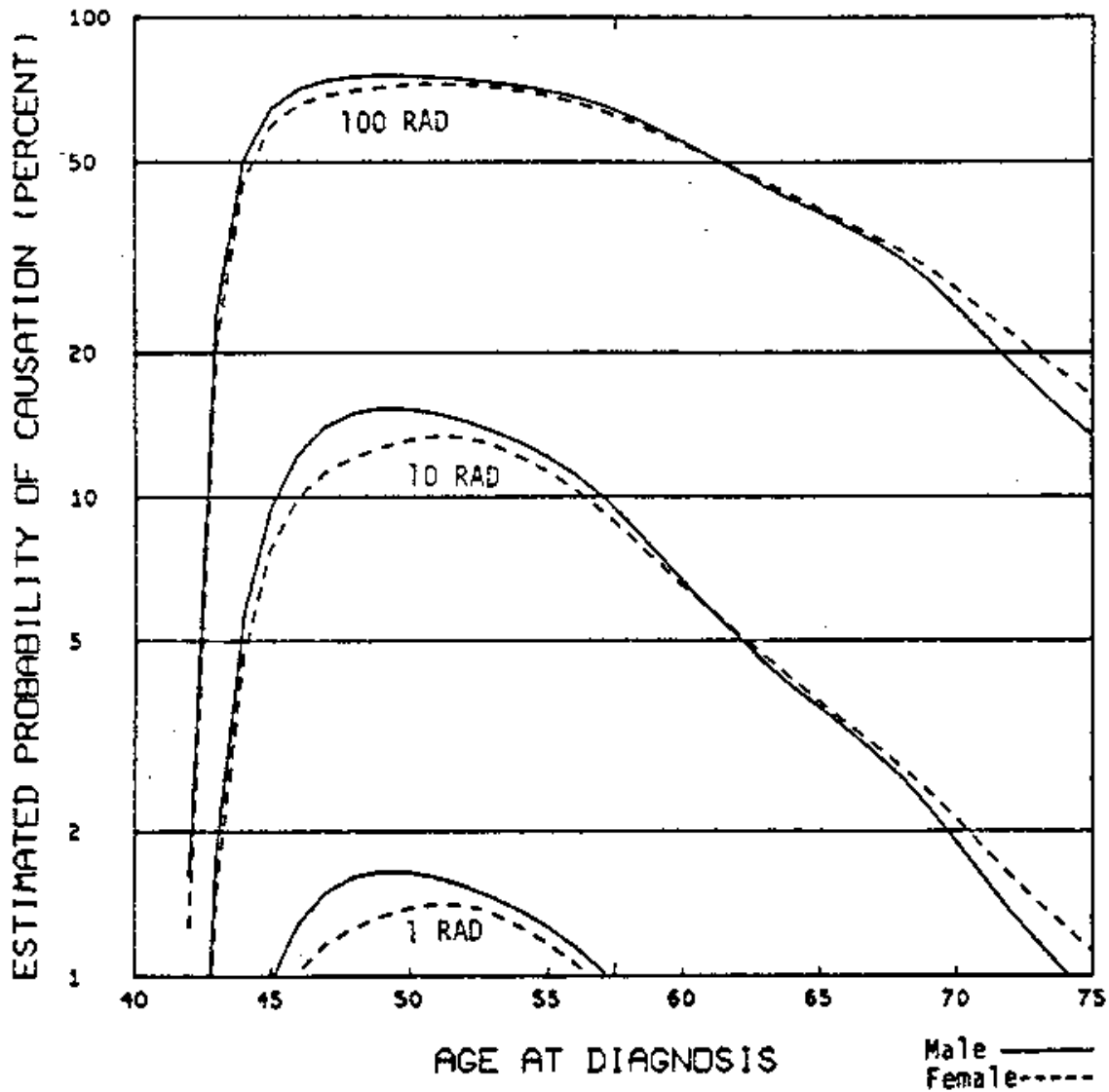


Fig X-1-B-6

ACUTE LEUKEMIA
EXPOSURE AGE 50

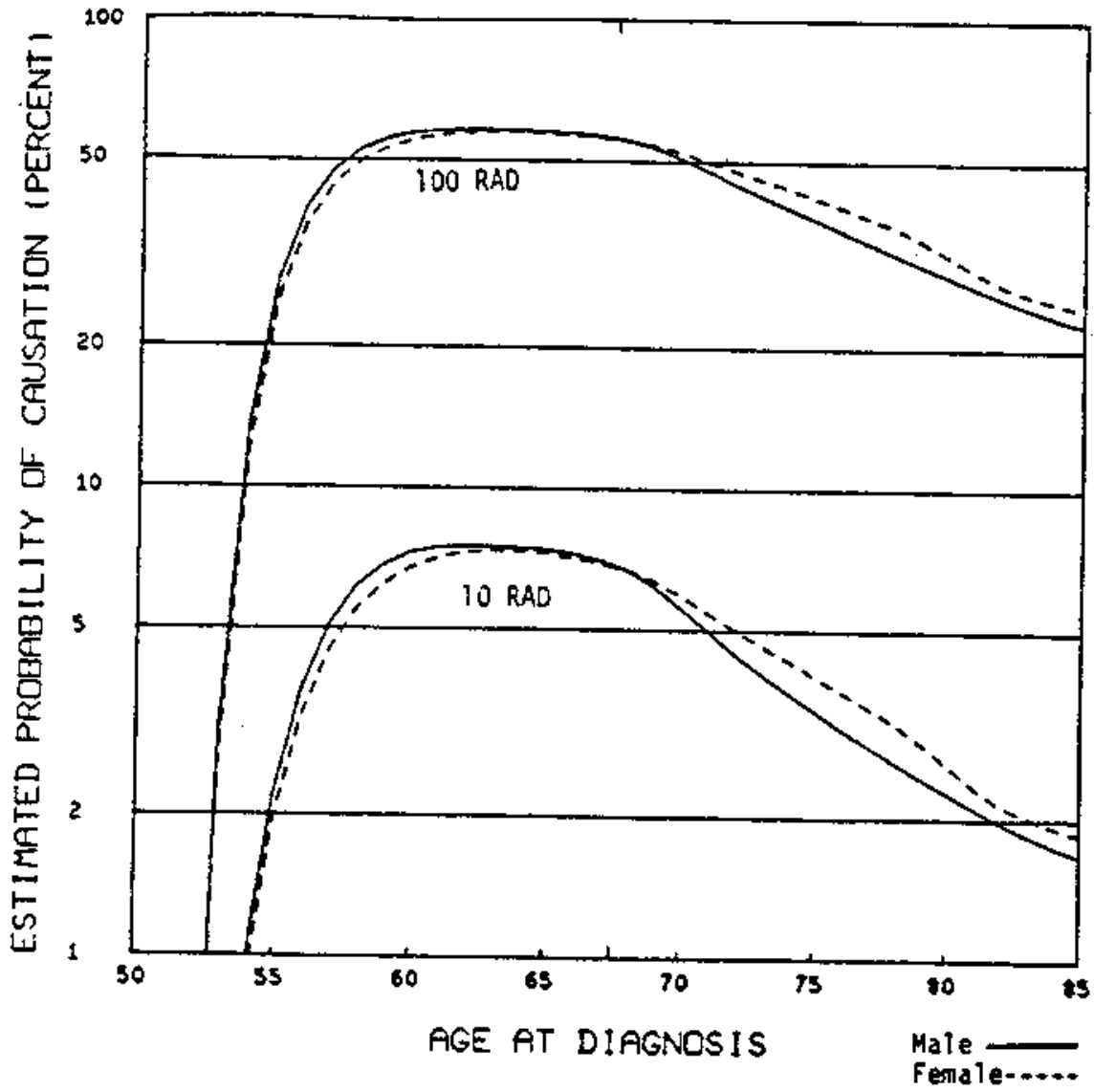
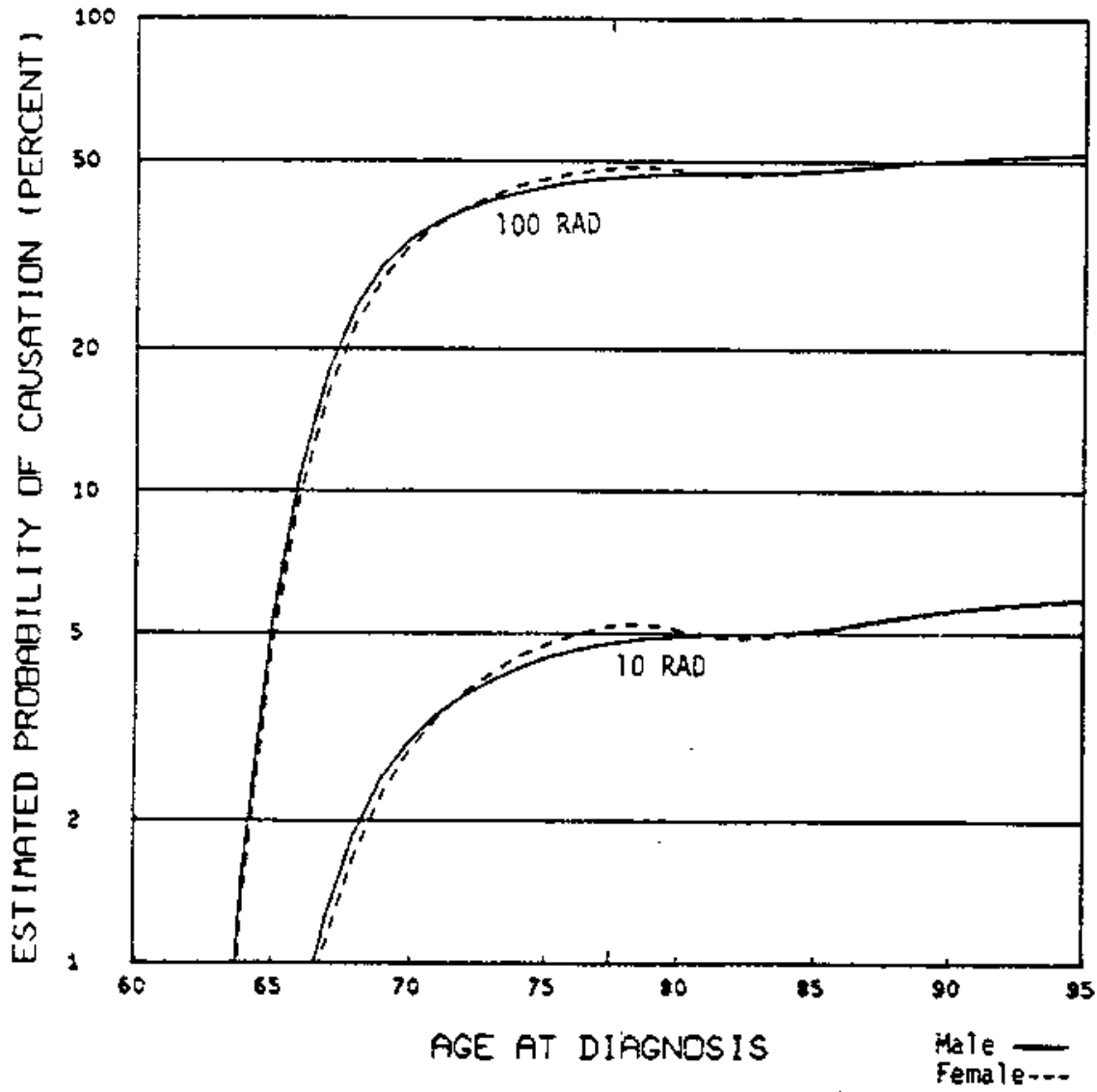


Fig X-1-B-7

ACUTE LEUKEMIA
EXPOSURE AGE 60



ACUTE LEUKEMIA
EXPOSURE AGE 70

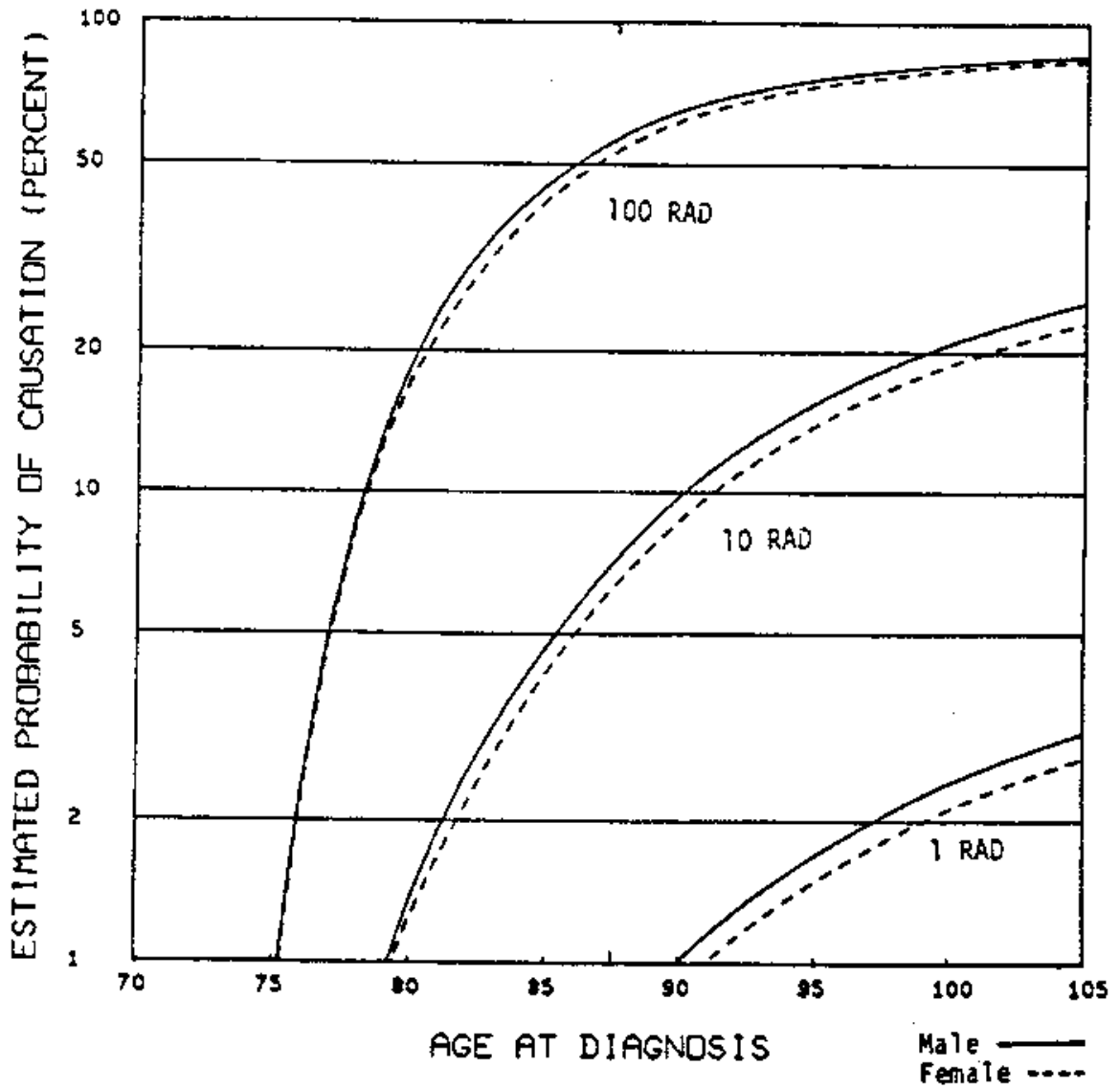


Fig X-1-C-1

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 0

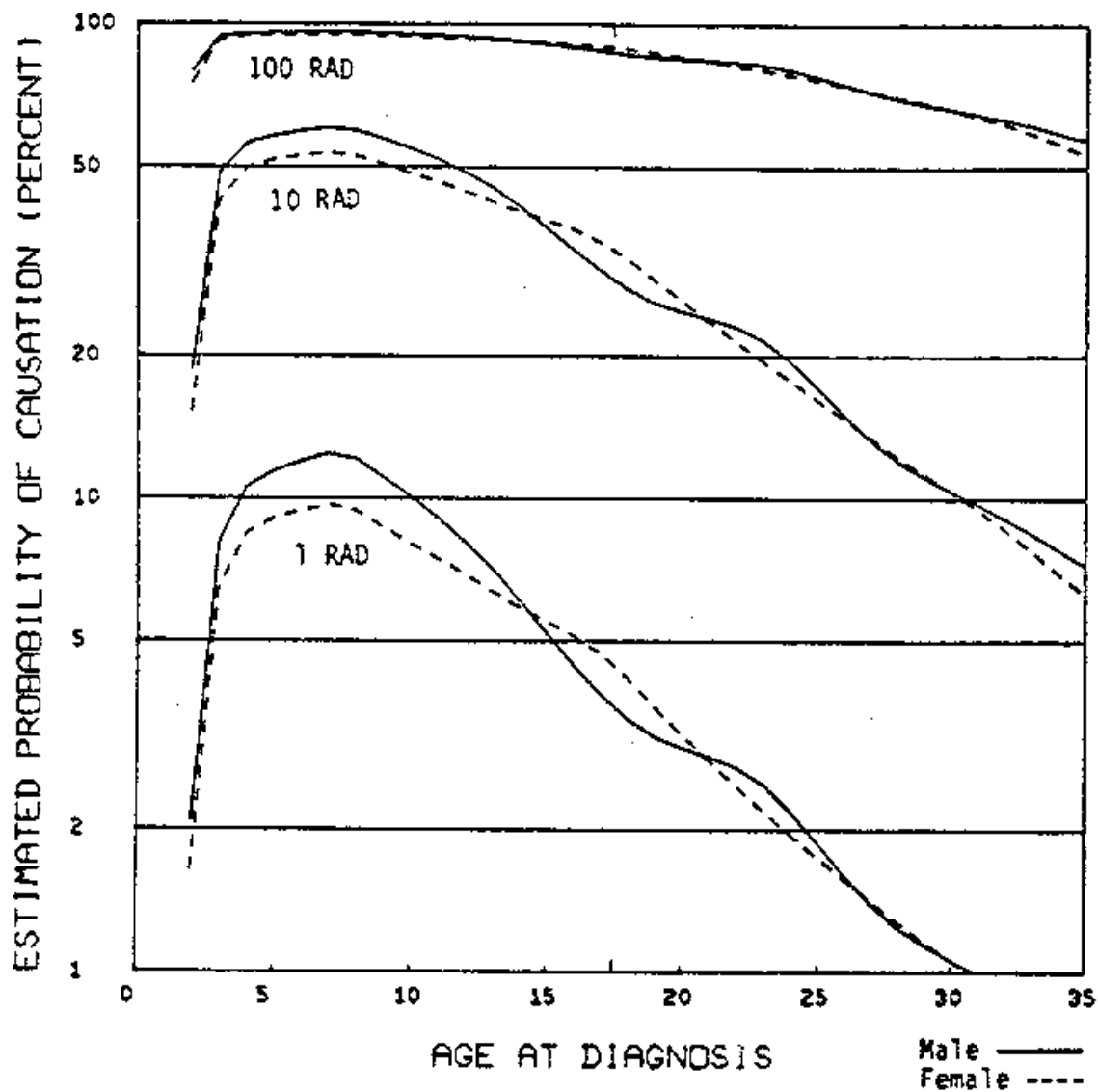


Fig X-1-C-2

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 10

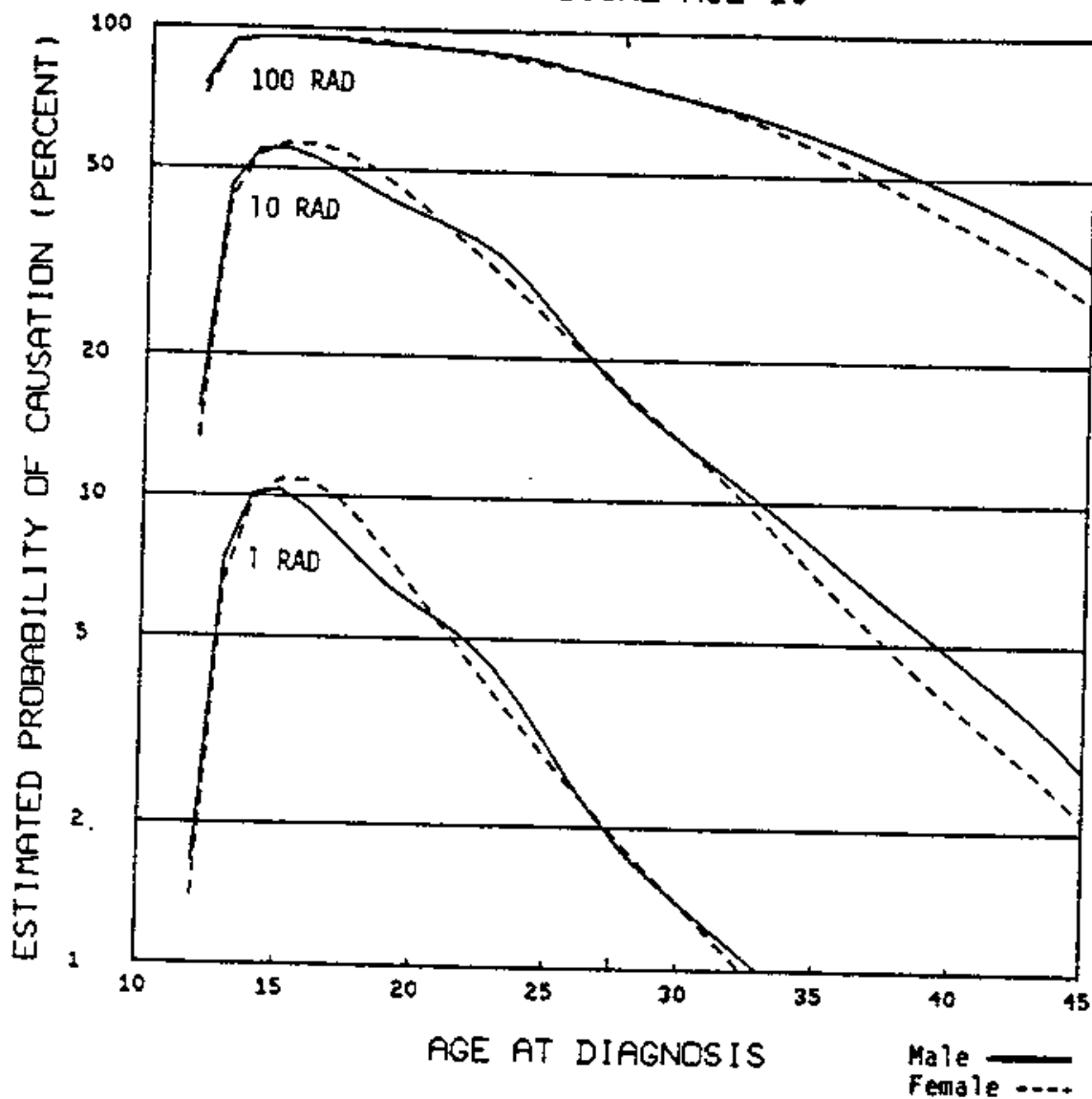
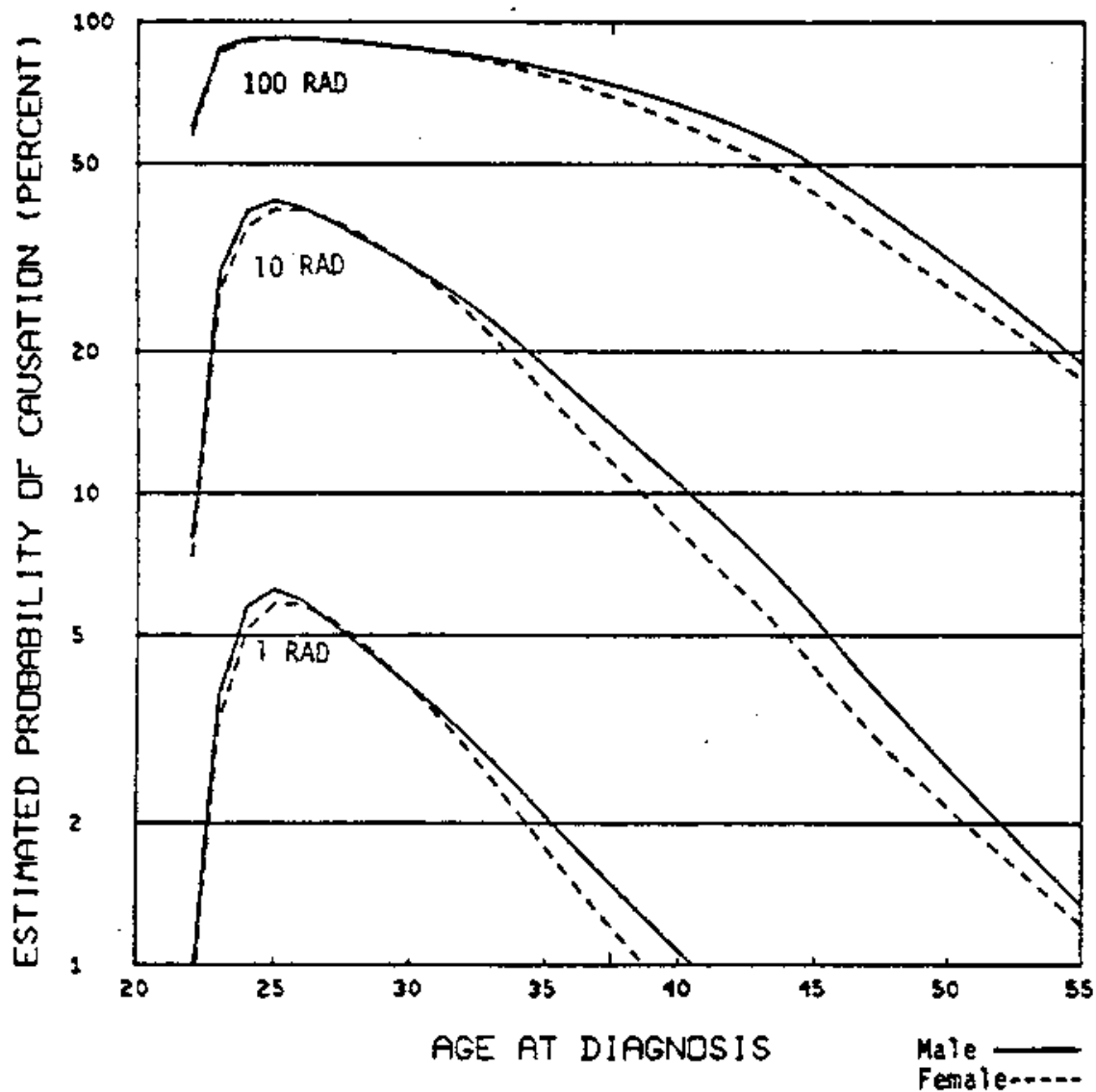


Fig X-1-C-3

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 20



LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 30

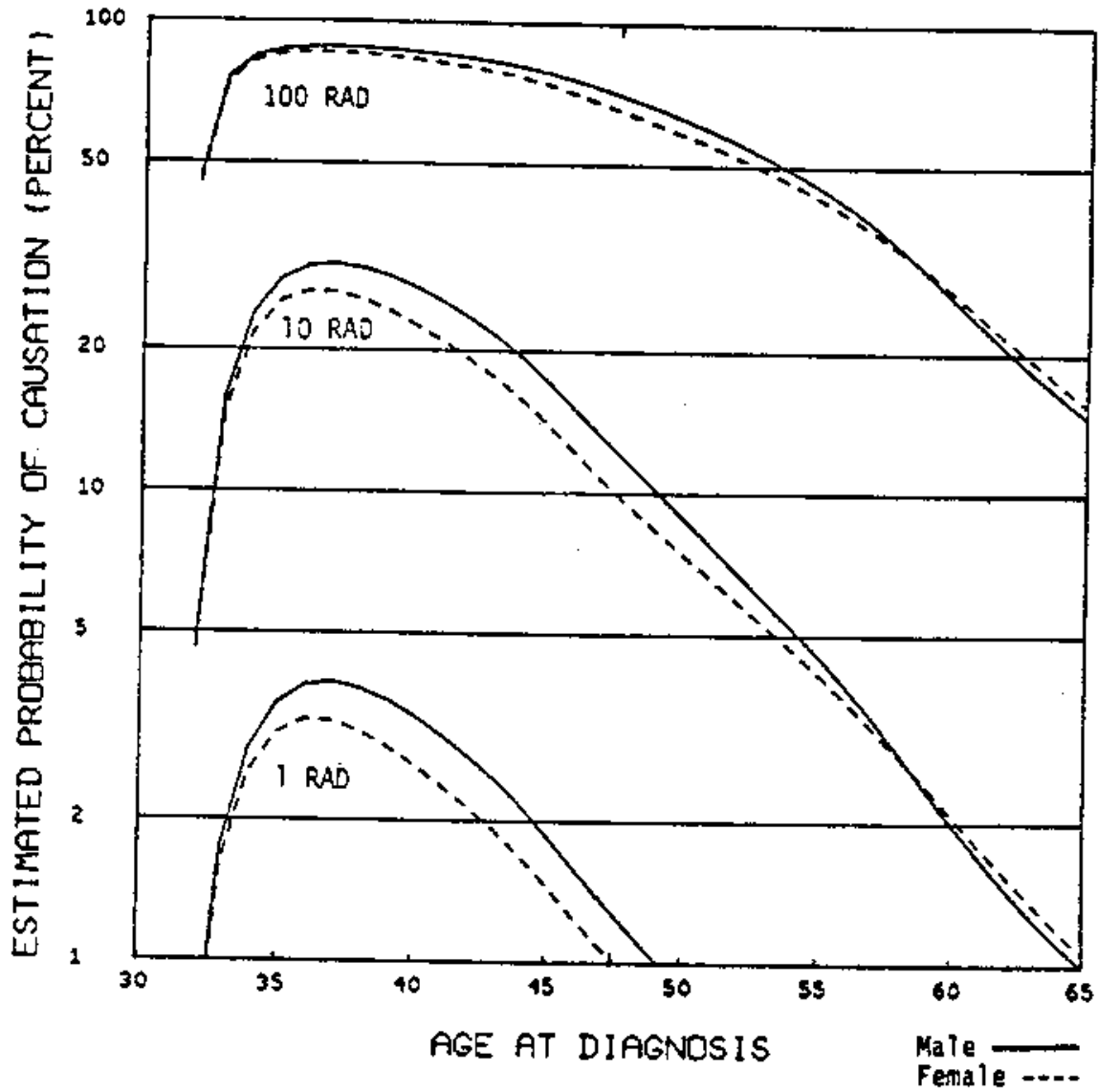


Fig X-1-C-5

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 40

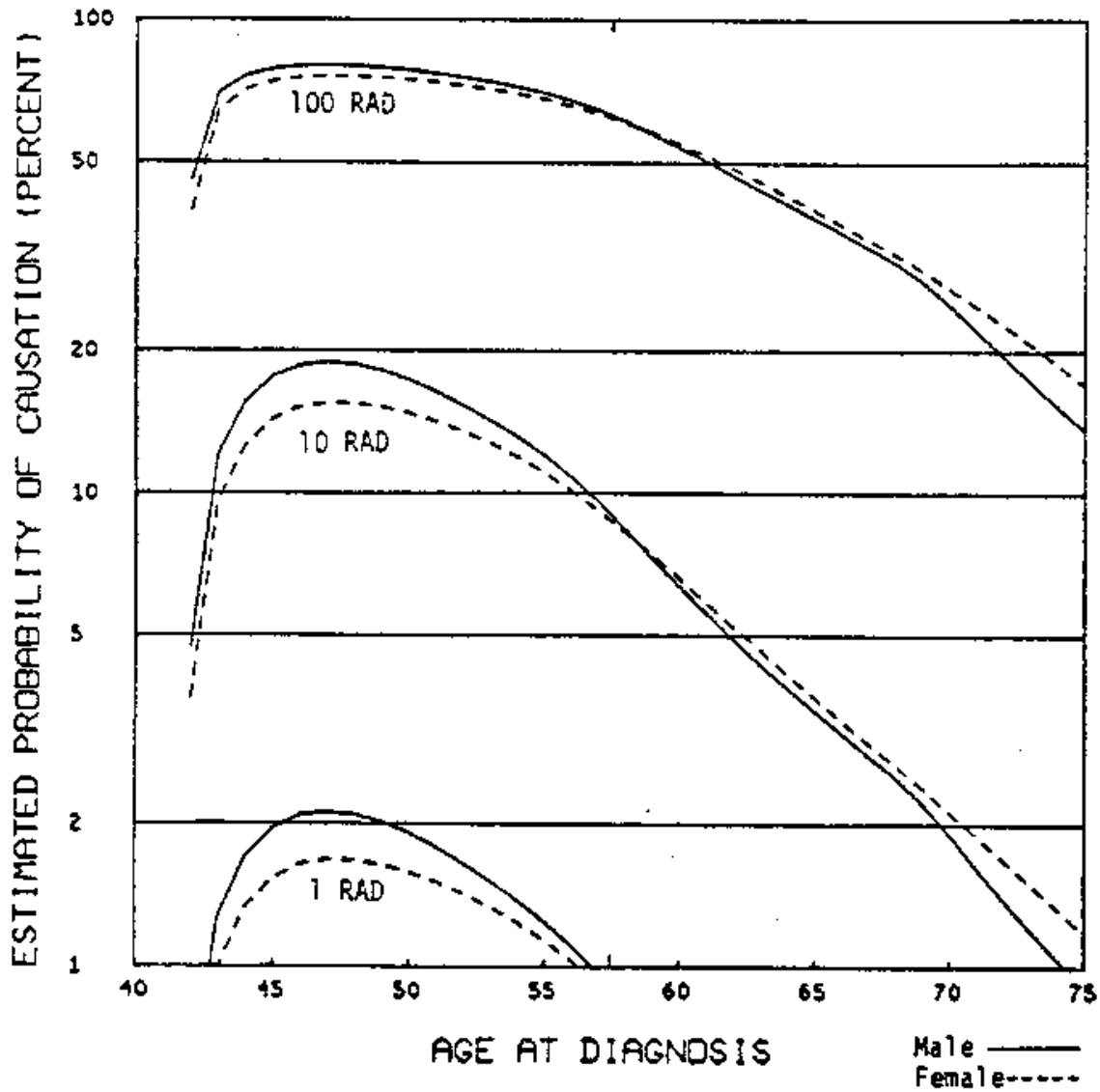
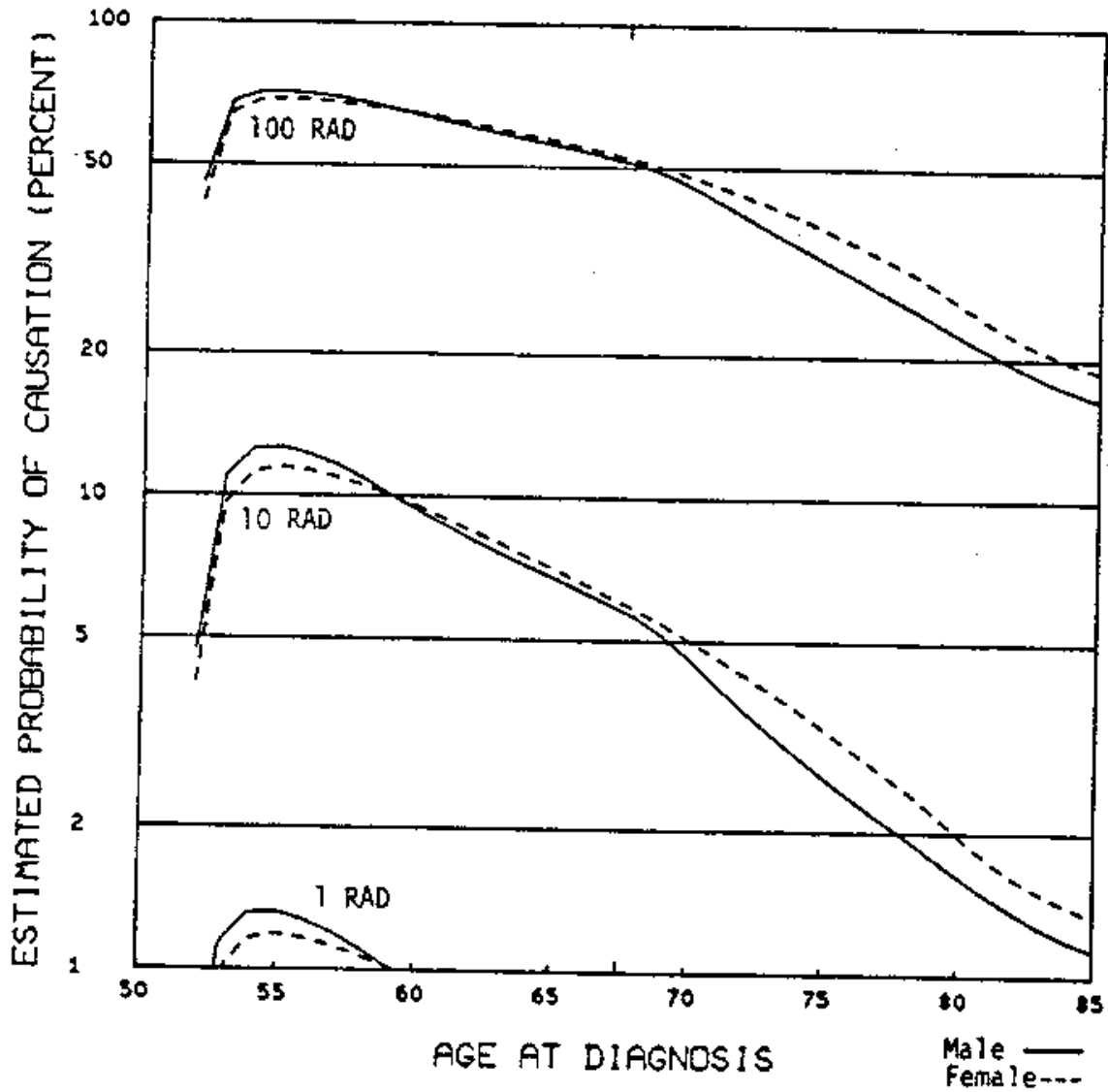


Fig X-1-C-6

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 50



LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 60

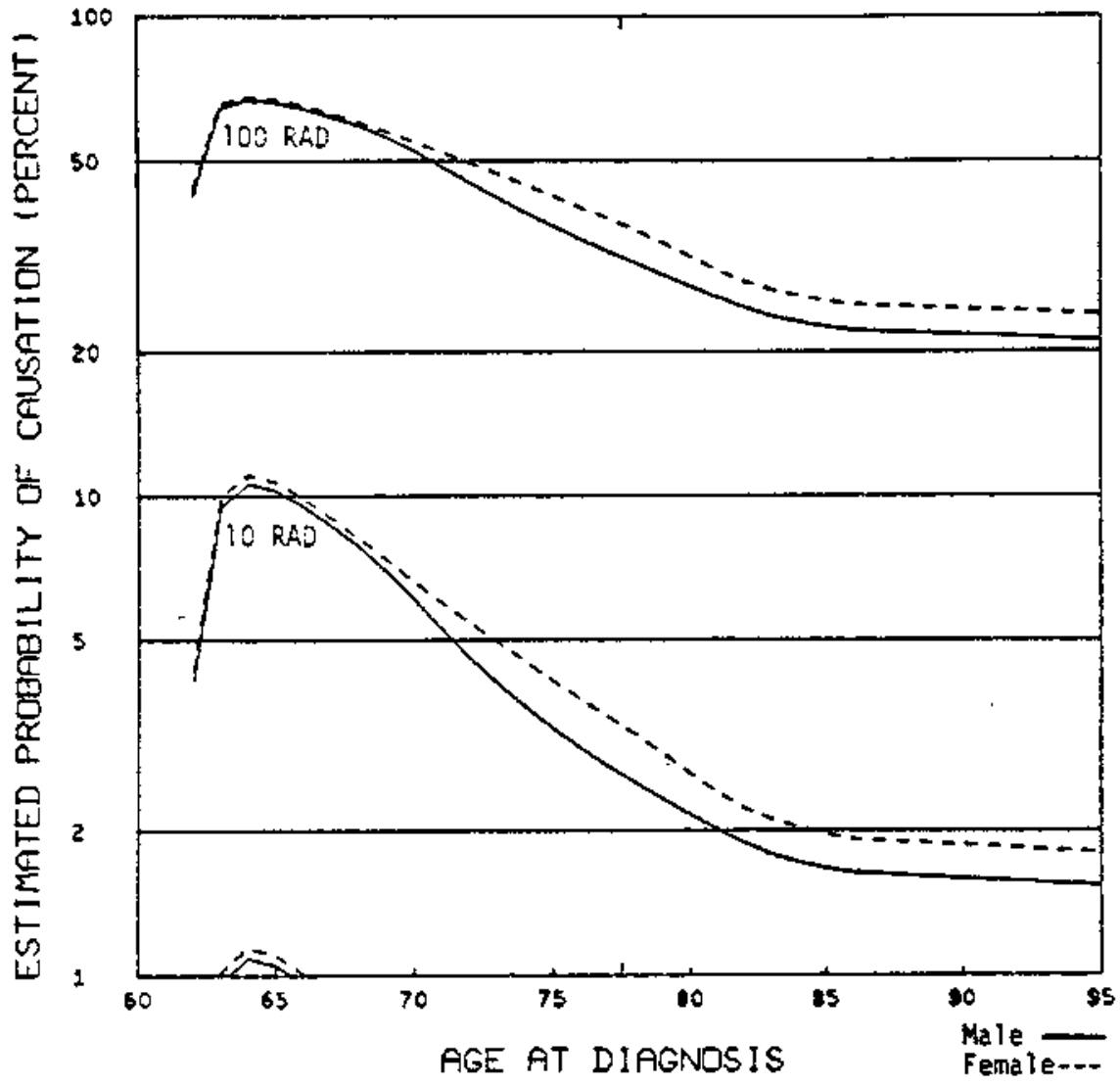


Fig X-1-C-8

LEUKEMIA: ALL TYPES EXCEPT CLL
EXPOSURE AGE 70

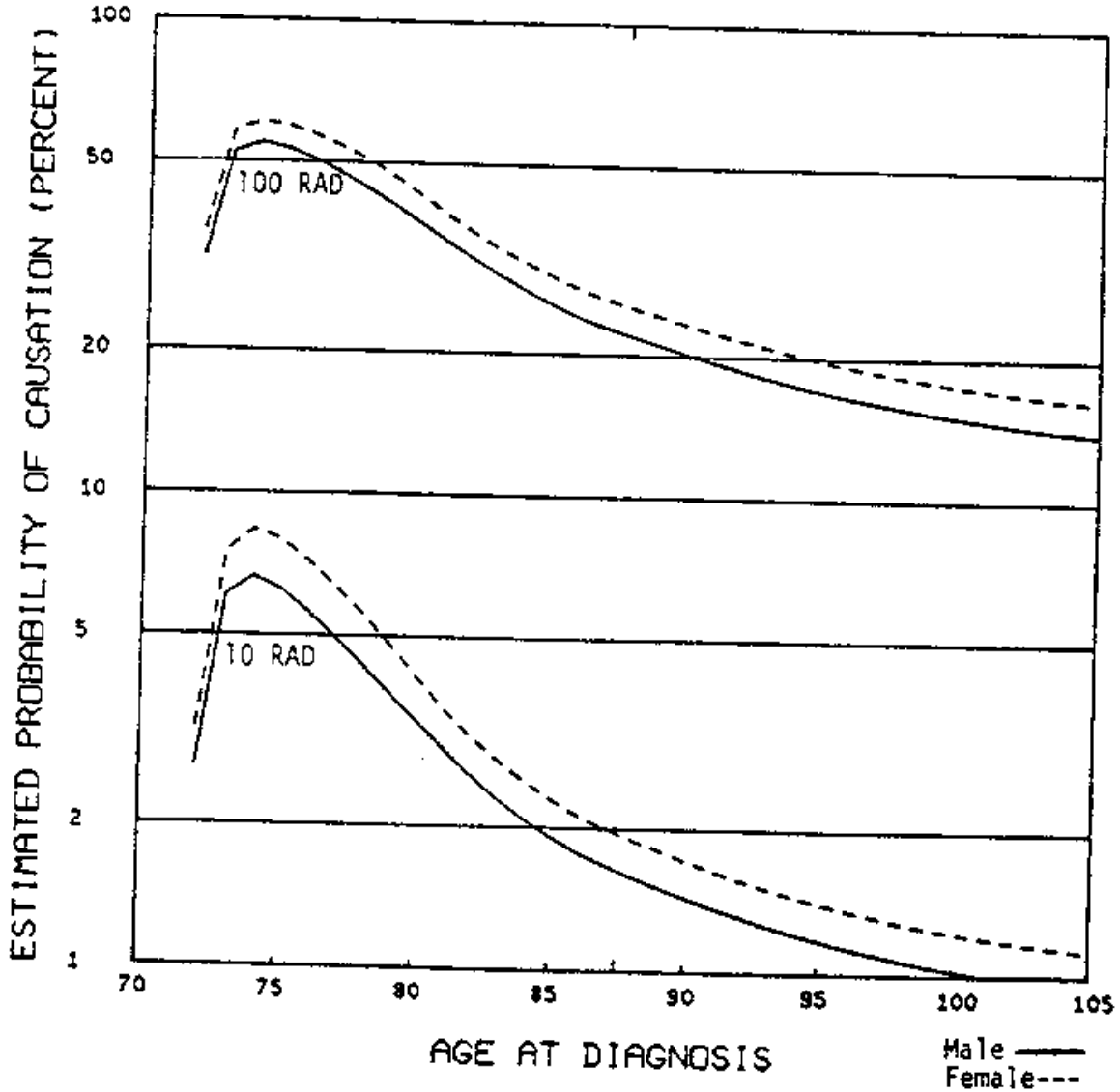


Table X-1-A. Chronic Granulocytic Leukemia:
 Temporal Distribution T(Y) by Year Y
 After Exposure

Y	T(Y)	Y	T(Y)
0	0	25	.0128
1	0	26	.0121
2	.0146	27	.0115
3	.0384	28	.0109
4	.0461	29	.0103
5	.0472	30	.00982
6	.0456	31	.00934
7	.0431	32	.00889
8	.0402	33	.00847
9	.0374	34	.00808
10	.0347	35	.00771
11	.0322	36	.00736
12	.0298	37	.00704
13	.0277	38	.00673
14	.0258	39	.00644
15	.0240	40	.00617
16	.0224	41	.00592
17	.0209	42	.00568
18	.0196	43	.00545
19	.0184	44	.00523
20	.0172	45	.00503
21	.0162	46	.00483
22	.0152	47	.00465
23	.0144	48	.00447
24	.0136	49	.00431

Table X-1-B. Chronic Granulocytic Leukemia: Risk Coefficient $E(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	2.78	1.77	38	1.15	.742
1	2.63	1.67	39	1.17	.754
2	2.47	1.57	40	1.19	.767
3	2.31	1.47	41	1.21	.781
4	2.15	1.37	42	1.23	.795
5	1.99	1.27	43	1.25	.811
6	1.84	1.17	44	1.27	.827
7	1.69	1.08	45	1.30	.844
8	1.55	.992	46	1.32	.861
9	1.43	.911	47	1.35	.879
10	1.31	.838	48	1.38	.897
11	1.21	.775	49	1.41	.915
12	1.13	.723	50	1.43	.934
13	1.07	.684	51	1.46	.953
14	1.03	.659	52	1.49	.972
15	1.01	.647	53	1.52	.991
16	1.00	.638	54	1.55	1.01
17	.990	.631	55	1.58	1.03
18	.981	.626	56	1.61	1.05
19	.975	.622	57	1.64	1.07
20	.972	.619	58	1.67	1.09
21	.970	.618	59	1.70	1.11
22	.971	.619	60	1.73	1.12
23	.974	.621	61	1.76	1.14
24	.980	.625	62	1.78	1.16
25	.987	.630	63	1.81	1.17
26	.997	.636	64	1.84	1.19
27	1.01	.644	65	1.86	1.20
28	1.02	.653	66	1.89	1.22
29	1.03	.661	67	1.91	1.23
30	1.05	.669	68	1.94	1.25
31	1.06	.677	69	1.96	1.26
32	1.07	.685	70	1.98	1.27
33	1.08	.694	71	2.01	1.28
34	1.09	.702	72	2.03	1.29
35	1.11	.711	73	2.05	1.30
36	1.12	.721	74	2.07	1.31
37	1.13	.731	75	2.10	1.32

Table X-1-C. Chronic Granulocytic Leukemia: Baseline Incidence $I(A_2, S)$ by Age at Diagnosis A_2 and Sex S

A_2	Sex		A_2	Sex	
	Male	Female		Male	Female
0	.100	.0500	43	1.12	1.01
1	.100	.0500	44	1.14	.949
2	.100	.0500	45	1.16	.918
3	.100	.0542	46	1.18	.885
4	.100	.0645	47	1.20	.900
5	.100	.0777	48	1.26	.983
6	.100	.0906	49	1.37	1.11
7	.100	.100	50	1.53	1.26
8	.100	.103	51	1.71	1.40
9	.100	.102	52	1.90	1.50
10	.100	.0984	53	2.10	1.57
11	.100	.0968	54	2.31	1.62
12	.100	.100	55	2.53	1.67
13	.106	.113	56	2.76	1.73
14	.123	.134	57	3.01	1.80
15	.147	.158	58	3.28	1.90
16	.174	.182	59	3.56	2.01
17	.200	.200	60	3.85	2.13
18	.229	.202	61	4.14	2.26
19	.265	.190	62	4.41	2.40
20	.307	.178	63	4.66	2.57
21	.352	.177	64	4.87	2.78
22	.400	.200	65	5.08	3.00
23	.477	.240	66	5.29	3.21
24	.592	.280	67	5.52	3.41
25	.719	.320	68	5.82	3.47
26	.831	.360	69	6.21	3.39
27	.900	.400	70	6.67	3.30
28	.910	.440	71	7.19	3.31
29	.878	.480	72	7.77	3.52
30	.832	.520	73	8.48	3.91
31	.797	.560	74	9.34	4.37
32	.800	.600	75	10.3	4.87
33	.838	.640	76	11.3	5.41
34	.884	.680	77	12.4	5.95
35	.931	.720	78	13.8	6.51
36	.972	.760	79	15.7	7.10
37	1.00	.800	80	17.4	7.68
38	1.02	.840	81	18.6	8.25
39	1.04	.880	82	19.0	8.78
40	1.06	.920	83	19.0	9.28
41	1.08	.960	84	19.0	9.74
42	1.10	1.00	85	19.0	10.1

Table X-1-B. Acute Leukemia: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

Y	A ₁									
	0	1	2	3	4	5	6	7	8	9
1	0	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0	0
3	0.0229	0.0219	0.0208	0.0198	0.187	0.176	0.165	0.153	0.144	0
4	0.105	0.102	0.098	0.0954	0.0922	0.0898	0.0873	0.0847	0.0822	0.0788
5	0.134	0.133	0.131	0.129	0.127	0.125	0.122	0.119	0.117	0.115
6	0.169	0.168	0.167	0.166	0.165	0.164	0.163	0.162	0.161	0.16
7	0.205	0.204	0.203	0.202	0.201	0.200	0.199	0.198	0.197	0.196
8	0.243	0.242	0.241	0.240	0.239	0.238	0.237	0.236	0.235	0.234
9	0.283	0.282	0.281	0.280	0.279	0.278	0.277	0.276	0.275	0.274
10	0.328	0.327	0.326	0.325	0.324	0.323	0.322	0.321	0.320	0.319
11	0.380	0.379	0.378	0.377	0.376	0.375	0.374	0.373	0.372	0.371
12	0.439	0.438	0.437	0.436	0.435	0.434	0.433	0.432	0.431	0.430
13	0.505	0.504	0.503	0.502	0.501	0.500	0.499	0.498	0.497	0.496
14	0.580	0.579	0.578	0.577	0.576	0.575	0.574	0.573	0.572	0.571
15	0.665	0.664	0.663	0.662	0.661	0.660	0.659	0.658	0.657	0.656
16	0.760	0.759	0.758	0.757	0.756	0.755	0.754	0.753	0.752	0.751
17	0.865	0.864	0.863	0.862	0.861	0.860	0.859	0.858	0.857	0.856
18	0.980	0.979	0.978	0.977	0.976	0.975	0.974	0.973	0.972	0.971
19	1.105	1.104	1.103	1.102	1.101	1.100	1.099	1.098	1.097	1.096
20	1.240	1.239	1.238	1.237	1.236	1.235	1.234	1.233	1.232	1.231
21	1.385	1.384	1.383	1.382	1.381	1.380	1.379	1.378	1.377	1.376
22	1.540	1.539	1.538	1.537	1.536	1.535	1.534	1.533	1.532	1.531
23	1.705	1.704	1.703	1.702	1.701	1.700	1.699	1.698	1.697	1.696
24	1.880	1.879	1.878	1.877	1.876	1.875	1.874	1.873	1.872	1.871
25	2.065	2.064	2.063	2.062	2.061	2.060	2.059	2.058	2.057	2.056
26	2.260	2.259	2.258	2.257	2.256	2.255	2.254	2.253	2.252	2.251
27	2.465	2.464	2.463	2.462	2.461	2.460	2.459	2.458	2.457	2.456
28	2.680	2.679	2.678	2.677	2.676	2.675	2.674	2.673	2.672	2.671
29	2.905	2.904	2.903	2.902	2.901	2.900	2.899	2.898	2.897	2.896
30	3.140	3.139	3.138	3.137	3.136	3.135	3.134	3.133	3.132	3.131
31	3.385	3.384	3.383	3.382	3.381	3.380	3.379	3.378	3.377	3.376
32	3.640	3.639	3.638	3.637	3.636	3.635	3.634	3.633	3.632	3.631
33	3.905	3.904	3.903	3.902	3.901	3.900	3.899	3.898	3.897	3.896
34	4.180	4.179	4.178	4.177	4.176	4.175	4.174	4.173	4.172	4.171
35	4.465	4.464	4.463	4.462	4.461	4.460	4.459	4.458	4.457	4.456
36	4.760	4.759	4.758	4.757	4.756	4.755	4.754	4.753	4.752	4.751
37	5.065	5.064	5.063	5.062	5.061	5.060	5.059	5.058	5.057	5.056
38	5.380	5.379	5.378	5.377	5.376	5.375	5.374	5.373	5.372	5.371
39	5.705	5.704	5.703	5.702	5.701	5.700	5.699	5.698	5.697	5.696
40	6.040	6.039	6.038	6.037	6.036	6.035	6.034	6.033	6.032	6.031
41	6.385	6.384	6.383	6.382	6.381	6.380	6.379	6.378	6.377	6.376
42	6.740	6.739	6.738	6.737	6.736	6.735	6.734	6.733	6.732	6.731
43	7.105	7.104	7.103	7.102	7.101	7.100	7.099	7.098	7.097	7.096
44	7.480	7.479	7.478	7.477	7.476	7.475	7.474	7.473	7.472	7.471
45	7.865	7.864	7.863	7.862	7.861	7.860	7.859	7.858	7.857	7.856
46	8.260	8.259	8.258	8.257	8.256	8.255	8.254	8.253	8.252	8.251
47	8.665	8.664	8.663	8.662	8.661	8.660	8.659	8.658	8.657	8.656
48	9.080	9.079	9.078	9.077	9.076	9.075	9.074	9.073	9.072	9.071
49	9.505	9.504	9.503	9.502	9.501	9.500	9.499	9.498	9.497	9.496
50	9.940	9.939	9.938	9.937	9.936	9.935	9.934	9.933	9.932	9.931
51	10.385	10.384	10.383	10.382	10.381	10.380	10.379	10.378	10.377	10.376
52	10.840	10.839	10.838	10.837	10.836	10.835	10.834	10.833	10.832	10.831
53	11.305	11.304	11.303	11.302	11.301	11.300	11.299	11.298	11.297	11.296
54	11.780	11.779	11.778	11.777	11.776	11.775	11.774	11.773	11.772	11.771
55	12.265	12.264	12.263	12.262	12.261	12.260	12.259	12.258	12.257	12.256
56	12.760	12.759	12.758	12.757	12.756	12.755	12.754	12.753	12.752	12.751
57	13.265	13.264	13.263	13.262	13.261	13.260	13.259	13.258	13.257	13.256
58	13.780	13.779	13.778	13.777	13.776	13.775	13.774	13.773	13.772	13.771
59	14.305	14.304	14.303	14.302	14.301	14.300	14.299	14.298	14.297	14.296
60	14.840	14.839	14.838	14.837	14.836	14.835	14.834	14.833	14.832	14.831
61	15.385	15.384	15.383	15.382	15.381	15.380	15.379	15.378	15.377	15.376
62	15.940	15.939	15.938	15.937	15.936	15.935	15.934	15.933	15.932	15.931
63	16.505	16.504	16.503	16.502	16.501	16.500	16.499	16.498	16.497	16.496
64	17.080	17.079	17.078	17.077	17.076	17.075	17.074	17.073	17.072	17.071
65	17.665	17.664	17.663	17.662	17.661	17.660	17.659	17.658	17.657	17.656
66	18.260	18.259	18.258	18.257	18.256	18.255	18.254	18.253	18.252	18.251
67	18.865	18.864	18.863	18.862	18.861	18.860	18.859	18.858	18.857	18.856
68	19.480	19.479	19.478	19.477	19.476	19.475	19.474	19.473	19.472	19.471
69	20.105	20.104	20.103	20.102	20.101	20.100	20.099	20.098	20.097	20.096
70	20.740	20.739	20.738	20.737	20.736	20.735	20.734	20.733	20.732	20.731
71	21.385	21.384	21.383	21.382	21.381	21.380	21.379	21.378	21.377	21.376
72	22.040	22.039	22.038	22.037	22.036	22.035	22.034	22.033	22.032	22.031
73	22.705	22.704	22.703	22.702	22.701	22.700	22.699	22.698	22.697	22.696
74	23.380	23.379	23.378	23.377	23.376	23.375	23.374	23.373	23.372	23.371
75	24.065	24.064	24.063	24.062	24.061	24.060	24.059	24.058	24.057	24.056
76	24.760	24.759	24.758	24.757	24.756	24.755	24.754	24.753	24.752	24.751
77	25.465	25.464	25.463	25.462	25.461	25.460	25.459	25.458	25.457	25.456
78	26.180	26.179	26.178	26.177	26.176	26.175	26.174	26.173	26.172	26.171
79	26.905	26.904	26.903	26.902	26.901	26.900	26.899	26.898	26.897	26.896
80	27.640	27.639	27.638	27.637	27.636	27.635	27.634	27.633	27.632	27.631
81	28.385	28.384	28.383	28.382	28.381	28.380	28.379	28.378	28.377	28.376
82	29.140	29.139	29.138	29.137	29.136	29.135	29.134	29.133	29.132	29.131
83	29.905	29.904	29.903	29.902	29.901	29.900	29.899	29.898	29.897	29.896
84	30.680	30.679	30.678	30.677	30.676	30.675	30.674	30.673	30.672	30.671
85	31.465	31.464	31.463	31.462	31.461	31.460	31.459	31.458	31.457	31.456
86	32.260	32.259	32.258	32.257	32.256	32.255	32.254	32.253	32.252	32.251
87	33.065	33.064	33.063	33.062	33.061	33.060	33.059	33.058	33.057	33.056
88	33.880	33.879	33.878	33.877	33.876	33.875	33.874	33.873	33.872	33.871
89	34.705	34.704	34.703	34.702	34.701	34.700	34.699	34.698	34.697	34.696
90	35.540	35.539	35.538	35.537	35.536	35.535	35.534	35.533	35.532	35.531
91	36.385	36.384	36.383	36.382	36.381	36.380	36.379	36.378	36.377	36.376
92	37.240	37.239	37.238	37.237	37.236	37.235	37.234	37.233	37.232	37.231
93	38.105	38.104	38.103	38.102	38.101	38.100	38.099	38.098	38.097	38.096
94	38.980	38.979	38.978	38.977	38.976	38.975	38.974	38.973	38.972	38.971
95	39.865	39.864	39.863	39.862	39.861	39.860	39.859	39.858	39.857	39.856
96	40.760	40.759	40.758	40.757	40.756	40.755	40.754	40.753	40.752	40.751
97	41.665	41.664	41.663	41.662	41.661	41.660	41.659	41.658	41.657	41.656
98	42.580	42.579	42.578	42.577	42.576	42.575	42.574	42.573	42.572	42.571
99	43.505	43.504	43.503	43.502	43.501	43.500	43.499	43.498	43.497	43.496
100	44.440	44.439	44.438	44.437	44.436	44.435	44.434	44.433	44.432	44.431

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $f(A, Y)$ by Year Y After Exposure at Age A_1

Y	9	10	11	12	13	14	15	16	17
1	0	0	0	0	0	0	0	0	0
2	0.134	0.124	0.114	0.103	0.0955	0.0888	0.0786	0.0708	0.0634
3	0.743	0.706	0.669	0.631	0.594	0.557	0.520	0.484	0.449
4	1.69	1.61	1.53	1.45	1.37	1.29	1.21	1.13	1.05
5	3.13	3.04	2.96	2.88	2.80	2.72	2.64	2.56	2.48
6	4.63	4.52	4.41	4.31	4.21	4.11	4.01	3.91	3.81
7	6.19	6.07	5.95	5.83	5.71	5.59	5.47	5.35	5.23
8	7.82	7.69	7.56	7.43	7.30	7.17	7.04	6.91	6.78
9	9.53	9.39	9.25	9.11	8.97	8.83	8.69	8.55	8.41
10	11.32	11.17	11.02	10.87	10.72	10.57	10.42	10.27	10.12
11	13.19	13.03	12.87	12.71	12.55	12.39	12.23	12.07	11.91
12	15.14	14.97	14.80	14.63	14.46	14.29	14.12	13.95	13.78
13	17.17	16.99	16.81	16.63	16.45	16.27	16.09	15.91	15.73
14	19.28	19.09	18.90	18.71	18.52	18.33	18.14	17.95	17.76
15	21.47	21.27	21.07	20.87	20.67	20.47	20.27	20.07	19.87
16	23.74	23.53	23.32	23.11	22.90	22.69	22.48	22.27	22.06
17	26.09	25.87	25.65	25.43	25.21	24.99	24.77	24.55	24.33
18	28.52	28.29	28.06	27.83	27.60	27.37	27.14	26.91	26.68
19	31.03	30.79	30.54	30.29	30.04	29.79	29.54	29.29	29.04
20	33.62	33.37	33.11	32.85	32.59	32.33	32.07	31.81	31.55
21	36.29	35.93	35.56	35.20	34.83	34.46	34.09	33.72	33.35
22	39.04	38.57	38.09	37.71	37.32	36.93	36.54	36.15	35.76
23	41.87	41.29	40.70	40.31	39.91	39.51	39.11	38.71	38.31
24	44.78	44.09	43.49	43.09	42.68	42.27	41.86	41.45	41.04
25	47.77	46.97	46.16	45.75	45.33	44.91	44.49	44.07	43.65
26	50.84	49.93	49.01	48.59	48.16	47.73	47.30	46.87	46.44
27	53.98	52.96	51.93	51.50	51.06	50.62	50.18	49.74	49.30
28	57.19	56.06	54.92	54.48	54.03	53.58	53.13	52.68	52.23
29	60.47	59.23	58.08	57.63	57.17	56.71	56.25	55.79	55.33
30	63.82	62.47	61.21	60.75	60.28	59.81	59.34	58.87	58.40
31	67.24	65.78	64.51	64.04	63.56	63.08	62.60	62.12	61.64
32	70.73	69.16	67.88	67.40	66.91	66.42	65.93	65.44	64.95
33	74.29	72.61	71.32	70.83	70.33	69.83	69.33	68.83	68.33
34	77.92	76.13	74.83	74.33	73.82	73.31	72.80	72.29	71.78
35	81.61	79.71	78.40	77.89	77.37	76.85	76.33	75.81	75.29
36	85.36	83.35	82.03	81.51	80.98	80.45	79.92	79.39	78.86
37	89.17	87.05	85.72	85.19	84.65	84.11	83.57	83.03	82.49
38	93.04	90.81	89.47	88.93	88.38	87.83	87.28	86.73	86.18
39	96.97	94.63	93.28	92.73	92.17	91.61	91.05	90.49	89.93
40	100.96	98.51	97.15	96.59	96.02	95.45	94.88	94.31	93.74
41	105.01	102.45	101.08	100.51	99.93	99.35	98.77	98.19	97.61
42	109.12	106.45	105.07	104.49	103.90	103.31	102.72	102.13	101.54
43	113.29	110.51	109.12	108.53	107.93	107.33	106.73	106.13	105.53
44	117.52	114.63	113.23	112.63	112.02	111.41	110.80	110.19	109.58
45	121.81	118.81	117.40	116.79	116.17	115.55	114.93	114.31	113.69
46	126.16	123.05	121.63	121.01	120.38	119.75	119.12	118.49	117.86
47	130.57	127.35	125.92	125.29	124.65	124.01	123.37	122.72	122.08
48	135.04	131.71	130.27	129.63	128.98	128.33	127.68	127.03	126.38
49	139.57	136.13	134.68	134.03	133.37	132.71	132.05	131.39	130.73

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_i, Y)$ by Year Y After Exposure at Age A_1

Y	18	19	20	21	22	23	24	25	26
1	.00344	.00382	.00443	.00589	.00848	.01295	.02058	.03219	.05107
2	.04195	.05282	.07150	.10119	.13919	.19262	.26910	.37452	.51388
3	.07338	.09496	.12899	.18161	.24973	.34485	.48446	.67607	.92688
4	.08878	.11835	.16227	.22789	.32474	.46933	.66878	.93885	1.29442
5	.08223	.11600	.16528	.23874	.34818	.50093	.70400	.98453	1.36680
6	.07444	.10737	.15288	.22651	.33846	.49039	.68330	.95620	1.33493
7	.06680	.09658	.13822	.20881	.31686	.46879	.66200	.91571	1.26565
8	.05784	.08309	.12073	.18517	.28519	.42152	.59201	.81520	1.11818
9	.04804	.06845	.10019	.15081	.23214	.34685	.50521	.71240	.98518
10	.03844	.05496	.08150	.11819	.18019	.27262	.39910	.56452	.78388
11	.03078	.04496	.06899	.10161	.15073	.22485	.33446	.48607	.68688
12	.02444	.03600	.05428	.08074	.11818	.17693	.26400	.38453	.54493
13	.01944	.02896	.04388	.06651	.09814	.14685	.21921	.32520	.47118
14	.01538	.02335	.03527	.05289	.07974	.11893	.17646	.26385	.38288
15	.01228	.01929	.02880	.04312	.06523	.09819	.14646	.21921	.32520
16	.00984	.01527	.02288	.03523	.05281	.07973	.11892	.17646	.26385
17	.00784	.01200	.01835	.02819	.04314	.06522	.09818	.14646	.21921
18	.00624	.00977	.01488	.02281	.03522	.05280	.07972	.11891	.17645
19	.00504	.00758	.01149	.01819	.02813	.04311	.06520	.09817	.14644
20	.00414	.00615	.00916	.01469	.02274	.03519	.05279	.07971	.11890
21	.00344	.00512	.00744	.01116	.01714	.02619	.03921	.05620	.08318
22	.00284	.00422	.00616	.00936	.01414	.02119	.03121	.04520	.06618
23	.00234	.00348	.00516	.00774	.01174	.01719	.02521	.03620	.05218
24	.00194	.00288	.00436	.00674	.01014	.01519	.02221	.03220	.04618
25	.00164	.00248	.00376	.00574	.00814	.01219	.01821	.02620	.03818
26	.00144	.00216	.00324	.00494	.00714	.01019	.01521	.02220	.03218
27	.00124	.00188	.00276	.00414	.00594	.00819	.01221	.01820	.02618
28	.00104	.00168	.00246	.00364	.00524	.00719	.01021	.01520	.02218
29	.00084	.00136	.00204	.00304	.00444	.00619	.00821	.01220	.01818
30	.00064	.00108	.00166	.00246	.00364	.00519	.00721	.01020	.01518
31	.00044	.00072	.00114	.00184	.00284	.00419	.00571	.00820	.01218
32	.00034	.00052	.00076	.00124	.00194	.00294	.00421	.00570	.00818
33	.00024	.00036	.00054	.00084	.00134	.00204	.00304	.00420	.00568
34	.00014	.00024	.00036	.00054	.00084	.00124	.00184	.00264	.00372
35	.00008	.00012	.00018	.00028	.00044	.00064	.00094	.00134	.00192
36	.00004	.00006	.00009	.00014	.00022	.00034	.00048	.00068	.00098
37	.00002	.00003	.00004	.00006	.00010	.00016	.00024	.00034	.00048
38	.00001	.00002	.00003	.00004	.00006	.00009	.00014	.00020	.00028
39	.00000	.00001	.00001	.00002	.00003	.00004	.00006	.00009	.00012
40	.00000	.00000	.00000	.00001	.00001	.00002	.00003	.00004	.00006
41	.00000	.00000	.00000	.00000	.00000	.00001	.00001	.00002	.00003
42	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00001	.00001
43	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
44	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
45	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
46	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
47	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
48	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000
49	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000	.00000

Table X-1-0 (Continued). Acute Leukemia: Temporal Distribution T(A₁, Y) by Year Y After Exposure at Age A₁

Y	27	28	29	30	31	32	33	34	35
1	.00158	.00133	.00111	.000925	.000743	.000625	.000508	.000409	.003277
2	.0167	.0147	.0128	.0112	.00960	.00833	.00711	.00604	.00504
3	.0376	.0345	.0310	.0279	.0249	.0222	.0198	.0172	.0150
4	.0529	.0491	.0454	.0417	.0381	.0347	.0314	.0282	.0253
5	.0608	.0573	.0538	.0503	.0468	.0433	.0399	.0366	.0334
6	.0632	.0604	.0575	.0545	.0514	.0483	.0452	.0420	.0389
7	.0624	.0602	.0580	.0556	.0531	.0504	.0477	.0450	.0421
8	.0595	.0580	.0564	.0544	.0524	.0504	.0483	.0460	.0436
9	.0557	.0547	.0536	.0524	.0509	.0496	.0474	.0458	.0438
10	.0514	.0507	.0503	.0495	.0485	.0474	.0461	.0447	.0431
11	.0474	.0469	.0467	.0462	.0456	.0449	.0440	.0430	.0418
12	.0439	.0436	.0436	.0429	.0426	.0422	.0416	.0407	.0400
13	.0400	.0399	.0395	.0394	.0394	.0394	.0391	.0387	.0381
14	.0360	.0358	.0356	.0354	.0354	.0354	.0354	.0354	.0354
15	.0329	.0328	.0328	.0328	.0328	.0328	.0328	.0328	.0328
16	.0299	.0299	.0299	.0299	.0299	.0299	.0299	.0299	.0299
17	.0269	.0269	.0269	.0269	.0269	.0269	.0269	.0269	.0269
18	.0234	.0234	.0234	.0234	.0234	.0234	.0234	.0234	.0234
19	.0204	.0204	.0204	.0204	.0204	.0204	.0204	.0204	.0204
20	.0174	.0174	.0174	.0174	.0174	.0174	.0174	.0174	.0174
21	.0144	.0144	.0144	.0144	.0144	.0144	.0144	.0144	.0144
22	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114
23	.0084	.0084	.0084	.0084	.0084	.0084	.0084	.0084	.0084
24	.0054	.0054	.0054	.0054	.0054	.0054	.0054	.0054	.0054
25	.0024	.0024	.0024	.0024	.0024	.0024	.0024	.0024	.0024
26	.0019	.0019	.0019	.0019	.0019	.0019	.0019	.0019	.0019
27	.0016	.0016	.0016	.0016	.0016	.0016	.0016	.0016	.0016
28	.0013	.0013	.0013	.0013	.0013	.0013	.0013	.0013	.0013
29	.0010	.0010	.0010	.0010	.0010	.0010	.0010	.0010	.0010
30	.0007	.0007	.0007	.0007	.0007	.0007	.0007	.0007	.0007
31	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
32	.0002	.0002	.0002	.0002	.0002	.0002	.0002	.0002	.0002
33	.0001	.0001	.0001	.0001	.0001	.0001	.0001	.0001	.0001
34	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
35	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
36	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
37	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
38	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
39	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
40	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
41	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
42	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
43	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
44	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
45	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
46	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
47	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
48	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
49	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution I(A_i, Y) by Year Y After Exposure at Age A_i

Y	36	37	38	39	40	41	42	43	44
1	0	0	0	0	0	0	0	0	0
2	.00260	.00204	.00159	.00123	.000944	.000717	.000539	.000401	.000294
3	.00424	.00354	.00291	.00236	.00193	.00156	.00124	.000928	.000769
4	.0130	.0112	.00957	.00813	.00685	.00572	.00475	.00390	.00318
5	.0224	.0198	.0174	.0152	.0131	.0113	.00962	.00814	.00683
6	.0324	.0272	.0244	.0217	.0192	.0168	.0147	.0127	.0109
7	.0431	.0358	.0294	.0259	.0222	.0186	.0152	.0124	.0101
8	.0541	.0446	.0364	.0308	.0261	.0216	.0172	.0139	.0112
9	.0611	.0504	.0408	.0334	.0281	.0228	.0182	.0144	.0113
10	.0644	.0524	.0418	.0328	.0268	.0212	.0164	.0124	.0094
11	.0644	.0519	.0404	.0314	.0254	.0194	.0144	.0104	.0074
12	.0604	.0474	.0354	.0264	.0204	.0144	.0094	.0064	.0044
13	.0594	.0454	.0324	.0234	.0174	.0114	.0064	.0034	.0014
14	.0574	.0424	.0294	.0204	.0144	.0084	.0034	.0004	.0004
15	.0554	.0394	.0264	.0174	.0114	.0054	.0004	.0004	.0004
16	.0534	.0374	.0244	.0154	.0094	.0034	.0004	.0004	.0004
17	.0514	.0354	.0224	.0134	.0074	.0014	.0004	.0004	.0004
18	.0494	.0334	.0204	.0114	.0054	.0004	.0004	.0004	.0004
19	.0474	.0314	.0184	.0094	.0034	.0004	.0004	.0004	.0004
20	.0454	.0294	.0164	.0074	.0014	.0004	.0004	.0004	.0004
21	.0434	.0274	.0144	.0054	.0004	.0004	.0004	.0004	.0004
22	.0414	.0254	.0124	.0034	.0004	.0004	.0004	.0004	.0004
23	.0394	.0234	.0104	.0014	.0004	.0004	.0004	.0004	.0004
24	.0374	.0214	.0084	.0004	.0004	.0004	.0004	.0004	.0004
25	.0354	.0194	.0064	.0004	.0004	.0004	.0004	.0004	.0004
26	.0334	.0174	.0044	.0004	.0004	.0004	.0004	.0004	.0004
27	.0314	.0154	.0024	.0004	.0004	.0004	.0004	.0004	.0004
28	.0294	.0134	.0004	.0004	.0004	.0004	.0004	.0004	.0004
29	.0274	.0114	.0004	.0004	.0004	.0004	.0004	.0004	.0004
30	.0254	.0094	.0004	.0004	.0004	.0004	.0004	.0004	.0004
31	.0234	.0074	.0004	.0004	.0004	.0004	.0004	.0004	.0004
32	.0214	.0054	.0004	.0004	.0004	.0004	.0004	.0004	.0004
33	.0194	.0034	.0004	.0004	.0004	.0004	.0004	.0004	.0004
34	.0174	.0014	.0004	.0004	.0004	.0004	.0004	.0004	.0004
35	.0154	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
36	.0134	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
37	.0114	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
38	.0094	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
39	.0074	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
40	.0054	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
41	.0034	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
42	.0014	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
43	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
44	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
45	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
46	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
47	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
48	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004
49	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004	.0004

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(A_i, Y)$ by Year Y After Exposure at Age A_i

Y	45	46	47	48	49	50	51	52	53
1	0	0	0	0	0	0	0	0	0
2	.000214	.000156	.000111	.000078	.000054	.000037	.000025	.000017	.000011
3	.000597	.000454	.000349	.000263	.000196	.000145	.000106	.000076	.000054
4	.001277	.000904	.000684	.000511	.000380	.000281	.000208	.000153	.000111
5	.002649	.001922	.001454	.001111	.000827	.000614	.000453	.000336	.000254
6	.004826	.003582	.002756	.002122	.001627	.001214	.000893	.000662	.000491
7	.008159	.006139	.004729	.003622	.002822	.002175	.001657	.001230	.000891
8	.012608	.009865	.007645	.005926	.004622	.003571	.002722	.002034	.001482
9	.018208	.014065	.010912	.008426	.006422	.004851	.003665	.002754	.002082
10	.025008	.019265	.014622	.011122	.008422	.006251	.004722	.003522	.002654
11	.033208	.025865	.019622	.014622	.011122	.008422	.006251	.004722	.003522
12	.043008	.033265	.024622	.018122	.013622	.010122	.007622	.005722	.004322
13	.055408	.042265	.030622	.022622	.017122	.012622	.009122	.006722	.005022
14	.070608	.054265	.039622	.029622	.022622	.017122	.012622	.009122	.006722
15	.088808	.068265	.050622	.037622	.029622	.022622	.017122	.012622	.009122
16	.110208	.084265	.062622	.046622	.035622	.027622	.021122	.015622	.011122
17	.134808	.102265	.076622	.057622	.044622	.033622	.026122	.019622	.014122
18	.162608	.123265	.094622	.071622	.056622	.042622	.032122	.024622	.018122
19	.193808	.148265	.116622	.086622	.064622	.048622	.036122	.027622	.020122
20	.228608	.178265	.144622	.108622	.082622	.060622	.046122	.035622	.026622
21	.267208	.204265	.170622	.130622	.100622	.076622	.058622	.045622	.034622
22	.309808	.238265	.196622	.150622	.118622	.092622	.070622	.054622	.040622
23	.356608	.280265	.232622	.180622	.144622	.114622	.088622	.068622	.050622
24	.407808	.330265	.280622	.220622	.180622	.144622	.114622	.088622	.068622
25	.463608	.388265	.330622	.260622	.214622	.174622	.138622	.108622	.082622
26	.524208	.454265	.394622	.310622	.254622	.214622	.174622	.138622	.108622
27	.590808	.528265	.474622	.370622	.304622	.264622	.224622	.184622	.144622
28	.663608	.608265	.554622	.440622	.364622	.324622	.284622	.244622	.204622
29	.742808	.698265	.634622	.520622	.434622	.394622	.354622	.314622	.274622
30	.828608	.788265	.714622	.600622	.514622	.474622	.434622	.394622	.354622
31	.920808	.880265	.794622	.680622	.594622	.554622	.514622	.474622	.434622
32	.101808	.970265	.874622	.760622	.674622	.634622	.594622	.554622	.514622
33	.114808	.1080265	.1014622	.094622	.088622	.082622	.076622	.070622	.064622
34	.129808	.123265	.116622	.110622	.104622	.098622	.092622	.086622	.080622
35	.146808	.140265	.133622	.127622	.121622	.115622	.109622	.103622	.097622
36	.165808	.158265	.151622	.145622	.139622	.133622	.127622	.121622	.115622
37	.186808	.178265	.171622	.165622	.159622	.153622	.147622	.141622	.135622
38	.209808	.200265	.193622	.187622	.181622	.175622	.169622	.163622	.157622
39	.234808	.224265	.217622	.211622	.205622	.199622	.193622	.187622	.181622
40	.261808	.250265	.243622	.237622	.231622	.225622	.219622	.213622	.207622
41	.290808	.278265	.271622	.265622	.259622	.253622	.247622	.241622	.235622
42	.321808	.308265	.301622	.295622	.289622	.283622	.277622	.271622	.265622
43	.354808	.340265	.333622	.327622	.321622	.315622	.309622	.303622	.297622
44	.389808	.374265	.367622	.361622	.355622	.349622	.343622	.337622	.331622
45	.426808	.410265	.403622	.397622	.391622	.385622	.379622	.373622	.367622
46	.465808	.448265	.441622	.435622	.429622	.423622	.417622	.411622	.405622
47	.506808	.488265	.481622	.475622	.469622	.463622	.457622	.451622	.445622
48	.549808	.530265	.523622	.517622	.511622	.505622	.499622	.493622	.487622
49	.594808	.574265	.567622	.561622	.555622	.549622	.543622	.537622	.531622

Table X-1-B (Continued). Acute Leukemia: Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

Y	54	55	56	57	58	59	60	61	62
1	0	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0	0
3	0	0	0	0	0	0	0	0	0
4	0	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	0	0	0
19	0	0	0	0	0	0	0	0	0
20	0	0	0	0	0	0	0	0	0
21	0	0	0	0	0	0	0	0	0
22	0	0	0	0	0	0	0	0	0
23	0	0	0	0	0	0	0	0	0
24	0	0	0	0	0	0	0	0	0
25	0	0	0	0	0	0	0	0	0
26	0	0	0	0	0	0	0	0	0
27	0	0	0	0	0	0	0	0	0
28	0	0	0	0	0	0	0	0	0
29	0	0	0	0	0	0	0	0	0
30	0	0	0	0	0	0	0	0	0
31	0	0	0	0	0	0	0	0	0
32	0	0	0	0	0	0	0	0	0
33	0	0	0	0	0	0	0	0	0
34	0	0	0	0	0	0	0	0	0
35	0	0	0	0	0	0	0	0	0
36	0	0	0	0	0	0	0	0	0
37	0	0	0	0	0	0	0	0	0
38	0	0	0	0	0	0	0	0	0
39	0	0	0	0	0	0	0	0	0
40	0	0	0	0	0	0	0	0	0
41	0	0	0	0	0	0	0	0	0
42	0	0	0	0	0	0	0	0	0
43	0	0	0	0	0	0	0	0	0
44	0	0	0	0	0	0	0	0	0
45	0	0	0	0	0	0	0	0	0
46	0	0	0	0	0	0	0	0	0
47	0	0	0	0	0	0	0	0	0
48	0	0	0	0	0	0	0	0	0
49	0	0	0	0	0	0	0	0	0
50	0	0	0	0	0	0	0	0	0

Table X-1-D (Continued). Acute Leukemia: Temporal Distribution $T(h, Y)$ by Year Y After Exposure at Age A_1

Y	72	73	74	75
0	0	0	0	0
1	0	0	0	0
2	0	0	0	0
3	0	0	0	0
4	0	0	0	0
5	.000085	.000083	.000081	.000081
6	.000019	.000011	.000006	.000003
7	.000048	.000030	.000018	.000010
8	.000100	.000043	.000039	.000025
9	.000181	.000116	.000073	.000052
10	.000295	.000192	.000123	.000077
11	.000467	.000295	.000192	.000123
12	.000639	.000426	.000282	.000183
13	.000823	.000592	.000395	.000239
14	.001155	.000788	.000522	.000333
15	.00147	.00102	.000694	.000465
16	.00181	.00128	.000880	.000598
17	.00222	.00157	.00109	.000746
18	.00266	.00189	.00133	.000916
19	.00313	.00225	.00159	.00118
20	.00363	.00263	.00187	.00139
21	.00416	.00303	.00217	.00153
22	.00472	.00344	.00250	.00174
23	.00530	.00391	.00284	.00203
24	.00591	.00439	.00321	.00231
25	.00653	.00488	.00358	.00260
26	.00717	.00538	.00398	.00290
27	.00782	.00590	.00439	.00321
28	.00848	.00644	.00481	.00354
29	.00915	.00698	.00523	.00388
30	.00983	.00753	.00569	.00423
31	.0105	.00809	.00614	.00459
32	.0112	.00866	.00660	.00495
33	.0119	.00923	.00707	.00533
34	.0126	.00980	.00754	.00571
35	.0133	.0104	.00801	.00609
36	.0139	.0110	.00849	.00648
37	.0144	.0115	.00897	.00687
38	.0153	.0121	.00945	.00727
39	.0159	.0127	.00993	.00767
40	.0164	.0132	.0104	.00807
41	.0172	.0138	.0109	.00847
42	.0179	.0144	.0114	.00888
43	.0185	.0149	.0119	.00928
44	.0191	.0155	.0123	.00968
45	.0197	.0160	.0128	.01007
46	.0203	.0165	.0133	.01045
47	.0209	.0171	.0137	.01083
48	.0215	.0174	.0142	.0112
49	.0220	.0181	.0146	.0117

Table X-1-E. Acute Leukemia: Risk Coefficient $E(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	4.62	2.95	38	2.24	1.43
1	4.34	2.77	39	2.38	1.52
2	4.05	2.58	40	2.53	1.61
3	3.76	2.40	41	2.71	1.72
4	3.47	2.22	42	2.92	1.85
5	3.19	2.04	43	3.17	2.00
6	2.92	1.87	44	3.45	2.17
7	2.67	1.71	45	3.79	2.37
8	2.43	1.56	46	4.18	2.60
9	2.21	1.42	47	4.65	2.88
10	2.02	1.29	48	5.21	3.20
11	1.86	1.19	49	5.87	3.58
12	1.72	1.10	50	6.68	4.04
13	1.62	1.04	51	7.65	4.59
14	1.55	.992	52	8.85	5.26
15	1.52	.969	53	10.3	6.07
16	1.49	.952	54	12.2	7.08
17	1.47	.937	55	14.5	8.33
18	1.45	.926	56	17.4	9.89
19	1.44	.918	57	21.1	11.9
20	1.43	.914	58	25.9	14.4
21	1.43	.912	59	32.3	17.7
22	1.43	.914	60	40.6	22.1
23	1.44	.919	61	51.9	27.8
24	1.45	.927	62	67.2	35.5
25	1.47	.939	63	88.3	46.1
26	1.50	.955	64	118.	60.8
27	1.53	.975	65	160.	81.5
28	1.56	.998	66	221.	111.
29	1.60	1.02	67	311.	154.
30	1.64	1.05	68	445.	218.
31	1.69	1.08	69	650.	315.
32	1.74	1.11	70	969.	464.
33	1.80	1.15	71	1470.	699.
34	1.87	1.19	72	2290.	1080.
35	1.94	1.24	73	3640.	1690.
36	2.03	1.30	74	5920.	2730.
37	2.13	1.36	75	9850.	4490.

Table X-1-F. Acute Leukemia: Baseline Incidence I(A₁,S)
by Age at Diagnosis A₂ and Sex S

A ₁	Sex		A ₂	Sex	
	Male	Female		Male	Female
0	6.90	5.70	43	3.17	2.44
1	6.90	5.70	44	3.47	2.73
2	6.90	5.70	45	3.79	3.05
3	6.55	5.43	46	4.10	3.34
4	5.72	4.76	47	4.40	3.60
5	4.69	3.94	48	4.69	3.73
6	3.76	3.18	49	4.97	3.78
7	3.20	2.70	50	5.24	3.81
8	2.94	2.45	51	5.52	3.87
9	2.73	2.22	52	5.81	4.00
10	2.56	2.02	53	6.10	4.21
11	2.45	1.84	54	6.44	4.45
12	2.40	1.70	55	6.87	4.76
13	2.41	1.57	56	7.45	5.14
14	2.45	1.43	57	8.23	5.61
15	2.50	1.32	58	9.18	6.14
16	2.52	1.23	59	10.2	6.68
17	2.50	1.20	60	11.3	7.22
18	2.38	1.22	61	12.4	7.77
19	2.19	1.27	62	13.5	8.31
20	1.99	1.33	63	14.4	8.86
21	1.84	1.38	64	15.2	9.40
22	1.80	1.40	65	16.1	9.95
23	1.84	1.40	66	17.1	10.5
24	1.88	1.40	67	18.3	11.1
25	1.92	1.40	68	20.2	11.9
26	1.96	1.40	69	22.7	12.9
27	2.00	1.40	70	25.5	14.1
28	2.04	1.40	71	28.6	15.3
29	2.08	1.40	72	31.5	16.5
30	2.12	1.41	73	34.4	17.6
31	2.16	1.44	74	37.2	18.9
32	2.20	1.50	75	40.1	20.1
33	2.24	1.58	76	42.9	21.4
34	2.28	1.66	77	45.8	22.7
35	2.32	1.74	78	48.6	24.4
36	2.36	1.82	79	51.4	26.9
37	2.40	1.90	80	54.1	29.4
38	2.44	1.98	81	56.7	31.5
39	2.49	2.06	82	59.2	32.7
40	2.56	2.14	83	61.2	33.6
41	2.70	2.22	84	62.6	34.2
42	2.90	2.30	85	63.6	34.7

Table X-1-0. Leukemia. All Types Except CLL: Temporal Distribution T(A₁, Y) by Year Y After Exposure at Age A₁

Y	0	1	2	3	4	5	6	7	8
1	0	0	0	0	0	0	0	0	0
2	.4705	.0196	.0764	.0181	.0174	.0167	.0159	.0152	.0143
3	.4835	.0294	.0723	.0273	.0250	.0227	.0203	.0178	.0153
4	.487	.0405	.064	.0399	.0350	.0280	.0239	.0197	.0155
5	.487	.051	.0583	.0494	.0404	.0327	.0262	.0209	.0157
6	.487	.0627	.0483	.0380	.0276	.0197	.0142	.0097	.0052
7	.4821	.0746	.0348	.0227	.0150	.0103	.0067	.0038	.0014
8	.4821	.0876	.0227	.0150	.0103	.0067	.0038	.0014	.0002
9	.4821	.101	.0115	.0074	.0048	.0031	.0019	.0011	.0006
10	.4821	.1146	.0058	.0037	.0024	.0016	.001	.0005	.0003
11	.4821	.1282	.0034	.0022	.0014	.0009	.0005	.0003	.0002
12	.4821	.1418	.0021	.0013	.0008	.0005	.0003	.0002	.0001
13	.4821	.1554	.0013	.0008	.0005	.0003	.0002	.0001	.0001
14	.4821	.169	.0008	.0005	.0003	.0002	.0001	.0001	.0001
15	.4821	.1826	.0005	.0003	.0002	.0001	.0001	.0001	.0001
16	.4821	.1962	.0003	.0002	.0001	.0001	.0001	.0001	.0001
17	.4821	.2098	.0002	.0001	.0001	.0001	.0001	.0001	.0001
18	.4821	.2234	.0001	.0001	.0001	.0001	.0001	.0001	.0001
19	.4821	.237	.0001	.0001	.0001	.0001	.0001	.0001	.0001
20	.4821	.2507	.0001	.0001	.0001	.0001	.0001	.0001	.0001
21	.4821	.2643	.0001	.0001	.0001	.0001	.0001	.0001	.0001
22	.4821	.2779	.0001	.0001	.0001	.0001	.0001	.0001	.0001
23	.4821	.2915	.0001	.0001	.0001	.0001	.0001	.0001	.0001
24	.4821	.3051	.0001	.0001	.0001	.0001	.0001	.0001	.0001
25	.4821	.3187	.0001	.0001	.0001	.0001	.0001	.0001	.0001
26	.4821	.3323	.0001	.0001	.0001	.0001	.0001	.0001	.0001
27	.4821	.3459	.0001	.0001	.0001	.0001	.0001	.0001	.0001
28	.4821	.3595	.0001	.0001	.0001	.0001	.0001	.0001	.0001
29	.4821	.3731	.0001	.0001	.0001	.0001	.0001	.0001	.0001
30	.4821	.3867	.0001	.0001	.0001	.0001	.0001	.0001	.0001
31	.4821	.4003	.0001	.0001	.0001	.0001	.0001	.0001	.0001
32	.4821	.4139	.0001	.0001	.0001	.0001	.0001	.0001	.0001
33	.4821	.4275	.0001	.0001	.0001	.0001	.0001	.0001	.0001
34	.4821	.4411	.0001	.0001	.0001	.0001	.0001	.0001	.0001
35	.4821	.4547	.0001	.0001	.0001	.0001	.0001	.0001	.0001
36	.4821	.4683	.0001	.0001	.0001	.0001	.0001	.0001	.0001
37	.4821	.4819	.0001	.0001	.0001	.0001	.0001	.0001	.0001
38	.4821	.4955	.0001	.0001	.0001	.0001	.0001	.0001	.0001
39	.4821	.5091	.0001	.0001	.0001	.0001	.0001	.0001	.0001
40	.4821	.5227	.0001	.0001	.0001	.0001	.0001	.0001	.0001
41	.4821	.5363	.0001	.0001	.0001	.0001	.0001	.0001	.0001
42	.4821	.5499	.0001	.0001	.0001	.0001	.0001	.0001	.0001
43	.4821	.5635	.0001	.0001	.0001	.0001	.0001	.0001	.0001
44	.4821	.5771	.0001	.0001	.0001	.0001	.0001	.0001	.0001
45	.4821	.5907	.0001	.0001	.0001	.0001	.0001	.0001	.0001
46	.4821	.6043	.0001	.0001	.0001	.0001	.0001	.0001	.0001
47	.4821	.6179	.0001	.0001	.0001	.0001	.0001	.0001	.0001
48	.4821	.6315	.0001	.0001	.0001	.0001	.0001	.0001	.0001
49	.4821	.6451	.0001	.0001	.0001	.0001	.0001	.0001	.0001

Table X-1-0 (Continued). Leukemia. All Types Except CLL: Temporal Distribution T(A, Y) by Year Y After Exposure at Age A

Y	18	19	20	21	22	23	24	25	26
1	0	0	0	0	0	0	0	0	0
2	.0082	.0088	.0076	.0073	.0069	.0068	.0064	.0061	.0059
3	.0405	.0382	.0361	.0340	.0320	.0301	.0283	.0268	.0251
4	.0649	.0621	.0592	.0564	.0536	.0508	.0481	.0455	.0429
5	.0743	.0719	.0694	.0668	.0643	.0617	.0590	.0564	.0537
6	.0690	.0668	.0646	.0624	.0601	.0578	.0554	.0530	.0506
7	.0635	.0613	.0591	.0568	.0545	.0522	.0500	.0477	.0454
8	.0568	.0546	.0524	.0501	.0478	.0455	.0432	.0409	.0386
9	.0504	.0482	.0460	.0437	.0414	.0391	.0368	.0345	.0322
10	.0444	.0422	.0400	.0377	.0354	.0331	.0308	.0285	.0262
11	.0394	.0372	.0350	.0327	.0304	.0281	.0258	.0235	.0212
12	.0354	.0332	.0310	.0287	.0264	.0241	.0218	.0195	.0172
13	.0324	.0302	.0280	.0257	.0234	.0211	.0188	.0165	.0142
14	.0308	.0286	.0264	.0241	.0218	.0195	.0172	.0149	.0126
15	.0273	.0251	.0229	.0206	.0183	.0160	.0137	.0114	.0091
16	.0242	.0220	.0198	.0175	.0152	.0129	.0106	.0083	.0060
17	.0216	.0194	.0172	.0149	.0126	.0103	.0080	.0057	.0034
18	.0193	.0171	.0149	.0126	.0103	.0080	.0057	.0034	.0011
19	.0173	.0151	.0129	.0106	.0083	.0060	.0037	.0014	.0001
20	.0156	.0134	.0112	.0089	.0066	.0043	.0020	.0007	.0004
21	.0141	.0119	.0097	.0074	.0051	.0028	.0015	.0012	.0009
22	.0127	.0105	.0083	.0060	.0037	.0024	.0021	.0018	.0015
23	.0116	.0094	.0072	.0049	.0026	.0013	.0010	.0007	.0004
24	.0105	.0083	.0061	.0038	.0015	.0002	.0009	.0006	.0003
25	.0094	.0072	.0050	.0027	.0004	.0001	.0008	.0005	.0002
26	.0084	.0062	.0040	.0017	.0004	.0001	.0008	.0005	.0002
27	.0074	.0052	.0030	.0007	.0004	.0001	.0008	.0005	.0002
28	.0064	.0042	.0020	.0007	.0004	.0001	.0008	.0005	.0002
29	.0054	.0032	.0010	.0007	.0004	.0001	.0008	.0005	.0002
30	.0044	.0022	.0000	.0007	.0004	.0001	.0008	.0005	.0002
31	.0034	.0012	.0000	.0007	.0004	.0001	.0008	.0005	.0002
32	.0024	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
33	.0014	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
34	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
35	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
36	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
37	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
38	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
39	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
40	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
41	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
42	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
43	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
44	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
45	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
46	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
47	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
48	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002
49	.0004	.0002	.0000	.0007	.0004	.0001	.0008	.0005	.0002

Table X-1-0 (Continued). Leukemia. All Types Except CIL: Temporal Distribution $T(A_i, Y)$ by Year Y After Exposure at Age A_i

Y	27	28	29	30	31	32	33	34	35
1	0	0	0	0	0	0	0	0	0
2	.00375	.00398	.00563	.00550	.00319	.00509	.00202	.00595	.00809
3	.0216	.0221	.0210	.0199	.0189	.0179	.0171	.0164	.0157
4	.0405	.0381	.0359	.0337	.0317	.0298	.0281	.0264	.0250
5	.0511	.0485	.0459	.0434	.0410	.0387	.0364	.0343	.0323
6	.0549	.0516	.0482	.0448	.0414	.0379	.0344	.0309	.0273
7	.0528	.0493	.0458	.0423	.0388	.0353	.0318	.0282	.0246
8	.0523	.0487	.0451	.0415	.0379	.0343	.0307	.0271	.0235
9	.0524	.0488	.0452	.0416	.0380	.0344	.0308	.0272	.0236
10	.0490	.0454	.0418	.0382	.0346	.0310	.0274	.0238	.0202
11	.0453	.0417	.0381	.0345	.0309	.0273	.0237	.0201	.0165
12	.0416	.0380	.0344	.0308	.0272	.0236	.0200	.0164	.0128
13	.0380	.0344	.0308	.0272	.0236	.0200	.0164	.0128	.0092
14	.0347	.0311	.0275	.0239	.0203	.0167	.0131	.0095	.0059
15	.0317	.0281	.0245	.0209	.0173	.0137	.0101	.0065	.0029
16	.0289	.0253	.0217	.0181	.0145	.0109	.0073	.0037	.0001
17	.0263	.0227	.0191	.0155	.0119	.0083	.0047	.0011	.0000
18	.0248	.0212	.0176	.0140	.0104	.0068	.0032	.0000	.0000
19	.0207	.0171	.0135	.0099	.0063	.0027	.0000	.0000	.0000
20	.0200	.0164	.0128	.0092	.0056	.0020	.0000	.0000	.0000
21	.0184	.0148	.0112	.0076	.0040	.0004	.0000	.0000	.0000
22	.0155	.0119	.0083	.0047	.0011	.0000	.0000	.0000	.0000
23	.0142	.0106	.0070	.0034	.0000	.0000	.0000	.0000	.0000
24	.0131	.0095	.0059	.0023	.0000	.0000	.0000	.0000	.0000
25	.0121	.0085	.0049	.0013	.0000	.0000	.0000	.0000	.0000
26	.0114	.0078	.0042	.0006	.0000	.0000	.0000	.0000	.0000
27	.0107	.0071	.0035	.0000	.0000	.0000	.0000	.0000	.0000
28	.0093	.0057	.0021	.0000	.0000	.0000	.0000	.0000	.0000
29	.00854	.00494	.00134	.0000	.0000	.0000	.0000	.0000	.0000
30	.00824	.00464	.00104	.0000	.0000	.0000	.0000	.0000	.0000
31	.00766	.00406	.00046	.0000	.0000	.0000	.0000	.0000	.0000
32	.00714	.00354	.00004	.0000	.0000	.0000	.0000	.0000	.0000
33	.00666	.00306	.00000	.0000	.0000	.0000	.0000	.0000	.0000
34	.00622	.00262	.00000	.0000	.0000	.0000	.0000	.0000	.0000
35	.00581	.00221	.00000	.0000	.0000	.0000	.0000	.0000	.0000
36	.00544	.00184	.00000	.0000	.0000	.0000	.0000	.0000	.0000
37	.00518	.00158	.00000	.0000	.0000	.0000	.0000	.0000	.0000
38	.00478	.00118	.00000	.0000	.0000	.0000	.0000	.0000	.0000
39	.00439	.00079	.00000	.0000	.0000	.0000	.0000	.0000	.0000
40	.00423	.00063	.00000	.0000	.0000	.0000	.0000	.0000	.0000
41	.00423	.00063	.00000	.0000	.0000	.0000	.0000	.0000	.0000
42	.00398	.00038	.00000	.0000	.0000	.0000	.0000	.0000	.0000
43	.00354	.00004	.00000	.0000	.0000	.0000	.0000	.0000	.0000
44	.00324	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000
45	.00316	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000
46	.00294	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000
47	.00284	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000
48	.00249	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000
49	.00249	.00000	.00000	.0000	.0000	.0000	.0000	.0000	.0000

Table X-1-0 (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A, Y) by Year Y After Exposure at Age A1

Y	A1										
	36	37	38	39	40	41	42	43	44	45	46
0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0
2	.00485	.00487	.00478	.00475	.00473	.00472	.00471	.00470	.00469	.00469	.00469
3	.0152	.0147	.0143	.0139	.0136	.0133	.0131	.0129	.0128	.0128	.0128
4	.0234	.0224	.0213	.0203	.0194	.0186	.0180	.0174	.0169	.0169	.0169
5	.0316	.0296	.0274	.0254	.0234	.0226	.0216	.0206	.0206	.0206	.0206
6	.0397	.0361	.0312	.0253	.0204	.0180	.0166	.0152	.0152	.0152	.0152
7	.0478	.0411	.0340	.0251	.0182	.0153	.0140	.0126	.0126	.0126	.0126
8	.0559	.0461	.0357	.0238	.0169	.0135	.0122	.0108	.0108	.0108	.0108
9	.0639	.0501	.0364	.0224	.0155	.0117	.0104	.0090	.0090	.0090	.0090
10	.0719	.0539	.0364	.0211	.0142	.0100	.0085	.0071	.0071	.0071	.0071
11	.0799	.0566	.0358	.0199	.0132	.0094	.0077	.0063	.0063	.0063	.0063
12	.0879	.0560	.0337	.0188	.0122	.0085	.0067	.0053	.0053	.0053	.0053
13	.0959	.0544	.0316	.0177	.0111	.0077	.0058	.0044	.0044	.0044	.0044
14	.1039	.0528	.0295	.0166	.0100	.0069	.0049	.0035	.0035	.0035	.0035
15	.1119	.0512	.0274	.0155	.0089	.0060	.0040	.0026	.0026	.0026	.0026
16	.1199	.0496	.0253	.0144	.0078	.0051	.0031	.0017	.0017	.0017	.0017
17	.1279	.0480	.0232	.0133	.0067	.0040	.0020	.0006	.0006	.0006	.0006
18	.1359	.0464	.0211	.0122	.0056	.0031	.0011	.0000	.0000	.0000	.0000
19	.1439	.0448	.0190	.0111	.0045	.0020	.0000	.0000	.0000	.0000	.0000
20	.1519	.0432	.0169	.0100	.0034	.0010	.0000	.0000	.0000	.0000	.0000
21	.1599	.0416	.0148	.0089	.0023	.0000	.0000	.0000	.0000	.0000	.0000
22	.1679	.0400	.0127	.0078	.0012	.0000	.0000	.0000	.0000	.0000	.0000
23	.1759	.0384	.0106	.0067	.0001	.0000	.0000	.0000	.0000	.0000	.0000
24	.1839	.0368	.0085	.0056	.0000	.0000	.0000	.0000	.0000	.0000	.0000
25	.1919	.0352	.0064	.0045	.0000	.0000	.0000	.0000	.0000	.0000	.0000
26	.1999	.0336	.0043	.0034	.0000	.0000	.0000	.0000	.0000	.0000	.0000
27	.2079	.0320	.0022	.0023	.0000	.0000	.0000	.0000	.0000	.0000	.0000
28	.2159	.0304	.0001	.0012	.0000	.0000	.0000	.0000	.0000	.0000	.0000
29	.2239	.0288	.0000	.0001	.0000	.0000	.0000	.0000	.0000	.0000	.0000
30	.2319	.0272	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
31	.2399	.0256	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
32	.2479	.0240	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
33	.2559	.0224	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
34	.2639	.0208	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
35	.2719	.0192	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
36	.2799	.0176	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
37	.2879	.0160	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
38	.2959	.0144	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
39	.3039	.0128	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
40	.3119	.0112	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
41	.3199	.0096	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
42	.3279	.0080	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
43	.3359	.0064	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
44	.3439	.0048	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
45	.3519	.0032	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
46	.3599	.0016	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
47	.3679	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
48	.3759	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
49	.3839	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
50	.3919	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
51	.3999	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
52	.4079	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
53	.4159	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
54	.4239	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
55	.4319	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
56	.4399	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
57	.4479	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
58	.4559	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
59	.4639	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
60	.4719	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
61	.4799	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
62	.4879	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
63	.4959	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
64	.5039	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
65	.5119	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
66	.5199	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
67	.5279	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
68	.5359	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
69	.5439	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
70	.5519	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
71	.5599	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
72	.5679	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
73	.5759	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
74	.5839	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
75	.5919	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
76	.5999	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
77	.6079	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
78	.6159	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
79	.6239	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
80	.6319	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
81	.6399	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
82	.6479	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
83	.6559	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
84	.6639	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
85	.6719	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
86	.6799	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
87	.6879	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
88	.6959	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
89	.7039	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
90	.7119	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
91	.7199	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
92	.7279	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
93	.7359	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
94	.7439	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
95	.7519	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
96	.7599	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
97	.7679	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
98	.7759	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000
99	.7839	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000	.0000

Table X-1-0 (Continued). Laukaa, All Types Except CII: Temporal Distribution (A₁, Y) by Year Y After Exposure at Age A₁

Y	A ₁										
	45	46	47	48	49	50	51	52	53	54	55
1	0	0	0	0	0	0	0	0	0	0	0
2	0.0468	0.0460	0.0468	0.0464	0.0467	0.0467	0.0467	0.0467	0.0467	0.0467	0.0467
3	0.127	0.126	0.125	0.124	0.124	0.124	0.124	0.124	0.124	0.124	0.124
4	0.165	0.162	0.159	0.158	0.158	0.158	0.158	0.158	0.158	0.158	0.158
5	0.190	0.183	0.177	0.176	0.176	0.176	0.176	0.176	0.176	0.176	0.176
6	0.209	0.199	0.190	0.188	0.188	0.188	0.188	0.188	0.188	0.188	0.188
7	0.225	0.212	0.202	0.199	0.199	0.199	0.199	0.199	0.199	0.199	0.199
8	0.237	0.223	0.211	0.209	0.209	0.209	0.209	0.209	0.209	0.209	0.209
9	0.246	0.232	0.218	0.216	0.216	0.216	0.216	0.216	0.216	0.216	0.216
10	0.252	0.237	0.223	0.221	0.221	0.221	0.221	0.221	0.221	0.221	0.221
11	0.255	0.241	0.227	0.225	0.225	0.225	0.225	0.225	0.225	0.225	0.225
12	0.256	0.242	0.229	0.227	0.227	0.227	0.227	0.227	0.227	0.227	0.227
13	0.255	0.242	0.229	0.227	0.227	0.227	0.227	0.227	0.227	0.227	0.227
14	0.253	0.240	0.228	0.226	0.226	0.226	0.226	0.226	0.226	0.226	0.226
15	0.249	0.237	0.224	0.222	0.222	0.222	0.222	0.222	0.222	0.222	0.222
16	0.244	0.234	0.221	0.219	0.219	0.219	0.219	0.219	0.219	0.219	0.219
17	0.238	0.229	0.216	0.214	0.214	0.214	0.214	0.214	0.214	0.214	0.214
18	0.232	0.224	0.211	0.209	0.209	0.209	0.209	0.209	0.209	0.209	0.209
19	0.225	0.218	0.205	0.202	0.202	0.202	0.202	0.202	0.202	0.202	0.202
20	0.218	0.212	0.200	0.197	0.197	0.197	0.197	0.197	0.197	0.197	0.197
21	0.211	0.206	0.194	0.191	0.191	0.191	0.191	0.191	0.191	0.191	0.191
22	0.205	0.199	0.188	0.185	0.185	0.185	0.185	0.185	0.185	0.185	0.185
23	0.198	0.193	0.182	0.179	0.179	0.179	0.179	0.179	0.179	0.179	0.179
24	0.189	0.186	0.175	0.172	0.172	0.172	0.172	0.172	0.172	0.172	0.172
25	0.182	0.180	0.170	0.167	0.167	0.167	0.167	0.167	0.167	0.167	0.167
26	0.175	0.173	0.164	0.161	0.161	0.161	0.161	0.161	0.161	0.161	0.161
27	0.168	0.167	0.158	0.155	0.155	0.155	0.155	0.155	0.155	0.155	0.155
28	0.162	0.161	0.152	0.149	0.149	0.149	0.149	0.149	0.149	0.149	0.149
29	0.155	0.155	0.146	0.143	0.143	0.143	0.143	0.143	0.143	0.143	0.143
30	0.149	0.149	0.140	0.137	0.137	0.137	0.137	0.137	0.137	0.137	0.137
31	0.143	0.144	0.135	0.132	0.132	0.132	0.132	0.132	0.132	0.132	0.132
32	0.138	0.138	0.129	0.126	0.126	0.126	0.126	0.126	0.126	0.126	0.126
33	0.132	0.133	0.124	0.121	0.121	0.121	0.121	0.121	0.121	0.121	0.121
34	0.127	0.126	0.117	0.114	0.114	0.114	0.114	0.114	0.114	0.114	0.114
35	0.122	0.123	0.114	0.111	0.111	0.111	0.111	0.111	0.111	0.111	0.111
36	0.117	0.119	0.110	0.107	0.107	0.107	0.107	0.107	0.107	0.107	0.107
37	0.112	0.114	0.105	0.102	0.102	0.102	0.102	0.102	0.102	0.102	0.102
38	0.108	0.110	0.101	0.098	0.098	0.098	0.098	0.098	0.098	0.098	0.098
39	0.103	0.106	0.097	0.094	0.094	0.094	0.094	0.094	0.094	0.094	0.094
40	0.099	0.102	0.093	0.090	0.090	0.090	0.090	0.090	0.090	0.090	0.090
41	0.095	0.097	0.088	0.085	0.085	0.085	0.085	0.085	0.085	0.085	0.085
42	0.091	0.094	0.085	0.082	0.082	0.082	0.082	0.082	0.082	0.082	0.082
43	0.087	0.090	0.081	0.078	0.078	0.078	0.078	0.078	0.078	0.078	0.078
44	0.084	0.087	0.078	0.075	0.075	0.075	0.075	0.075	0.075	0.075	0.075
45	0.081	0.084	0.075	0.072	0.072	0.072	0.072	0.072	0.072	0.072	0.072
46	0.078	0.081	0.072	0.069	0.069	0.069	0.069	0.069	0.069	0.069	0.069
47	0.074	0.077	0.068	0.065	0.065	0.065	0.065	0.065	0.065	0.065	0.065
48	0.070	0.073	0.064	0.061	0.061	0.061	0.061	0.061	0.061	0.061	0.061
49	0.066	0.069	0.060	0.057	0.057	0.057	0.057	0.057	0.057	0.057	0.057

Table X-1-0 (Continued). Leukemia. All Types Except CLL. Temporal Distribution T(A₁,Y) by Year Y After Exposure at Age A₁

Y	A ₁												
	54	55	56	57	58	59	60	61	62	63	64	65	66
0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123
4	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149
5	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156	.0156
6	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126
7	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151
8	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152	.0152
9	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150
10	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150	.0150
11	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149
12	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149	.0149
13	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148
14	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148
15	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147
16	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147
17	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147
18	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147	.0147
19	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146	.0146
20	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145	.0145
21	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143	.0143
22	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142	.0142
23	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140	.0140
24	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139	.0139
25	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137	.0137
26	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135	.0135
27	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133	.0133
28	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131	.0131
29	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129	.0129
30	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127	.0127
31	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126	.0126
32	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125	.0125
33	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124	.0124
34	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123
35	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122	.0122
36	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121	.0121
37	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120	.0120
38	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119	.0119
39	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118	.0118
40	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117	.0117
41	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116	.0116
42	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115	.0115
43	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114	.0114
44	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113	.0113
45	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112	.0112
46	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111	.0111
47	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110	.0110
48	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109	.0109
49	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108	.0108

Table X-1-0 (Continued). Leukemia, All Types Except CLL: Temporal Distribution T(A_i, Y) by Year Y After Exposure at Age A_i

Y	63	64	65	66	67	68	69	70	71
0	0	0	0	0	0	0	0	0	0
1	0	0	0	0	0	0	0	0	0
2	.00447	.00467	.00487	.00467	.00467	.00467	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123	.0123
4	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148	.0148
5	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151	.0151
6	.0147	.0146	.0144	.0146	.0146	.0146	.0144	.0144	.0144
7	.0139	.0139	.0138	.0138	.0138	.0138	.0138	.0138	.0138
8	.0131	.0130	.0130	.0130	.0129	.0129	.0129	.0129	.0129
9	.0123	.0122	.0121	.0121	.0121	.0120	.0120	.0120	.0120
10	.0114	.0115	.0114	.0113	.0112	.0112	.0112	.0111	.0111
11	.0109	.0108	.0106	.0106	.0105	.0104	.0104	.0104	.0103
12	.0104	.0102	.0100	.00980	.00980	.00973	.00968	.00964	.00961
13	.00984	.00964	.00945	.00931	.00920	.00911	.00904	.00899	.00896
14	.00944	.00918	.00896	.00879	.00866	.00855	.00847	.00841	.00836
15	.00907	.00878	.00854	.00834	.00818	.00805	.00796	.00788	.00782
16	.00874	.00844	.00816	.00794	.00776	.00761	.00750	.00741	.00734
17	.00850	.00814	.00784	.00759	.00738	.00722	.00709	.00699	.00691
18	.00827	.00787	.00754	.00728	.00704	.00687	.00672	.00661	.00652
19	.00808	.00767	.00731	.00702	.00677	.00656	.00640	.00627	.00616
20	.00792	.00749	.00710	.00678	.00651	.00629	.00611	.00596	.00585
21	.00778	.00732	.00692	.00658	.00629	.00605	.00583	.00569	.00556
22	.00764	.00716	.00675	.00640	.00610	.00582	.00562	.00545	.00531
23	.00754	.00706	.00663	.00625	.00592	.00565	.00542	.00523	.00508
24	.00747	.00698	.00653	.00611	.00577	.00548	.00524	.00504	.00487
25	.00739	.00689	.00641	.00600	.00563	.00534	.00508	.00486	.00469
26	.00732	.00680	.00632	.00590	.00553	.00521	.00491	.00471	.00452
27	.00724	.00673	.00624	.00581	.00542	.00509	.00481	.00457	.00437
28	.00721	.00667	.00617	.00573	.00533	.00500	.00471	.00444	.00423
29	.00716	.00662	.00611	.00566	.00524	.00490	.00459	.00433	.00411
30	.00712	.00657	.00604	.00560	.00519	.00482	.00450	.00423	.00400
31	.00708	.00653	.00600	.00556	.00514	.00475	.00443	.00416	.00390
32	.00704	.00649	.00597	.00550	.00505	.00463	.00430	.00406	.00374
33	.00700	.00642	.00588	.00540	.00493	.00448	.00415	.00387	.00366
34	.00696	.00638	.00584	.00534	.00486	.00440	.00407	.00374	.00354
35	.00692	.00633	.00578	.00526	.00478	.00431	.00398	.00363	.00345
36	.00689	.00630	.00575	.00522	.00474	.00426	.00393	.00357	.00337
37	.00685	.00626	.00571	.00517	.00468	.00420	.00387	.00351	.00331
38	.00681	.00622	.00567	.00512	.00463	.00415	.00382	.00346	.00326
39	.00677	.00618	.00563	.00508	.00459	.00411	.00378	.00342	.00322
40	.00673	.00614	.00559	.00504	.00455	.00407	.00374	.00338	.00318
41	.00670	.00611	.00556	.00501	.00452	.00404	.00371	.00335	.00315
42	.00666	.00607	.00552	.00497	.00448	.00400	.00367	.00331	.00311
43	.00661	.00602	.00547	.00492	.00443	.00395	.00362	.00326	.00306
44	.00657	.00598	.00543	.00488	.00439	.00391	.00358	.00322	.00302
45	.00653	.00594	.00539	.00484	.00435	.00387	.00354	.00318	.00298
46	.00649	.00590	.00535	.00480	.00431	.00383	.00350	.00314	.00294
47	.00644	.00585	.00530	.00475	.00426	.00378	.00345	.00309	.00289
48	.00640	.00581	.00526	.00471	.00422	.00374	.00341	.00305	.00285
49	.00635	.00576	.00521	.00466	.00417	.00369	.00336	.00300	.00280

Table X-1-g (Continued). leukemia. All Types Except CLL: Temporal Distribution T(A), Y) by Year Y After Exposure at Age A₁

Y	72	73	74	75
1	0	0	0	0
2	.00447	.00467	.00467	.00467
3	.0123	.0123	.0123	.0123
4	.0148	.0148	.0148	.0148
5	.0151	.0151	.0151	.0151
6	.0146	.0146	.0146	.0146
7	.0138	.0138	.0138	.0138
8	.0129	.0129	.0129	.0129
9	.0120	.0120	.0120	.0120
10	.0111	.0111	.0111	.0111
11	.0103	.0103	.0103	.0103
12	.00959	.00957	.00957	.00954
13	.0083	.00841	.00848	.00869
14	.00833	.00830	.00827	.00827
15	.00778	.00775	.00773	.00771
16	.00729	.00725	.00723	.00721
17	.00665	.00668	.00677	.00675
18	.00645	.00639	.00636	.00633
19	.00609	.00603	.00598	.00595
20	.00576	.00569	.00564	.00561
21	.00547	.00539	.00533	.00529
22	.00520	.00511	.00505	.00500
23	.00494	.00486	.00479	.00474
24	.00474	.00464	.00456	.00450
25	.00454	.00445	.00434	.00428
26	.00437	.00425	.00415	.00408
27	.00421	.00408	.00397	.00389
28	.00406	.00392	.00381	.00373
29	.00393	.00378	.00366	.00357
30	.00381	.00365	.00353	.00343
31	.00378	.00354	.00341	.00338
32	.00361	.00345	.00329	.00318
33	.00352	.00334	.00319	.00307
34	.00344	.00325	.00310	.00297
35	.00337	.00317	.00301	.00288
36	.00330	.00310	.00293	.00280
37	.00325	.00304	.00286	.00272
38	.00319	.00298	.00280	.00265
39	.00315	.00292	.00274	.00258
40	.00310	.00288	.00268	.00252
41	.00307	.00283	.00263	.00247
42	.00303	.00279	.00259	.00242
43	.00300	.00274	.00253	.00237
44	.00297	.00273	.00251	.00235
45	.00295	.00270	.00248	.00232
46	.00293	.00267	.00245	.00229
47	.00291	.00265	.00242	.00226
48	.00289	.00263	.00240	.00224
49	.00288	.00261	.00238	.00222
50	.00286	.00259	.00236	.00220
51	.00285	.00257	.00234	.00218
52	.00284	.00255	.00232	.00216
53	.00283	.00253	.00230	.00214
54	.00282	.00251	.00228	.00212
55	.00281	.00249	.00226	.00210
56	.00280	.00247	.00224	.00208
57	.00279	.00245	.00222	.00206
58	.00278	.00243	.00220	.00204
59	.00277	.00241	.00218	.00202
60	.00276	.00239	.00216	.00200
61	.00275	.00237	.00214	.00198
62	.00274	.00235	.00212	.00196
63	.00273	.00233	.00210	.00194
64	.00272	.00231	.00208	.00192
65	.00271	.00229	.00206	.00190
66	.00270	.00227	.00204	.00188
67	.00269	.00225	.00202	.00186
68	.00268	.00223	.00200	.00184
69	.00267	.00221	.00198	.00182
70	.00266	.00219	.00196	.00180
71	.00265	.00217	.00194	.00178
72	.00264	.00215	.00192	.00176
73	.00263	.00213	.00190	.00174
74	.00262	.00211	.00188	.00172
75	.00261	.00209	.00186	.00170
76	.00260	.00207	.00184	.00168
77	.00259	.00205	.00182	.00166
78	.00258	.00203	.00180	.00164
79	.00257	.00201	.00178	.00162
80	.00256	.00199	.00176	.00160
81	.00255	.00197	.00174	.00158
82	.00254	.00195	.00172	.00156
83	.00253	.00193	.00170	.00154
84	.00252	.00191	.00168	.00152
85	.00251	.00189	.00166	.00150
86	.00250	.00187	.00164	.00148
87	.00249	.00185	.00162	.00146
88	.00248	.00183	.00160	.00144
89	.00247	.00181	.00158	.00142
90	.00246	.00179	.00156	.00140
91	.00245	.00177	.00154	.00138
92	.00244	.00175	.00152	.00136
93	.00243	.00173	.00150	.00134
94	.00242	.00171	.00148	.00132
95	.00241	.00169	.00146	.00130
96	.00240	.00167	.00144	.00128
97	.00239	.00165	.00142	.00126
98	.00238	.00163	.00140	.00124
99	.00237	.00161	.00138	.00122
100	.00236	.00159	.00136	.00120

Table X-1-H. Leukemia, All Types Except CLL: Risk Coefficient $E(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	7.31	4.66	38	3.39	2.17
1	6.87	4.38	39	3.54	2.27
2	6.42	4.10	40	3.72	2.38
3	5.97	3.81	41	3.92	2.50
4	5.53	3.53	42	4.14	2.64
5	5.09	3.25	43	4.39	2.80
6	4.67	2.99	44	4.67	2.97
7	4.27	2.73	45	4.98	3.16
8	3.90	2.50	46	5.32	3.37
9	3.56	2.28	47	5.71	3.61
10	3.26	2.09	48	6.13	3.86
11	3.00	1.92	49	6.60	4.15
12	2.79	1.78	50	7.11	4.46
13	2.62	1.68	51	7.67	4.80
14	2.52	1.61	52	8.27	5.17
15	2.46	1.57	53	8.92	5.57
16	2.42	1.55	54	9.61	6.00
17	2.39	1.53	55	10.3	6.45
18	2.36	1.51	56	11.1	6.93
19	2.34	1.50	57	11.9	7.42
20	2.33	1.49	58	12.6	7.92
21	2.33	1.49	59	13.4	8.42
22	2.33	1.49	60	14.2	8.92
23	2.34	1.50	61	14.9	9.40
24	2.36	1.51	62	15.6	9.86
25	2.39	1.53	63	16.2	10.3
26	2.43	1.55	64	16.8	10.7
27	2.47	1.58	65	17.3	11.0
28	2.52	1.61	66	17.8	11.3
29	2.58	1.65	67	18.2	11.6
30	2.63	1.68	68	18.5	11.9
31	2.70	1.73	69	18.9	12.1
32	2.77	1.77	70	19.2	12.2
33	2.84	1.82	71	19.5	12.4
34	2.93	1.88	72	19.7	12.5
35	3.02	1.94	73	20.0	12.7
36	3.13	2.01	74	20.2	12.8
37	3.25	2.08	75	20.5	12.9

Table X-1-1. Leukemia, All Types Except CLL: Baseline Incidence $I(a_1, S)$ by Age at Diagnosis a_1 and Sex S

a_1	Sex		a_1	Sex	
	Male	Female		Male	Female
0	7.00	5.70	43	4.22	3.47
1	7.00	5.70	44	4.52	3.70
2	7.00	5.70	45	4.87	3.97
3	6.65	5.44	46	5.24	4.25
4	5.83	4.80	47	5.60	4.50
5	4.80	4.01	48	5.98	4.73
6	3.86	3.27	49	6.38	4.95
7	3.30	2.80	50	6.80	5.16
8	3.04	2.54	51	7.25	5.38
9	2.81	2.31	52	7.71	5.60
10	2.64	2.10	53	8.20	5.85
11	2.54	1.93	54	8.77	6.15
12	2.50	1.80	55	9.47	6.51
13	2.53	1.68	56	10.3	6.92
14	2.58	1.56	57	11.4	7.41
15	2.65	1.46	58	12.7	7.97
16	2.69	1.40	59	14.0	8.60
17	2.70	1.40	60	15.3	9.29
18	2.63	1.44	61	16.7	10.0
19	2.49	1.48	62	18.0	10.7
20	2.34	1.52	63	19.2	11.5
21	2.23	1.56	64	20.4	12.2
22	2.20	1.60	65	21.6	13.0
23	2.29	1.64	66	22.9	13.8
24	2.45	1.68	67	24.2	14.6
25	2.64	1.72	68	26.2	15.5
26	2.80	1.76	69	28.9	16.6
27	2.90	1.80	70	32.3	17.7
28	2.93	1.84	71	35.9	18.9
29	2.94	1.88	72	39.6	20.2
30	2.94	1.93	73	43.3	21.6
31	2.96	2.00	74	47.1	23.3
32	3.00	2.10	75	50.9	25.1
33	3.07	2.22	76	54.8	27.0
34	3.15	2.34	77	58.6	29.0
35	3.23	2.46	78	62.8	31.5
36	3.31	2.58	79	67.2	34.5
37	3.40	2.70	80	71.6	37.5
38	3.49	2.82	81	75.8	40.2
39	3.59	2.94	82	79.4	42.1
40	3.71	3.06	83	82.1	43.5
41	3.84	3.18	84	84.0	44.6
42	4.00	3.30	85	85.3	45.5

2. Cancer of Bones and Joints (170 in ICDA-8)

Bone cancer is relatively uncommon and radiogenic bone cancer has been seen mainly in association with internally deposited isotopes of radium, especially in radium-dial painters exposed to long-lived radium-226 and -228 (10), and in German patients treated with short-lived radium-224 for tuberculosis and ankylosing spondylitis (11). Radiogenic bone cancer has also been reported following high doses of X rays (4), especially among ankylosing spondylitis patients. It has not been seen in the A-bomb survivors (4).

For the BEIR III report, risk coefficients were first calculated for repeated acute exposures to radium-224 and the "provisional" low-LET coefficients, as they are termed in the BEIR report, were derived from them through the use of the ICRP quality factor of 20 for alpha particles. Tables were prepared for leukemia plus bone cancer and not for each separately. This was done because the temporal distribution of excess bone cancer is rather like that for leukemia: the latent period is short, four years or less, and the total period of expression, perhaps 20-25 years.

Since the only human data on the risk of bone cancer following exposure to low-LET radiation pertain to therapeutic levels of dose, the Working Group decided that it should not make PC estimates for bone cancer resulting from low-LET radiation but should confine its calculations to the alpha radiation on which the BEIR estimates rest. The BEIR III linear estimate, based on the radium-224 experience, is one excess bone cancer per million persons per year per rad of alpha radiation to endosteal tissue (4). Hence Table X-2-B will not be used for the purpose of PC estimation for exposure to low-LET radiation, or to greatly protracted high-LET radiation from, e.g., radium-226.

The BEIR report provides little basis for a choice for either the dose-response or the time-response model. The linear function is assumed for high-LET radiation, but more for consistency with experimental results for tumors generally rather than because of the empirical evidence on the induction of bone cancer in man following exposure to radium-224. For alpha particles from radium-224 the BEIR risk coefficient of 1 per million persons per year per rad of endosteal dose is a fairly stable linear estimate, being based on 54 cases vs. an expectation of only 0.2 cases (11). Information on variation with age is only fair, but the indications are that younger patients experienced a risk very little higher than that of adult patients, and no sex differential was observed (4). The lowest doses at which excess cases have been observed in the radium-224 series are above 50 rad of alpha radiation to the endosteum, so that the applicability of the data to lower doses remains uncertain. The best PC estimates would be those for doses of radium-224 alpha radiation within the observed range, average skeletal doses being mostly above 90 rad.

The BEIR committee employed a constant absolute risk (plateau) for bone cancer in combining it with leukemia, with no dose threshold, but the Working Group has used a wave function, as it has for leukemia, and for this assumption there is good recent evidence (12). Published data from the German radium-224 series were used to fit a lognormal induction

period model (13). The fitted model had a minimum induction period of 1.52 years and the natural logarithm of time after the minimum had a mean of 2.12 and a variance of 0.48.

United States incidence data for cancers of bones and joints have been taken from the SEER data bank for 1973-1981 (8). As may be seen from Tables VII-1 and VII-2, there is relatively little variation among the SEER reporting areas (8), although a sex differential is well established, females having about 60 percent of the level reported for males. Radiation is the only environmental factor that is known to play an etiologic role in bone cancer (14). Statistical studies of racial differences in the incidence of Ewing's tumor and studies of family aggregations point to the influence of genetic factors on some forms of bone cancer (15). If an individual is known to be a member of a sub-population with an elevated baseline risk, then the PC estimate obtained on the basis of the SEER rates will be excessive (see Chapter IV-G and Chapter IX).

For bone cancer, as for leukemia, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F \times T \times K$$

where $F = F(D)$ represents the alpha radiation dose to endosteal tissue (D); $T = T(Y)$ represents the influence of the interval from exposure to diagnosis; and $K = K(A_1, A_2, S)$ represents relative excess of bone cancer for a person of sex S and ages A_1 and A_2 at exposure and diagnosis, respectively, when both F and T = 1. Here K is found as

$$K = E(A_1, S)/I(A_2, S)$$

where $E(A_1, S)$ is derived from BEIR III and is an estimate of the probability that a radiation-induced bone cancer will be diagnosed at some time after exposure to radium-224, and is expressed in units of dose. For each exposure age A_1 and sex S, $E(A_1, S)$ was determined such that the average of $E(A_1, S) \times T(Y)$ over the BEIR III plateau period ($Y = 2$ through 28) was equal to the BEIR coefficient, 0.1 excess cancers per hundred thousand persons per year per rad.

Look-up tables are provided below for the following coefficients:

$T(Y)$, Table X-2-A;

$E(A_1, S)$, Table X-2-B;

$I(A_2, S)$, Table X-2-C.

Here, under the linear model assumed for high-LET radiation, the endosteal dose in rad is

$$F = D.$$

The constant relative risk model for time to response was not assumed to hold for bone cancer, which appears to follow a "wave" function, and therefore the factor T is the probability that a cancer caused by an exposure at age A_1 will be diagnosed Y years later.

A few examples are given below to illustrate the use of the tables in deriving the PC values.

Example #1 A typical male, exposed to 50 rad of brief alpha radiation to endosteal tissue at age 10, with a diagnosis of bone cancer 6.5 years later, at age 16. Then $A_1 = 10$, $A_2 = 16$, $Y = 6$, and $D = 50$

$$F(D) = 50$$

$$T(Y) = T(6) = .0874$$

$$E(A_1, S) = E(10, m) = 2.79$$

$$I(A_2, S) = I(16, m) = 1.54$$

$$K = E/I = 2.79/1.54 = 1.812$$

$$\text{then } R = F \times T \times K = 50 \times .0874 \times 1.812 = 7.91$$

$$\text{and } PC = R/(1 + R) = 7.91/8.91 = .89 \text{ or } 89\%.$$

Example #2 A typical female exposed to 100 rad of brief alpha radiation to endosteal tissue at age 7, with a diagnosis of bone cancer at age 20, 12.5 years after exposure. Then $A_1 = 7$, $A_2 = 20$, $Y = 12$, and $D = 100$.

$$F(D) = 100$$

$$T(12) = .0485$$

$$E(7, f) = 2.81$$

$$I(20, f) = .781$$

$$K = E/I = 2.81/.781 = 3.60$$

$$\text{then } R = F \times T \times K = 100 \times .0485 \times 3.60 = 17.5$$

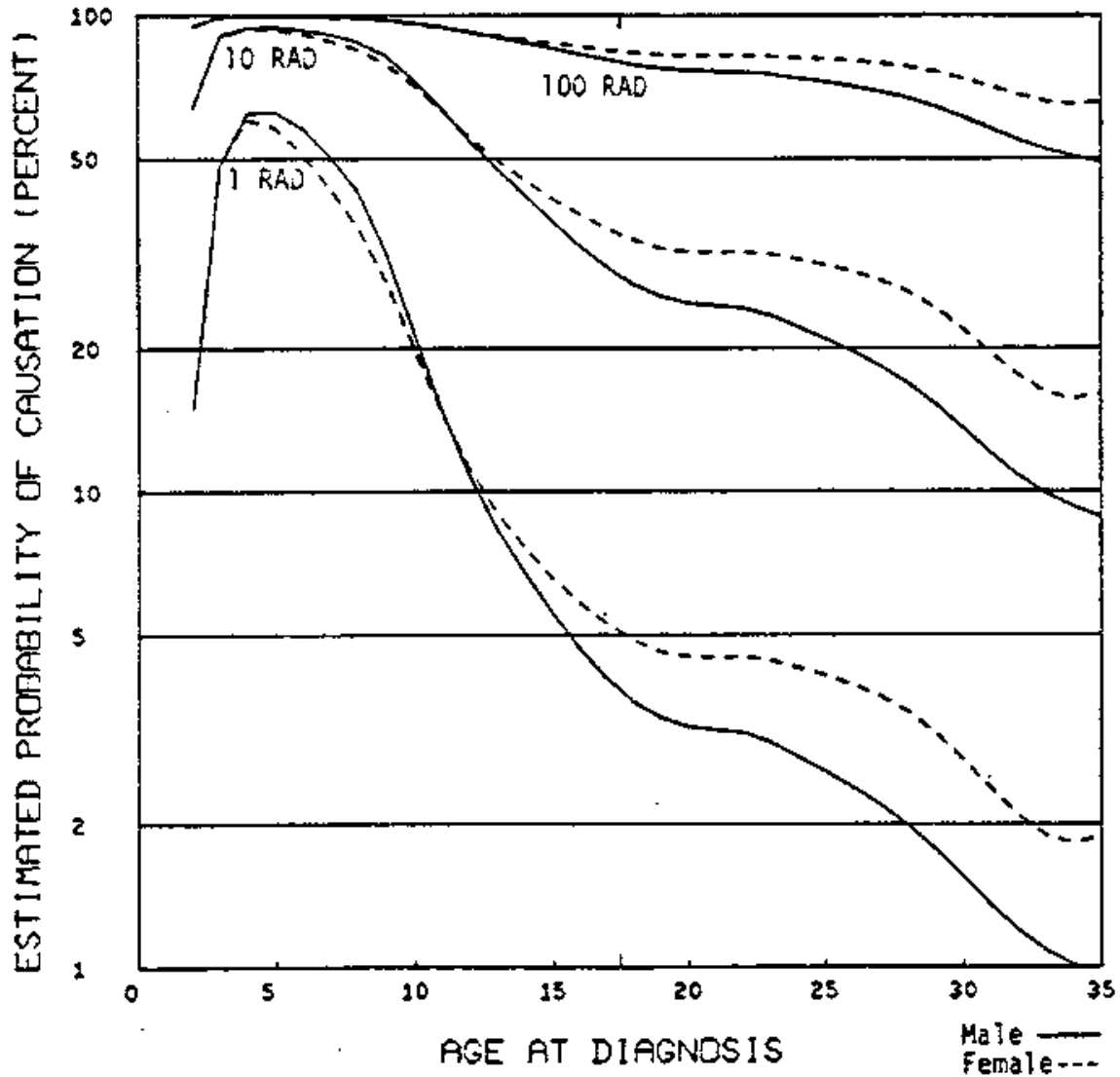
$$\text{and } PC = R/(1+R) = 17.5/18.5 = .946 \text{ or } 95\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide some orientation to the general magnitude of the PC values resulting from the procedures described here for bone cancer, Fig. X-2 has been drawn for endosteal doses of 1, 10, and 100 rad to show the PC values by age at exposure and sex. The figure is in 8 parts corresponding to ages 0, 10, 20, 30, 40, 50, 60, and 70 at exposure. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

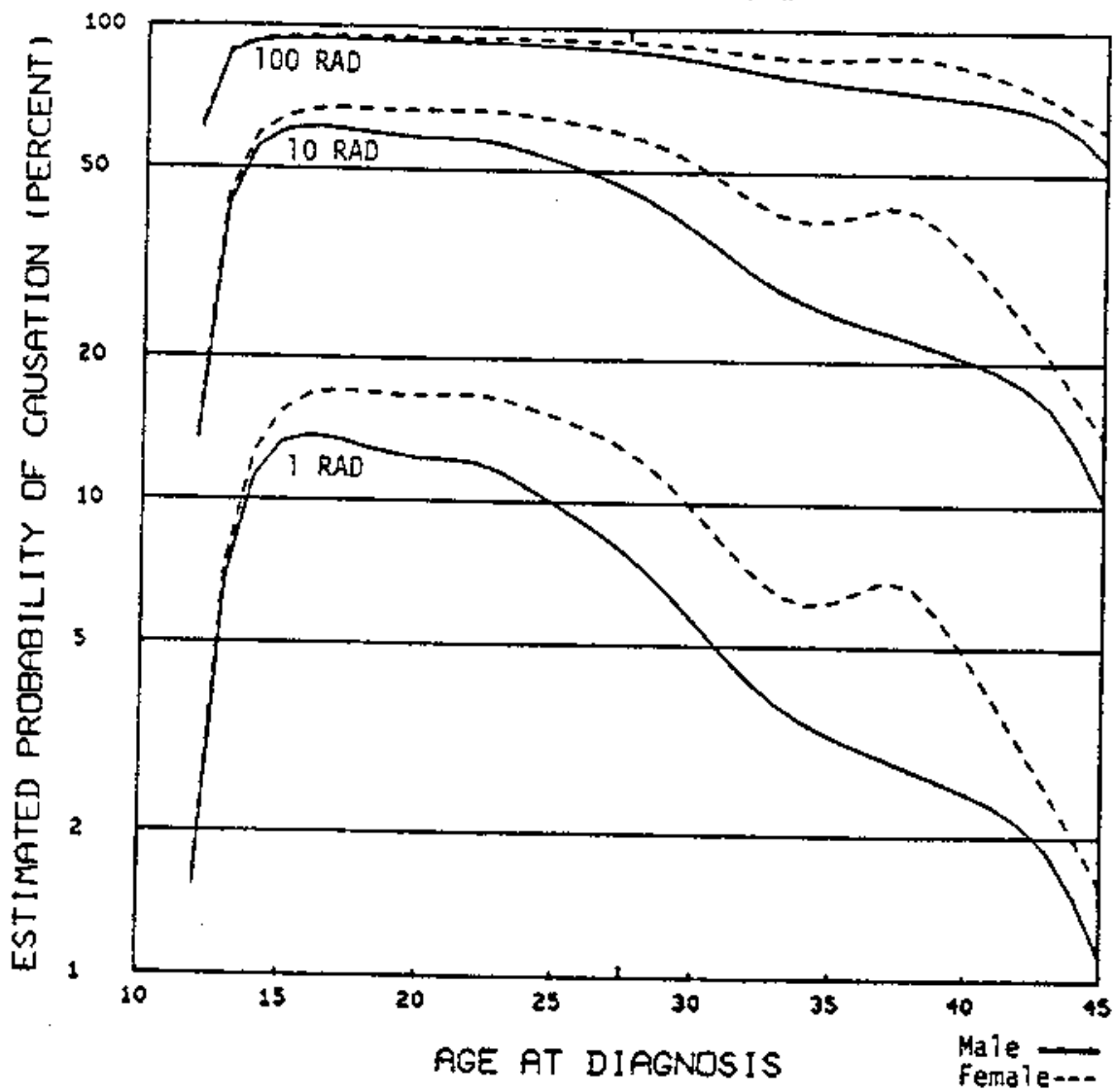
Fig X-2-1

BONE AND JOINT CANCER *
EXPOSURE AGE 0



*Alpha radiation from radium-224 only

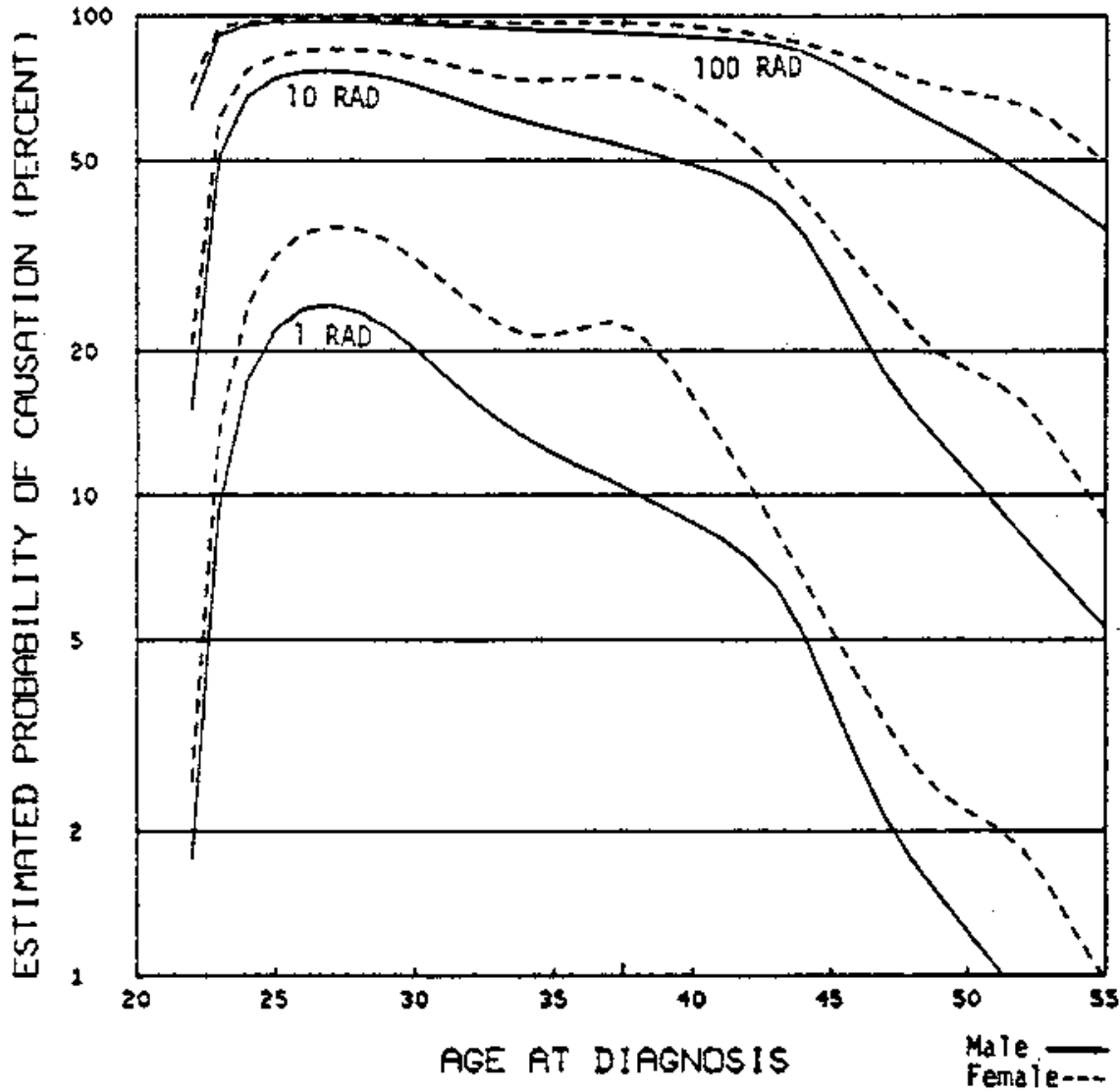
BONE AND JOINT CANCER*
EXPOSURE AGE 10



*Alpha radiation from radium-224 only

Fig X-2-3

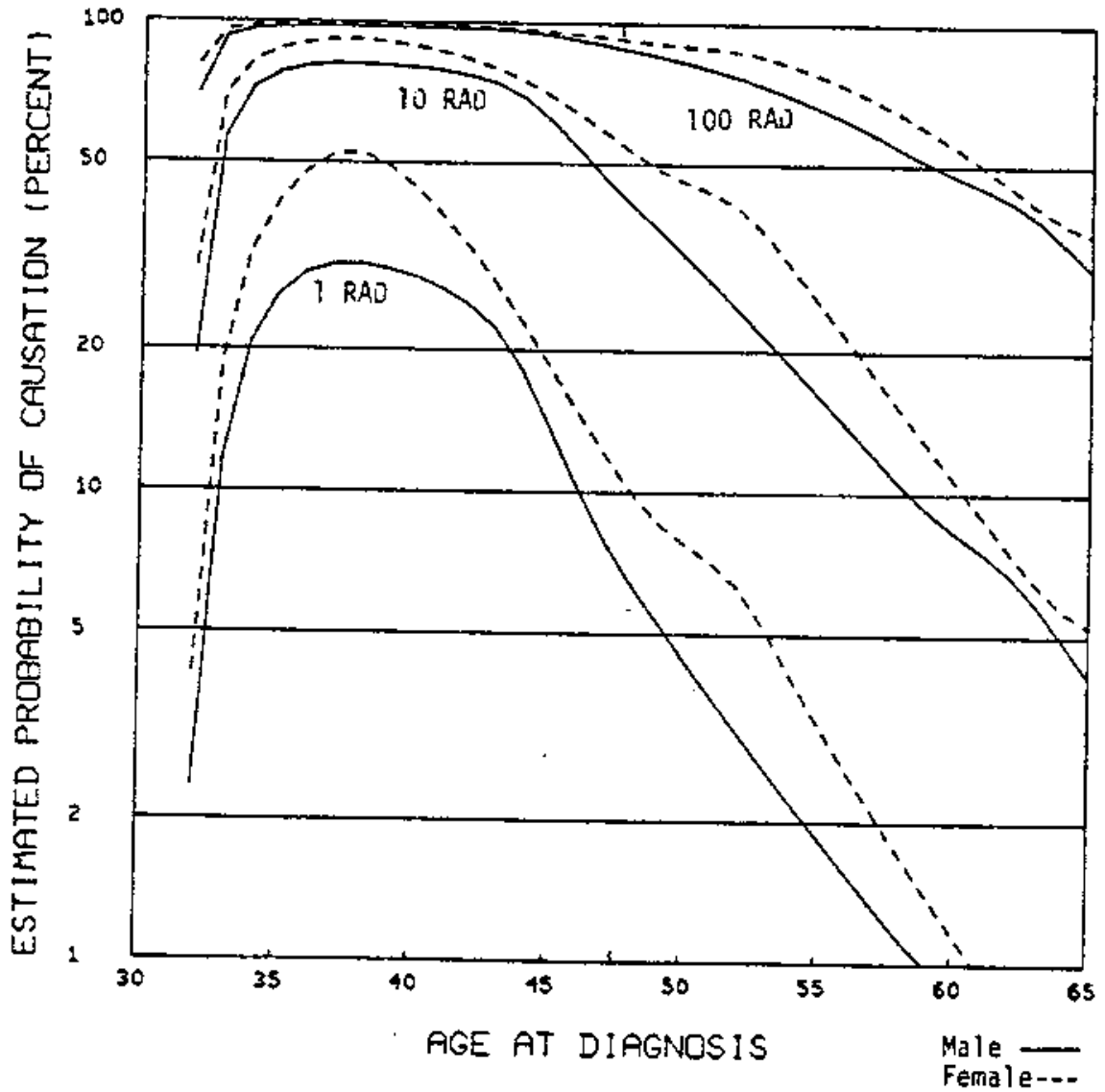
BONE AND JOINT CANCER *
EXPOSURE AGE 20



*Alpha radiation from radium-224 only

Fig X-2-4

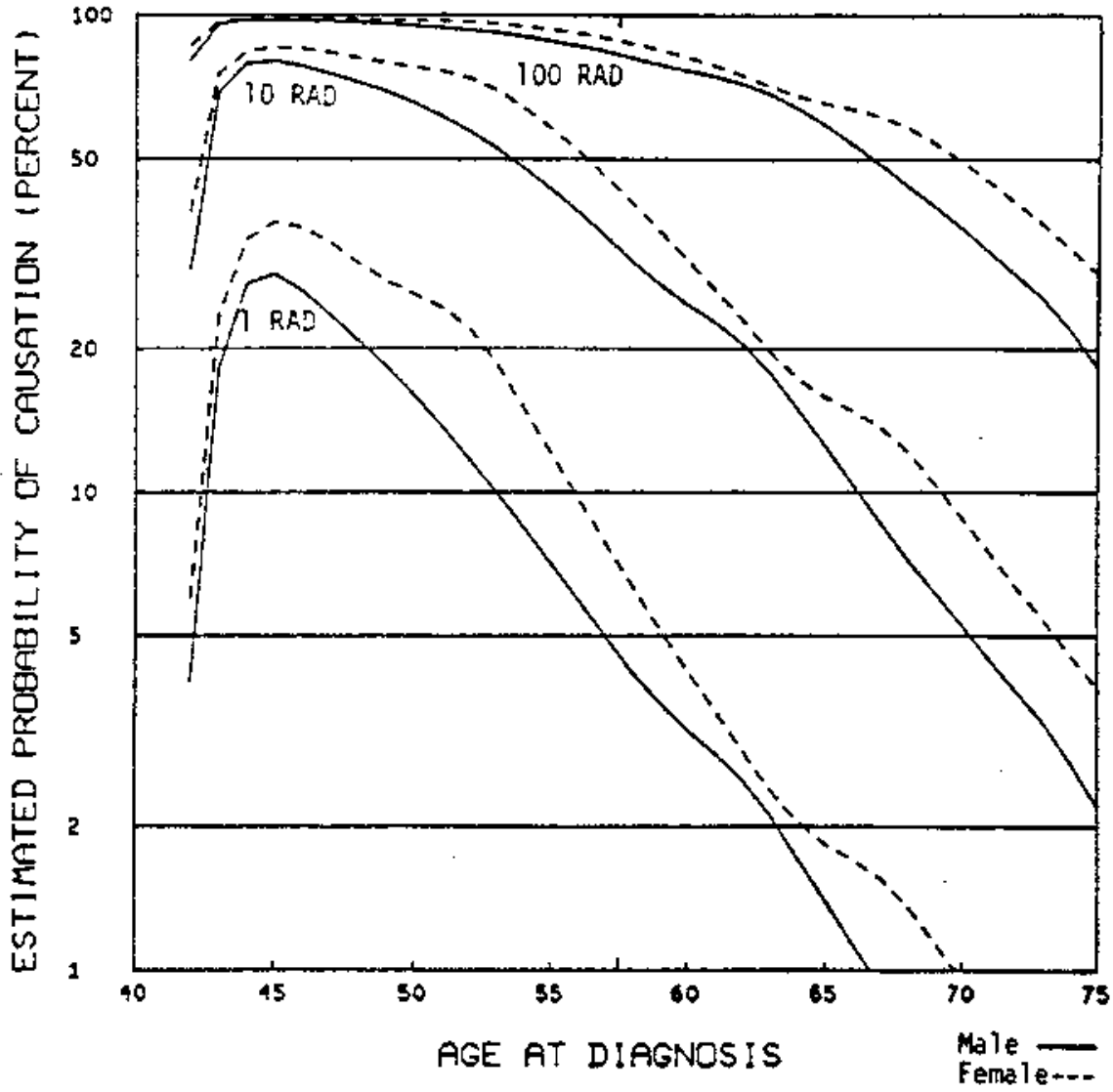
BONE AND JOINT CANCER*
EXPOSURE AGE 30



*Alpha radiation from radium-224 only

Fig X-2-5

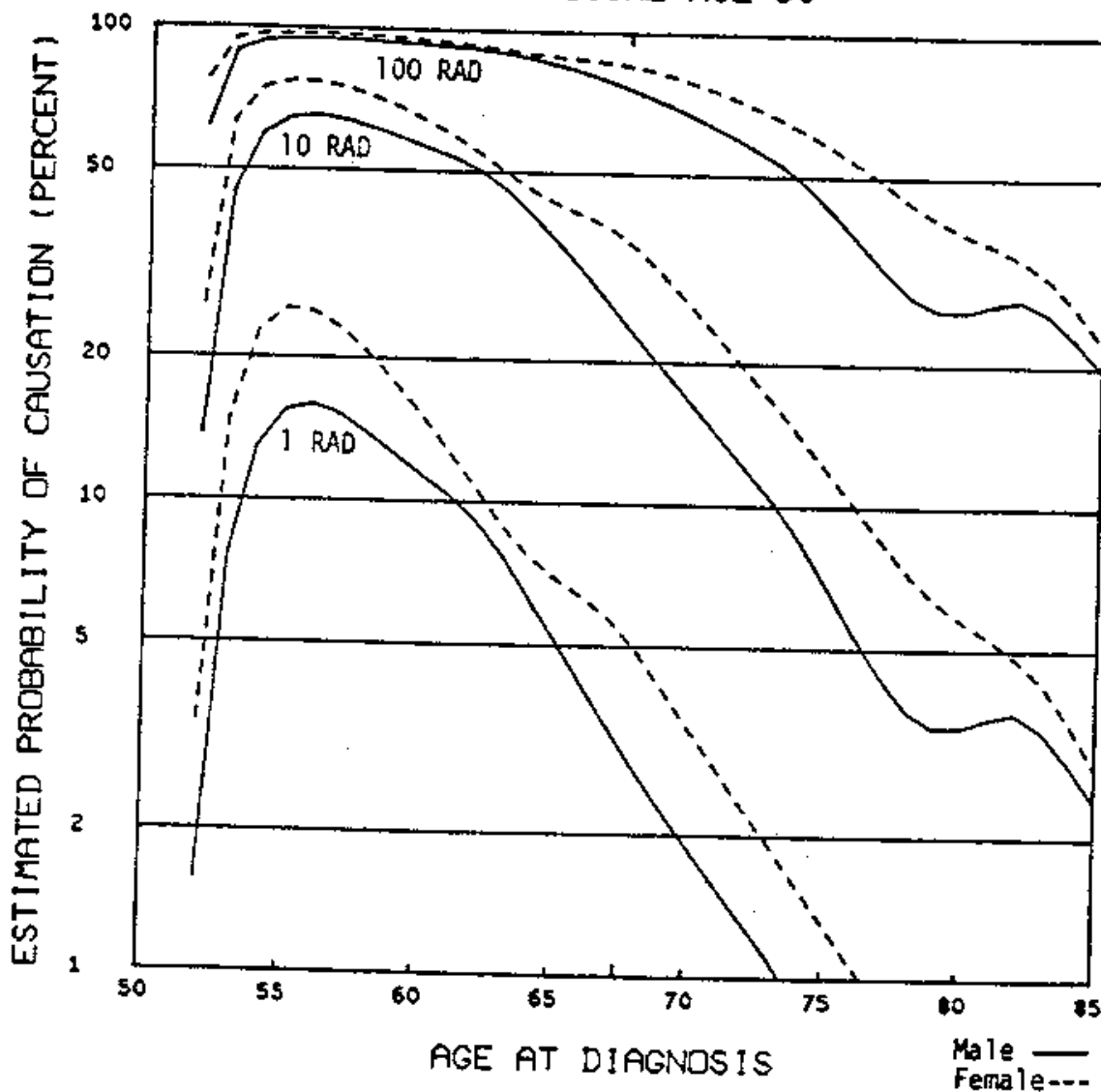
BONE AND JOINT CANCER *
EXPOSURE AGE 40



*Alpha radiation from radium-224 only

Fig X-2-6

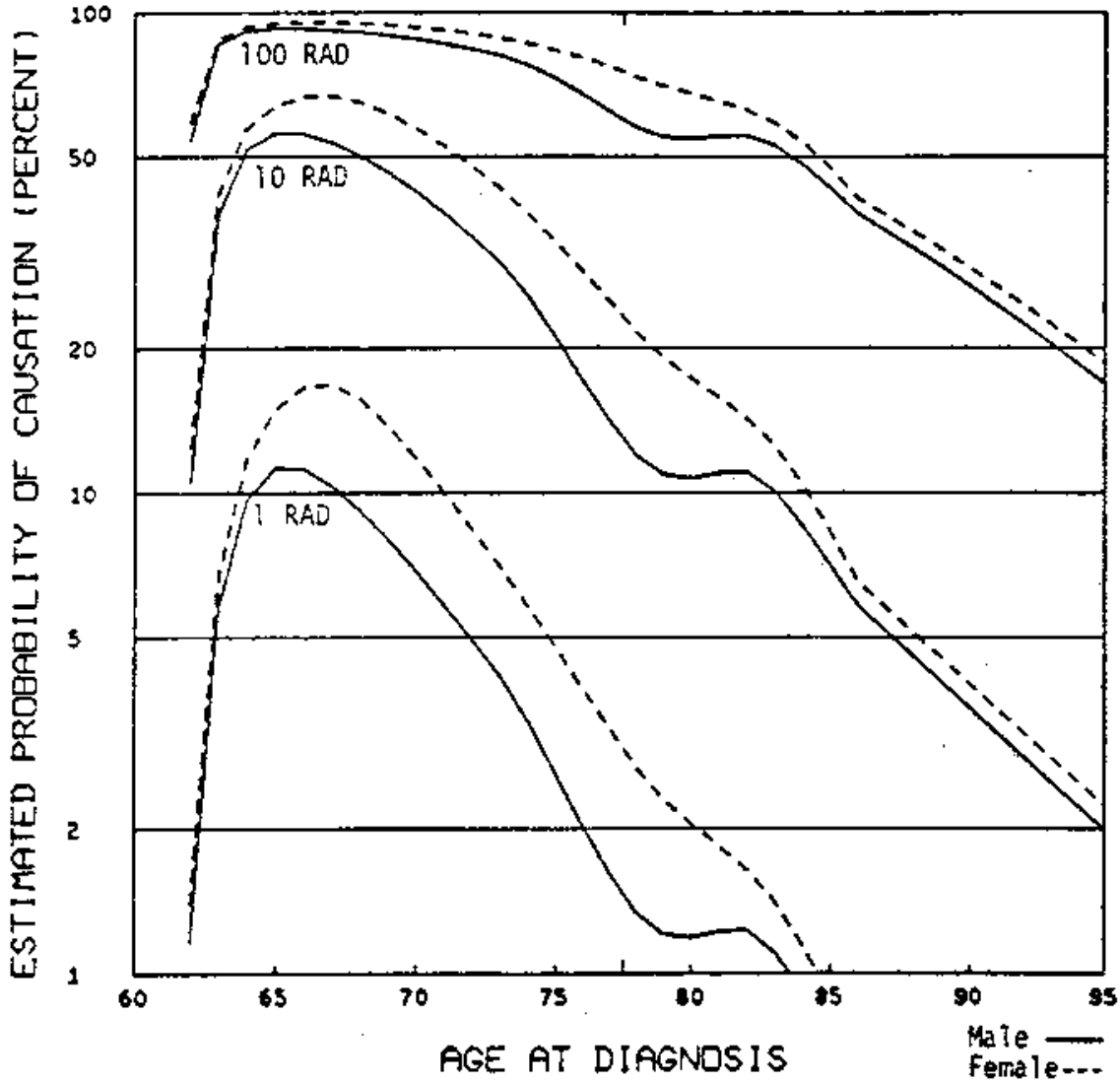
BONE AND JOINT CANCER*
EXPOSURE AGE 50



*Alpha radiation from radium-224 only

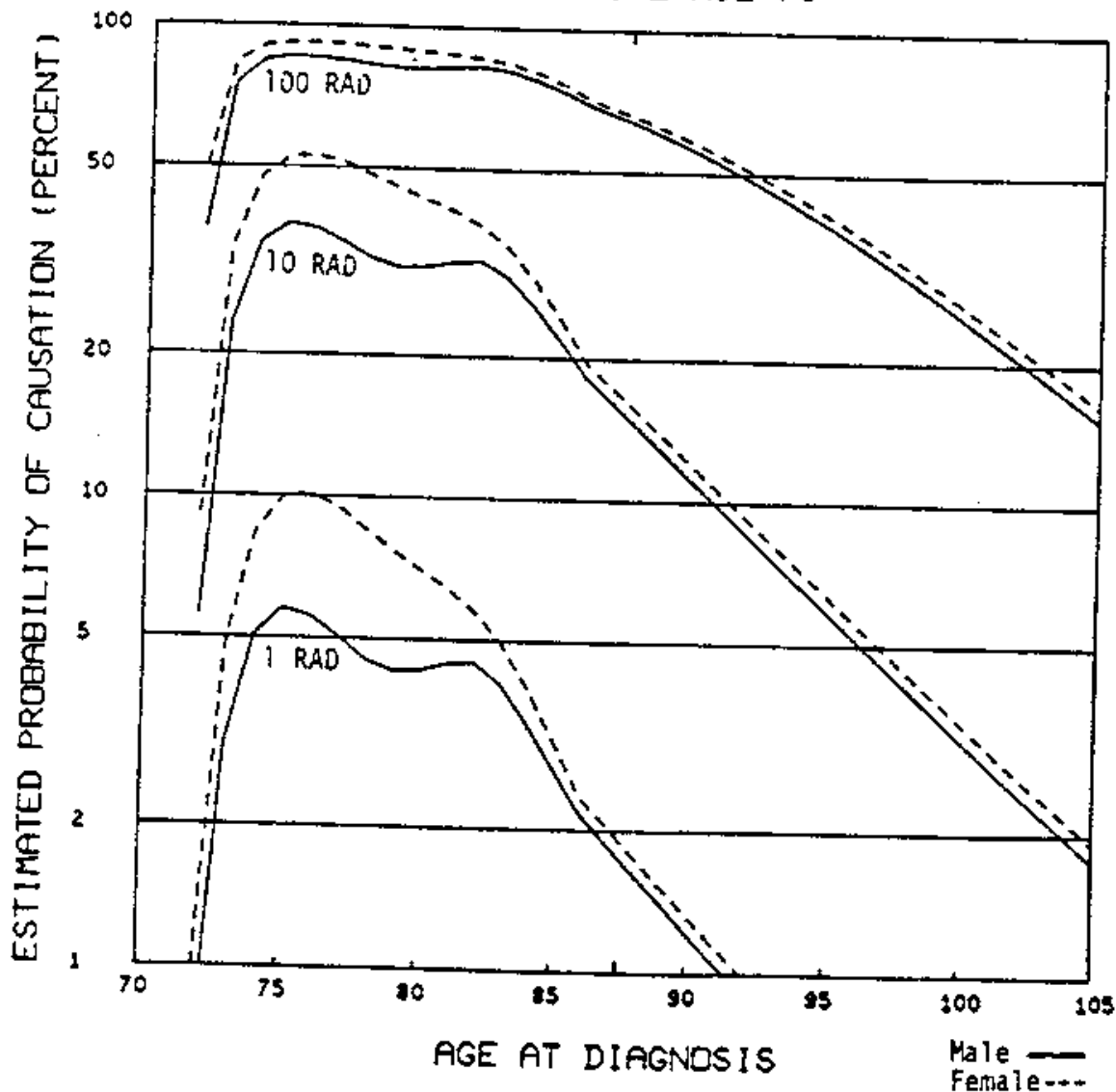
Fig X-2-7

BONE AND JOINT CANCER*
EXPOSURE AGE 60



*Alpha radiation from radium-224 only

BONE AND JOINT CANCER*
EXPOSURE AGE 70



*Alpha radiation from radium-224 only

Table X-2-A. Bone and Joint Cancer:
 Temporal Distribution T(Y) by Year Y
 After Exposure

Y	T(Y)	Y	T(Y)
0	0	25	.00750
1	.0000190	26	.00657
2	.00629	27	.00577
3	.0338	28	.00507
4	.0637	29	.00446
5	.0814	30	.00394
6	.0874	31	.00348
7	.0857	32	.00308
8	.0798	33	.00274
9	.0720	34	.00243
10	.0638	35	.00216
11	.0558	36	.00193
12	.0485	37	.00172
13	.0419	38	.00154
14	.0362	39	.00138
15	.0312	40	.00124
16	.0269	41	.00111
17	.0232	42	.00100
18	.0200	43	.000900
19	.0173	44	.000812
20	.0150	45	.000733
21	.0130	46	.000662
22	.0113	47	.000600
23	.00984	48	.000543
24	.00858	49	.000493

Table X-2-B. Bone and Joint Cancer: Risk Coefficient $E(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	2.80	2.81	38	2.65	2.73
1	2.80	2.81	39	2.63	2.72
2	2.80	2.81	40	2.62	2.71
3	2.80	2.81	41	2.60	2.71
4	2.80	2.81	42	2.59	2.70
5	2.80	2.81	43	2.57	2.69
6	2.80	2.81	44	2.55	2.68
7	2.79	2.81	45	2.53	2.67
8	2.79	2.81	46	2.51	2.65
9	2.79	2.81	47	2.49	2.64
10	2.79	2.81	48	2.47	2.63
11	2.79	2.81	49	2.45	2.61
12	2.79	2.81	50	2.42	2.59
13	2.79	2.81	51	2.40	2.58
14	2.79	2.81	52	2.37	2.55
15	2.79	2.80	53	2.35	2.53
16	2.79	2.80	54	2.32	2.51
17	2.79	2.80	55	2.30	2.48
18	2.78	2.80	56	2.27	2.46
19	2.78	2.80	57	2.24	2.43
20	2.78	2.80	58	2.21	2.40
21	2.78	2.80	59	2.18	2.37
22	2.77	2.79	60	2.16	2.33
23	2.77	2.79	61	2.13	2.30
24	2.77	2.79	62	2.10	2.26
25	2.76	2.79	63	2.07	2.23
26	2.76	2.78	64	2.04	2.19
27	2.75	2.78	65	2.02	2.15
28	2.74	2.78	66	1.99	2.12
29	2.74	2.77	67	1.97	2.08
30	2.73	2.77	68	1.95	2.05
31	2.72	2.77	69	1.92	2.02
32	2.71	2.76	70	1.91	1.98
33	2.71	2.76	71	1.89	1.96
34	2.70	2.75	72	1.87	1.93
35	2.68	2.75	73	1.86	1.90
36	2.67	2.74	74	1.85	1.88
37	2.66	2.74	75	1.84	1.86

Table X-2-C. Bone and Joint Cancer: Baseline Incidence
I(A₁,S) by Age at Diagnosis A₂ and Sex S

A ₂	Sex		A ₂	Sex	
	Male	Female		Male	Female
0	.100	.100	43	.444	.337
1	.100	.100	44	.532	.379
2	.100	.100	45	.638	.424
3	.109	.118	46	.736	.465
4	.136	.165	47	.801	.500
5	.178	.234	48	.841	.510
6	.233	.315	49	.881	.493
7	.300	.400	50	.921	.471
8	.431	.528	51	.961	.467
9	.646	.714	52	1.00	.501
10	.896	.916	53	1.04	.561
11	1.13	1.09	54	1.08	.621
12	1.30	1.20	55	1.12	.681
13	1.41	1.24	56	1.16	.741
14	1.49	1.25	57	1.20	.801
15	1.54	1.22	58	1.21	.861
16	1.54	1.17	59	1.20	.921
17	1.50	1.10	60	1.17	.981
18	1.40	1.01	61	1.16	1.04
19	1.27	.895	62	1.20	1.10
20	1.12	.781	63	1.29	1.12
21	.987	.677	64	1.39	1.09
22	.900	.600	65	1.50	1.03
23	.845	.543	66	1.61	.991
24	.795	.494	67	1.71	1.00
25	.753	.453	68	1.79	1.05
26	.720	.421	69	1.87	1.11
27	.700	.400	70	1.95	1.17
28	.696	.392	71	2.03	1.24
29	.703	.396	72	2.11	1.30
30	.713	.404	73	2.28	1.38
31	.715	.408	74	2.54	1.46
32	.700	.400	75	2.83	1.55
33	.667	.369	76	3.07	1.63
34	.627	.318	77	3.21	1.71
35	.582	.263	78	3.07	1.72
36	.538	.218	79	2.71	1.68
37	.500	.200	80	2.29	1.62
38	.465	.205	81	1.97	1.59
39	.434	.220	82	1.91	1.61
40	.409	.242	83	2.00	1.74
41	.396	.269	84	2.15	1.95
42	.400	.300	85	2.31	2.21

3. Salivary Gland Cancer (142 in ICDA-8)

The 1980 BEIR report (4) included the salivary glands among the sites sensitive to radiation carcinogenesis, but probably only at high dose levels, and summary risk coefficients were not presented. The evidence for a radiation effect rests mainly on follow-up studies of patients with histories of therapeutic irradiation to the head and neck during infancy or childhood, with doses to the salivary gland ranging from about 40 rad for X-ray epilation of the scalp to as much as 800 rad for irradiation of the thymus gland or the tonsils (16-22). A recent review (23) included a linear regression analysis of dose response in which data from these studies were combined. The several studies agreed reasonably well with an estimated excess risk per rad of 0.26 cases per million person-years, when a minimal induction period of 5 years was assumed. Estimates also were derived from two studies of A-bomb survivors (24,25), but these estimates seemed less reliable because of limited data in one and uncertain dosimetry and uncertain numbers of person-years in the other.

The Working Group considers that available data support an estimated risk of 0.26 excess salivary gland cancers per million person-years per rad following a radiation exposure during infancy or childhood, that is, before age 15. This level of risk applies 10 years after exposure, with somewhat lower risks 5-9 years after exposure. No estimate was calculated for exposures at older ages.

The available data are much too fragile for critical examination of dose-response and time-response models appropriate to the salivary glands, and the Working Group has assumed that excess cancer of the salivary glands could be adequately described by means of the linear-quadratic dose-response model and the constant relative risk time-response model. The standard assumptions as to absence of threshold and 10-year latent period, smoothed as described in Chapter VI, have also been made.

Incidence data for the U.S. have been extracted from the data bank for the SEER program of the National Cancer Institute. The rates used to represent normal or baseline incidence are for the period 1973-1981, all races combined, and all reporting areas combined except Puerto Rico. There is little variation among the reporting areas as to level of risk, but the rates for females are about 75 percent of those for males (8).

As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures will be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

The procedures for calculating PC values for cancers of the salivary glands based on the assumptions and principles of Chapter V and are detailed in Chapters VI and IX. For cancers of the salivary glands, as

for cancers of most other sites, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the tissue dose (D) in rad, T(Y) the influence of the time from exposure to diagnosis (Y), and K(A₁, S) the relative excess risk of salivary gland cancer for a person of age at exposure A₁ and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for cancers of the salivary gland, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancers of the salivary glands, the influence of time, T, depends entirely upon completed years from exposure to diagnosis (Y). The function T is tabulated below.

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess cancer of the salivary glands, K, is given in the accompanying table for low-LET radiation and for each sex and year of age (completed years) from birth to age 14.

A few examples should clarify the actual computational procedures for cancers of the salivary glands following exposure to ionizing radiation.

Example #1 A typical female, exposed at age 5 to 3 rad of low-LET radiation to the salivary glands, with diagnosis at age 12, 7.2 years after exposure. Then D = 3, A₁ = 5, and Y = 7.

$$F(D) = 3 + 3^2/116 = 3.1$$

$$T(Y) = T(7) = 0.5$$

$$K(A_1, S) = K(5, f) = .0300$$

and R may be found from the relation

$$R = F \times T \times K = 3.1 \times 0.5 \times .030 = .0465$$

$$\text{and } PC = R/(1+R) = .0465/1.0465 = .044, \text{ or } 4\%.$$

Example #2 A typical male, exposed at age 18 to 5 rad of low-LET radiation to the salivary glands, with diagnosis at age 30. No estimate can be made because the information is not available for estimating the risk associated with exposure after age 14.

Example #3 A typical male, aged 7 at first exposure to 6 rad of low-LET radiation to the salivary glands, and aged 12 at the second exposure to 5 rad of low-LET radiation, with diagnosis at age 20, 8.3 years after the second exposure and more than 10 years after the first. This example requires that two estimates of R be made, one for each exposure.

Exposure at age 7, when $D = 6$, $A_1 = 7$, and $Y = 13$

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(13) = 1$$

$$K(7,m) = .0311$$

$$\text{and } R(7) = F \times T \times K = 6.31 \times 1 \times .0311 = .196$$

Exposure at age 12, when $D = 5$, $A_1 = 12$, and $Y = 8$

$$F(5) = 5 + 5^2/116 = 5.22$$

$$T(8) = .741$$

$$K(12,m) = .0214$$

$$R(12) = 5.22 \times .741 \times .0214 = .0828$$

$$\text{then } R = R(7) + R(12) = .196 + .083 = .279$$

$$\text{and } PC = R/(1 + R) = .279/1.279 = .22 \text{ or } 22\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide some orientation to the general magnitude of the PC values resulting from the procedures described here for the salivary glands, Fig X-3 has been drawn for tissue doses of 1, 10, and 100 rad to show the PC values by age at exposure and sex. The calculations were performed with $T(Y) = 1$, i.e., on the assumption that the interval from exposure to diagnosis was 10 or more years. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-3

SALIVARY GLAND CANCER

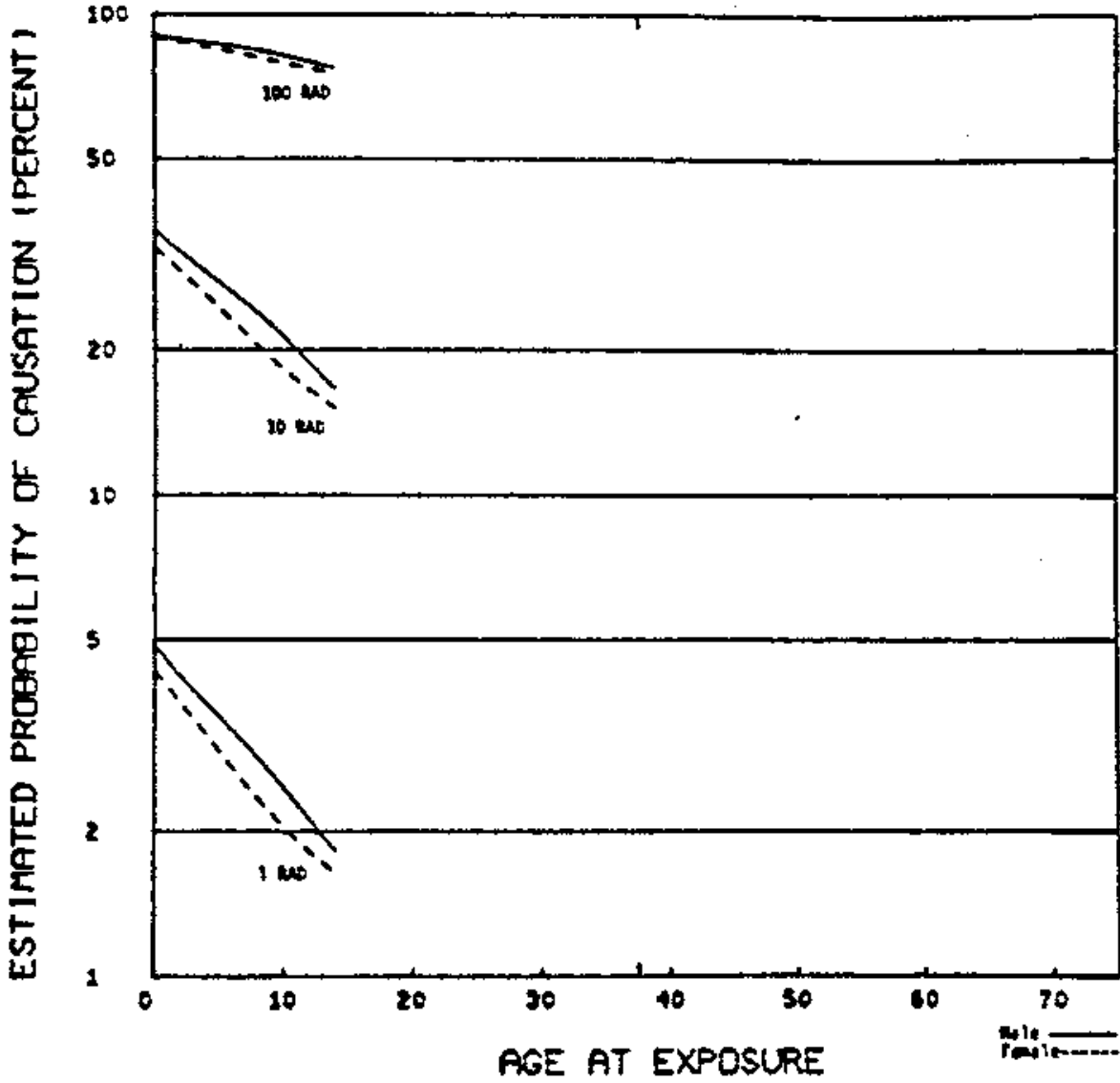


Table X-3. Salivary Gland Cancer: Relative Excess
 $K(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	.0509	.0446	8	.0290	.0237
1	.0467	.0412	9	.0270	.0221
2	.0433	.0380	10	.0250	.0206
3	.0405	.0351	11	.0231	.0194
4	.0379	.0325	12	.0214	.0183
5	.0355	.0300	13	.0198	.0174
6	.0332	.0277	14	.0184	.0165
7	.0311	.0256			

4. Esophageal Cancer (150 in ICDA-8)

The esophagus is apparently not especially sensitive to the carcinogenic influence of ionizing radiation, but is included among the sites for which risk estimates have been made by both the BEIR III committee (4) and the UN committee in its 1977 report (2). The Working Group has employed the BEIR III risk coefficients (adjusted to the period 11-30 years after exposure) for individuals exposed after age 20; those for exposure under age 20 were considered unreliable for the present purpose (see Chapter VII-F). The BEIR III committee relied heavily on both experimental and human data in selecting the esophagus for inclusion among the sites for which risk might be estimated. Human data, however, are rather few and derive largely from the small series among the British ankylosing spondylitis patients (26) and the larger series among A-bomb survivors (27). The BEIR committee used the risk coefficients for fatal esophageal cancer among the A-bomb survivors as its incidence estimates, since the case-fatality of esophageal cancer is so very high. More recent reports on the experience of the A-bomb survivors have not altered the evidence of the relative sensitivity of esophageal tissue to the carcinogenic action of radiation (28-30).

Neither the dose-response nor the time-response characteristics of radiation-induced esophageal cancer have been studied sufficiently to provide independent evidence as to the functions most suitable for this site. The Working Group has chosen, therefore, to employ the linear-quadratic dose-response function, with no threshold, and the constant relative risk model to describe the distribution of excess cases over time with a latent period of 10 years smoothed as described in Chapter V-C.

Estimates of baseline incidence are based on the SEER data bank of the National Cancer Institute (8). The rates are for the period 1973-1981, for all races combined, and for all reporting areas combined except Puerto Rico. As noted in Chapter VII-C, Tables VII-1 and VII-2, there is considerable variation among the SEER reporting areas with respect to the incidence of esophageal cancer. The major risk factors that have been identified are alcohol consumption and cigarette smoking (31). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures will be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased. Day and Munoz (31) cite the data of Tuyns *et al.* (32) as providing evidence that a multiplicative model fits well the combined influence of alcohol consumption and smoking upon the risk of esophageal cancer. There are, however, no good data bearing on the issue with respect to ionizing radiation and no numerical adjustment is provided here.

For esophageal cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the contribution of the tissue dose, T(Y) represents the conditioning influence of years from exposure to diagnosis (Y), and K(A₁, S) represents the relative excess risk of esophageal cancer for a person of sex S and age at exposure A₁, when both F and T = 1.

Under the linear-quadratic model assumed for esophageal cancer when exposure is to low-LET radiation

$$F = D + D^2/116$$

For the esophagus the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y). The function T is tabulated below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess esophageal cancer, K, is given in the accompanying Table X.4 for low-LET radiation and for each sex and year of age (completed years) from 20 to 75.

A few examples should make it clear how the PC values are to be calculated in individual cases:

Example 1 A male, exposed to 5 rad of low-LET radiation to the esophagus at age 20, with a diagnosis of esophageal cancer at age 50, otherwise typical of his age-sex classification with respect to the risk of esophageal cancer. Here D = 5, A₁ = 20, and Y = 30.

$$F(D) = 5 + 5^2/116 = 5.22$$

$$T(Y) = T(30) = 1$$

$$K(A_1, S) = K(20, m) = .00207$$

$$\text{then } R = 5.22 \times 1 \times .00207 = .0108$$

$$\text{and } PC = R/(1 + R) = .011 \text{ or } 1\%.$$

Example 2 A typical male, exposed at age 55 to 19 rad of low-LET radiation to the esophagus, with a diagnosis of esophageal cancer at age 59, 4.6 years after exposure. Here D = 19, A₁ = 55, and Y = 4.

$$F = 19 + 19^2/116 = 22.11$$

$$T(4) = 0$$

$$K(55, m) = .000603$$

then $R = 0$

and $PC = 0$ also

Example 3 An esophageal cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the esophagus, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis, ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20, f) = .00562$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00562 = .0057$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20, f) = .00562$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00562 = .0114$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00497$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00497 = .0153$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00497$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00497 = .0314$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00153$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00153 = .0035$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0057$$

$$+ .0114 + .0153 + .0314 + .0035 = .0673$$

$$PC = R/(1+R) = .0673/1.0673 = .063 = 6\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-4 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-4

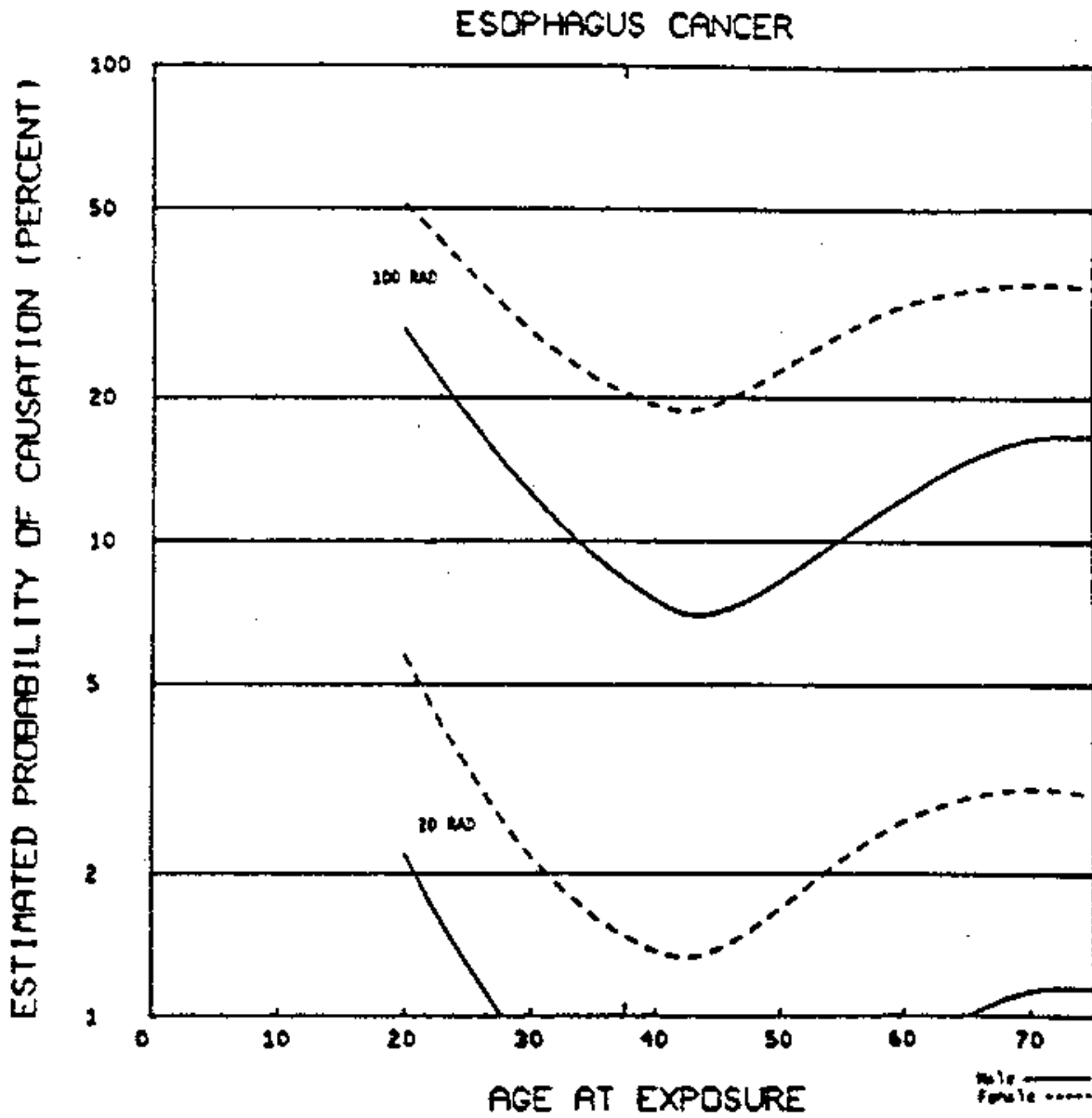


Table X-4. Esophagus Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00207	.00562	48	.000446	.00144
21	.00184	.00497	49	.000464	.00151
22	.00164	.00442	50	.000483	.00158
23	.00147	.00396	51	.000504	.00166
24	.00132	.00355	52	.000527	.00174
25	.00120	.00320	53	.000551	.00183
26	.00109	.00289	54	.000576	.00192
27	.000992	.00262	55	.000603	.00201
28	.000908	.00239	56	.000630	.00210
29	.000835	.00220	57	.000658	.00219
30	.000771	.00204	58	.000688	.00228
31	.000716	.00190	59	.000719	.00237
32	.000667	.00179	60	.000752	.00245
33	.000624	.00169	61	.000786	.00253
34	.000586	.00160	62	.000822	.00259
35	.000554	.00153	63	.000857	.00265
36	.000525	.00146	64	.000891	.00270
37	.000499	.00140	65	.000924	.00274
38	.000477	.00136	66	.000955	.00279
39	.000457	.00132	67	.000982	.00282
40	.000439	.00128	68	.00101	.00285
41	.000423	.00126	69	.00103	.00287
42	.000411	.00125	70	.00105	.00288
43	.000405	.00124	71	.00106	.00288
44	.000405	.00126	72	.00107	.00287
45	.000410	.00129	73	.00107	.00284
46	.000419	.00133	74	.00108	.00281
47	.000431	.00138	75	.00107	.00278

5. Stomach Cancer (151 in ICDA-8)

The risk coefficients used in the derivation of PC values for stomach cancer are taken from the BEIR III report (4) and adjusted to the period 11-30 years after exposure, but the BEIR coefficient for those exposed under age 10 is not used for reasons presented in Chapter VII. The inclusion of stomach cancer in the list of radiogenic cancers rests primarily on the experience of the British patients with ankylosing spondylitis treated by X rays (26) and of the A-bomb survivors (27) but is supported by animal experimentation (4). On the other hand, the recently published series on cervical cancer patients treated with X ray and radium had 201 observed cases of stomach cancer, several times the size of the ankylosing spondylitis series, but lacked evidence of a carcinogenic effect on stomach tissue (5). The relationship in the A-bomb survivors at the time the BEIR III report was prepared rested entirely on the experience of the Hiroshima survivors (27), but more recent data on the Nagasaki survivors indicate that the effect is by no means confined to the Hiroshima sample (28,29). The numbers are very large, 1754 deaths from stomach cancer through 1978, 1443 in Hiroshima, 311 in Nagasaki, but relative risk estimates are low: Kato and Schull estimate that only 42 of the deaths from stomach cancer may have been caused by radiation (28).

The Nagasaki Tumor Registry data on stomach cancer incidence were examined by Wakabayashi et al. for goodness of fit to the linear, linear-quadratic, and "pure" quadratic functions, and none of the models could be rejected by the usual statistical criterion (29). The Working Group has adopted the linear-quadratic dose-response function for stomach cancer as for most tumors in the expectation that further accumulation of data may in time demonstrate non-linearity, which is suggested by the combined A-bomb data of the two cities.

The Working Group has adopted the constant relative risk time-response model on the basis of Land and Tokunaga's analysis of other sites (33) and the demonstration by Kato and Schull (28) that, for all sites combined except leukemia, the picture is one of constant relative risk rather than absolute risk over time. (See also Chapter V-C.)

Environmental factors evidently play a dominant role in the etiology of stomach cancer, the incidence of which has been falling rapidly in the U.S. and many other countries, but few specific etiologic factors have been identified. The influence of smoking and alcohol is described as equivocal, but many studies have yielded crude associations between various aspects of diet and the risk of stomach cancer (34). There is no information on the joint effect of ionizing radiation and other risk factors. When the SEER incidence data, used here as the baseline data on the risk of stomach cancer, are examined by reporting area a wide range of variation is seen (Tables VII-1 and VII-2). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk

factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased. Caution should be exercised, however, because the appropriate interaction model for radiation in combination with any other carcinogens for stomach cancer is not known.

The calculational routine for stomach cancer is based on the assumptions and procedures detailed in Chapters V, VI, and IX. For stomach cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the contribution of a low-LET radiation dose to the relevant tissue (D), T(Y) represents the conditioning influence of years from exposure to diagnosis, and K(A₁, S) represents the standardized relative excess risk of stomach cancer per rad for a person of sex S and age at exposure A₁, when both F and T = 1.

Under the linear-quadratic model assumed for stomach cancer when exposure is to low-LET radiation,

$$F = D + D^2/116.$$

For the stomach the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y). The function T is tabled below.

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess cancer, K, is given in the accompanying Table X-5 for low-LET radiation and for each sex and year of age (completed years) from 10 to 75.

A few examples should make it clear how PC values are to be obtained for stomach cancer.

Example 1 A typical woman aged 25 with an exposure of 10 rad of X rays to the stomach, and with a diagnosis of stomach cancer at age 50, 25 years later. Then D = 10, A₁ = 25, and Y = 25.

$$F(10) = 10 + 10^2/116 = 10.86$$

$$T(25) = 1$$

$$K(25, f) = .00782$$

$$\text{then } R = F \times T \times K = 10.86 \times 1 \times .00782 = .0849$$

$$\text{and } PC = R/(1 + R) = .0849/1.0849 = .078 \text{ or } 8\%.$$

Example 2 A stomach cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the stomach, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1=20$) but 23 years and 10 months before diagnosis ($Y = 20$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(1) = 1 + 1^2/116 = 1.01$$

$$T(24) = 1$$

$$K(20,f) = .0100$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .0100 = .0101$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .0100$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .0100 = .0203$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00959$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00959 = .0295$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00959$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00959 = .0605$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00458$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00458 = .0104$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0101$$

$$+ .0203 + .0295 + .0605 + .0104 = .131$$

$$PC = R/(1 + R) = .131/1.131 = .116 = 12\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-5 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-5

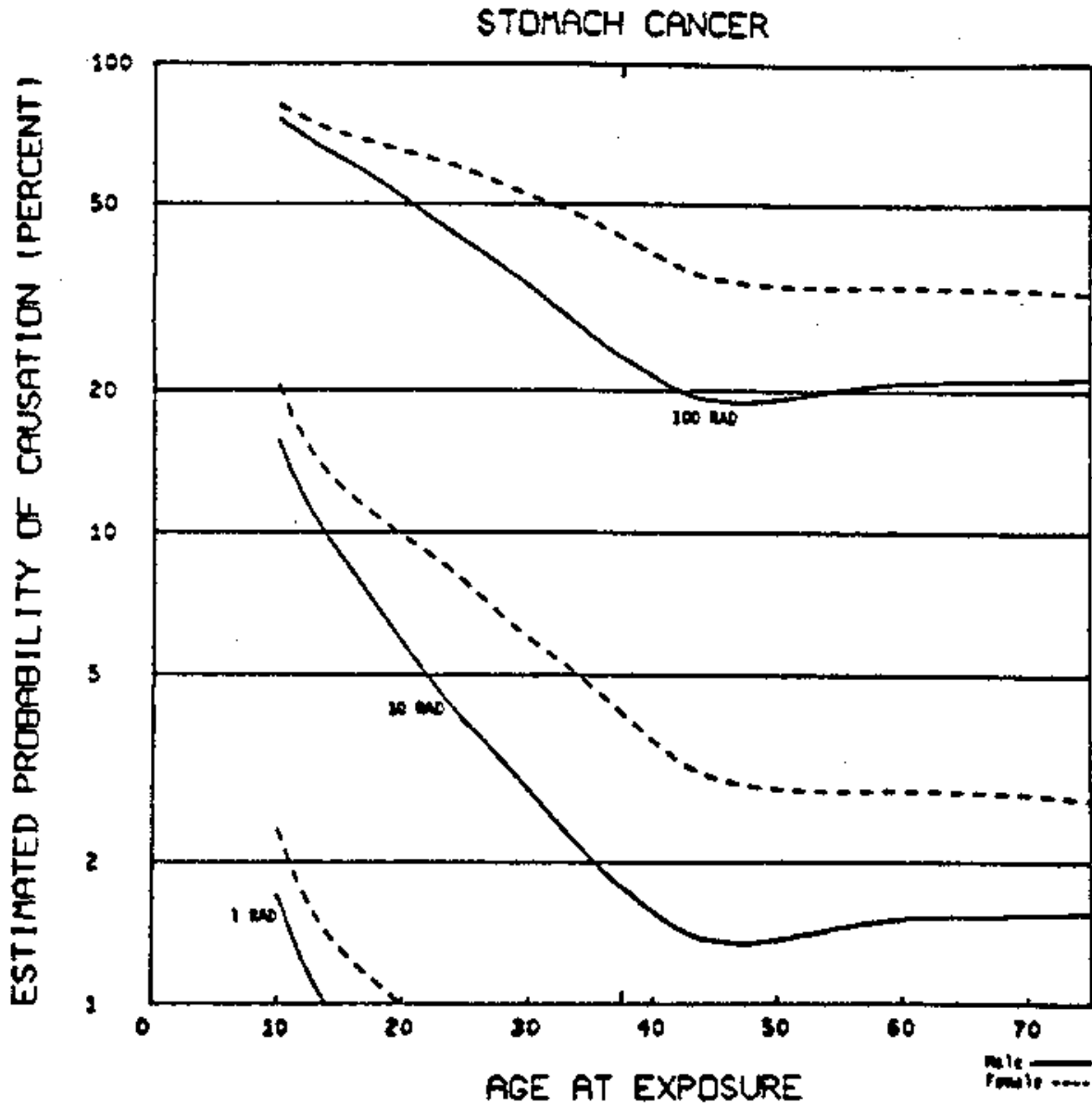


Table X-5. Stomach Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
10	.0172	.0238	43	.00131	.00302
11	.0145	.0201	44	.00129	.00294
12	.0125	.0175	45	.00127	.00287
13	.0111	.0156	46	.00126	.00282
14	.00995	.0142	47	.00126	.00278
15	.00907	.0132	48	.00126	.00276
16	.00826	.0124	49	.00127	.00274
17	.00751	.0117	50	.00128	.00272
18	.00684	.0111	51	.00129	.00271
19	.00523	.0105	52	.00130	.00270
20	.00569	.0100	53	.00132	.00270
21	.00522	.00959	54	.00134	.00270
22	.00479	.00915	55	.00135	.00270
23	.00442	.00872	56	.00137	.00270
24	.00410	.00827	57	.00138	.00270
25	.00381	.00782	58	.00140	.00270
26	.00356	.00736	59	.00141	.00270
27	.00333	.00692	60	.00142	.00270
28	.00311	.00652	61	.00142	.00270
29	.00290	.00616	62	.00143	.00270
30	.00270	.00585	63	.00143	.00269
31	.00251	.00558	64	.00143	.00269
32	.00234	.00533	65	.00143	.00268
33	.00218	.00508	66	.00143	.00267
34	.00204	.00483	67	.00143	.00267
35	.00192	.00458	68	.00144	.00266
36	.00180	.00434	69	.00144	.00266
37	.00171	.00410	70	.00144	.00265
38	.00162	.00388	71	.00144	.00263
39	.00154	.00367	72	.00144	.00262
40	.00147	.00348	73	.00145	.00260
41	.00141	.00330	74	.00145	.00258
42	.00135	.00314	75	.00145	.00257

6. Colon Cancer (153 in ICDA-8)

The colon has long been considered an organ of apparent, but uncertain, sensitivity to radiation carcinogenesis, based on studies of patient populations irradiated for benign or malignant pelvic disease and the British series of patients treated with radiation for ankylosing spondylitis. The uncertainty arose because, although remarkable excess risks were seen in some studies (35,36), there was none in others with comparable levels of exposure (37,38). Moreover, the excess risk seen among spondylitis patients treated with X rays was discounted because of known associations among spondylitis, ulcerative colitis, and colon cancer (3,26). In fact, an excess risk was seen soon after treatment began, well before the expiration of a 10-, or even 5-year, minimum induction period for radiation-induced cancer.

More recently, excess colon cancer has been observed in mortality data for survivors of the Hiroshima A-bomb (28) and in tumor-registry data for survivors of the Nagasaki bomb (29). At about the same time, however, in a large international series of women in Europe and North America treated by irradiation for cervical cancer, no excess mortality was seen for colon cancer despite an average dose of about 500 rad to the colon, possibly because average follow-up is only 7.6 years (5).

At the present time the evidence for excess colon cancer associated with radiation exposure rests mainly upon the A-bomb survivor data, perhaps because colon cancer normally is rare in Japan in comparison with the United States, and a modest excess may therefore be easier to detect. The most recent A-bomb survivor data are consistent with the risk estimates given in the 1980 BEIR report (4,23) except that the data do not appear adequate to support a risk estimate for exposures before age 20 (see Chapter VII-F). The BEIR III coefficients for ages 20+, adjusted to the period 11-30 years after exposure, are the basic risk estimates used by the Working Group.

There has been no analysis of colon cancer to establish the most appropriate dose-response function or to determine whether the relative risk model is superior to the absolute risk model for distributing radiogenic cases over time. The Working Group has assumed that the preferred linear-quadratic dose-response model of the BEIR III committee and the constant relative risk time-response model would provide a suitable basis for the calculation of PC values for this site. These general assumptions are discussed in Chapter V.

The normal incidence of colon cancer in the U.S. is best represented by the SEER data of the National Cancer Institute which, however, are subject to some variation among reporting areas (8). (See Chapter VII-C and Tables VII-1 and VII-2.) The base-line rates employed here are those for all races combined and for all areas combined except for Puerto Rico, and are age- and sex-specific. They are taken from computer tapes for the period 1973-1981.

Migrant studies have underscored the role environmental factors, including nutrition, must play in the etiology of colon cancer, especially the dietary intake of meat and animal fat. Epidemiologic studies have

also identified a number of familial and hereditary factors that influence the risk of colon cancer and have shown that persons with chronic ulcerative colitis are at high risk of colon cancer (39). For none of these factors are quantitative estimates of relative risk firm enough for specific guidance in this context. Nor is there information on any interaction between such risk factors and radiation in the etiology of colon cancer. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and if the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

The procedures for calculating PC values for colon cancer rest on the general strategy outlined in Chapters V, VI, and IX. For colon cancer, as for other sites, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents the influence of years from exposure to the diagnosis of colon cancer (Y), and K(A₁, S) represents the relative excess risk of colon cancer for a person of age at exposure A₁ and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for colon cancer when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For colon cancer the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabulated below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess colon cancer, K, is given in the accompanying Table X-6 for low-LET radiation, for each sex and completed year of age from 20 to 75.

A few specific examples should illustrate the way in which PC values for colon cancer may be derived from the material presented here.

Example 1 A typical female aged 45 given 5 rad of low-LET radiation to the colon, with a diagnosis of colon cancer at age 48, 3.5 years after

exposure. Then $D = 5$, $A_1 = 45$, and $Y = 3$.

$$F(5) = 5 + 5^2/116 = 5.22$$

$$T(3) = 0$$

$$K(45, f) = .000340$$

$$\text{then } R = F \times T \times K = 0$$

and $PC = 0$ also.

Example 2 A typical male exposed to an acute dose of 2 rad of low-LET radiation to the colon at age 36, and with a diagnosis of colon cancer at age 55. Then $D = 2$, $A_1 = 36$, and $Y = 19$.

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(19) = 1$$

$$K(36, m) = .000493$$

$$\text{then } R = F \times T \times K = 2.03 \times 1 \times .000493 = .0010$$

$$\text{and } PC = R/(1 + R) = .0010/1.0010 = .001 = 0.1\%$$

Example 3 A colon cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the colon, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y=23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The partition giving the maximum risk estimate assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(1) = 1 + 1^2/116 = 1.01$$

$$T(24) = 1$$

$$K(20, f) = .00153$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00153 = .00155$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00153$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00153 = .00311$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00143$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00143 = .00440$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00143$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00143 = .00902$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .000558$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .000558 = .00127$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00155$$

$$+ .00311 + .00440 + .00902 + .00127 = .0194$$

$$PC = R/(1+R) = .0194/1.0194 = .0190 \text{ or } 2\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig. X-6 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values

plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-6

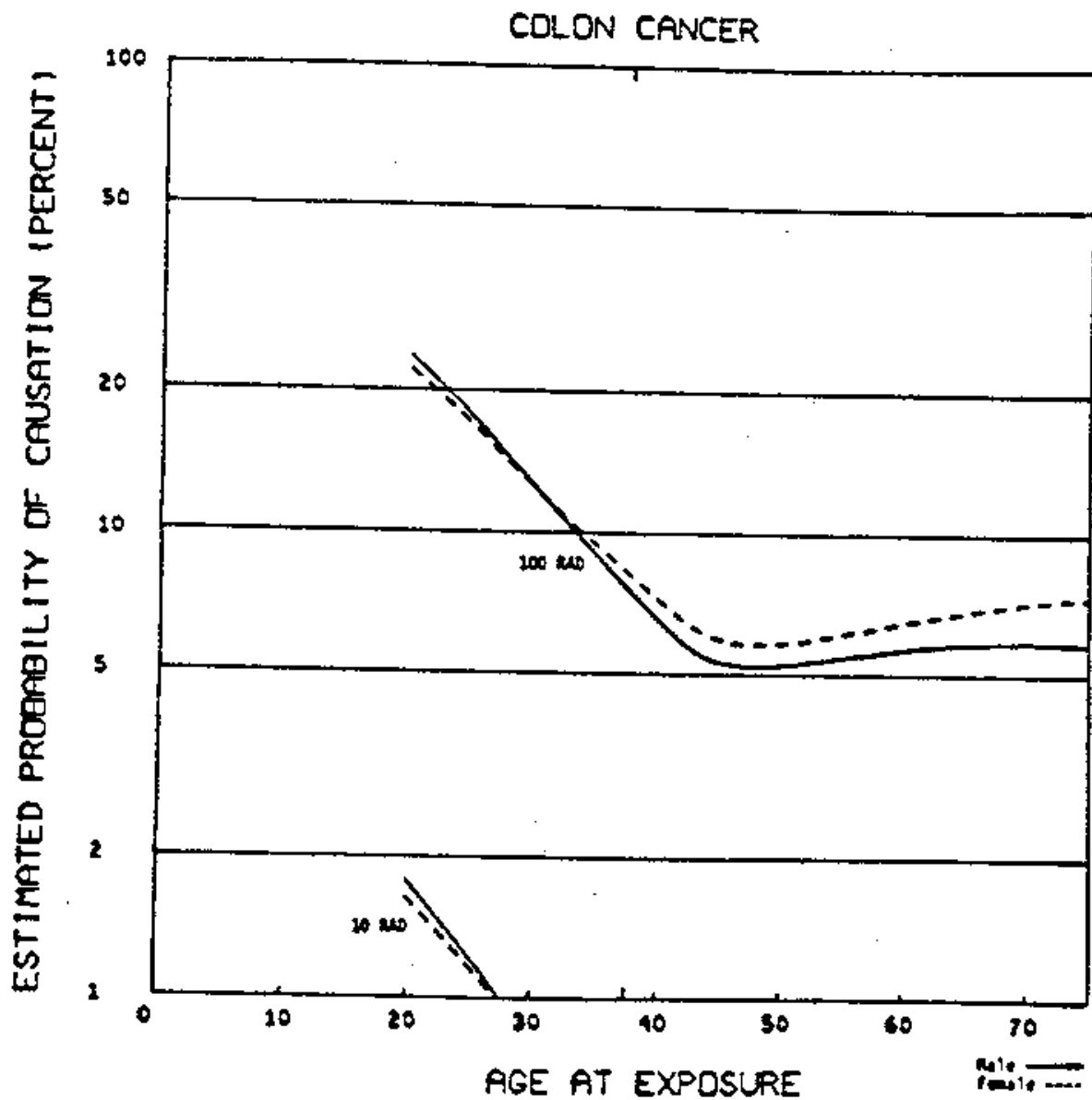


Table X-6. Colon Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00167	.00153	48	.000296	.000331
21	.00155	.00143	49	.000296	.000331
22	.00144	.00134	50	.000298	.000333
23	.00134	.00125	51	.000300	.000335
24	.00124	.00117	52	.000302	.000338
25	.00115	.00109	53	.000305	.000342
26	.00106	.00102	54	.000307	.000346
27	.000979	.000947	55	.000310	.000350
28	.000905	.000882	56	.000313	.000354
29	.000837	.000822	57	.000316	.000359
30	.000774	.000768	58	.000319	.000363
31	.000716	.000718	59	.000321	.000368
32	.000663	.000673	60	.000324	.000372
33	.000615	.000631	61	.000326	.000377
34	.000571	.000593	62	.000328	.000381
35	.000530	.000558	63	.000330	.000385
36	.000493	.000526	64	.000332	.000389
37	.000460	.000496	65	.000333	.000393
38	.000429	.000468	66	.000334	.000397
39	.000401	.000442	67	.000335	.000402
40	.000376	.000418	68	.000336	.000406
41	.000353	.000395	69	.000336	.000410
42	.000333	.000375	70	.000336	.000414
43	.000319	.000359	71	.000336	.000417
44	.000309	.000348	72	.000335	.000419
45	.000302	.000340	73	.000334	.000421
46	.000298	.000335	74	.000333	.000423
47	.000296	.000332	75	.000332	.000423

7. Cancer of the Liver (155.0 and 197.8 in ICDA-8)

Primary cancer of the liver is well known as a late effect of radiography employing the contrast medium, Thorotrast, a colloidal thorium dioxide compound emitting alpha particles (2,4,40). There is, however, some uncertainty as to the etiologic significance of its chemical vs. its radiation properties. Human data on the association between ionizing radiation and liver cancer are otherwise sparse. In the British series of ankylosing spondylitis patients treated by X rays no excess liver cancer was found, but the liver was classified as one of the "lightly irradiated sites", for which the observed numbers of deaths from cancer were not significantly greater than expectation based on the British mortality statistics (3). The 1977 UNSCEAR report (2) provides a "tentative risk assessment" of 10-20 excess cancers per million persons per rad of alpha radiation. With a mean latency of 25 years these coefficients become approximately 0.40 to 0.80 per million per year per rad. The BEIR III report (4) provides an estimate of 300 per million persons per rad of alpha radiation, 15 per million persons per rad of low-LET radiation on the assumption of a RBE of 20, and an annualized risk coefficient of 0.70 excess cancers per million per year per rad of low-LET radiation.

The most extensive human data on liver cancer following external exposure to ionizing radiation derive from the experience of the Japanese A-bomb survivors: 55 incident cases in Nagasaki (29) and 118 in Hiroshima (30). The Nagasaki Tumor Registry report for 1959-1978 yields a risk estimate of 0.70 ± 0.52 excess cancers per million persons per year per rad (29), and the Hiroshima Tumor Registry for the same period an estimate of $0.72 \pm .18$ (30). The death certificate diagnoses for the Life Span Study sample of 82,000 A-bomb survivors have not been tabulated for liver cancer in the most recent report (1950-1978) (28) but cancers of the liver are included in the category of "other or unspecified digestive organs," that is, cancers of digestive organs other than the esophagus, stomach, pancreas, colon, and rectum and rectosigmoid junction. Thus, cancer of the liver is a significant part of the "all other" category that includes 595 deaths and for which a test of trend with dose returns a highly significant p of .0033.

None of the reports cited provides age- or sex-specific risk estimates for cancer of the liver, but trend tests on the age-specific mortality tables of Kato and Schull (28) for "all other" gastrointestinal organs yield p-values as follows for the observed numbers of deaths in tests of the relation between mortality and dose:

<u>Age at exposure</u>	<u>Number of deaths</u>	<u>p in Test of Trend with Dose</u>
0-9	4	.64
10-19	30	.02
20-34	82	.08
35-49	284	.04
50+	195	.20

The sex-specific tests of trend with dose result in p-values of .03 for males and .02 for females (28).

Overall, the more recent data support the BEIR III risk coefficients for liver cancer, except that the data are too fragile, for persons exposed under age 20, for the BEIR estimate for that age-group to be used (see Chapter VII-F). The BEIR III coefficients have been adjusted to the period 11-30 years after exposure.

Neither dose-response nor time-response has been adequately investigated for cancer of the liver and, except for the Thorotrast patients, whose irradiation is essentially continuous, there are too few cases of radiogenic liver cancer for such analyses. Accordingly, the Working Group has assumed that the appropriate dose-response functions are linear-quadratic for low-LET and linear for high-LET radiation and the appropriate time-response function the constant relative risk model.

The baseline risk of liver cancer in the US population has been taken from the data of the SEER program of the National Cancer Institute for the years 1973-1981. Published data from the contributing registries for the years 1973-1977 (8) reveal great variation (see Tables VII-1 and VII-2) and it should be stressed that it is the set of rates for all areas (except Puerto Rico) combined and for all races combined that is used in the calculations here.

Although ionizing radiation is clearly a risk factor for liver cancer, there are far more important risk factors. These include exposure to arsenic, vinyl chloride, probably hepatitis B virus, and alcohol (41). For none of these factors are quantitative estimates of relative risk firm enough for specific guidance in this context. Nor is there information on any interaction between such risk factors and radiation in the etiology of liver cancer. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

The procedures for calculating PC values for liver cancer are based on the assumptions and principles of Chapter V and the procedures of Chapters VI and IX. As with most other sites, for liver cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the influence of the tissue dose (D) in rad of low-

LET radiation, $T(Y)$ represents the variation in R over time in years (Y) after exposure, and $K(A_1, S)$ represents the relative excess risk of liver cancer for a person of age at exposure A_1 and sex S , when both F and $T = 1$.

Under the linear-quadratic model assumed for liver cancer, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For liver cancer the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess liver cancer, K , is given in the accompanying Table X-7 for low-LET radiation and for each sex and year of completed age from 20 to 75. A few examples should clarify the actual computational procedures for liver cancer following exposure to ionizing radiation.

Example 1 A typical male, exposed at age 31 to 10 rad of low-LET radiation to the liver, with diagnosis of liver cancer at age 59. Then $D = 10$, $A_1 = 31$, and $Y = 28$.

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(28) = 1$$

$$K(A_1, S) = K(31, m) = .00755$$

$$\text{then } R = F \times T \times K = 10.86 \times 1 \times .00755 = .0820$$

$$\text{and } PC = R/(1 + R) = .0820/1.0820 = .076 \text{ or } 8\%.$$

Example 2 A typical female given 10 rad of low-LET radiation to the liver at age 36, with a diagnosis of liver cancer at age 55, 19 years after exposure. Then $D = 10$, $A_1 = 36$, and $Y = 19$.

$$F(10) = 10 + 10^2/116 = 10.86$$

$$T(19) = 1$$

$$K(36, f) = .0129$$

$$\text{then } R = F \times T \times K = 10.86 \times 1 \times .0129 = .140$$

$$\text{and } PC = R/(1+R) = .140/(1.140) = .123 \text{ or } 12\%.$$

Example 3 A liver cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the liver, occurred at age 20, 24 years and 2 months before

diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20, f) = .0503$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .0503 = .0508$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20, f) = .0503$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .0503 = .102$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21, f) = .0463$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .0463 = .143$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21, f) = .0463$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .0463 = .292$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .0139$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .0139 = .0315$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .0508 + .102 \\ + .143 + .292 + .0315 = .619$$

$$PC = R/(1+R) = .619/1.619 = .382 = 38\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-7 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-7

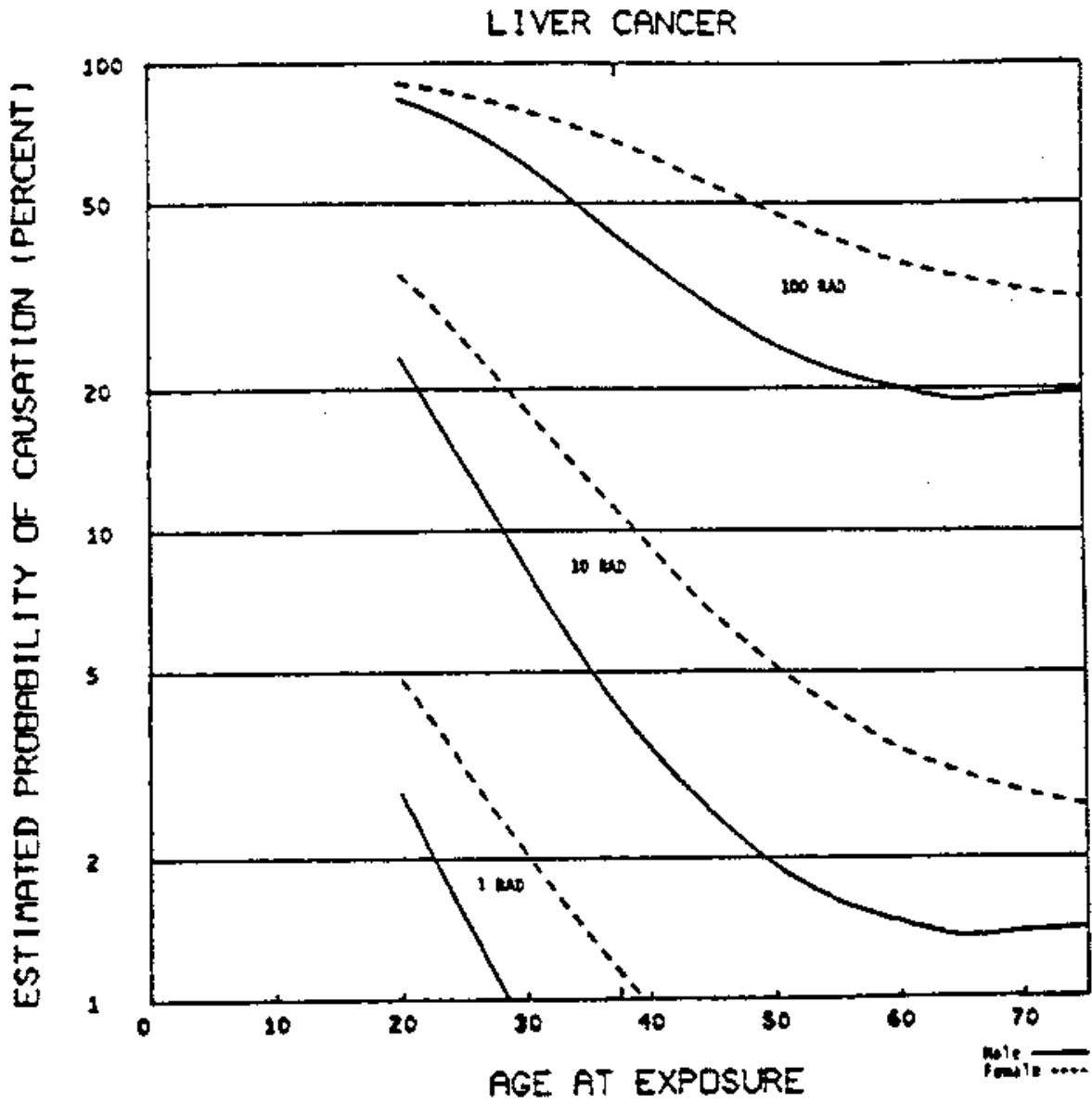


Table X-7. Liver Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.0281	.0503	48	.00199	.00559
21	.0246	.0463	49	.00190	.00530
22	.0216	.0424	50	.00181	.00503
23	.0191	.0387	51	.00174	.00478
24	.0170	.0352	52	.00167	.00455
25	.0151	.0320	53	.00161	.00435
26	.0134	.0292	54	.00156	.00415
27	.0119	.0267	55	.00152	.00397
28	.0106	.0244	56	.00148	.00380
29	.00943	.0224	57	.00144	.00365
30	.00843	.0206	58	.00141	.00350
31	.00755	.0189	59	.00138	.00337
32	.00678	.0175	60	.00136	.00326
33	.00612	.0162	61	.00133	.00317
34	.00555	.0150	62	.00131	.00309
35	.00504	.0139	63	.00129	.00301
36	.00460	.0129	64	.00127	.00295
37	.00421	.0119	65	.00126	.00288
38	.00387	.0111	66	.00126	.00283
39	.00357	.0103	67	.00126	.00277
40	.00331	.00954	68	.00127	.00272
41	.00308	.00884	69	.00128	.00267
42	.00287	.00819	70	.00128	.00263
43	.00269	.00762	71	.00129	.00258
44	.00252	.00712	72	.00130	.00255
45	.00237	.00667	73	.00130	.00251
46	.00223	.00627	74	.00131	.00248
47	.00210	.00591	75	.00131	.00246

8. Cancer of the Pancreas (157 in ICDA-8)

Risk estimates for pancreatic cancer are less reliable than those for most sites, perhaps because most data are derived from death certificate diagnoses that do not fare well in pathology reviews. The UNSCEAR (2) and BEIR III (4) reports rely heavily on the excess reported for the British ankylosing spondylitis patients treated with X rays (26), but the relationship is weak in the most recent report on that series (3). The pancreas was a "heavily irradiated site," and although Doll and his colleagues have yet to publish a dose estimate for the pancreas, the BEIR III report gives a value of 90 rad. There were 18 deaths from pancreatic cancer vs. 9.5 expected in the latest report, but 5 occurred within the first two years after treatment (vs. 1 expected) and the 13 vs. 8.5 comparison for the period 3+ years after therapy returns a p-value in excess of .10. Land has calculated an estimate of $0.70 + .61$ excess deaths per million per year per rad for this experience (23). The BEIR III estimate is .90 for males and .99 for females, with age-specific coefficients varying in direct proportion to those for all gastrointestinal cancer deaths among the A-bomb survivors, 1950-1974.

Death certificate diagnoses for the large Life Span Study sample of A-bomb survivors reveal no statistical evidence that the risk of pancreatic cancer depends on dose ($p = .67$ in a test of linear trend on 148 deaths) (28), but the pathology confirmation and detection percentages for cancer of the pancreas are low, 62 and 37 respectively, in a series of 61 autopsy cases (42). In a report on 36 cases in the Nagasaki Tumor Registry series for 1959-1978, Wakabayashi et al. report a trend p of .06, for which the risk coefficient is $1.15 + .92$ (29). In the unpublished Hiroshima Tumor Registry report for the same time period there are 143 cases with a non-significant risk coefficient of .18 (90-percent confidence interval of $-.14$ to $+.50$) (30). Overall, therefore, the experience of the A-bomb survivors provides very weak support for a relationship between pancreatic cancer and radiation dose.

In their first report on deaths among workers at the Hanford Works in Richland, Washington, Mancuso et al. reported a probable excess of 6 deaths from pancreatic cancer among 31, and estimated the doubling dose at 7.4 rad (43). The statistical significance of the association was verified by Hutchison et al. in independent calculations (44) and by Gilbert and Marks in a cohort analysis of the worker population (45). These and numerous other commentators stressed the fragility of the data (death certificate diagnosis and the likelihood of exposure to carcinogenic chemicals). The association was later weakened by the finding that, for 1 of the 4 critical deaths in the 15+ rem dose group, medical records showed that the primary cancer was probably in the stomach (46).

The pancreas barely meets the criteria for inclusion among the sites for which PC estimates are to be made. There are human data from which the necessary risk coefficients can be derived, but the statistical reliability of the association between cancer and dose is low and consistency among the few available series is minimal.

The Working Group chose to employ the BEIR III coefficients except for exposure before the age of 20, the basis for the BEIR III coefficient

for younger individuals having been judged insufficient for the present purpose (Chapter VII-F). The BEIR coefficients were, however, adjusted to the period 11-30 years after exposure. There appears to be no published analysis of dose-response functions appropriate for the pancreas, and the available data are too few to make such analysis very meaningful. Accordingly, the Working Group has employed the preferred linear-quadratic dose-response model for this site as for most of the solid tumors. Similarly, although time-response models have not been explored, the Working Group considered that the constant relative risk model was a reasonable choice.

The baseline data needed for the calculation of PC values have been taken from the data tapes for the SEER program of the National Cancer Institute for the years 1973-1981 and for all races combined and all areas combined except Puerto Rico. Published data for the reporting areas in the period 1973-1977 show only a moderate degree of variation, but an appreciable difference between the sexes, males having the higher rates (8). (See Tables VII-1 and VII-2.)

Cancer of the pancreas is also associated with alcohol consumption, exposure to certain chemicals, and smoking (47). The Working Group found no information on the pattern of interaction between such well-established risk factors and radiation. As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

The procedures for calculating PC values for the pancreas are based on the principles and assumptions of Chapter V and the procedures of Chapters VI and IX. As with most sites, for cancer of the pancreas the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents the variation in R over time in years (Y) after exposure, and K(A₁, S) represents the relative excess of pancreatic cancer for a person of age A₁ and sex S, when both F and T = 1.

Under the linear-quadratic dose-response model assumed for pancreatic cancer, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancer of the pancreas the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess cancer of the pancreas, K, is given in the accompanying Table X-8 for low-LET radiation exposure in rad and for each sex and age in completed years from 20 to 75.

A few examples may clarify the actual computational procedures for pancreatic cancer following exposure to ionizing radiation.

Example 1 A typical female, exposed at age 35 to 10 rad of low-LET radiation to the pancreas, with diagnosis at age 50. Then $D = 10$, $A_1 = 35$, and $Y = 15$.

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(15) = 1$$

$$K(A_1, S) = K(35, f) = .00184$$

$$\text{then } R = F \times T \times K = 10.86 \times 1 \times .00184 = .020$$

$$\text{and } PC = R/(1 + R) = .020/1.020 = .0196 \text{ or } 2\%.$$

Example 2 A typical male, exposed to 5 rad of low-LET radiation to the pancreas at age 40, with a diagnosis at age 51, 11 years after exposure. Then $D = 5$, $A_1 = 40$, and $Y = 11$.

$$F(5) = 5 + 5^2/116 = 5.22$$

$$T(11) = 1$$

$$K(40, m) = .000933$$

$$\text{then } R = F \times T \times K = 5.22 \times 1 \times .000933 = .00487$$

$$\text{and } PC = R/(1 + R) = .00487/1.00487 = .0049 \text{ or less than } 1\%.$$

Example 3 A pancreatic cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the pancreas, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y, and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .00739$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00739 = .00746$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00739$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00739 = .0150$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00664$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00664 = .0204$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00664$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00664 = .0419$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00184$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00184 = .00417$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00746$$

$$+ .0150 + .0204 + .0419 + .00417 = .089$$

$$PC = R/(1 + R) = .089/1.089 = .082 = 8\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide a general orientation to the magnitude of the PC values that result from the procedures described here, Fig. X-8 has been prepared for pancreatic cancer. It gives PC values for 1, 10, and 100 rad of low-LET radiation to pancreatic tissue by age at diagnosis, separately for males and females. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-8

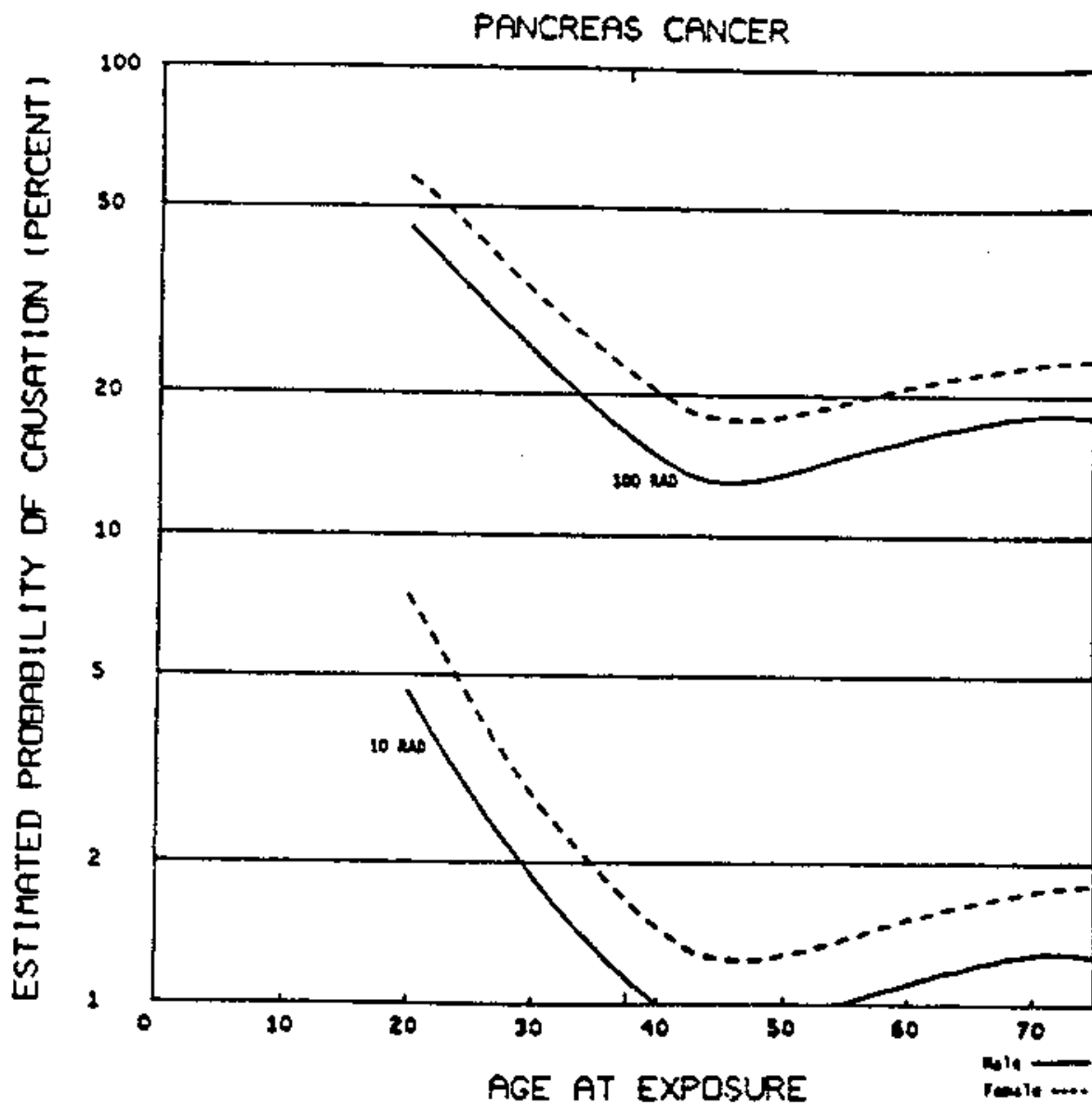


Table X-8. Pancreas Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00446	.00739	48	.000821	.00117
21	.00400	.00664	49	.000832	.00118
22	.00360	.00596	50	.000846	.00119
23	.00325	.00534	51	.000863	.00121
24	.00295	.00478	52	.000881	.00123
25	.00269	.00429	53	.000901	.00125
26	.00246	.00386	54	.000921	.00127
27	.00226	.00349	55	.000940	.00129
28	.00208	.00317	56	.000960	.00132
29	.00191	.00289	57	.000979	.00134
30	.00176	.00265	58	.000998	.00137
31	.00163	.00245	59	.00102	.00140
32	.00151	.00227	60	.00103	.00142
33	.00141	.00211	61	.00105	.00145
34	.00131	.00197	62	.00107	.00147
35	.00123	.00184	63	.00109	.00149
36	.00116	.00172	64	.00111	.00151
37	.00109	.00162	65	.00112	.00153
38	.00103	.00152	66	.00114	.00155
39	.000980	.00144	67	.00116	.00158
40	.000933	.00136	68	.00117	.00160
41	.000891	.00130	69	.00119	.00162
42	.000855	.00124	70	.00120	.00164
43	.000831	.00121	71	.00120	.00165
44	.000817	.00118	72	.00120	.00166
45	.000810	.00117	73	.00120	.00168
46	.000809	.00116	74	.00119	.00168
47	.000813	.00116	75	.00118	.00169

9. Lung Cancer (162.1 in ICDA-8)

Introduction

The association between ionizing radiation and cancer of the lung and bronchus has been most clearly evident in various studies of underground miners who are exposed to radon and its daughter products (48-50). The results of the studies on miners are broadly consistent with other studies of the relation of X rays and gamma rays to respiratory cancer, notably those of the Japanese A-bomb survivors (28) and the British ankylosing spondylitis patients who were treated with X rays (3).

The BEIR III assessment of lung cancer risk following exposure to ionizing radiation was a synthesis of epidemiologic data from a number of studies of mining populations with occupational exposure to alpha radiation from inhaled radon daughters, and from the Japanese A-bomb survivor studies and the British series of patients given X-ray therapy for ankylosing spondylitis, both representing exposure to external, mainly low-LET, radiation. In that assessment it was concluded that, among miners, excess lung cancer risk was proportional to cumulative exposure to radon daughters, measured in "working level months" (WLM), and that excess risk was proportional to cumulative dose from low-LET radiation, with approximate equivalence of effect between one WLM and 6 rad low-LET dose to the bronchial epithelium. (One "working level" (WL) is defined as the activity in air that gives 13,000 MeV of alpha radiation per liter from ultimate decay of the short-lived daughters; one WLM is defined as exposure to 1 WL for 170 hours.) In the BEIR assessment, age at observation was a far more important determinant of excess risk than age at exposure. For a given cumulative exposure, and after a minimum latent period, estimated risk increased approximately linearly with age at observation, from zero before age 35 to a maximal value at about age 70 and older (4, pp. 198, 325-327).

The Working Group found the BEIR analysis difficult to use, partly because the formula of a linear increase in excess risk with increasing age at observation is inconsistent with the constant relative risk model for time from exposure to diagnosis, a model that the A-bomb survivor lung cancer mortality data for 1950-1978 appear to support (28,33). Also, there is some evidence that the two kinds of radiation may differ in their carcinogenic effects. The shape of the dose-response relationship is probably different for the two types of radiation (see Chapters III-1 and V-B). Moreover, the A-bomb survivor data strongly suggest an additive relationship between exposure to low-LET radiation and smoking in the causation of lung cancer (51), whereas the relevant data for radon daughter exposure and smoking, while mixed (52-54), tend, on the whole, to suggest a multiplicative interaction model (49,55-59). It was also noted that there is no real necessity to base risk estimates on the combined data from the two kinds of exposure; there are sufficient data to support separate lung cancer risk analyses for external, low-LET radiation and exposure to inhaled radon daughter products.

Estimates for high-LET radiation

The many studies of lung cancer risk in mining populations exposed to

radon daughter products are remarkable for the diversity of risk estimates produced. Estimates based on reasonably large mining populations range from 0.3 percent relative excess per WLM for U.S. uranium miners (59) to 3 percent or more in Swedish metal miners and Canadian uranium miners (55). Reviews of the mining population data have tended to differ in the amount of weight given to the various studies. In a recent proportional hazard model analysis of data from Czech, U.S., and Canadian uranium miners, Jacobi et al. obtained estimates of, respectively, 1.5, 0.7 and (about) 1.5 percent relative excess risk per WLM with a weighted average of 1.2 percent per WLM (60). Another review, by Thomas and McNeill, placed less weight on the U.S. uranium miner data and, using a different analytical approach, obtained an overall estimate of 2.3 percent per WLM (55).

Another source of variability in studies and reviews by expert committees is the assumed distribution of excess risk over time following exposure. Lundin et al. (61) postulated a lognormal model for time to response in their analysis of U.S. uranium miner data, while Whittemore and McMillan assumed a constant relative risk model in their analysis of substantially the same data (59). The authors of NCRP Report No. 78 (62) assumed a decreasing absolute risk model with a 20-year half-life for stem cells transformed by alpha radiation (63). Recently, Jacobi et al. introduced a proportional hazards model, incorporating the constant relative risk model (60). Previously, Jacobi and the ICRP had employed the constant absolute risk model (64,65). Ellett and Nelson (66) have used lung cancer data from smoking and non-smoking iron miners in Sweden to test various time-to-response models for lung cancer induced by exposure to radon daughters. Their analysis found that the constant relative risk model gave a reasonably good fit to the observed age-at-diagnosis data, whereas the BEIR model gave a marginally unsatisfactory fit; the constant absolute risk model and the decreasing absolute risk model of NCRP Report No. 78, on the other hand, deviated markedly from these data.

Expert committees of the ICRP and the U.S. National Academy of Sciences are now preparing, or will soon prepare, assessments of lung cancer risk associated with exposure to radon daughters. In the meantime, there is no one "official" estimate that appears to take precedence over all others. The estimate most nearly consistent with the approach of the present Working Group is that calculated by Jacobi et al. (60); according to that estimate, the relative excess risk R associated with a single exposure of reasonably short duration, measured in WLM, might be calculated as

$$R = U \times T(Y) \times 1.2 \text{ percent per WLM}$$

where U is the exposure in WLM, and the temporal factor T(Y) is defined in the same way as for lung cancer following external, low-LET radiation. The method of estimating exposure for U.S. uranium miners prior to 1961 appears to have been different from that used after that date and those used in other countries, and is considered on the whole to have over-estimated exposure (55,61). There is, therefore, some justification for using a different risk factor for U.S. miner exposures before 1961, such as the value of 0.7% per WLM estimated by Jacobi et al. (60). Because

the U.S. data for exposures before 1961 are included in the weighted average calculated by Jacobi, there is also reason to use a higher risk factor, such as the value 1.5 percent per WLM calculated from Czech and Canadian data (60), for later exposures. The Working Group wishes to emphasize, however, that the range of published risk estimates is somewhat greater than from 0.7 to 1.5 percent per WLM, and that reviews by expert committees may provide us with different estimates within the next year or so.

One marked difference between the above algorithm and that recommended below for low-LET radiation is that in the above expression relative excess does not depend upon age at exposure. In fact, age at exposure is difficult to study in mining populations because exposure tends to be spread out over many years. Moreover, given the uncertainty of age-specific risk coefficients derived from the A-bomb survivor data, it is entirely possible that, over the age ranges at which most mining exposures are received, there is little variation in susceptibility by age at exposure.

Another difference is that, for alpha radiation from inhaled radon daughter products, a multiplicative interaction is assumed to hold with respect to smoking. Thus, unlike the algorithm for external, low-LET radiation, the relative excess is invariant under differences in smoking level.

Estimates for low-LET radiation

Estimates based on the A-bomb survivor series and the British spondylitis series are in good agreement (67). Accordingly, new risk coefficients were calculated for low-LET radiation, based on the A-bomb survivor lung cancer mortality data for 1955-1978 (28). Regression coefficients calculated separately for exposure ages 10-19, 20-34, 35-49, and 50+ conformed to a roughly linear pattern of dependence on exposure age; the absolute risk coefficients in Table VI-1, and the coefficients for relative excess in Table X-9-A therefore incorporate a linear dependence on age at exposure, plus a correction for an estimated 30 percent underascertainment from death certificates. This correction allows for some improvement in ascertainment efficiency since the report of Steer et al., which was largely based on autopsy and death certificate data from the 1960s (68).

Lung cancer is not one of the cancers reliably identified by those who fill out death certificates, but the errors are mostly in the direction of under-reporting primary cancer of the lung and bronchus.

The NCI SEER data on the incidence of lung cancer in the US by age and sex, for the years 1973-1981, are used for the normal risk of lung cancer in calculating PC values for low-LET radiation. As may be seen in Tables VII-1 and VII-2, the SEER reporting areas differ considerably in their reported baseline levels of incidence (the range is 42 to 113 for males) (8). Although the main risk factor for lung cancer is smoking, for which adjustments can be made as discussed in Chapter IV, Section H, and in Chapter IX, there are other important etiologic agents that may pose difficulties, notably asbestos, polycyclic hydrocarbons, chloromethyl ethers, chromium, nickel, and inorganic arsenic (69). As noted in Chapter IV-G and in Chapter IX, risk co-factors other than smoking may be taken

into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

For lung cancer, the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the contribution of the low-LET tissue dose (D) in rad, T(Y) represents the variation in R over time in years (Y) after exposure, and K(A₁, S) represents the relative excess risk of lung cancer for a person of sex S and age A₁ at exposure, when both F and T = 1.

Under the linear-quadratic model assumed for the lung when exposure is to low-LET radiation,

$$F = D + D^2/116.$$

For the lung, the influence of time (T) on the relative risk depends only on years from exposure to diagnosis (Y).

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess lung cancer, K, is given in the accompanying Table X-9-A for low-LET radiation and for each sex and completed year of age at exposure from 10 to 75.

Because cigarette smoking dominates the risk of lung cancer in the general population, the PC estimate should, if possible, take smoking history into account. As explained in Chapter IV, the multiplicative interaction model would require no adjustment for smoking history, but the additive interaction model seems more appropriate for lung cancer, at least for low-LET radiation. This requires that the influence of smoking history be incorporated into the expression for R when calculating PC's. This results in a multiplier for R, calculated as the average population risk divided by the average risk in the relevant smoking category. This ratio is W in the Chapter IV discussion, and the values developed there are repeated in Table X-9-B. Then the value of R, modified to show the influence of smoking status, becomes

$$R = F \times T \times K \times W.$$

A few examples should make it clear how the PC values are to be obtained for individual cases:

Example 1 A non-smoking male, exposed to 5 rad of low-LET radiation to the lung at age 20, with a diagnosis at age 50, otherwise typical of his age-sex group with respect to the risk of lung cancer. Then $D = 5$, $A_1 = 20$, $Y = 30$, and $W = 6.81$

$$F(D) = 5 + 5^2/116 = 5.22$$

$$T(Y) = T(30) = 1$$

$$K(A_1, S) = K(20, m) = .00122$$

$$W = 6.81$$

$$\text{then } R = F \times T \times K \times W = 5.22 \times 1 \times .00122 \times 6.81 = .0434$$

$$\text{and } PC = R/(1 + R) = .0434/1.0434 = .042 \text{ or } 4\%.$$

Example 2 A lung cancer was diagnosed at age 44 in a non-smoking woman following several exposures to low-LET radiation at various ages. The first, of one rad to the lung, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9 rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$). For a non-smoking female $W = 4.64$.

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The partition giving the maximum risk estimate assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(A_1, S) = K(20, f) = .00230$$

$$R_1 = F \times T \times K \times W = 1.01 \times 1 \times .00230 \times 4.64 = .0108$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00230$$

$$R_2 = F \times T \times K \times W = 2.03 \times 1 \times .00230 \times 4.64 = .0217$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00214$$

$$R_{3a} = F \times T \times K \times W = 3.08 \times 1 \times .00214 \times 4.64 = .0306$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00214$$

$$R_{3b} = F \times T \times K \times W = 6.31 \times 1 \times .00214 \times 4.64 = .0627$$

Exposures 4, 5 and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00104$$

$$R_{4,5,6} = F \times T \times K \times W = 2.45 \times .926 \times .00104 \times 4.64 = .0109$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} =$$

$$+ .0108 + .0217 + .0306 + .0627 + .0109 = .1367$$

$$PC = R/(1 + R) = .1367/1.1367 = .120 \text{ or } 12\%$$

Example 3 A lung cancer was diagnosed in a man whose only known radiation exposure was to inhaled radon and radon daughters while employed as a uranium miner during the period 1950-1968. The most recent exposure occurred more than 10 years before diagnosis. Total recorded exposure was to 140 WLM, of which 100 WLM was before 1961 and 40 WLM afterward. If the risk factor .012 per WLM is applied to the total exposure, the calculated relative excess is

$$R = 140 \times .012 = 1.68$$

and the PC is

$$PC = R/(1 + R) = 1.68/2.68 = .626 = 63\%.$$

The same result is obtained by looking up in Table PC-9-I (Appendix I) the PC for 140 WLM with an assumed excess risk of 1.2%. However, it may be desirable to use different relative excess risks because of employment as a miner both before and after 1961. In this case, Table PC-9-I cannot be used and calculations are as follows:

If the factor .007 is applied to exposures before 1961 and the factor .015 to exposures afterward, the relative excess is

$$R = 100 \times .007 + 40 \times .015 = 1.30,$$

and the PC is

$$PC = 1.30/2.30 = .565 = 57\%.$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-O includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-9 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, on the assumption that the minimal latent period has been satisfied and with no information with respect to smoking history. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig X-9

LUNG CANCER

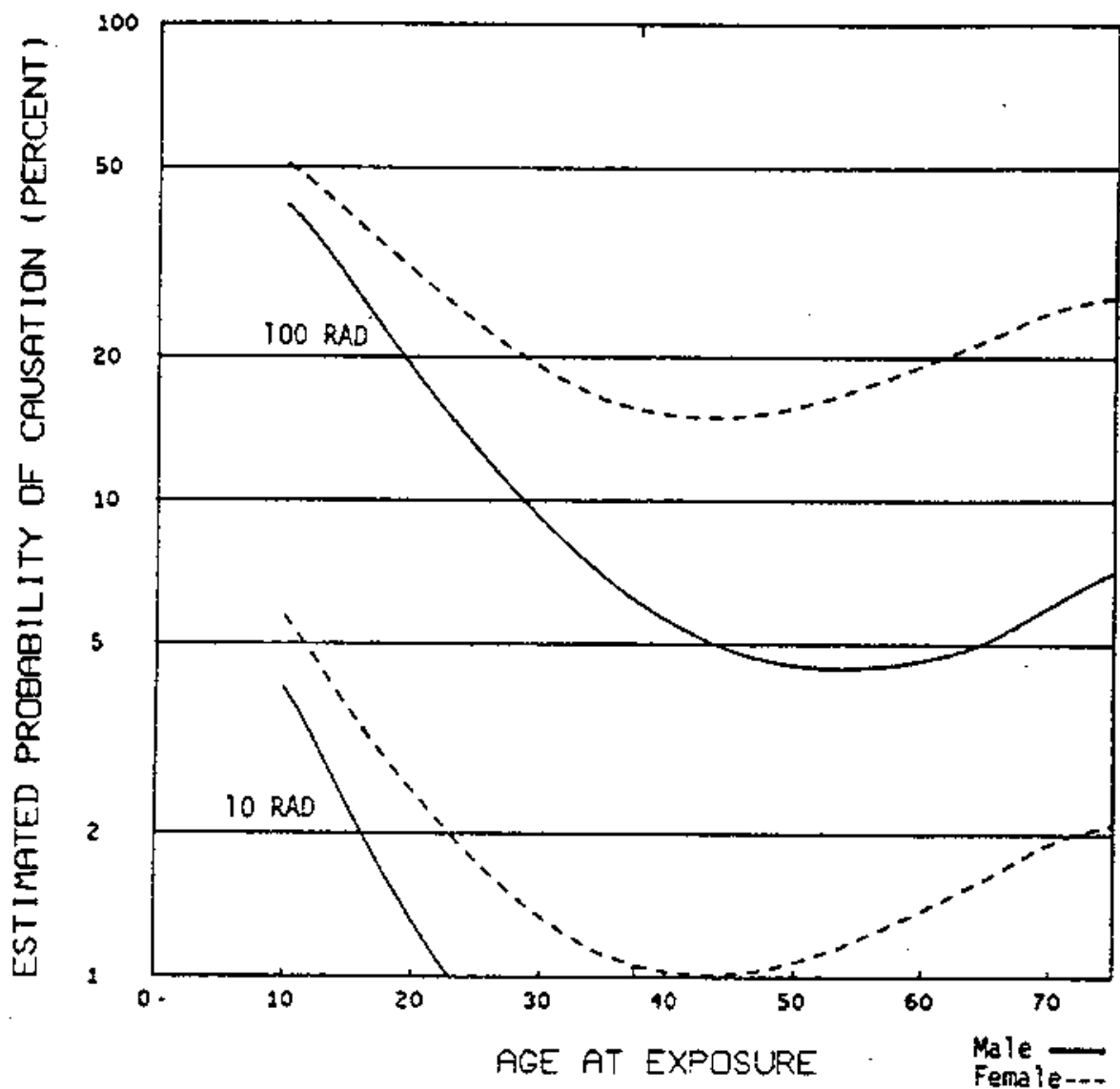


Table X-9-A Lung Cancer: Relative Excess $K(A, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A	Sex	
	Male	Female		Male	Female
10	.00387	.00557	43	.000288	.000942
11	.00349	.00510	44	.000280	.000942
12	.00311	.00465	45	.000274	.000945
13	.00275	.00422	46	.000268	.000950
14	.00243	.00383	47	.000263	.000959
15	.00214	.00349	48	.000260	.000970
16	.00190	.00318	49	.000256	.000985
17	.00169	.00292	50	.000254	.00100
18	.00151	.00269	51	.000252	.00102
19	.00136	.00248	52	.000251	.00104
20	.00122	.00230	53	.000250	.00106
21	.00111	.00214	54	.000250	.00109
22	.00101	.00199	55	.000251	.00112
23	.000925	.00186	56	.000252	.00115
24	.000849	.00174	57	.000253	.00118
25	.000781	.00163	58	.000255	.00122
26	.000721	.00154	59	.000258	.00125
27	.000667	.00145	60	.000261	.00129
28	.000619	.00138	61	.000265	.00133
29	.000576	.00131	62	.000269	.00137
30	.000537	.00125	63	.000274	.00142
31	.000503	.00120	64	.000280	.00146
32	.000472	.00115	65	.000288	.00151
33	.000444	.00111	66	.000297	.00156
34	.000419	.00107	67	.000308	.00162
35	.000397	.00104	68	.000319	.00168
36	.000377	.00102	69	.000331	.00174
37	.000359	.000998	70	.000344	.00179
38	.000344	.000981	71	.000357	.00184
39	.000330	.000968	72	.000370	.00188
40	.000318	.000957	73	.000384	.00191
41	.000307	.000950	74	.000398	.00194
42	.000297	.000945	75	.000411	.00197

Table X-9-B

W, The Factor Used To Adjust Average
Population Incidence for Smoking History

Smoking Category	W	
	Males	Females
Total	1.00	1.00
Nonsmokers	6.81	4.64
Former smokers	1.71	1.17
Present cigarette smokers, all	0.604	0.412
under 10/day	1.75	1.19
10 - 20/day	0.707	0.482
21 - 39/day	0.408	0.278
40 +/day	0.287	0.196

10. Cancer of the Female Breast (174 in ICDA-8)

Risk estimates for radiation-induced cancer of the female breast are the most secure for any site. The 1980 BEIR report was preceded by publication of incidence data on the Life Span Study sample of Japanese A-bomb survivors (70), former patients at Massachusetts tuberculosis sanatoria who received substantial cumulative breast doses from multiple fluoroscopic examinations (71), and women treated with X rays for acute postpartum mastitis (72). The estimates in the 1980 BEIR report were based on an analysis in parallel of data from these three sources (73,74).

A remarkable feature of the analysis in parallel was that similar estimates of the absolute magnitude of risk were obtained from the three samples for similar ages at exposure and lengths of follow-up, despite 3 to 5-fold differences in baseline risk between Japanese and US women (75). A possible interpretation of this finding is that factors in the American lifestyle responsible for the difference (American women of Japanese descent have breast cancer rates approaching those of other American women) are additive with radiation in the causation of breast cancer. The data also were highly consistent with proportionality between radiation dose and excess risk, and with the constant relative risk model for induction period.

Estimates for women exposed after age 40 were uncertain because the two medical series contained few relevant data and the A-bomb survivor data, which were consistent with little or no excess risk, suggested the possibility that a radiation effect on ovarian function might have reduced the risk of breast cancer among older women. Evidence for excess risk among Swedish women treated with X rays for benign breast disease (76) at ages above 40 seemed questionable because of the possibility that the excess might be attributable to the indication for treatment, e.g., chronic cystic mastitis, known to be a risk factor for breast cancer. This uncertainty was resolved by the BEIR committee at the time by applying risk coefficients for exposures at ages 20-39 to those at older ages, with the implicit understanding that this might overestimate risk from exposure after age 40.

At the time of the 1980 BEIR report no persuasive evidence of excess breast cancer risk in women irradiated before about age 10 had been presented, and while it seemed possible that an excess would appear when the youngest A-bomb survivors reached ages at which breast cancer normally reaches appreciable levels, it also seemed possible that lack of differentiated breast target tissue might preclude a carcinogenic effect of radiation. Further follow-up studies of A-bomb survivors (77,78) and American women treated in infancy for supposedly enlarged thymus gland (79) have shown that irradiation during early childhood does increase the risk of breast cancer, that this risk does not appear until after about age 30, when breast cancer rates normally increase, and that the excess, when it does appear, is comparable to that seen in women irradiated during their teens, previously considered to be the ages of greatest sensitivity. The two studies make it plain that the BEIR coefficient of 0 for women exposed under ten years of age is inappropriate and should be replaced. Moreover, the more recent study of A-bomb survivors (78) is based on a sufficiently large experience at the older ages to provide adequate estimates for

women aged 40 or older and these indicate that the flat projection of risk from age 20 in the BEIR report can no longer be supported. Accordingly, age-specific coefficients developed from that more recent study have been substituted for those given in the BEIR report (see Chapter V-D).

Other recent developments include a record-linkage study (80) of breast cancer mortality among some 110,000 Canadian women given multiple chest fluoroscopies during treatment at tuberculosis sanatoria in Canada. The radiation exposures were highly fractionated and delivered over periods of years. The data from this study were interpreted as suggestive of a strongly quadratic, rather than linear, dose response. This interpretation, which seems contradictory to the general observation from experimental radiobiology that fractionation and protraction of dose reduce nonlinear components of the dose response (81), appears to rest on a difference between data from Nova Scotia, where total doses tended to be high, and other Canadian provinces, where doses tended to be lower because patients usually were examined with their backs to the X-ray source. Considerable uncertainty surrounds the dosimetry data for the Canadian series, and it is of interest that the initial publication of a small Nova Scotia series (82), which employed incidence rather than mortality, suggested linearity of dose-response to the first BEIR committee (83).

Despite its general preference for the linear-quadratic dose-response function, the Working Group considered that all the data for breast cancer except those in the recent Canadian report were so strongly linear that it was important to make an exception of breast cancer and to assume linearity of dose-response in developing the PC estimation procedure for this site. The time-response data on breast cancer definitely point to the constant relative risk model as the basis for distributing excess cases over time, with a latent period (for incidence) of 10 years smoothed as described in Chapter V-C. Since the underlying data on breast cancer are extensive, are derived from numerous exposure situations, and are relatively non-controversial, PC estimates for this site are probably more reliable than for any other site. The general procedures for estimating PC values are described in Chapters VI and IX.

Breast cancer baseline rates vary somewhat by geographic region. Tables VII-1 and VII-2 illustrate the variability seen in the SEER data of the National Cancer Institute from which the baseline or normal incidence data were taken (8). There are many risk factors for breast cancer in addition to exposure to ionizing radiation, especially early menarche, nulliparity, delayed age at first completed pregnancy, positive family history, and pre-existing proliferative breast disease (84). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. If it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased. For breast cancer the relative excess, R , in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1)$$

where $F(D)$ represents the influence of the low-LET tissue dose (D), $T(Y)$ represents the variation in R over time in years (Y) after exposure, and $K(A_1)$ represents the relative excess risk of breast cancer for a woman of age A_1 at exposure, when both F and $T = 1$.

Under the linear model assumed for breast cancer, $F = D$ for low-LET radiation.

For breast cancer the influence of time (T) on the relative risk does not vary by age at exposure but does depend on years from exposure to diagnosis (Y) in the following fashion:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1

The standardized relative risk of excess breast cancer, K , is given in the accompanying Table X-10 for low-LET radiation and for each completed year of age from birth to 75.

A few examples should illustrate how the PC values are to be obtained in individual cases.

Example 1 A typical female, aged 10 when exposed to 10 rad of low-LET radiation to breast tissue, with a diagnosis of breast cancer at age 35. That is, $D = 10$, $A_1 = 10$, and $Y = 25$.

$$F(D) = 10$$

$$T(Y) = T(25) = 1$$

$$K(A_1, S) = K(10) = .0144$$

$$\text{then } R = 10 \times 1 \times .0144 = .144$$

$$\text{and } PC = R/(1 + R) = .144/1.144 = .126 \text{ or } 13\%.$$

Example 2 A breast cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the breast in which cancer was later diagnosed, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1=20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours can be treated as a single exposure because estimated risk under the linear model depends only upon the total dose. Similarly, the three exposures at age 35 can be treated as a single exposure.

Exposure 1:

$$F(D) = F(1) = 1$$

$$T(Y) = T(24) = 1$$

$$K(A_1, S) = K(20, f) = .00606$$

$$R_1 = F \times T \times K = 1 \times 1 \times .00606 = .00606$$

Exposure 2:

$$F(2) = 2$$

$$T(23) = 1$$

$$K(20, f) = .00606$$

$$R_2 = F \times T \times K = 2 \times 1 \times .00606 = .0121$$

Exposure 3:

$$F(9) = 9$$

$$T(23) = 1$$

$$K(21, f) = .00523$$

$$R_3 = F \times T \times K = 9 \times 1 \times .00523 = .0471$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4$$

$$T(9) = .926$$

$$K(35, f) = .00214$$

$$R_{4,5,6} = F \times T \times K = 2.4 \times .926 \times .00214 = .00476$$

$$R = R_1 + R_2 + R_3 + R_{4,5,6} = .00606 + .0121 + .0471$$

$$+ .00476 = .0700$$

$$PC = R / (1 + R) = .0700 / 1.0700 = .0654 \text{ or } 7\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-10 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-10

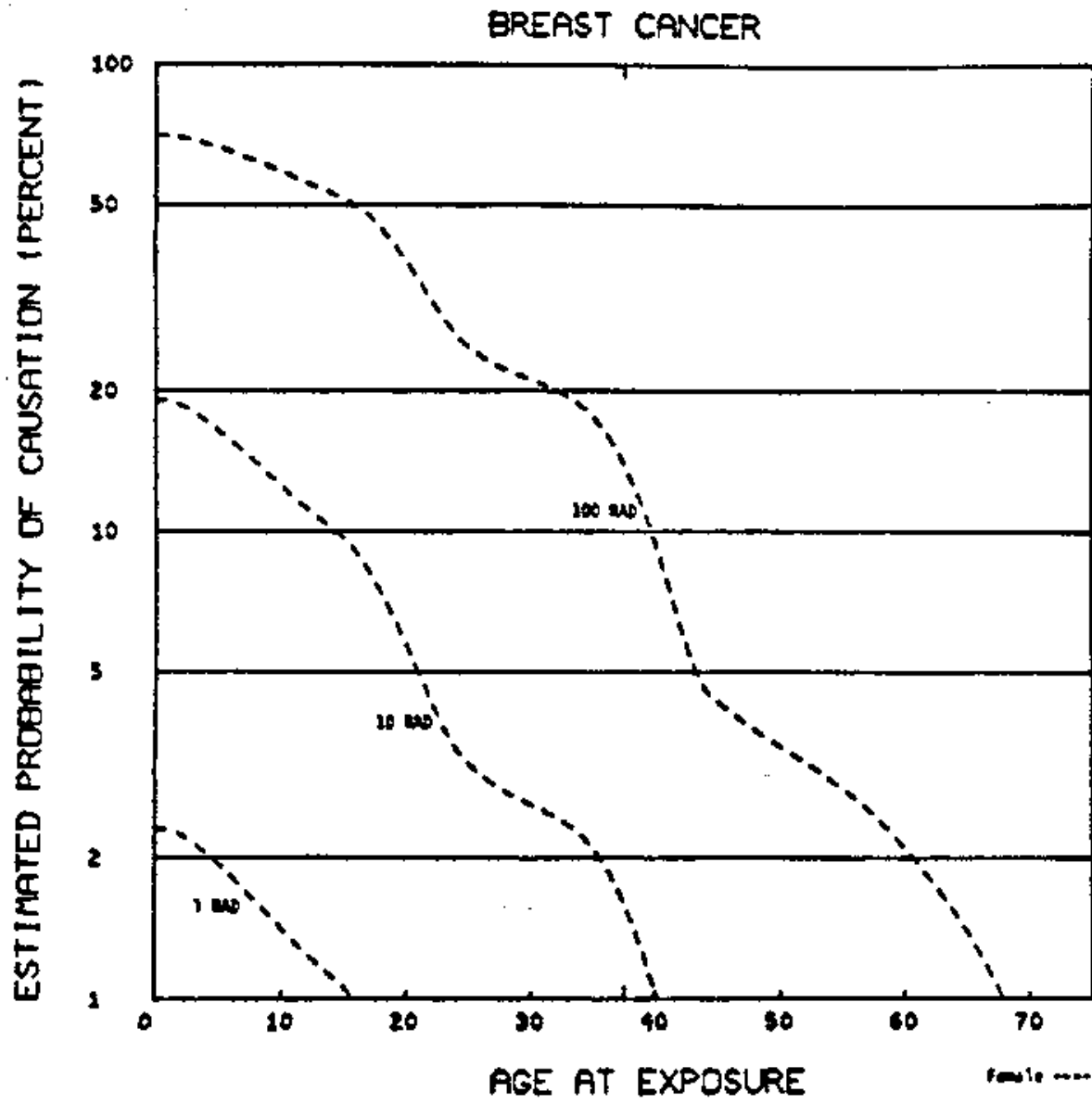


Table X-10. Female Breast Cancer: Relative Excess
 $K(A_1, S)$ by Exposure Age A_1

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	---	.0237	38	---	.00150
1	---	.0236	39	---	.00126
2	---	.0230	40	---	.00104
3	---	.0220	41	---	.000835
4	---	.0209	42	---	.000669
5	---	.0198	43	---	.000547
6	---	.0186	44	---	.000478
7	---	.0174	45	---	.000452
8	---	.0163	46	---	.000429
9	---	.0153	47	---	.000409
10	---	.0144	48	---	.000391
11	---	.0134	49	---	.000375
12	---	.0126	50	---	.000359
13	---	.0119	51	---	.000345
14	---	.0113	52	---	.000331
15	---	.0107	53	---	.000318
16	---	.00992	54	---	.000305
17	---	.00897	55	---	.000291
18	---	.00797	56	---	.000277
19	---	.00699	57	---	.000263
20	---	.00606	58	---	.000248
21	---	.00523	59	---	.000231
22	---	.00452	60	---	.000215
23	---	.00395	61	---	.000200
24	---	.00354	62	---	.000185
25	---	.00329	63	---	.000170
26	---	.00310	64	---	.000155
27	---	.00296	65	---	.000141
28	---	.00285	66	---	.000127
29	---	.00276	67	---	.000113
30	---	.00268	68	---	.0000996
31	---	.00260	69	---	.0000859
32	---	.00251	70	---	.0000720
33	---	.00241	71	---	.0000580
34	---	.00229	72	---	.0000437
35	---	.00214	73	---	.0000293
36	---	.00195	74	---	.0000148
37	---	.00173	75	---	0

11. Cancer of Kidney or Bladder (188, 189.0, 189.1 in ICDA-8)

Sensitivity to the carcinogenic effect of ionizing radiation is considered to be relatively low for both the kidney and the urinary bladder. Reported dose-specific risks are seldom high and in some studies no excess cancers have been found. Malignant tumors of the kidney, of the bladder, or of the undifferentiated "urinary organs" have been reported to be increased in frequency among the A-bomb survivors, persons treated with irradiation of the spine for ankylosing spondylitis, persons who received injections of Thorotrast in retrograde pyelography, and persons with cervical cancer treated by radiation (4,23). In some studies the relationship with radiation dose is uncertain or simply not demonstrable, and the data from the cervical cancer series are especially inconclusive (5). The strongest relationship is seen in the mortality experience of the A-bomb survivors over the period 1950-1978 (28), especially since it appears within each sex and within each city, but death certificate diagnoses are much less reliable for these sites than for many others.

The BEIR III coefficients, adjusted to the period 11-30 years after exposure, have been used in the PC calculations as described in Chapters VI and IX, except that estimates were not made for those under age 20 at exposure for the reasons given in Chapter VII-F.

The normal or baseline risk of cancers of the kidney and bladder has been taken from the data bank of the SEER program of the National Cancer Institute (8). The rates are for the period 1973-1981, for all races combined, and for all reporting areas combined except Puerto Rico. There is appreciable geographic variation within the US (see Tables VII-1 and VII-2) that apparently rests on differentials in industrial exposures that are of major importance for cancer of the bladder (85). Exposure to dyestuffs, rubber, leather, and certain organic chemicals has been associated with excess cancer of the bladder (86). An association between cigarette consumption and bladder cancer is well documented, and there is some evidence of an association with cancer of the kidney (85). As noted in Chapter IV-G and in Chapter IX, risk factors other than ionizing radiation may be taken into consideration in interpreting the PC values derived by the procedures presented here. If it is believed that some other risk factor operates additively with radiation, and the individual is thought to have been exposed to that risk factor to an extent greater than the average for the population generally, then the PC obtained from the present procedures may be somewhat excessive. But if it is believed that the second risk factor may combine with radiation to enhance risk in multiplicative fashion, the PC estimates based on these procedures should be unbiased.

The Working Group had no information available to it concerning the most appropriate dose-response function for cancers of the kidney and bladder, or the most suitable time-response function, or whether radiation may interact with other risk factors in multiplicative or additive fashion. It chose, therefore, to employ the preferred linear-quadratic model of dose-response, with no threshold, and the constant relative risk model for distributing excess cancers over time. The minimum latent period was taken as 10 years but smoothed as described in Chapter V-C.

The procedures for calculating PC values for cancers of the kidney and bladder are based on the assumptions and principles discussed in Chapter V and the procedures of Chapter VI and IX. As with most sites, for cancers of the kidney and bladder the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents variation in R over time in years (Y) after exposure, while K(A₁, S) represents the relative excess risk of cancer of the kidney or bladder for a person of age at exposure A₁ and sex S, when both F and T = 1.

Under the linear-quadratic model assumed for cancers of the kidney and bladder, when exposure is to low-LET radiation

$$F = D + D^2/116.$$

For cancers of the kidney and bladder the influence of time (T) on the relative risk depends entirely on years from exposure to diagnosis (Y). The function T is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative excess risk for cancer of the kidney or bladder, K, is given in the accompanying Table X-11 for low-LET radiation and for each sex and year of age (completed years) from 20 to 75.

A few examples should clarify the actual computational procedures for cancers of the kidney and bladder following exposure to ionizing radiation.

Example 1 A typical female, aged 35 when exposed to 10 rad of low-LET radiation to bladder tissue with diagnosis at age 55, 20 years after exposure. Then D = 10, A₁ = 35, and Y = 20

$$F(D) = 10 + 10^2/116 = 10.86$$

$$T(Y) = T(20) = 1$$

$$K(A_1, S) = K(35, f) = .00142$$

$$R = F \times T \times K = 10.86 \times 1 \times .00142 = .01542$$

$$\text{and } PC = .0154/1.0154 = .015 \text{ or } 2\%.$$

Example 2 A typical male, aged 55 at exposure to 5 rad of low-LET radiation to the kidney, with diagnosis at age 60, 4.9 years after exposure. That is, $D = 5$, $A_1 = 55$, and $Y = 4$.

$$F = 5 + 5^2/116 = 5.22$$

$$T(4) = 0$$

$$K(55,m) = .000275$$

$$\text{then } R = F \times T \times K = 5.22 \times 0 \times .000275 = 0$$

$$\text{and } PC = 0$$

Example 3 A kidney cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the kidney, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$).

The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y , and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours should be treated as 2 exposures because it required more than one day, but less than two. The suggested partition assigns a 3-rad exposure to one 24-hour period and 6 rad to another. The three exposures at age 35 can be treated as one because they correspond to the same values of A_1 and Y , and because the total dose is less than 5 rad.

Exposure 1:

$$F(D) = F(1) = 1 + 1^2/116 = 1.01$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .00301$$

$$R_1 = F \times T \times K = 1.01 \times 1 \times .00301 = .00304$$

Exposure 2:

$$F(2) = 2 + 2^2/116 = 2.03$$

$$T(23) = 1$$

$$K(20,f) = .00301$$

$$R_2 = F \times T \times K = 2.03 \times 1 \times .00301 = .00611$$

Exposure 3a:

$$F(3) = 3 + 3^2/116 = 3.08$$

$$T(23) = 1$$

$$K(21,f) = .00287$$

$$R_{3a} = F \times T \times K = 3.08 \times 1 \times .00287 = .00884$$

Exposure 3b:

$$F(6) = 6 + 6^2/116 = 6.31$$

$$T(23) = 1$$

$$K(21,f) = .00287$$

$$R_{3b} = F \times T \times K = 6.31 \times 1 \times .00287 = .0181$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4 + 2.4^2/116 = 2.45$$

$$T(9) = .926$$

$$K(35,f) = .00142$$

$$R_{4,5,6} = F \times T \times K = 2.45 \times .926 \times .00142 = .00322$$

$$R = R_1 + R_2 + R_{3a} + R_{3b} + R_{4,5,6} = .00304$$

$$+ .00611 + .00884 + .0181 + .00322 = .0393$$

$$PC = R/(1+R) = .0393/1.0393 = .038 = 4\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-11 has been drawn for tissue doses of 10 and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only two radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-11

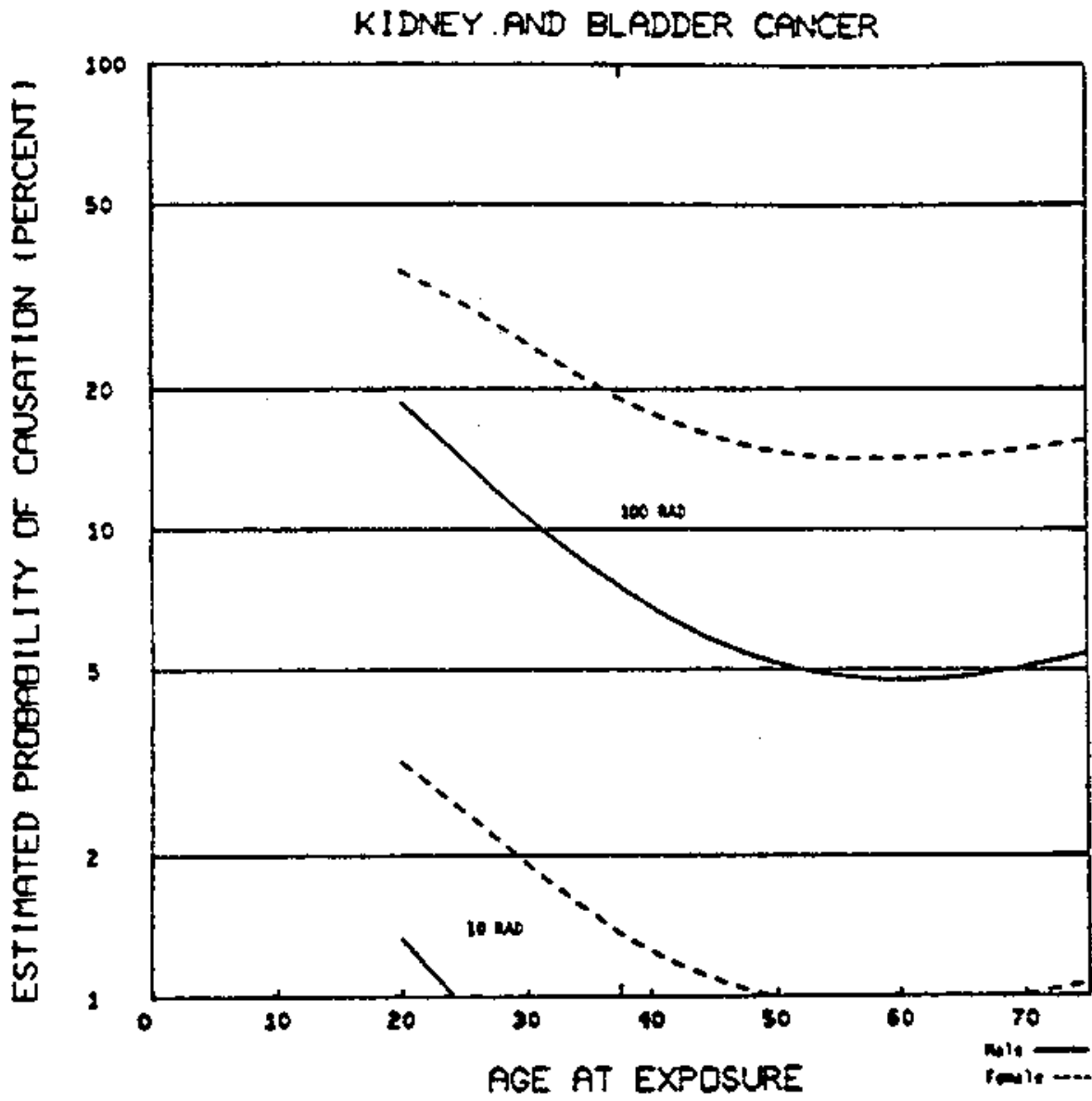


Table X-11. Kidney and Bladder Cancer: Relative Excess
 $K(A_1, S)$ by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
20	.00124	.00301	48	.000306	.000958
21	.00116	.00287	49	.000300	.000943
22	.00108	.00273	50	.000294	.000930
23	.00101	.00260	51	.000289	.000920
24	.000945	.00247	52	.000285	.000911
25	.000883	.00235	53	.000281	.000904
26	.000826	.00223	54	.000278	.000898
27	.000772	.00211	55	.000275	.000895
28	.000724	.00200	56	.000273	.000892
29	.000680	.00190	57	.000271	.000891
30	.000642	.00180	58	.000270	.000892
31	.000607	.00172	59	.000269	.000893
32	.000575	.00163	60	.000269	.000894
33	.000546	.00156	61	.000269	.000896
34	.000519	.00149	62	.000269	.000898
35	.000495	.00142	63	.000270	.000901
36	.000472	.00136	64	.000271	.000904
37	.000451	.00130	65	.000272	.000908
38	.000431	.00125	66	.000274	.000913
39	.000413	.00121	67	.000276	.000919
40	.000396	.00117	68	.000279	.000925
41	.000380	.00113	69	.000283	.000932
42	.000366	.00110	70	.000286	.000940
43	.000353	.00107	71	.000290	.000949
44	.000341	.00104	72	.000294	.000958
45	.000331	.00102	73	.000299	.000968
46	.000322	.000995	74	.000303	.000980
47	.000314	.000975	75	.000308	.000993

12. Thyroid Cancer (193 in ICDA-8)

The thyroid tables were constructed on the basis of the assumptions and principles of Chapter V and the procedures described in Chapters VI and IX. The risk coefficients used in making the tables, however, were modified from the published BEIR III values and are given in Table VI-1. The BEIR III coefficients were based largely on the exposure of children and the data available in 1978-79, when the report was prepared, seemed insufficient to support clinical impressions of age differentials in risk (4). A central value of 4.0 excess cancers per million persons per year per rad was postulated on the basis of the literature available at that time, and the female/male ratio of risk, 2.6, was taken from preliminary data (40 clinical cases) on the A-bomb survivors (87) to yield estimates of 5.8 for females and 2.2 for males, regardless of age at exposure.

Data concerning the incidence of thyroid cancer are especially uncertain because of difficulty of ascertainment. Thyroid cancers are usually indolent; they are often slow growing and may not come to medical attention unless they are sought by active investigation. Since active screening for thyroid cancer will often be undertaken upon population groups in which it is suspected that thyroid cancers may have been induced by radiation, excesses may be found, not only because the incidence is increased but because diligent investigation has identified cancers that would otherwise not come to attention.

Since the BEIR III report was prepared, additional data have been published on the Israeli tinea capitis series (88) and on the A-bomb survivors (29,89). In addition, the Working Group has had access to a near-final manuscript on 178 clinical cases among the A-bomb survivors (90). The Israeli series is limited to persons who were children at the time of exposure, but the recent reports on the A-bomb survivors contain clear evidence of age variation in risk and also provide a more stable estimate of the ratio of female to male risk coefficients, 3.5. The US literature suggests an average risk coefficient of about 3.3 excess cancers per million persons per year per rad for those exposed as children, and the Working Group has employed this value, rather than 4.0, together with the female/male ratio of 3.5, to obtain the final coefficients of 1.5 for males and 5.0 for females. Since the observed risks in A-bomb survivors 20 or older at exposure are about one-third of those for survivors exposed before age 20, this fraction was used to estimate approximate coefficients for the older group, 0.5 for males and 1.5 for females.

Although there is some evidence favoring a minimum latent period of 5 years for thyroid cancer (91), it was decided to use the standard assumption of 10 years (smoothed over the interval 5-10 years) made for all solid tumors as described in Chapter V-C. Published dose-response information on radiation-induced thyroid cancer is not extensive, but it clearly suggests linearity (91). In addition, in the large unpublished series of Ishimaru et al. the excess thyroid cancer incidence among A-bomb survivors is best fitted by a linear function of dose (90). Despite its general preference for the linear-quadratic dose-response function, therefore, the Working Group chose to base its PC estimation procedures for thyroid cancer on linearity. The distribution of radiation-induced cases over time was assumed to follow the relative risk model

although there is very little published thyroid cancer information with which to test this assumption.

The PC estimates calculated for thyroid cancer pertain to external X and gamma irradiation, not to the radioisotopes of iodine. Although iodine-131 is thought to be the major source of irradiation of thyroid tissues in individuals exposed to fallout from the weapons tests, the existing human data are not of sufficient cogency to provide a direct basis for quantitative estimates of risks; furthermore, there is controversy over the biological effectiveness of iodine-131 beta radiation relative to X rays and gamma rays. An Ad Hoc Working Group on Thyroid/Iodine Assessment, also mandated by the Orphan Drug Act (Public Law 97-414, Section 7a) is currently reviewing the available data and research needs in this area.

It is the SEER data on the incidence of thyroid cancer for all reporting areas combined except Puerto Rico, and all races combined, for the period 1973-1981, that is the source of the normal incidence rates employed here (8). For thyroid cancer known risk factors are neither numerous nor influential (92); there is, however, some variation in the SEER tables for individual reporting areas (see Tables VII-1 and VII-2).

For thyroid cancer the relative excess, R, in the basic equation

$$PC = R/(1 + R)$$

is found as the product of three functions, i.e.,

$$R = F(D) \times T(Y) \times K(A_1, S)$$

where F(D) represents the influence of the low-LET tissue dose (D), T(Y) represents variation in R over time in years (Y) after exposure, and K(A₁, S) represents the relative excess thyroid cancer per rad for a person of sex S and age at exposure A₁, when both F and T = 1.

Under the linear model assumed for thyroid cancer, F = D where D is the low-LET tissue dose in rad. For the thyroid the influence of time (T) on relative risk depends only on years from exposure to diagnosis (Y). The simple function T, the latency factor, is tabled below:

Y	0-4	5	6	7	8	9	10+
T	0	.074	.259	.500	.741	.926	1.

The standardized relative risk of excess thyroid cancer, K, is given in the accompanying Table X-12 for each sex and individual year of age (completed years) from birth to 75.

A few examples should make it clear how the PC values are to be obtained.

Example 1 A female, aged 10 when exposed to 5 rad of low-LET radiation to thyroid tissue, with diagnosis 9.9 years later, and assumed to be typical of her age and sex with respect to the normal risk of thyroid cancer. That is, D = 5, A₁ = 10, and Y = 9.

$$F(D) = 5$$

$$T(Y) = T(9) = .926$$

$$K(A_1, S) = K(10, f) = .0594$$

$$\text{then } R = F \times T \times K = 5 \times .926 \times .0594 = .275$$

$$\text{and } PC = R/(1 + R) = .275/1.275 = .216 \text{ or } 22\%.$$

Example 2 A female exposed twice to low-LET radiation to thyroid tissue, 5 rad at age 10 and 2 rad at age 15, with diagnosis of thyroid cancer at age 25, 9.8 years after the latter exposure. Again, it is assumed that she is representative of her age and sex with respect to the normal risk of thyroid cancer. We must combine two values of R, one for each exposure.

Exposure 1, at age 10, when $D = 5$, $A_1 = 10$, and $Y = 15$

$$F(D) = 5$$

$$T(15) = 1$$

$$K(10, f) = .0594$$

$$\text{then } R_1 = F \times T \times K = 5 \times 1 \times .0594 = .297$$

Exposure 2, at age 15, when $D = 2$, $A_1 = 15$, and $Y = 9$

$$F(D) = 2$$

$$T(9) = .926$$

$$K(15, f) = .0535$$

$$\text{then } R_2 = F \times T \times K = 2 \times .926 \times .0535 = .0991$$

$$\text{the total } R = R_1 + R_2 = .297 + .099 = .396$$

$$\text{and } PC = R/(1 + R) = .396/1.396 = .284, \text{ or } 28\%.$$

Example 3 A thyroid cancer was diagnosed at age 44 in a woman following several exposures to low-LET radiation at various ages. The first, of one rad to the thyroid, occurred at age 20, 24 years and 2 months before diagnosis ($Y = 24$). The second, to 2 rad, occurred 4 months later, at the same age ($A_1 = 20$) but 23 years and 10 months before diagnosis ($Y = 23$). At age 21, 23 years and 3 months before diagnosis, a 9-rad total dose was received over a 36-hour period at the continuous rate of 250 millirad per hour ($Y = 23$). Finally, at age 35, three exposures, to 1.1, 0.6, and 0.7 rad, respectively, were received on consecutive days, 9 years and 2 months prior to diagnosis ($Y = 9$). The first, second, and third exposures should be considered separately, because exposures 1 and 2 correspond to different values of Y, and exposures 2 and 3 to different exposure ages. The 9-rad continuous exposure delivered over 36 hours can be treated as a

single exposure because estimated risk under the linear model depends only upon the total dose. Similarly, the three exposures at age 35 can be treated as a single exposure.

Exposure 1:

$$F(D) = 1$$

$$T(Y) = T(24) = 1$$

$$K(20,f) = .0374$$

$$R_1 = F \times T \times K = 1 \times 1 \times .0374 = .0374$$

Exposure 2:

$$F(D) = 2$$

$$T(23) = 1$$

$$K(20,f) = .0374$$

$$R_2 = F \times T \times K = 2 \times 1 \times .0374 = .0748$$

Exposure 3:

$$F(D) = 9$$

$$T(23) = 1$$

$$K(21,f) = .0331$$

$$R_3 = F \times T \times K = 9 \times 1 \times .0331 = .2979$$

Exposures 4, 5, and 6:

$$F(1.1 + 0.6 + 0.7) = F(2.4) = 2.4$$

$$T(9) = .926$$

$$K(35,f) = .0175$$

$$R_{4,5,6} = F \times T \times K = 2.4 \times .926 \times .0175 = .0389$$

$$R = R_1 + R_2 + R_3 + R_{4,5,6} = .0374 + .0748$$

$$+ .2979 + .0389 = .449$$

$$PC = R/(1 + R) = .449/1.449 = .310 \text{ or } 31\%$$

The uncertainty surrounding PC estimates is discussed in Chapter VII, and Section VII-0 includes a derivation of approximate 90 percent credibility intervals for PC estimates.

To provide an orientation to the general magnitude of the PC values that result from the procedures described here, Fig X-12 has been drawn for tissue doses of 1, 10, and 100 rad of low-LET radiation, and PC values plotted by age at exposure, for both males and females, and on the assumption that the minimal latent period has been satisfied. The vertical scale is logarithmic and curves are presented for only three radiation dose levels. For these and other reasons interpolation is to be discouraged.

Fig. X-12

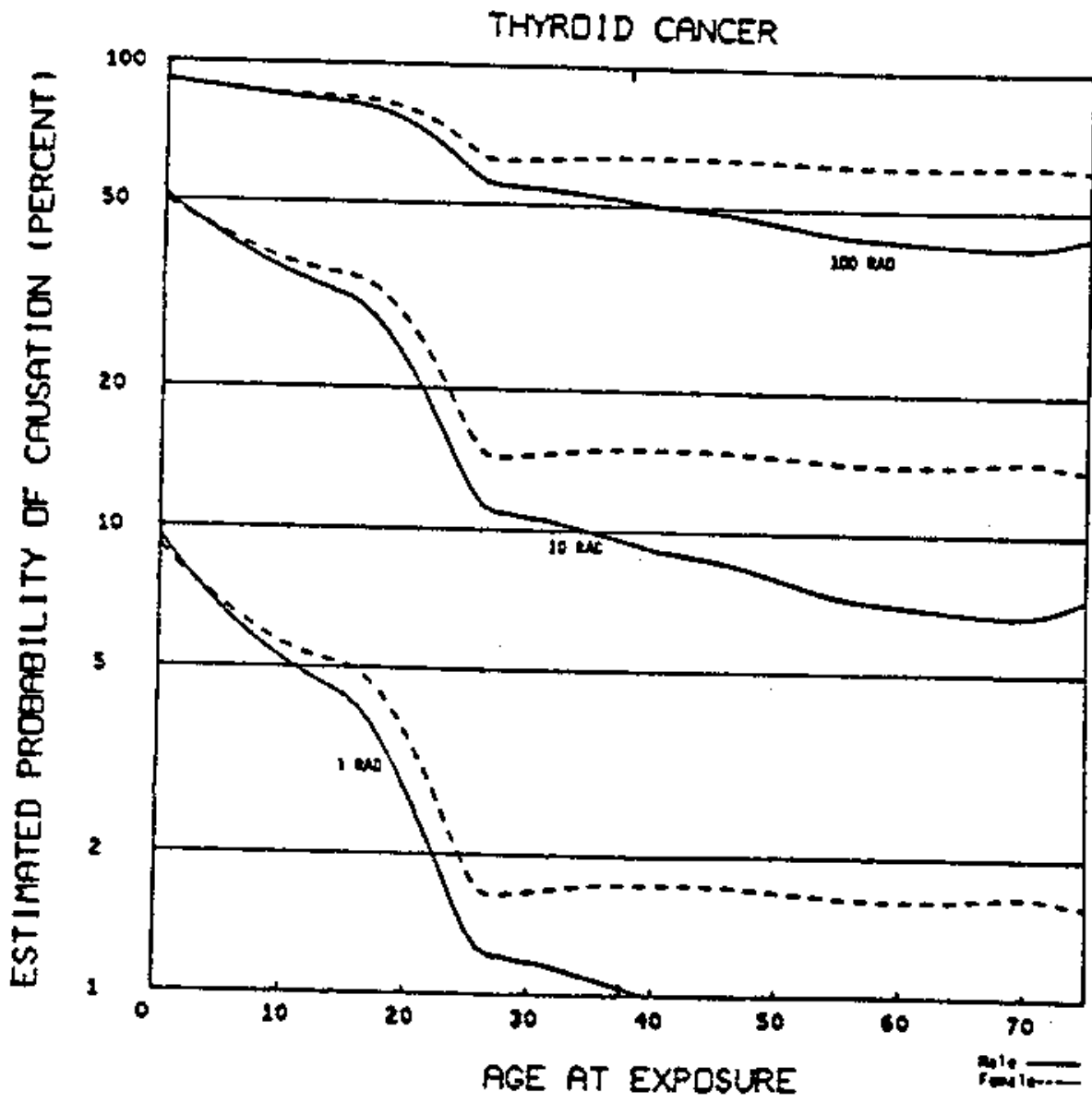


Table X-12. Thyroid Cancer: Relative Excess $K(A_1, S)$
by Exposure Age A_1 and Sex S

A_1	Sex		A_1	Sex	
	Male	Female		Male	Female
0	.106	.100	38	.0104	.0176
1	.0965	.0931	39	.0102	.0176
2	.0885	.0871	40	.0101	.0176
3	.0819	.0820	41	.00992	.0176
4	.0762	.0775	42	.00981	.0176
5	.0713	.0735	43	.00971	.0176
6	.0671	.0700	44	.00961	.0176
7	.0634	.0668	45	.00949	.0175
8	.0601	.0640	46	.00935	.0175
9	.0573	.0615	47	.00919	.0174
10	.0547	.0594	48	.00902	.0173
11	.0525	.0577	49	.00884	.0172
12	.0505	.0563	50	.00866	.0171
13	.0487	.0552	51	.00848	.0170
14	.0471	.0543	52	.00831	.0169
15	.0455	.0535	53	.00814	.0168
16	.0430	.0517	54	.00799	.0167
17	.0397	.0490	55	.00786	.0166
18	.0359	.0456	56	.00776	.0165
19	.0320	.0416	57	.00769	.0165
20	.0282	.0374	58	.00763	.0164
21	.0246	.0331	59	.00758	.0164
22	.0213	.0289	60	.00752	.0164
23	.0184	.0250	61	.00747	.0164
24	.0158	.0215	62	.00741	.0164
25	.0139	.0188	63	.00736	.0164
26	.0127	.0171	64	.00731	.0164
27	.0123	.0166	65	.00726	.0165
28	.0122	.0167	66	.00722	.0166
29	.0120	.0168	67	.00718	.0166
30	.0119	.0169	68	.00714	.0167
31	.0118	.0170	69	.00712	.0168
32	.0116	.0172	70	.00713	.0169
33	.0116	.0173	71	.00719	.0168
34	.0112	.0174	72	.00729	.0167
35	.0110	.0175	73	.00745	.0164
36	.0108	.0176	74	.00764	.0162
37	.0106	.0176	75	.00784	.0160

13. Excluded Sites

Although it is generally accepted that ionizing radiation may increase the risk of virtually any form of cancer, for many sites compelling human data on its causative role are lacking, and for still others the existing data are inadequate for the present purpose. For example, the BEIR III report lists the following sites or tissues under the category of those in which radiation-induced cancer has not been observed: prostate, uterus and cervix, testis, mesentery and mesothelium, and chronic lymphocytic leukemia. Sites or tissues in which the magnitude of the dose-specific risk is uncertain are specified as: larynx, nasal sinuses, parathyroid, ovary, and connective tissues (4). In addition, the BEIR III committee presented estimates for lymphoma that no longer seem supportable; if, indeed, certain malignant lymphomas are radiogenic, the evidence remains too tenuous and inadequate to serve as the basis of PC calculations. Although excess mortality from malignant lymphoma has been reported in the British ankylosing spondylitis series (3), among the U.S. radiologists (93), and among the Japanese A-bomb survivors (94), most of the evidence has been based on death certificate diagnoses and on small numbers. No statistically significant excess is evident in the most recent report on mortality among the A-bomb survivors (28) or in the reports based on the tumor registries (29,30). In their 1972 review of the evidence Anderson et al. pointed to differences in the pathogenesis of leukemia and malignant lymphoma and concluded that radiation-induced malignant lymphoma can be observed only following very high-dose, possibly near-lethal, exposures (95).

Multiple myeloma is a special case, worthy of further discussion. Popularized as a radiogenic form of cancer by the first Hanford report (43), multiple myeloma continues to have uncertain status as a radiogenic tumor. Cuzik has summarized the data from 12 irradiated populations in which some association has been reported between multiple myeloma and exposure to ionizing radiation, but these provide no basis for quantitative risk estimates (96). Miller and Beebe have questioned Cuzik's pooling of dissimilar studies, some of which do not show a wave of leukemia before small excesses of multiple myeloma (97). Another perplexing factor was that, in no study, no matter how heavy the dose, was the excess of multiple myeloma more than marginal. A numerical basis for risk estimation can be derived from recent reports on mortality from multiple myeloma among A-bomb survivors (28,98) but histologically confirmed cases in the Nagasaki Tumor Registry (29) and the Hiroshima Tumor Registry (30) are considerably fewer and place the relationship in doubt.

Brain cancer has been reported in both of the tinea capitis series (20,88) but not in sufficient numbers to provide stable statistical estimates. Skin cancer is well-established as an effect of exposure to ionizing radiation but not to low doses. No threshold dose has been agreed upon and there is no quantitative basis for risk estimates in the region of practical interest (4).

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APPENDIX I

ILLUSTRATIVE PC TABLES

The complexity of the algorithms of the PC calculation is such that systematic tables of the extent called for in the Orphan Drug Act would prove unwieldy in practice and might invite more error than the alternative procedure of ad hoc calculation based on a few reference tables for each site. In adopting the latter route in its presentation, the Working Group nevertheless was persuaded that some illustrative PC tables would usefully supplement the graphic summaries of Chapter X.

PC tables have been prepared for tissue doses of 1, 10 and 100 rad, and, for lung cancer (Table PC-9-1), for increments of cumulative exposure, in WLM, to inhaled radon and radon daughter products. For the latter table only, alternative PC values are presented, reflecting various choices of risk coefficients as discussed in Chapter X-9. All other tables, with the exception of the tables for bone cancer associated with exposure to alpha particle radiation from radium-224, pertain only to low-LET radiation and may not be used for exposure to high-LET radiation. Except for leukemia and bone cancer, the tabulated coefficients from which the PC values are calculated do not depend upon age at diagnosis. With the same exceptions, dependence on time after exposure is restricted to multiplication of the relative excess risk by a factor T(Y) which increases from zero during years $Y = 0-4$ to one for $Y \geq 10$. Thus it is sufficient to tabulate PC values by radiation dose, sex, and age at exposure, for $Y \geq 10$. For leukemia and bone cancer, on the other hand, the PC depends upon age at diagnosis as well, and in the interests of brevity, separate tables of PC, tabulated by sex, dose, and age at diagnosis, are presented only for exposure ages 0 to 70 in steps of 10.

Interpolation on exposure age is not recommended for leukemia or bone cancer because of the added complexity of dependence upon age at diagnosis, and is unnecessary for other cancer sites. Interpolation on dose is impracticable, except for interpolation on WLM in Table PC-9-1, because PC values are given for only three dose values. It is, in any case, easy to calculate PC values from the relevant tables in Chapter X.

A simple mathematical relationship holds between the PC values corresponding to any two dose values, for any site, provided that all other factors, like age at exposure, time from exposure to cancer diagnosis, and sex, are the same. Let PC_1 denote the tabulated PC value for dose D_1 , and let PC_2 denote the (untabulated) value for dose D_2 . Then

$$\frac{1}{PC_2} = 1 + \frac{1-PC_1}{PC_1} \frac{F(D_1)}{F(D_2)}$$

where $F(D) = D$ for breast or thyroid cancer following exposure to low-LET radiation or for bone cancer following exposure to radium-224, and $F(D) = D + D^2/116$ for other cancers following exposure to low-LET radiation. The above relationship is not recommended for routine use because the tabulated PC values are given to a lower degree of precision than the risk coefficients in Chapter X.

The tables appearing below are:

- PC-1-A Chronic granulocytic leukemia
- PC-1-B Acute leukemia
- PC-1-C All leukemia except CLL
- PC-2 Bone cancer following exposure to radium-224
- PC-3 Salivary gland cancer
- PC-4 Esophageal cancer
- PC-5 Stomach cancer
- PC-6 Colon cancer
- PC-7 Liver cancer
- PC-8 Pancreatic cancer
- PC-9 Lung cancer
- PC-10 Cancer of the female breast
- PC-11 Kidney or bladder cancer
- PC-12 Thyroid cancer.

Table PC-1-A-0. Chronic Granulocytic Leukemia Following Exposure at Age 0, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation: PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	29.	82.	99.	34.	85.	99.
3	52.	92.	99.	56.	93.	99.
4	56.	93.	99.	56.	93.	99.
5	57.	93.	99.	52.	92.	99.
6	56.	93.	99.	47.	91.	99.
7	55.	93.	99.	43.	89.	99.
8	53.	92.	99.	41.	88.	99.
9	51.	92.	99.	40.	88.	99.
10	49.	91.	99.	39.	87.	99.
11	47.	91.	99.	37.	86.	99.
12	46.	90.	99.	35.	85.	99.
13	42.	89.	99.	30.	83.	99.
14	37.	86.	99.	26.	79.	98.
15	31.	83.	99.	21.	74.	98.
16	27.	80.	99.	18.	70.	98.
17	23.	76.	98.	16.	67.	97.
18	19.	72.	98.	15.	65.	97.
19	16.	68.	97.	15.	65.	97.
20	14.	63.	97.	15.	65.	97.
21	11.	58.	96.	14.	64.	97.
22	9.7	54.	95.	12.	59.	96.
23	7.8	48.	94.	9.7	54.	95.
24	6.0	41.	92.	8.0	48.	94.
25	4.8	35.	90.	6.7	44.	93.
26	3.9	31.	88.	5.7	39.	92.
27	3.5	28.	87.	4.9	36.	90.
28	3.2	27.	86.	4.2	32.	89.
29	3.2	26.	85.	3.7	29.	88.
30	3.2	26.	86.	3.3	27.	86.
31	3.2	26.	86.	2.9	24.	85.
32	3.0	25.	85.	2.6	22.	83.
33	2.8	23.	84.	2.3	20.	81.
34	2.5	22.	83.	2.1	19.	80.
35	2.3	20.	81.	1.9	17.	78.

Table PC-1-A-10. Chronic Granulocytic Leukemia Following Exposure at Age 10, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	16.	67.	97.	11.	57.	96.
13	32.	84.	99.	22.	76.	98.
14	33.	84.	99.	23.	76.	98.
15	30.	82.	99.	20.	73.	98.
16	26.	79.	98.	17.	70.	98.
17	22.	75.	98.	15.	66.	97.
18	19.	71.	98.	14.	64.	97.
19	16.	67.	97.	14.	64.	97.
20	13.	62.	96.	14.	64.	97.
21	11.	57.	96.	13.	62.	97.
22	9.0	51.	95.	11.	58.	96.
23	7.1	45.	93.	8.9	51.	95.
24	5.4	38.	91.	7.2	46.	93.
25	4.2	32.	89.	6.0	41.	92.
26	3.4	28.	87.	5.0	36.	91.
27	3.0	25.	85.	4.2	32.	89.
28	2.8	23.	84.	3.6	29.	87.
29	2.7	23.	84.	3.1	26.	86.
30	2.7	23.	83.	2.7	23.	84.
31	2.6	22.	83.	2.4	21.	82.
32	2.5	21.	82.	2.1	19.	80.
33	2.2	20.	81.	1.9	17.	78.
34	2.0	18.	79.	1.7	15.	76.
35	1.8	16.	77.	1.5	14.	74.
36	1.6	15.	75.	1.3	13.	71.
37	1.5	14.	74.	1.2	12.	69.
38	1.4	13.	72.	1.1	11.	67.
39	1.3	12.	71.	.98	9.7	65.
40	1.2	12.	69.	.89	8.9	62.
41	1.1	11.	68.	.82	8.1	60.
42	1.1	10.	66.	.75	7.5	58.
43	.99	9.7	65.	.70	7.1	57.
44	.93	9.2	63.	.70	7.1	57.
45	.87	8.6	62.	.70	7.1	57.

Table PC-1-A-20. Chronic Granulocytic Leukemia Following Exposure at Age 20, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. ² PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
22	3.5	28.	87.	6.4	33.	89.
23	7.3	46.	94.	9.1	52.	95.
24	7.1	45.	93.	9.3	53.	95.
25	6.0	41.	92.	8.4	50.	94.
26	5.1	37.	91.	7.3	46.	94.
27	4.5	34.	90.	6.3	42.	93.
28	4.2	32.	89.	5.4	38.	91.
29	4.0	31.	89.	4.6	34.	90.
30	3.9	31.	88.	4.0	31.	88.
31	3.8	30.	88.	3.5	28.	87.
32	3.5	28.	87.	3.0	25.	85.
33	3.1	26.	86.	2.6	23.	83.
34	2.8	24.	84.	2.3	20.	81.
35	2.5	21.	82.	2.0	18.	79.
36	2.2	20.	81.	1.8	17.	77.
37	2.0	18.	79.	1.6	15.	75.
38	1.8	17.	78.	1.4	14.	73.
39	1.7	16.	76.	1.3	12.	71.
40	1.6	15.	75.	1.2	11.	68.
41	1.4	14.	73.	1.0	10.	66.
42	1.3	13.	71.	.94	9.3	64.
43	1.2	12.	70.	.88	8.7	62.
44	1.2	11.	68.	.87	8.6	62.
45	1.1	10.	67.	.86	8.6	62.
46	1.0	9.8	65.	.85	8.4	61.
47	.93	9.2	63.	.79	7.9	60.
48	.84	8.4	61.	.69	6.9	56.
49	.73	7.4	58.	.58	5.9	52.
50	.63	6.3	54.	.48	5.0	47.
51	.53	5.3	50.	.41	4.3	43.
52	.46	4.7	46.	.37	3.8	41.
53	.39	4.1	42.	.34	3.5	38.
54	.34	3.6	39.	.31	3.2	36.
55	.30	3.1	36.	.29	3.0	35.

Table PC-1-A-30. Chronic Granulocytic Leukemia Following Exposure at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
32	1.9	17.	78.	1.6	15.	75.
33	4.6	34.	90.	3.9	30.	88.
34	5.2	37.	91.	4.4	33.	89.
35	5.1	37.	91.	4.2	32.	89.
36	4.7	35.	90.	3.9	30.	88.
37	4.4	33.	89.	3.5	28.	87.
38	4.0	31.	89.	3.1	26.	86.
39	3.7	29.	88.	2.8	24.	84.
40	3.3	27.	86.	2.5	22.	82.
41	3.1	25.	85.	2.2	20.	81.
42	2.8	24.	84.	2.0	18.	79.
43	2.6	22.	83.	1.8	17.	77.
44	2.3	21.	82.	1.8	16.	77.
45	2.1	19.	80.	1.7	16.	77.
46	2.0	18.	79.	1.7	16.	76.
47	1.8	17.	77.	1.5	14.	74.
48	1.6	15.	75.	1.3	13.	71.
49	1.4	13.	72.	1.1	11.	67.
50	1.2	11.	69.	.91	9.0	63.
51	.99	9.7	65.	.77	7.8	59.
52	.84	8.4	61.	.68	6.9	56.
53	.72	7.2	57.	.61	6.2	53.
54	.62	6.3	53.	.56	5.7	51.
55	.53	5.5	50.	.52	5.3	49.
56	.46	4.8	46.	.47	4.8	47.
57	.40	4.2	43.	.43	4.4	44.
58	.35	3.6	39.	.39	4.0	42.
59	.31	3.2	36.	.35	3.6	39.
60	.27	2.8	33.	.31	3.2	36.
61	.24	2.5	31.	.28	2.9	34.
62	.21	2.2	28.	.25	2.6	32.
63	.19	2.0	26.	.22	2.3	29.
64	.18	1.9	24.	.20	2.1	27.
65	.16	1.7	23.	.17	1.8	24.

Table PC-1-A-40. Chronic Granulocytic Leukemia Following Exposure at Age 40, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation.² PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	1.6	15.	75.	1.1	11.	68.
43	3.9	31.	88.	2.9	24.	84.
44	4.6	34.	90.	3.6	28.	87.
45	4.7	34.	90.	3.8	30.	88.
46	4.4	33.	90.	3.8	30.	88.
47	4.1	32.	89.	3.6	29.	87.
48	3.7	29.	88.	3.1	25.	85.
49	3.2	26.	86.	2.5	22.	83.
50	2.6	23.	83.	2.1	19.	80.
51	2.2	20.	81.	1.7	16.	77.
52	1.9	17.	78.	1.5	14.	74.
53	1.6	15.	75.	1.3	13.	72.
54	1.3	13.	71.	1.2	12.	69.
55	1.1	11.	68.	1.1	11.	67.
56	.96	9.5	64.	.99	9.7	65.
57	.83	8.2	61.	.89	8.8	62.
58	.71	7.2	57.	.79	7.9	60.
59	.61	6.2	53.	.70	7.1	57.
60	.53	5.5	50.	.62	6.3	54.
61	.47	4.8	46.	.55	5.6	51.
62	.41	4.3	43.	.49	5.0	48.
63	.37	3.8	41.	.43	4.5	44.
64	.33	3.5	38.	.38	3.9	41.
65	.30	3.2	36.	.33	3.4	38.
66	.27	2.9	34.	.29	3.1	35.
67	.25	2.6	32.	.26	2.7	32.
68	.22	2.4	29.	.24	2.5	31.
69	.20	2.1	27.	.24	2.5	30.
70	.18	1.9	25.	.23	2.4	30.
71	.16	1.7	22.	.22	2.3	29.
72	.14	1.5	20.	.20	2.1	27.
73	.12	1.3	18.	.17	1.8	24.
74	.10	1.1	16.	.14	1.5	21.
75	.090	.96	14.	.12	1.3	18.

Table PC-1-A-50. Chronic Granulocytic Leukemia Following Exposure at Age 50, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
52	1.1	11.	67.	.91	9.0	63.
53	2.6	22.	83.	2.2	20.	81.
54	2.8	24.	84.	2.6	22.	83.
55	2.6	22.	83.	2.6	22.	83.
56	2.3	20.	81.	2.4	21.	82.
57	2.0	18.	79.	2.2	20.	81.
58	1.7	16.	77.	2.0	18.	79.
59	1.5	14.	74.	1.7	16.	76.
60	1.3	12.	71.	1.5	14.	74.
61	1.1	11.	67.	1.3	13.	71.
62	.97	9.5	64.	1.2	11.	68.
63	.85	8.5	61.	1.0	9.9	65.
64	.76	7.6	58.	.87	8.6	62.
65	.68	6.8	55.	.75	7.5	58.
66	.61	6.2	53.	.65	6.6	55.
67	.54	5.6	50.	.57	5.9	52.
68	.48	5.0	47.	.53	5.4	50.
69	.42	4.4	44.	.51	5.2	48.
70	.37	3.9	41.	.49	5.0	48.
71	.32	3.4	37.	.46	4.7	46.
72	.28	3.0	34.	.41	4.2	43.
73	.24	2.6	31.	.34	3.6	39.
74	.21	2.2	28.	.29	3.1	35.
75	.18	1.9	25.	.25	2.6	31.
76	.15	1.6	22.	.21	2.2	28.
77	.13	1.4	20.	.18	1.9	25.
78	.11	1.2	17.	.16	1.7	23.
79	.095	1.0	15.	.14	1.5	20.
80	.081	.87	13.	.12	1.3	18.
81	.072	.77	12.	.11	1.1	16.
82	.067	.72	11.	.095	1.0	15.
83	.064	.69	11.	.086	.92	14.
84	.061	.66	10.	.078	.83	13.
85	.058	.63	9.8	.072	.77	12.

Table PC-1-A-60. Chronic Granulocytic Leukemia Following Exposure at Age 60, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
62	.57	5.9	52.	.68	6.9	56.
63	1.4	13.	73.	1.7	15.	76.
64	1.6	15.	75.	1.8	17.	78.
65	1.6	15.	75.	1.7	16.	77.
66	1.5	14.	74.	1.6	15.	75.
67	1.3	13.	72.	1.4	13.	72.
68	1.2	11.	69.	1.3	12.	71.
69	1.0	10.	66.	1.2	12.	70.
70	.90	8.9	63.	1.2	11.	69.
71	.77	7.8	59.	1.1	11.	67.
72	.67	6.7	55.	.95	9.3	64.
73	.57	5.8	51.	.79	7.9	60.
74	.48	4.9	47.	.66	6.7	55.
75	.41	4.2	43.	.55	5.7	51.
76	.34	3.6	39.	.47	4.8	46.
77	.29	3.1	35.	.40	4.1	42.
78	.25	2.6	31.	.34	3.5	39.
79	.20	2.1	27.	.29	3.0	35.
80	.17	1.8	24.	.25	2.7	32.
81	.15	1.6	22.	.22	2.3	29.
82	.14	1.5	21.	.20	2.1	27.
83	.13	1.4	20.	.17	1.8	24.
84	.12	1.3	19.	.16	1.7	23.
85	.12	1.3	18.	.14	1.5	21.
86	.11	1.2	17.	.14	1.4	20.
87	.11	1.1	16.	.13	1.4	19.
88	.10	1.1	16.	.12	1.3	18.
89	.095	1.0	15.	.12	1.2	18.
90	.090	.96	14.	.11	1.2	17.
91	.086	.92	14.	.10	1.1	16.
92	.082	.87	13.	.099	1.1	16.
93	.078	.83	13.	.095	1.0	15.
94	.074	.79	12.	.090	.96	14.
95	.071	.76	12.	.086	.92	14.

Table PC-1-A-70. Chronic Granulocytic Leukemia Following Exposure at Age 70, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
72	.37	3.9	41.	.53	5.4	50.
73	.90	8.9	63.	1.2	12.	70.
74	.98	9.6	65.	1.3	13.	71.
75	.91	9.0	63.	1.2	12.	70.
76	.80	8.0	60.	1.1	10.	67.
77	.69	7.0	56.	.92	9.1	63.
78	.58	5.9	52.	.79	7.9	59.
79	.47	4.9	47.	.67	6.8	55.
80	.40	4.1	42.	.58	5.9	52.
81	.34	3.6	39.	.50	5.1	48.
82	.31	3.3	37.	.43	4.3	45.
83	.29	3.0	35.	.38	4.0	41.
84	.27	2.8	33.	.34	3.5	38.
85	.25	2.6	32.	.30	3.2	36.
86	.23	2.5	30.	.28	3.0	34.
87	.22	2.3	29.	.26	2.8	33.
88	.21	2.2	28.	.25	2.6	31.
89	.19	2.0	26.	.23	2.4	30.
90	.18	1.9	25.	.22	2.3	29.
91	.17	1.8	24.	.20	2.2	27.
92	.16	1.7	23.	.19	2.0	26.
93	.15	1.6	22.	.18	1.9	25.
94	.14	1.5	21.	.17	1.8	24.
95	.13	1.4	20.	.16	1.7	23.
96	.13	1.4	19.	.15	1.6	22.
97	.12	1.3	18.	.15	1.5	21.
98	.11	1.2	17.	.14	1.5	20.
99	.11	1.2	17.	.13	1.4	19.
100	.10	1.1	16.	.12	1.3	19.
101	.098	1.0	15.	.12	1.3	18.
102	.093	1.0	15.	.11	1.2	17.
103	.089	.95	14.	.11	1.1	17.
104	.085	.91	14.	.10	1.1	16.
105	.081	.87	13.	.098	1.0	15.

Table PC-1-B-0. Acute Leukemia Following Exposure at Age 0, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	1.5	14.	74.	1.2	11.	69.
3	6.9	45.	93.	5.4	38.	91.
4	9.9	54.	95.	7.8	48.	94.
5	11.	58.	96.	8.8	51.	95.
6	12.	59.	96.	9.3	52.	95.
7	12.	58.	96.	9.0	51.	95.
8	10.	55.	95.	8.1	49.	94.
9	9.0	52.	95.	7.2	46.	94.
10	7.9	48.	94.	6.5	43.	93.
11	6.7	44.	93.	5.8	40.	92.
12	5.7	39.	92.	5.1	37.	91.
13	4.7	35.	90.	4.6	34.	90.
14	3.8	30.	88.	4.1	32.	89.
15	3.1	26.	86.	3.7	29.	88.
16	2.6	22.	83.	3.3	27.	86.
17	2.2	19.	80.	2.9	24.	85.
18	1.9	17.	78.	2.4	21.	82.
19	1.8	16.	77.	1.9	18.	79.
20	1.7	15.	76.	1.6	15.	75.
21	1.5	14.	74.	1.3	12.	71.
22	1.3	13.	71.	1.1	11.	67.
23	1.1	11.	68.	.95	9.3	64.
24	.95	9.4	64.	.82	8.1	60.
25	.81	8.0	60.	.71	7.1	57.
26	.68	6.9	56.	.61	6.2	53.
27	.58	6.0	52.	.53	5.5	50.
28	.50	5.1	48.	.47	4.8	46.
29	.43	4.4	44.	.41	4.2	43.
30	.37	3.9	41.	.36	3.7	40.
31	.32	3.3	37.	.31	3.2	36.
32	.28	2.9	34.	.26	2.7	32.
33	.24	2.5	31.	.22	2.5	29.
34	.21	2.2	28.	.18	2.0	25.
35	.18	1.9	25.	.16	1.7	22.

Table PC-1-B-10. Acute Leukemia Following Exposure at Age 10, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	1.0	10.	66.	.94	9.3	64.
13	5.6	39.	92.	5.5	39.	92.
14	8.1	49.	94.	8.8	51.	95.
15	8.3	49.	94.	9.8	54.	95.
16	7.6	47.	94.	9.8	54.	95.
17	6.8	44.	93.	8.8	51.	95.
18	6.1	41.	92.	7.5	47.	94.
19	5.6	39.	92.	6.1	41.	92.
20	5.2	37.	91.	5.0	36.	91.
21	4.7	35.	90.	4.1	31.	89.
22	4.1	31.	89.	3.4	27.	87.
23	3.4	27.	87.	2.9	24.	84.
24	2.8	24.	84.	2.4	21.	82.
25	2.3	21.	82.	2.1	18.	80.
26	2.0	18.	79.	1.8	16.	77.
27	1.6	15.	76.	1.5	14.	74.
28	1.4	13.	72.	1.3	12.	71.
29	1.2	11.	69.	1.1	11.	67.
30	.99	9.7	65.	.95	9.4	64.
31	.84	8.4	61.	.81	8.1	60.
32	.72	7.2	57.	.67	6.8	56.
33	.62	6.3	53.	.56	5.7	51.
34	.55	5.4	50.	.46	4.8	46.
35	.46	4.7	46.	.39	4.0	42.
36	.39	4.1	42.	.33	3.4	38.
37	.34	3.6	39.	.28	2.9	34.
38	.30	3.1	35.	.23	2.5	30.
39	.26	2.7	32.	.20	2.1	27.
40	.22	2.3	29.	.17	1.8	24.
41	.19	2.0	26.	.15	1.5	21.
42	.16	1.7	22.	.13	1.3	19.
43	.13	1.4	19.	.10	1.1	16.
44	.10	1.1	16.	.085	.90	14.
45	.086	.91	14.	.068	.73	11.

Table PC-1-B-20. Acute Leukemia Following Exposure at Age 20, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
22	.35	3.7	40.	.29	3.0	35.
23	2.7	23.	84.	2.3	20.	81.
24	4.8	35.	90.	4.1	32.	89.
25	5.7	39.	92.	5.0	36.	91.
26	5.7	40.	92.	5.2	37.	91.
27	5.4	38.	91.	5.0	36.	91.
28	4.9	36.	90.	4.6	34.	90.
29	4.3	33.	89.	4.1	32.	89.
30	3.8	30.	88.	3.7	29.	88.
31	3.3	27.	86.	3.2	26.	86.
32	2.9	24.	85.	2.7	23.	84.
33	2.5	22.	82.	2.3	20.	81.
34	2.1	19.	80.	1.9	17.	78.
35	1.9	17.	78.	1.6	15.	75.
36	1.6	15.	75.	1.3	13.	71.
37	1.4	13.	72.	1.1	11.	68.
38	1.2	12.	69.	.96	9.4	64.
39	1.0	10.	66.	.81	8.1	60.
40	.90	9.0	63.	.69	7.0	56.
41	.76	7.6	59.	.59	6.0	52.
42	.63	6.4	54.	.51	5.2	49.
43	.51	5.3	49.	.42	4.4	44.
44	.42	4.3	44.	.34	3.6	39.
45	.34	3.6	39.	.27	2.9	34.
46	.28	3.0	35.	.22	2.3	29.
47	.24	2.5	31.	.19	2.0	26.
48	.20	2.1	27.	.16	1.7	23.
49	.17	1.8	24.	.14	1.5	21.
50	.15	1.6	21.	.13	1.4	19.
51	.13	1.3	19.	.11	1.2	17.
52	.11	1.2	17.	.10	1.1	16.
53	.093	1.0	15.	.086	.92	14.
54	.080	.86	13.	.074	.79	12.
55	.068	.73	11.	.063	.68	10.

Table PC-1-B-30. Acute Leukemia Following Exposure at Age 30, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
32	.070	.74	11.	.065	.70	11.
33	.82	8.2	60.	.74	7.5	58.
34	2.0	18.	79.	1.7	16.	77.
35	2.9	24.	85.	2.5	21.	82.
36	3.4	28.	87.	2.8	24.	84.
37	3.6	29.	87.	2.9	25.	85.
38	3.6	29.	87.	2.9	24.	85.
39	3.5	28.	87.	2.7	23.	84.
40	3.3	27.	86.	2.5	22.	83.
41	2.9	25.	85.	2.3	20.	81.
42	2.6	22.	83.	2.1	19.	80.
43	2.2	19.	81.	1.8	17.	77.
44	1.9	17.	78.	1.5	14.	74.
45	1.6	15.	75.	1.2	12.	70.
46	1.3	13.	71.	1.0	10.	66.
47	1.1	11.	68.	.89	8.9	62.
48	.98	9.6	65.	.79	7.9	60.
49	.85	8.4	61.	.72	7.2	57.
50	.74	7.4	58.	.65	6.6	55.
51	.64	6.5	54.	.59	6.0	52.
52	.56	5.7	51.	.52	5.3	49.
53	.49	5.0	48.	.45	4.7	46.
54	.43	4.4	44.	.39	4.1	42.
55	.37	3.8	40.	.34	3.5	39.
56	.31	3.2	37.	.29	3.0	35.
57	.26	2.7	32.	.24	2.6	31.
58	.21	2.3	28.	.20	2.2	27.
59	.18	1.9	25.	.17	1.8	24.
60	.15	1.6	21.	.15	1.6	21.
61	.12	1.3	19.	.13	1.3	19.
62	.11	1.1	16.	.11	1.2	17.
63	.091	.98	14.	.095	1.0	15.
64	.080	.86	13.	.083	.89	13.
65	.070	.75	11.	.073	.78	12.

Table PC-1-B-40. Acute Leukemia Following Exposure at Age 40, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	.008	.089	1.5	.006	.072	1.2
43	.16	1.6	22.	.13	1.4	19.
44	.50	5.1	48.	.41	4.2	43.
45	.88	8.7	62.	.69	7.0	56.
46	1.2	11.	69.	.92	9.1	63.
47	1.4	13.	72.	1.1	11.	67.
48	1.5	14.	74.	1.2	12.	69.
49	1.6	15.	74.	1.3	12.	71.
50	1.6	15.	74.	1.4	13.	72.
51	1.5	14.	74.	1.4	13.	72.
52	1.5	14.	73.	1.4	13.	72.
53	1.4	13.	72.	1.3	12.	71.
54	1.3	12.	71.	1.2	11.	69.
55	1.2	11.	69.	1.1	11.	67.
56	1.1	10.	66.	.98	9.6	65.
57	.93	9.2	63.	.87	8.6	62.
58	.80	8.0	60.	.76	7.6	59.
59	.69	7.0	56.	.67	6.8	56.
60	.60	6.1	53.	.59	6.0	52.
61	.52	5.3	49.	.53	5.4	49.
62	.45	4.7	46.	.47	4.8	47.
63	.41	4.2	43.	.42	4.3	44.
64	.36	3.8	40.	.38	3.9	41.
65	.33	3.4	38.	.34	3.5	38.
66	.29	3.1	35.	.30	3.2	36.
67	.26	2.7	32.	.27	2.9	33.
68	.22	2.3	29.	.24	2.5	31.
69	.19	2.0	26.	.21	2.2	28.
70	.16	1.7	23.	.18	1.9	25.
71	.13	1.4	20.	.16	1.7	23.
72	.12	1.2	18.	.14	1.5	21.
73	.10	1.1	16.	.12	1.3	19.
74	.088	.94	14.	.11	1.2	17.
75	.077	.83	13.	.098	1.0	15.

Table PC-1-8-50. Acute Leukemia Following Exposure at Age 50, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
52	.000	.004	.081	.000	.004	.071
53	.016	.17	2.9	.014	.15	2.5
54	.081	.86	13.	.071	.75	12.
55	.19	2.1	26.	.17	1.8	26.
56	.33	3.4	38.	.29	3.0	35.
57	.45	4.6	45.	.40	4.1	43.
58	.54	5.6	50.	.49	5.1	48.
59	.61	6.2	53.	.56	5.8	51.
60	.65	6.6	55.	.62	6.3	53.
61	.68	6.9	56.	.66	6.6	55.
62	.69	7.0	56.	.68	6.8	56.
63	.70	7.1	57.	.69	6.9	56.
64	.70	7.1	57.	.69	7.0	56.
65	.70	7.0	56.	.68	6.9	56.
66	.68	6.9	56.	.67	6.8	55.
67	.65	6.6	55.	.65	6.6	55.
68	.60	6.1	53.	.62	6.3	53.
69	.54	5.6	50.	.58	5.9	52.
70	.49	5.0	47.	.53	5.4	50.
71	.43	4.5	45.	.49	5.0	48.
72	.39	4.1	42.	.45	4.7	46.
73	.36	3.7	40.	.42	4.4	44.
74	.33	3.4	38.	.39	4.1	42.
75	.30	3.2	36.	.36	3.8	40.
76	.28	2.9	34.	.34	3.5	38.
77	.26	2.7	32.	.31	3.3	37.
78	.24	2.5	30.	.28	3.0	34.
79	.22	2.3	29.	.25	2.7	32.
80	.20	2.2	27.	.23	2.4	30.
81	.19	2.0	26.	.21	2.2	28.
82	.18	1.9	25.	.20	2.1	27.
83	.17	1.8	24.	.19	2.0	26.
84	.16	1.7	23.	.18	1.9	25.
85	.16	1.6	22.	.17	1.8	24.

Table PC-1-8-60. Acute Leukemia Following Exposure at Age 60, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
62	.000	.000	.002	.000	.000	.002
63	.001	.011	.19	.000	.009	.17
64	.008	.088	1.5	.007	.077	1.3
65	.028	.30	4.9	.025	.26	4.3
66	.062	.67	10.	.055	.59	9.3
67	.11	1.2	17.	.098	1.0	15.
68	.16	1.7	23.	.15	1.6	21.
69	.21	2.2	28.	.20	2.1	27.
70	.25	2.6	32.	.25	2.6	31.
71	.29	3.0	35.	.29	3.0	35.
72	.32	3.3	37.	.33	3.5	38.
73	.35	3.6	39.	.37	3.9	41.
74	.38	3.9	41.	.40	4.2	43.
75	.40	4.1	42.	.43	4.4	44.
76	.41	4.3	43.	.45	4.7	45.
77	.43	4.4	44.	.47	4.8	47.
78	.44	4.5	45.	.47	4.9	47.
79	.45	4.6	45.	.46	4.8	46.
80	.45	4.7	46.	.45	4.7	46.
81	.46	4.7	46.	.45	4.6	45.
82	.46	4.8	46.	.46	4.7	46.
83	.47	4.8	46.	.46	4.8	46.
84	.48	4.9	47.	.47	4.9	47.
85	.49	5.0	47.	.48	5.0	47.
86	.50	5.1	48.	.50	5.1	48.
87	.51	5.3	49.	.51	5.3	49.
88	.53	5.4	49.	.53	5.4	49.
89	.54	5.5	50.	.54	5.5	50.
90	.55	5.6	50.	.55	5.6	50.
91	.56	5.7	51.	.55	5.7	51.
92	.56	5.7	51.	.56	5.7	51.
93	.57	5.8	51.	.57	5.8	51.
94	.57	5.9	52.	.57	5.8	52.
95	.58	5.9	52.	.58	5.9	52.

Table PC-1-B-70. Acute Leukemia Following Exposure at Age 70, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
72	.000	.000	.000	.000	.000	.000
73	.000	.000	.011	.000	.000	.010
74	.000	.008	.15	.000	.008	.14
75	.003	.042	.72	.003	.040	.69
76	.012	.13	2.1	.011	.12	2.0
77	.026	.28	4.6	.025	.27	4.4
78	.049	.52	8.2	.046	.49	7.8
79	.080	.85	13.	.073	.78	12.
80	.12	1.3	18.	.11	1.1	16.
81	.17	1.8	24.	.14	1.5	21.
82	.22	2.4	29.	.19	2.0	26.
83	.29	3.0	35.	.25	2.6	32.
84	.35	3.8	40.	.32	3.3	37.
85	.45	4.6	45.	.39	4.1	42.
86	.54	5.6	50.	.48	4.9	47.
87	.65	6.6	55.	.57	5.8	51.
88	.76	7.7	59.	.67	6.8	55.
89	.88	8.8	62.	.78	7.8	59.
90	1.0	9.9	65.	.89	8.8	62.
91	1.1	11.	68.	1.0	9.8	65.
92	1.3	12.	70.	1.1	11.	68.
93	1.4	13.	73.	1.2	12.	70.
94	1.6	15.	74.	1.4	13.	72.
95	1.7	16.	76.	1.5	14.	74.
96	1.8	17.	78.	1.6	15.	75.
97	2.0	18.	79.	1.7	16.	77.
98	2.1	19.	80.	1.9	17.	78.
99	2.3	20.	81.	2.0	18.	79.
100	2.4	21.	82.	2.1	19.	80.
101	2.5	22.	83.	2.2	20.	81.
102	2.7	23.	84.	2.4	21.	82.
103	2.8	24.	84.	2.5	22.	82.
104	3.0	25.	85.	2.6	22.	83.
105	3.1	26.	85.	2.7	23.	84.

Table PC-t-C-0. Leukemia Excluding CLL Following Exposure at Age 0, by Age A, at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
2	2.1	19.	80.	1.6	15.	76.
3	8.5	50.	94.	6.7	44.	93.
4	12.	59.	96.	9.5	53.	95.
5	14.	63.	97.	11.	56.	96.
6	14.	65.	97.	11.	58.	96.
7	14.	64.	97.	11.	57.	96.
8	13.	62.	97.	10.	55.	95.
9	12.	59.	96.	9.5	53.	95.
10	11.	56.	96.	8.8	51.	95.
11	9.5	53.	95.	8.1	49.	94.
12	8.3	49.	94.	7.4	46.	94.
13	7.1	45.	93.	6.8	44.	93.
14	6.0	41.	92.	6.3	42.	93.
15	5.1	37.	91.	5.9	40.	92.
16	4.4	33.	90.	5.4	38.	91.
17	3.9	30.	88.	4.7	35.	90.
18	3.5	28.	87.	4.1	32.	89.
19	3.3	27.	86.	3.6	28.	87.
20	3.2	26.	86.	3.1	26.	86.
21	3.0	25.	85.	2.7	23.	84.
22	2.7	23.	84.	2.4	21.	82.
23	2.4	21.	82.	2.1	19.	80.
24	2.1	18.	79.	1.9	17.	78.
25	1.7	16.	77.	1.7	16.	76.
26	1.5	14.	74.	1.5	14.	74.
27	1.4	13.	72.	1.4	13.	72.
28	1.2	12.	70.	1.3	12.	70.
29	1.1	11.	68.	1.1	11.	68.
30	1.1	10.	67.	1.0	10.	66.
31	.99	9.7	65.	.93	9.2	63.
32	.91	9.0	63.	.83	8.3	61.
33	.83	8.3	61.	.74	7.4	58.
34	.76	7.6	59.	.66	6.6	55.
35	.70	7.1	57.	.59	6.0	52.

Table PC-1-C-10. Leukemia Excluding CLL Following Exposure at Age 10, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
12	1.7	16.	76.	1.5	14.	74.
13	7.3	46.	94.	7.0	45.	93.
14	10.	54.	95.	10.	56.	96.
15	10.	55.	95.	12.	58.	96.
16	9.3	53.	95.	11.	58.	96.
17	8.3	49.	94.	10.	55.	95.
18	7.5	46.	94.	8.6	50.	95.
19	6.8	44.	93.	7.3	46.	94.
20	6.3	42.	93.	6.2	42.	92.
21	5.7	39.	92.	5.2	37.	91.
22	5.0	36.	91.	4.4	33.	90.
23	4.2	32.	89.	3.8	30.	88.
24	3.4	28.	87.	3.2	26.	86.
25	2.8	24.	84.	2.8	23.	84.
26	2.3	20.	81.	2.4	21.	82.
27	2.0	18.	79.	2.0	18.	79.
28	1.7	16.	77.	1.8	16.	77.
29	1.6	15.	74.	1.6	15.	74.
30	1.4	13.	72.	1.4	13.	72.
31	1.2	12.	70.	1.2	11.	69.
32	1.1	11.	67.	1.0	9.9	65.
33	.98	9.6	65.	.87	8.6	62.
34	.87	8.6	62.	.75	7.5	58.
35	.77	7.7	59.	.65	6.6	55.
36	.69	7.0	56.	.57	5.8	51.
37	.62	6.3	53.	.50	5.1	48.
38	.55	5.7	51.	.44	4.5	45.
39	.50	5.1	48.	.39	4.0	42.
40	.45	4.6	45.	.35	3.6	39.
41	.40	4.1	43.	.31	3.2	36.
42	.36	3.7	40.	.28	2.9	34.
43	.32	3.3	37.	.25	2.6	31.
44	.28	2.9	34.	.22	2.3	29.
45	.24	2.5	31.	.19	2.0	26.

Table PC-1-C-20. Leukemia Excluding CLL Following Exposure at Age 20, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
22	.81	8.1	80.	.72	7.2	57.
23	3.6	29.	87.	3.2	26.	86.
24	5.4	38.	91.	5.0	36.	91.
25	5.8	40.	92.	5.7	40.	92.
26	5.6	39.	92.	5.7	39.	92.
27	5.2	37.	91.	5.3	38.	91.
28	4.8	35.	90.	4.8	35.	90.
29	4.3	33.	89.	4.3	33.	89.
30	3.9	30.	88.	3.8	30.	88.
31	3.5	28.	87.	3.3	27.	86.
32	3.1	25.	85.	2.8	24.	84.
33	2.7	23.	83.	2.4	21.	82.
34	2.3	20.	81.	2.0	18.	79.
35	2.0	18.	79.	1.7	16.	76.
36	1.8	16.	77.	1.5	14.	73.
37	1.5	14.	74.	1.2	12.	70.
38	1.4	13.	72.	1.1	10.	67.
39	1.2	11.	69.	.93	9.2	63.
40	1.0	10.	66.	.81	8.0	60.
41	.91	9.0	63.	.70	7.1	57.
42	.79	7.9	60.	.61	6.2	53.
43	.68	6.9	56.	.53	5.4	50.
44	.58	5.9	52.	.45	4.7	46.
45	.49	5.1	48.	.39	4.0	42.
46	.42	4.3	44.	.33	3.5	38.
47	.36	3.8	40.	.29	3.0	35.
48	.31	3.3	37.	.25	2.6	32.
49	.27	2.8	33.	.22	2.3	29.
50	.23	2.5	30.	.20	2.1	27.
51	.20	2.1	27.	.17	1.8	24.
52	.18	1.9	25.	.16	1.7	22.
53	.15	1.6	22.	.14	1.5	20.
54	.13	1.4	20.	.12	1.3	18.
55	.12	1.2	18.	.11	1.2	17.

Table PC-1-C-30. Leukemia Excluding CLL Following Exposure at Age 30, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
32	.67	4.8	46.	.43	4.4	44.
33	1.7	16.	76.	1.5	14.	74.
34	2.8	23.	84.	2.4	21.	82.
35	3.4	28.	87.	2.9	24.	85.
36	3.8	30.	88.	3.1	26.	86.
37	3.8	30.	83.	3.1	26.	85.
38	3.7	29.	88.	3.0	25.	85.
39	3.5	28.	87.	2.8	23.	84.
40	3.2	26.	86.	2.5	22.	83.
41	2.9	25.	85.	2.3	20.	81.
42	2.6	23.	83.	2.1	18.	80.
43	2.3	20.	82.	1.8	17.	77.
44	2.0	18.	79.	1.6	15.	75.
45	1.7	16.	77.	1.4	13.	72.
46	1.5	14.	74.	1.2	11.	69.
47	1.3	12.	71.	1.0	10.	66.
48	1.1	11.	67.	.90	8.9	63.
49	.96	9.5	64.	.79	7.9	60.
50	.83	8.3	61.	.70	7.1	57.
51	.72	7.3	57.	.62	6.3	54.
52	.63	6.4	54.	.55	5.6	51.
53	.54	5.6	50.	.49	5.0	47.
54	.47	4.8	47.	.43	4.4	44.
55	.40	4.2	43.	.38	3.9	41.
56	.34	3.6	39.	.33	3.4	38.
57	.29	3.0	35.	.28	3.0	34.
58	.24	2.5	31.	.25	2.6	31.
59	.20	2.1	27.	.21	2.2	28.
60	.17	1.8	24.	.18	1.9	25.
61	.15	1.6	21.	.16	1.7	23.
62	.13	1.4	19.	.14	1.5	20.
63	.11	1.2	17.	.12	1.3	18.
64	.099	1.1	15.	.11	1.1	16.
65	.087	.93	14.	.093	.99	15.

Table PC-1-C-40. Leukemia Excluding CLL Following Exposure at Age 40, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
42	.44	4.6	45.	.34	3.6	39.
43	1.2	12.	69.	.93	9.2	63.
44	1.6	15.	75.	1.2	12.	70.
45	1.8	17.	77.	1.4	14.	73.
46	1.9	18.	79.	1.5	14.	74.
47	2.0	18.	79.	1.6	15.	75.
48	2.0	18.	79.	1.6	15.	75.
49	1.9	17.	78.	1.6	15.	75.
50	1.8	16.	77.	1.5	14.	74.
51	1.7	16.	76.	1.5	14.	73.
52	1.6	15.	74.	1.4	13.	72.
53	1.4	14.	73.	1.3	12.	71.
54	1.3	12.	71.	1.2	11.	69.
55	1.2	11.	68.	1.1	11.	67.
56	1.0	10.	64.	.98	9.6	65.
57	.89	8.8	62.	.87	8.7	62.
58	.76	7.6	59.	.78	7.8	59.
59	.66	6.7	55.	.69	6.9	56.
60	.57	5.9	52.	.61	6.2	53.
61	.50	5.1	48.	.54	5.5	50.
62	.44	4.6	45.	.48	4.9	47.
63	.39	4.1	42.	.42	4.3	44.
64	.35	3.7	39.	.38	3.9	41.
65	.31	3.3	37.	.33	3.5	38.
66	.28	3.0	34.	.30	3.1	36.
67	.25	2.7	32.	.27	2.8	33.
68	.22	2.3	29.	.24	2.5	31.
69	.19	2.0	26.	.21	2.2	28.
70	.16	1.7	23.	.19	2.0	26.
71	.14	1.5	20.	.17	1.8	24.
72	.12	1.3	18.	.15	1.6	22.
73	.10	1.1	16.	.13	1.4	20.
74	.090	.96	14.	.12	1.2	18.
75	.079	.85	13.	.10	1.1	16.

Table PC-1-C-50. Leukemia Excluding CLL Following Exposure at Age 50, by Age A, at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
52	.43	4.5	45.	.37	3.9	41.
53	1.1	10.	67.	.94	9.3	64.
54	1.2	12.	70.	1.1	11.	67.
55	1.2	12.	70.	1.1	11.	68.
56	1.2	11.	69.	1.1	11.	67.
57	1.1	11.	67.	1.1	10.	66.
58	1.0	9.8	65.	1.0	9.8	65.
59	.93	9.2	63.	.95	9.3	64.
60	.86	8.6	62.	.89	8.8	62.
61	.80	8.0	60.	.84	8.4	61.
62	.75	7.5	58.	.79	7.9	60.
63	.71	7.1	57.	.74	7.5	58.
64	.67	6.8	55.	.70	7.1	57.
65	.63	6.4	54.	.66	6.6	55.
66	.59	6.0	52.	.62	6.3	53.
67	.56	5.7	51.	.58	5.9	52.
68	.51	5.2	48.	.56	5.5	50.
69	.45	4.7	46.	.50	5.1	48.
70	.40	4.1	43.	.46	4.7	46.
71	.35	3.7	40.	.42	4.4	44.
72	.31	3.3	37.	.39	4.0	42.
73	.28	3.0	34.	.35	3.7	40.
74	.25	2.7	32.	.32	3.4	37.
75	.23	2.4	30.	.29	3.1	35.
76	.21	2.2	28.	.26	2.8	33.
77	.19	2.0	26.	.24	2.5	31.
78	.17	1.8	24.	.22	2.3	29.
79	.16	1.7	23.	.19	2.0	26.
80	.14	1.5	21.	.17	1.8	24.
81	.13	1.4	20.	.16	1.7	22.
82	.12	1.3	18.	.14	1.5	21.
83	.12	1.2	18.	.14	1.4	20.
84	.11	1.2	17.	.13	1.4	19.
85	.10	1.1	16.	.12	1.3	19.

Table PC-1-C-60. Leukemia Excluding CLL Following Exposure at Age 60, by Age A, at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
62	.37	3.8	41.	.39	4.1	42.
63	.91	9.0	63.	.95	9.4	64.
64	1.0	10.	66.	1.1	11.	67.
65	1.0	9.8	65.	1.0	10.	66.
66	.92	9.0	63.	.95	9.4	64.
67	.83	8.3	61.	.86	8.6	62.
68	.73	7.3	58.	.77	7.7	59.
69	.63	6.4	54.	.69	6.9	56.
70	.54	5.5	50.	.61	6.2	53.
71	.46	4.8	46.	.55	5.6	51.
72	.40	4.2	43.	.50	5.1	48.
73	.36	3.7	40.	.45	4.6	46.
74	.32	3.3	37.	.41	4.2	43.
75	.29	3.0	35.	.37	3.8	41.
76	.24	2.8	33.	.34	3.5	38.
77	.24	2.6	31.	.31	3.2	36.
78	.22	2.6	29.	.28	2.9	34.
79	.21	2.2	28.	.25	2.7	32.
80	.19	2.0	26.	.23	2.4	30.
81	.18	1.9	25.	.21	2.2	28.
82	.17	1.8	24.	.20	2.1	27.
83	.16	1.7	23.	.19	2.0	26.
84	.16	1.7	23.	.19	2.0	26.
85	.16	1.6	22.	.18	1.9	25.
86	.15	1.6	22.	.18	1.9	25.
87	.15	1.6	22.	.18	1.9	25.
88	.15	1.6	22.	.18	1.9	25.
89	.15	1.6	22.	.18	1.9	25.
90	.15	1.6	22.	.18	1.9	25.
91	.15	1.6	22.	.18	1.9	24.
92	.15	1.6	21.	.17	1.8	24.
93	.15	1.6	21.	.17	1.8	24.
94	.15	1.5	21.	.17	1.8	24.
95	.14	1.5	21.	.17	1.8	24.

Table PC-1-C-70. Leukemia Excluding CLL Following Exposure at Age 70, by Age A, at Diagnosis, Sex, and Dose in Rad of Low-LET Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
72	.23	2.4	30.	.28	3.0	34.
73	.55	5.6	50.	.69	7.0	56.
74	.60	6.1	53.	.77	7.7	59.
75	.57	5.8	51.	.73	7.4	58.
76	.51	5.3	49.	.66	6.7	55.
77	.45	4.7	46.	.58	5.9	52.
78	.40	4.1	42.	.50	5.1	48.
79	.34	3.6	39.	.43	4.4	44.
80	.30	3.1	36.	.36	3.8	40.
81	.26	2.8	33.	.32	3.3	37.
82	.23	2.5	30.	.28	2.9	34.
83	.21	2.2	28.	.25	2.7	32.
84	.19	2.0	26.	.23	2.4	30.
85	.18	1.9	25.	.21	2.2	28.
86	.17	1.8	24.	.20	2.1	27.
87	.16	1.7	23.	.19	2.0	26.
88	.15	1.6	22.	.18	1.9	25.
89	.14	1.5	21.	.17	1.8	24.
90	.14	1.4	20.	.16	1.7	23.
91	.13	1.4	19.	.15	1.6	22.
92	.12	1.3	19.	.15	1.6	21.
93	.12	1.3	18.	.14	1.5	21.
94	.11	1.2	17.	.14	1.4	20.
95	.11	1.2	17.	.13	1.4	20.
96	.11	1.1	16.	.13	1.4	19.
97	.10	1.1	16.	.12	1.3	19.
98	.10	1.1	16.	.12	1.3	18.
99	.098	1.0	15.	.12	1.2	18.
100	.096	1.0	15.	.11	1.2	17.
101	.094	1.0	15.	.11	1.2	17.
102	.092	.98	15.	.11	1.2	17.
103	.091	.97	14.	.11	1.1	17.
104	.089	.95	14.	.11	1.1	16.
105	.088	.94	14.	.10	1.1	16.

Table PC-2-0. Bone and Joint Cancer Following Exposure at Age 0, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
1	.053	.53	5.1	.053	.53	5.1
2	15.	64.	95.	15.	64.	95.
3	46.	90.	99.	45.	89.	99.
4	57.	93.	99.	52.	92.	99.
5	56.	93.	99.	49.	91.	99.
6	51.	91.	99.	44.	89.	99.
7	44.	89.	99.	38.	86.	98.
8	34.	84.	98.	30.	81.	98.
9	24.	76.	97.	22.	74.	97.
10	17.	67.	95.	16.	66.	95.
11	12.	58.	93.	13.	59.	94.
12	9.3	51.	91.	10.	53.	92.
13	7.7	45.	89.	8.7	49.	90.
14	6.4	40.	87.	7.5	45.	89.
15	5.4	36.	85.	6.7	42.	88.
16	4.7	33.	83.	6.1	39.	87.
17	4.1	30.	81.	5.6	37.	86.
18	3.8	29.	80.	5.3	36.	85.
19	3.7	28.	79.	5.2	35.	84.
20	3.6	27.	79.	5.1	35.	84.
21	3.6	27.	79.	5.1	35.	84.
22	3.4	26.	78.	5.0	35.	84.
23	3.2	25.	77.	4.8	34.	84.
24	2.9	23.	75.	4.7	33.	83.
25	2.7	22.	74.	4.4	32.	82.
26	2.5	20.	72.	4.2	30.	81.
27	2.3	19.	70.	3.9	29.	80.
28	2.0	17.	67.	3.5	27.	78.
29	1.7	15.	64.	3.1	24.	76.
30	1.5	13.	61.	2.7	22.	73.
31	1.3	12.	58.	2.3	19.	71.
32	1.2	11.	55.	2.1	18.	68.
33	1.1	10.	53.	2.0	17.	68.
34	1.1	9.8	52.	2.1	18.	68.
35	1.0	9.4	51.	2.3	19.	70.

Table PC-2-10. Bone and Joint Cancer Following Exposure at Age 10, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
11	.004	.047	.47	.004	.049	.49
12	1.3	12.	57.	1.5	13.	60.
13	6.3	40.	87.	7.1	43.	88.
14	11.	54.	92.	13.	59.	93.
15	13.	60.	94.	16.	65.	95.
16	14.	61.	94.	17.	68.	95.
17	14.	61.	94.	18.	69.	96.
18	14.	61.	94.	18.	69.	96.
19	14.	61.	94.	18.	69.	96.
20	14.	61.	94.	19.	70.	96.
21	14.	61.	94.	19.	70.	96.
22	13.	60.	94.	19.	69.	96.
23	12.	58.	93.	18.	68.	96.
24	11.	56.	93.	17.	67.	95.
25	10.	54.	92.	16.	66.	95.
26	9.4	51.	91.	15.	64.	95.
27	8.5	48.	90.	14.	62.	94.
28	7.4	45.	89.	13.	59.	93.
29	6.4	41.	87.	11.	55.	92.
30	5.5	37.	85.	9.4	51.	91.
31	4.8	34.	84.	8.2	47.	90.
32	4.3	31.	82.	7.4	44.	89.
33	4.0	29.	80.	7.0	43.	88.
34	3.7	28.	79.	7.0	43.	88.
35	3.5	26.	78.	7.4	44.	89.
36	3.3	25.	77.	7.8	46.	89.
37	3.1	24.	76.	7.5	45.	89.
38	3.0	23.	75.	6.5	41.	87.
39	2.8	22.	74.	5.4	36.	85.
40	2.6	21.	73.	4.4	31.	82.
41	2.4	20.	71.	3.5	27.	78.
42	2.1	18.	68.	2.8	22.	74.
43	1.7	15.	63.	2.2	19.	70.
44	1.3	11.	56.	1.8	15.	64.
45	.94	8.6	49.	1.4	13.	59.

Table PC-2-20. Bone and Joint Cancer Following Exposure at Age 20, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
21	.005	.053	.53	.007	.079	.78
22	1.9	16.	66.	2.9	23.	75.
23	10.	53.	92.	15.	64.	95.
24	18.	69.	96.	27.	78.	97.
25	23.	75.	97.	33.	83.	98.
26	25.	77.	97.	37.	85.	98.
27	25.	77.	97.	37.	86.	98.
28	24.	76.	97.	36.	85.	98.
29	22.	74.	97.	34.	84.	98.
30	20.	71.	96.	31.	82.	98.
31	18.	68.	96.	28.	79.	97.
32	16.	66.	95.	25.	77.	97.
33	15.	64.	95.	24.	76.	97.
34	14.	62.	94.	24.	76.	97.
35	13.	60.	94.	25.	77.	97.
36	12.	58.	93.	26.	78.	97.
37	11.	56.	93.	25.	76.	97.
38	11.	54.	92.	21.	73.	96.
39	10.	53.	92.	18.	69.	96.
40	9.2	50.	91.	15.	63.	95.
41	8.4	48.	90.	12.	58.	93.
42	7.3	44.	89.	9.5	51.	91.
43	5.8	38.	86.	7.6	45.	89.
44	4.3	31.	82.	6.0	39.	86.
45	3.2	25.	77.	4.7	33.	83.
46	2.4	20.	71.	3.8	28.	80.
47	2.0	17.	67.	3.1	24.	76.
48	1.6	14.	63.	2.7	22.	74.
49	1.4	12.	58.	2.5	20.	72.
50	1.2	11.	54.	2.3	19.	70.
51	1.0	9.2	50.	2.0	17.	68.
52	.85	7.9	46.	1.7	15.	63.
53	.73	6.8	42.	1.3	12.	58.
54	.62	5.9	38.	1.1	9.9	52.
55	.53	5.1	35.	.88	8.2	47.

Table PC-2-30. Bone and Joint Cancer Following Exposure at Age 30, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
31	.007	.072	.72	.013	.13	1.3
32	2.4	20.	71.	4.2	30.	81.
33	12.	58.	93.	20.	72.	96.
34	22.	73.	97.	36.	85.	98.
35	28.	79.	97.	46.	90.	99.
36	31.	82.	98.	53.	92.	99.
37	32.	82.	98.	54.	92.	99.
38	32.	82.	98.	52.	92.	99.
39	31.	82.	98.	48.	90.	99.
40	30.	81.	98.	42.	88.	99.
41	28.	79.	97.	36.	85.	98.
42	25.	77.	97.	31.	82.	98.
43	20.	72.	96.	26.	78.	97.
44	16.	65.	95.	21.	73.	96.
45	12.	57.	93.	17.	67.	95.
46	9.1	50.	91.	14.	62.	94.
47	7.3	44.	89.	11.	56.	93.
48	6.1	39.	87.	9.8	52.	92.
49	5.1	35.	84.	8.9	49.	91.
50	4.3	31.	82.	8.1	47.	90.
51	3.6	27.	79.	7.2	44.	89.
52	3.0	24.	76.	5.9	38.	86.
53	2.5	21.	72.	4.6	33.	83.
54	2.1	18.	68.	3.7	28.	79.
55	1.8	15.	65.	3.0	23.	75.
56	1.5	13.	61.	2.4	20.	71.
57	1.3	12.	57.	2.0	17.	67.
58	1.1	10.	53.	1.6	14.	62.
59	1.0	9.2	50.	1.3	12.	57.
60	.91	8.4	48.	1.1	10.	53.
61	.81	7.6	45.	.92	8.5	48.
62	.70	6.6	41.	.77	7.2	44.
63	.58	5.5	37.	.67	6.3	40.
64	.48	4.6	32.	.61	5.8	38.
65	.39	3.8	28.	.58	5.5	37.

Table PC-2-40. Bone and Joint Cancer Following Exposure at Age 40, by Age A_2 at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_2	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	.013	.13	1.2	.019	.19	1.9
42	4.0	29.	80.	5.4	36.	85.
43	17.	67.	95.	21.	73.	96.
44	24.	76.	97.	31.	82.	98.
45	25.	77.	97.	34.	84.	98.
46	24.	76.	97.	34.	84.	98.
47	22.	74.	97.	32.	82.	98.
48	20.	71.	96.	30.	81.	98.
49	18.	68.	96.	28.	80.	98.
50	15.	64.	95.	27.	79.	97.
51	13.	60.	94.	24.	76.	97.
52	11.	56.	93.	21.	72.	96.
53	9.6	51.	91.	17.	67.	95.
54	8.1	47.	90.	14.	61.	94.
55	6.8	42.	88.	11.	55.	93.
56	5.7	38.	86.	9.0	50.	91.
57	4.8	34.	84.	7.3	44.	89.
58	4.2	30.	81.	5.9	39.	86.
59	3.6	27.	79.	4.8	34.	84.
60	3.2	25.	77.	4.0	29.	81.
61	2.9	23.	75.	3.3	25.	77.
62	2.4	20.	71.	2.7	22.	74.
63	2.0	17.	67.	2.3	19.	70.
64	1.6	14.	62.	2.1	18.	68.
65	1.3	12.	57.	1.9	16.	66.
66	1.1	9.7	52.	1.8	15.	64.
67	.88	8.1	47.	1.5	14.	61.
68	.74	6.9	43.	1.3	12.	57.
69	.62	5.9	38.	1.1	9.8	52.
70	.53	5.0	35.	.90	8.4	48.
71	.45	4.3	31.	.76	7.1	43.
72	.38	3.7	28.	.64	6.0	39.
73	.31	3.0	24.	.53	5.1	35.
74	.25	2.4	20.	.45	4.3	31.
75	.20	2.0	17.	.38	3.6	27.

Table PC-2-50. Bone and Joint Cancer Following Exposure at Age 50, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.004	.048	.48	.011	.11	1.0
52	1.5	13.	60.	3.2	25.	76.
53	7.3	44.	89.	14.	61.	94.
54	12.	59.	93.	21.	73.	96.
55	15.	64.	95.	24.	76.	97.
56	15.	65.	95.	23.	75.	97.
57	15.	63.	95.	22.	73.	97.
58	14.	61.	94.	19.	71.	96.
59	13.	59.	94.	17.	67.	95.
60	12.	57.	93.	14.	63.	94.
61	10.	54.	92.	12.	58.	93.
62	8.9	49.	91.	10.	53.	92.
63	7.3	44.	89.	8.8	49.	91.
64	5.9	39.	86.	7.9	46.	90.
65	4.8	33.	83.	7.3	44.	89.
66	3.9	29.	80.	6.6	41.	88.
67	3.2	25.	77.	5.7	38.	86.
68	2.6	21.	73.	4.7	33.	83.
69	2.2	18.	69.	3.9	29.	80.
70	1.8	16.	65.	3.2	25.	77.
71	1.5	13.	61.	2.6	21.	73.
72	1.3	11.	56.	2.2	18.	69.
73	1.0	9.5	51.	1.8	16.	65.
74	.81	7.6	45.	1.5	13.	60.
75	.64	6.0	39.	1.2	11.	56.
76	.52	4.9	34.	1.0	9.5	51.
77	.43	4.2	30.	.87	8.0	47.
78	.40	3.8	29.	.76	7.1	43.
79	.40	3.8	29.	.68	6.4	41.
80	.41	4.0	29.	.63	5.9	39.
81	.43	4.1	30.	.56	5.4	36.
82	.39	3.8	28.	.49	4.7	33.
83	.33	3.2	25.	.41	3.9	29.
84	.27	2.7	21.	.32	3.1	24.
85	.23	2.2	18.	.25	2.5	20.

Table PC-2-60. Bone and Joint Cancer Following Exposure at Age 60, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.003	.035	.35	.004	.043	.42
62	1.1	10.	53.	1.3	12.	57.
63	5.4	36.	85.	6.6	41.	88.
64	9.0	50.	91.	12.	58.	93.
65	10.	54.	92.	16.	65.	95.
66	10.	54.	92.	17.	67.	95.
67	9.8	52.	92.	17.	67.	95.
68	8.8	49.	91.	15.	64.	95.
69	7.7	45.	89.	13.	60.	94.
70	6.6	41.	88.	11.	56.	93.
71	5.5	37.	86.	9.5	51.	91.
72	4.7	33.	83.	8.0	46.	90.
73	3.8	28.	80.	6.6	41.	88.
74	3.0	24.	75.	5.5	37.	85.
75	2.3	19.	70.	4.5	32.	82.
76	1.9	16.	65.	3.7	28.	79.
77	1.5	13.	61.	3.1	24.	76.
78	1.4	12.	58.	2.6	21.	73.
79	1.4	12.	58.	2.3	19.	71.
80	1.4	12.	59.	2.1	18.	68.
81	1.4	12.	59.	1.9	16.	66.
82	1.3	11.	55.	1.6	14.	62.
83	1.1	9.6	52.	1.3	12.	57.
84	.85	7.9	46.	1.0	9.3	51.
85	.70	6.6	41.	.78	7.3	44.
86	.61	5.8	38.	.69	6.5	41.
87	.54	5.1	35.	.60	5.7	38.
88	.47	4.5	32.	.53	5.1	35.
89	.42	4.0	29.	.47	4.5	32.
90	.37	3.6	27.	.41	4.0	29.
91	.32	3.2	25.	.37	3.5	27.
92	.29	2.8	22.	.32	3.1	25.
93	.26	2.5	20.	.29	2.8	22.
94	.23	2.2	19.	.25	2.5	20.
95	.20	2.0	17.	.23	2.2	19.

Table PC-2-70. Bone and Joint Cancer Following Exposure at Age 70, by Age A₂ at Diagnosis, Sex, and Dose in Rad of Alpha Radiation. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₂	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
71	.001	.018	.18	.003	.030	.30
72	.57	5.4	36.	.95	8.7	49.
73	2.8	22.	74.	4.6	33.	83.
74	4.5	32.	83.	8.0	46.	90.
75	5.2	35.	85.	9.4	51.	91.
76	5.2	35.	84.	9.6	52.	91.
77	4.9	34.	84.	9.0	50.	91.
78	4.7	33.	83.	8.4	48.	90.
79	4.8	34.	84.	7.8	45.	89.
80	5.0	35.	84.	7.2	44.	89.
81	5.1	35.	84.	6.5	41.	87.
82	4.6	33.	83.	5.6	37.	86.
83	3.8	29.	80.	4.6	32.	83.
84	3.1	24.	76.	3.5	27.	79.
85	2.5	21.	72.	2.7	22.	74.
86	2.2	18.	69.	2.4	19.	71.
87	1.9	16.	66.	2.0	17.	68.
88	1.6	14.	62.	1.8	15.	64.
89	1.4	13.	59.	1.5	13.	61.
90	1.2	11.	55.	1.3	12.	57.
91	1.1	9.7	52.	1.2	10.	54.
92	.93	8.5	48.	1.0	9.2	50.
93	.81	7.5	45.	.87	8.1	47.
94	.70	6.6	42.	.76	7.1	43.
95	.62	5.8	38.	.67	6.3	40.
96	.54	5.2	35.	.59	5.6	37.
97	.47	4.6	32.	.51	4.9	34.
98	.42	4.0	30.	.45	4.3	31.
99	.37	3.6	27.	.40	3.8	29.
100	.32	3.2	25.	.35	3.4	26.
101	.29	2.8	22.	.31	3.0	24.
102	.25	2.5	20.	.26	2.7	22.
103	.23	2.2	18.	.24	2.4	20.
104	.20	2.0	17.	.22	2.1	18.
105	.18	1.8	15.	.19	1.9	16.

Table PC-3. Salivary Gland Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
0	4.9	36.	90.	4.3	33.	89.
1	4.5	34.	90.	4.0	31.	88.
2	4.2	32.	89.	3.7	29.	88.
3	3.9	31.	88.	3.4	28.	87.
4	3.7	29.	88.	3.2	26.	86.
5	3.5	28.	87.	2.9	25.	85.
6	3.2	27.	86.	2.7	23.	84.
7	3.0	25.	85.	2.5	22.	83.
8	2.8	24.	84.	2.3	20.	82.
9	2.7	23.	83.	2.2	19.	80.
10	2.5	21.	82.	2.0	18.	79.
11	2.3	20.	81.	1.9	17.	78.
12	2.1	19.	80.	1.8	17.	77.
13	2.0	18.	79.	1.7	16.	76.
14	1.8	17.	77.	1.6	15.	75.

Table PC-4. Esophagus Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.21	2.2	28.	.56	5.8	51.
21	.19	2.0	26.	.50	5.1	48.
22	.17	1.8	23.	.44	4.6	45.
23	.15	1.6	21.	.40	4.1	42.
24	.13	1.4	20.	.36	3.7	40.
25	.12	1.3	18.	.32	3.4	37.
26	.11	1.2	17.	.29	3.0	35.
27	.10	1.1	16.	.26	2.8	33.
28	.091	.98	14.	.24	2.5	31.
29	.084	.90	13.	.22	2.3	29.
30	.078	.83	13.	.21	2.2	28.
31	.072	.77	12.	.19	2.0	26.
32	.067	.72	11.	.18	1.9	25.
33	.063	.67	10.	.17	1.8	24.
34	.059	.63	9.8	.16	1.7	23.
35	.056	.60	9.4	.15	1.6	22.
36	.053	.57	8.9	.15	1.6	21.
37	.050	.54	8.3	.14	1.5	21.
38	.048	.52	8.2	.14	1.5	20.
39	.046	.49	7.8	.13	1.4	20.
40	.044	.47	7.6	.13	1.4	19.
41	.043	.46	7.3	.13	1.4	19.
42	.041	.44	7.1	.13	1.3	19.
43	.041	.44	7.0	.12	1.3	19.
44	.041	.44	7.0	.13	1.4	19.
45	.041	.44	7.1	.13	1.4	19.
46	.042	.43	7.2	.13	1.4	20.
47	.043	.47	7.4	.14	1.5	20.
48	.043	.48	7.7	.15	1.5	21.
49	.047	.50	8.0	.15	1.6	22.
50	.049	.52	8.3	.16	1.7	23.
51	.051	.54	8.6	.17	1.8	24.
52	.053	.57	8.9	.18	1.9	24.
53	.056	.59	9.3	.18	1.9	25.
54	.058	.62	9.7	.19	2.0	26.
55	.061	.65	10.	.20	2.1	27.
56	.064	.68	10.	.21	2.2	28.
57	.066	.71	11.	.22	2.3	29.
58	.069	.74	11.	.23	2.4	30.
59	.072	.77	12.	.24	2.5	31.
60	.075	.81	12.	.25	2.6	31.

Table PC-4 (Continued). Esophagus Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.079	.85	13.	.25	2.7	32.
62	.083	.88	13.	.26	2.7	33.
63	.086	.92	14.	.27	2.8	33.
64	.090	.96	14.	.27	2.8	33.
65	.093	.99	15.	.28	2.9	34.
66	.095	1.0	15.	.28	2.9	34.
67	.099	1.1	15.	.28	3.0	34.
68	.10	1.1	16.	.29	3.0	35.
69	.10	1.1	16.	.29	3.0	35.
70	.11	1.1	16.	.29	3.0	35.
71	.11	1.1	16.	.29	3.0	35.
72	.11	1.1	17.	.29	3.0	35.
73	.11	1.1	17.	.29	3.0	35.
74	.11	1.2	17.	.28	3.0	34.
75	.11	1.1	17.	.28	2.9	34.

Table PC-5. Stomach Cancer 10 or More Years After Exposure to low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	1.7	16.	76.	2.3	21.	82.
11	1.4	14.	73.	2.0	18.	79.
12	1.2	12.	70.	1.7	16.	77.
13	1.1	11.	67.	1.5	14.	74.
14	.99	9.8	65.	1.4	13.	73.
15	.91	9.0	63.	1.3	13.	71.
16	.83	8.2	61.	1.2	12.	70.
17	.75	7.5	58.	1.2	11.	69.
18	.69	6.9	56.	1.1	11.	67.
19	.62	6.3	54.	1.0	10.	66.
20	.57	5.8	51.	1.0	9.8	65.
21	.52	5.4	49.	.96	9.4	64.
22	.48	4.9	47.	.91	9.0	63.
23	.44	4.6	45.	.87	8.7	62.
24	.41	4.3	43.	.83	8.2	61.
25	.38	4.0	42.	.78	7.8	59.
26	.36	3.7	40.	.74	7.4	58.
27	.33	3.5	38.	.69	7.0	56.
28	.31	3.3	37.	.65	6.6	55.
29	.29	3.1	35.	.62	6.3	53.
30	.27	2.8	33.	.59	6.0	52.
31	.25	2.7	32.	.56	5.7	51.
32	.24	2.5	30.	.53	5.5	50.
33	.22	2.3	29.	.51	5.2	49.
34	.21	2.2	28.	.48	5.0	47.
35	.19	2.0	26.	.46	4.7	46.
36	.18	1.9	25.	.44	4.5	45.
37	.17	1.8	24.	.41	4.3	43.
38	.16	1.7	23.	.39	4.0	42.
39	.16	1.6	22.	.37	3.8	41.
40	.15	1.6	21.	.35	3.6	39.
41	.14	1.5	21.	.33	3.5	38.
42	.14	1.4	20.	.32	3.3	37.
43	.13	1.4	20.	.30	3.2	36.
44	.13	1.4	19.	.30	3.1	35.
45	.13	1.4	19.	.29	3.0	35.
46	.13	1.4	19.	.28	3.0	34.
47	.13	1.4	19.	.28	2.9	34.
48	.13	1.4	19.	.28	2.9	34.
49	.13	1.4	19.	.28	2.9	34.
50	.13	1.4	19.	.27	2.9	34.

Table PC-5 (Continued). Stomach Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.13	1.4	19.	.27	2.9	34.
52	.13	1.4	19.	.27	2.8	33.
53	.13	1.4	20.	.27	2.8	33.
54	.13	1.4	20.	.27	2.8	33.
55	.14	1.4	20.	.27	2.8	33.
56	.14	1.5	20.	.27	2.8	33.
57	.14	1.5	20.	.27	2.8	33.
58	.14	1.5	21.	.27	2.8	33.
59	.14	1.5	21.	.27	2.8	33.
60	.14	1.5	21.	.27	2.8	33.
61	.14	1.5	21.	.27	2.8	33.
62	.14	1.5	21.	.27	2.8	33.
63	.14	1.5	21.	.27	2.8	33.
64	.14	1.5	21.	.27	2.8	33.
65	.14	1.5	21.	.27	2.8	33.
66	.14	1.5	21.	.27	2.8	33.
67	.14	1.5	21.	.27	2.8	33.
68	.15	1.5	21.	.27	2.8	33.
69	.15	1.5	21.	.27	2.8	33.
70	.15	1.5	21.	.27	2.8	33.
71	.15	1.5	21.	.25	2.8	33.
72	.15	1.5	21.	.26	2.8	33.
73	.15	1.6	21.	.26	2.7	33.
74	.15	1.6	21.	.26	2.7	32.
75	.15	1.6	21.	.25	2.7	32.

Table PC-6. Colon Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A, at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.17	1.8	24.	.15	1.6	22.
21	.16	1.7	22.	.14	1.5	21.
22	.15	1.5	21.	.13	1.4	20.
23	.13	1.4	20.	.13	1.3	19.
24	.12	1.3	19.	.12	1.3	18.
25	.12	1.2	18.	.11	1.2	17.
26	.11	1.1	16.	.10	1.1	16.
27	.099	1.1	15.	.095	1.0	15.
28	.091	.97	14.	.089	.95	14.
29	.084	.90	13.	.083	.88	13.
30	.078	.83	13.	.077	.83	13.
31	.072	.77	12.	.072	.77	12.
32	.067	.72	11.	.068	.73	11.
33	.062	.66	10.	.064	.68	11.
34	.058	.62	9.6	.059	.64	9.9
35	.053	.57	9.0	.056	.60	9.4
36	.050	.53	8.4	.053	.57	8.9
37	.046	.50	7.9	.050	.54	8.5
38	.043	.46	7.4	.047	.51	8.0
39	.040	.43	6.9	.045	.48	7.6
40	.038	.41	6.5	.042	.45	7.2
41	.036	.38	6.2	.040	.43	6.9
42	.034	.36	5.8	.038	.41	6.5
43	.032	.35	5.6	.036	.39	6.3
44	.031	.33	5.4	.035	.38	6.1
45	.030	.33	5.3	.034	.37	6.0
46	.030	.32	5.3	.034	.36	5.9
47	.030	.32	5.2	.033	.36	5.8
48	.030	.32	5.2	.033	.36	5.8
49	.030	.32	5.2	.033	.36	5.8
50	.030	.32	5.3	.034	.36	5.8
51	.030	.32	5.3	.034	.36	5.9
52	.030	.33	5.3	.034	.37	5.9
53	.031	.33	5.4	.034	.37	6.0
54	.031	.33	5.4	.035	.37	6.1
55	.031	.34	5.5	.035	.38	6.1
56	.032	.34	5.5	.036	.38	6.2
57	.032	.34	5.6	.036	.39	6.3
58	.032	.35	5.6	.037	.39	6.3
59	.032	.35	5.6	.037	.40	6.4
60	.033	.35	5.7	.038	.40	6.5

Table PC-6 (Continued). Colon Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.033	.35	5.7	.038	.41	6.6
62	.033	.36	5.8	.038	.41	6.6
63	.033	.36	5.8	.039	.42	6.7
64	.033	.36	5.8	.039	.42	6.8
65	.034	.36	5.8	.040	.43	6.8
66	.034	.36	5.9	.040	.43	6.9
67	.034	.36	5.9	.041	.43	7.0
68	.034	.36	5.9	.041	.44	7.0
69	.034	.36	5.9	.041	.44	7.1
70	.034	.36	5.9	.042	.45	7.2
71	.034	.36	5.9	.042	.45	7.2
72	.034	.36	5.9	.042	.45	7.2
73	.034	.36	5.9	.042	.46	7.3
74	.034	.36	5.8	.043	.46	7.3
75	.033	.36	5.8	.043	.46	7.3

Table PC-7. Liver Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	2.8	23.	84.	4.8	35.	90.
21	2.4	21.	82.	4.5	33.	90.
22	2.1	19.	80.	4.1	32.	89.
23	1.9	17.	78.	3.8	30.	88.
24	1.7	16.	76.	3.4	28.	87.
25	1.5	14.	74.	3.1	26.	86.
26	1.3	13.	71.	2.9	24.	84.
27	1.2	11.	69.	2.6	22.	83.
28	1.1	10.	66.	2.4	21.	82.
29	.94	9.3	64.	2.2	20.	81.
30	.84	8.4	61.	2.0	18.	79.
31	.76	7.6	58.	1.9	17.	78.
32	.68	6.9	56.	1.7	16.	77.
33	.61	6.2	53.	1.6	15.	75.
34	.56	5.7	51.	1.5	14.	74.
35	.51	5.2	48.	1.4	13.	72.
36	.46	4.8	46.	1.3	12.	71.
37	.42	4.4	44.	1.2	11.	69.
38	.39	4.0	42.	1.1	11.	67.
39	.36	3.7	40.	1.0	10.	66.
40	.33	3.5	38.	.95	9.4	64.
41	.31	3.2	36.	.88	8.8	62.
42	.29	3.0	35.	.82	8.2	60.
43	.27	2.8	33.	.76	7.6	59.
44	.25	2.7	32.	.71	7.2	57.
45	.24	2.5	31.	.67	6.8	55.
46	.22	2.4	29.	.63	6.4	54.
47	.21	2.2	28.	.59	6.0	52.
48	.20	2.1	27.	.56	5.7	51.
49	.19	2.0	26.	.53	5.4	50.
50	.18	1.9	25.	.50	5.2	48.
51	.18	1.9	24.	.48	4.9	47.
52	.17	1.8	24.	.46	4.7	46.
53	.16	1.7	23.	.44	4.5	45.
54	.16	1.7	23.	.42	4.3	44.
55	.15	1.6	22.	.40	4.1	43.
56	.15	1.6	22.	.38	4.0	41.
57	.15	1.5	21.	.37	3.8	40.
58	.14	1.5	21.	.35	3.7	39.
59	.14	1.5	20.	.34	3.5	39.
60	.14	1.5	20.	.33	3.4	38.

Table PC-7 (Continued). Liver Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.13	1.4	20.	.32	3.3	37.
62	.13	1.4	20.	.31	3.2	37.
63	.13	1.4	19.	.30	3.2	36.
64	.13	1.4	19.	.30	3.1	35.
65	.13	1.4	19.	.29	3.0	35.
66	.13	1.4	19.	.28	3.0	35.
67	.13	1.4	19.	.28	2.9	34.
68	.13	1.4	19.	.27	2.9	34.
69	.13	1.4	19.	.27	2.8	33.
70	.13	1.4	19.	.26	2.8	33.
71	.13	1.4	19.	.26	2.7	32.
72	.13	1.4	19.	.26	2.7	32.
73	.13	1.4	19.	.25	2.7	32.
74	.13	1.4	20.	.25	2.6	32.
75	.13	1.4	20.	.25	2.6	31.

Table PC-8. Pancreas Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.45	4.6	45.	.74	7.4	58.
21	.40	4.2	43.	.67	6.7	55.
22	.36	3.8	40.	.60	6.1	53.
23	.33	3.4	38.	.54	5.5	50.
24	.30	3.1	35.	.48	4.9	47.
25	.27	2.8	33.	.43	4.5	44.
26	.25	2.6	31.	.39	4.0	42.
27	.23	2.4	30.	.35	3.7	39.
28	.21	2.2	28.	.32	3.3	37.
29	.19	2.0	26.	.29	3.0	35.
30	.18	1.9	25.	.27	2.8	33.
31	.16	1.7	23.	.25	2.6	31.
32	.15	1.6	22.	.23	2.4	30.
33	.14	1.5	21.	.21	2.2	28.
34	.13	1.4	20.	.20	2.1	27.
35	.12	1.3	19.	.19	2.0	26.
36	.12	1.2	18.	.17	1.8	24.
37	.11	1.2	17.	.16	1.7	23.
38	.10	1.1	16.	.15	1.6	22.
39	.099	1.1	15.	.15	1.5	21.
40	.094	1.0	15.	.14	1.5	20.
41	.090	.96	14.	.13	1.4	19.
42	.086	.92	14.	.12	1.3	19.
43	.084	.89	13.	.12	1.3	18.
44	.082	.88	13.	.12	1.3	18.
45	.082	.87	13.	.12	1.3	18.
46	.082	.87	13.	.12	1.2	18.
47	.082	.88	13.	.12	1.2	18.
48	.083	.88	13.	.12	1.3	18.
49	.084	.90	13.	.12	1.3	18.
50	.085	.91	14.	.12	1.3	18.
51	.087	.93	14.	.12	1.3	18.
52	.089	.95	14.	.12	1.3	19.
53	.091	.97	14.	.13	1.3	19.
54	.093	.99	15.	.13	1.4	19.
55	.095	1.0	15.	.13	1.4	19.
56	.097	1.0	15.	.13	1.4	20.
57	.099	1.1	15.	.13	1.4	20.
58	.10	1.1	16.	.14	1.5	20.
59	.10	1.1	16.	.14	1.5	21.
60	.10	1.1	16.	.14	1.5	21.

Table PC-8 (Continued). Pancreas Cancer 10 or More Years
 After Exposure to Low-LET Radiation, by Age A₁ at Exposure,
 Sex, and Dose in Rad. PC in Percent, to Two Significant
 Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.11	1.1	16.	.15	1.6	21.
62	.11	1.1	17.	.15	1.6	21.
63	.11	1.2	17.	.15	1.6	22.
64	.11	1.2	17.	.15	1.6	22.
65	.11	1.2	17.	.15	1.6	22.
66	.11	1.2	18.	.16	1.7	22.
67	.12	1.2	18.	.16	1.7	23.
68	.12	1.3	18.	.16	1.7	23.
69	.12	1.3	18.	.16	1.7	23.
70	.12	1.3	18.	.17	1.8	23.
71	.12	1.3	18.	.17	1.8	24.
72	.12	1.3	18.	.17	1.8	24.
73	.12	1.3	18.	.17	1.8	24.
74	.12	1.3	18.	.17	1.8	24.
75	.12	1.3	18.	.17	1.8	24.

Table PC-9-A. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad, Given No Information on Smoking. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.39	4.0	42.	.56	5.7	51.
11	.35	3.7	39.	.51	5.2	49.
12	.31	3.3	37.	.47	4.8	46.
13	.28	2.9	34.	.42	4.4	44.
14	.24	2.6	31.	.38	4.0	42.
15	.22	2.3	28.	.35	3.7	39.
16	.19	2.0	26.	.32	3.3	37.
17	.17	1.8	24.	.29	3.1	35.
18	.15	1.6	22.	.27	2.8	33.
19	.14	1.5	20.	.25	2.6	32.
20	.12	1.3	19.	.23	2.4	30.
21	.11	1.2	17.	.22	2.3	28.
22	.10	1.1	16.	.20	2.1	27.
23	.093	.99	15.	.19	2.0	26.
24	.086	.91	14.	.18	1.9	24.
25	.079	.84	13.	.16	1.7	23.
26	.073	.78	12.	.16	1.6	22.
27	.067	.72	11.	.15	1.6	21.
28	.062	.67	10.	.14	1.5	20.
29	.058	.62	9.7	.13	1.4	20.
30	.054	.58	9.1	.13	1.3	19.
31	.051	.54	8.6	.12	1.3	18.
32	.048	.51	8.1	.12	1.2	18.
33	.045	.48	7.6	.11	1.2	17.
34	.042	.45	7.2	.11	1.1	17.
35	.040	.43	6.9	.10	1.1	16.
36	.038	.41	6.6	.10	1.1	16.
37	.036	.39	6.3	.10	1.1	16.
38	.035	.37	6.0	.099	1.1	15.
39	.033	.36	5.8	.098	1.0	15.
40	.032	.34	5.6	.096	1.0	15.
41	.031	.33	5.4	.096	1.0	15.
42	.030	.32	5.2	.095	1.0	15.
43	.029	.31	5.1	.095	1.0	15.
44	.028	.30	5.0	.095	1.0	15.
45	.028	.30	4.9	.095	1.0	15.
46	.027	.29	4.8	.096	1.0	15.
47	.027	.28	4.7	.097	1.0	15.
48	.026	.28	4.6	.098	1.0	15.
49	.026	.28	4.6	.099	1.1	15.
50	.026	.28	4.5	.10	1.1	16.

Table PC-9-A (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad, Given No Information on Smoking. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.025	.27	4.5	.10	1.1	16.
52	.025	.27	4.5	.10	1.1	16.
53	.025	.27	4.4	.11	1.1	16.
54	.025	.27	4.4	.11	1.2	17.
55	.025	.27	4.5	.11	1.2	17.
56	.025	.27	4.5	.12	1.2	18.
57	.026	.27	4.5	.12	1.3	18.
58	.026	.28	4.5	.12	1.3	19.
59	.026	.28	4.6	.13	1.3	19.
60	.026	.28	4.6	.13	1.4	19.
61	.027	.29	4.7	.13	1.4	20.
62	.027	.29	4.8	.14	1.5	20.
63	.028	.30	4.9	.14	1.5	21.
64	.028	.30	5.0	.15	1.5	21.
65	.029	.31	5.1	.15	1.6	22.
66	.030	.32	5.2	.16	1.7	23.
67	.031	.33	5.4	.16	1.7	23.
68	.032	.35	5.6	.17	1.8	24.
69	.033	.36	5.8	.18	1.9	24.
70	.035	.37	6.0	.18	1.9	25.
71	.036	.39	6.2	.19	2.0	26.
72	.037	.40	6.4	.19	2.0	26.
73	.039	.42	6.7	.19	2.0	26.
74	.040	.43	6.9	.20	2.1	27.
75	.041	.44	7.1	.20	2.1	27.

Table PC-9-8. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad, for Nonsmokers. PC₁ in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	2.6	22.	83.	2.5	22.	83.
11	2.3	21.	82.	2.3	20.	82.
12	2.1	19.	80.	2.1	19.	80.
13	1.9	17.	78.	1.9	18.	78.
14	1.6	15.	75.	1.8	16.	77.
15	1.4	14.	73.	1.6	15.	75.
16	1.3	12.	71.	1.5	14.	73.
17	1.1	11.	68.	1.3	13.	72.
18	1.0	10.	66.	1.2	12.	70.
19	.93	9.1	63.	1.1	11.	68.
20	.83	8.3	61.	1.1	10.	67.
21	.76	7.6	58.	.99	9.7	65.
22	.69	7.0	56.	.92	9.1	63.
23	.63	6.4	54.	.86	8.6	62.
24	.58	5.9	52.	.81	8.1	60.
25	.53	5.5	50.	.76	7.6	58.
26	.49	5.1	48.	.72	7.2	57.
27	.46	4.7	46.	.67	6.8	56.
28	.42	4.4	44.	.64	6.3	54.
29	.39	4.1	42.	.61	6.2	53.
30	.37	3.8	41.	.58	5.9	52.
31	.34	3.6	39.	.56	5.7	51.
32	.32	3.4	37.	.54	5.5	50.
33	.30	3.2	36.	.52	5.3	49.
34	.29	3.0	35.	.50	5.1	48.
35	.27	2.9	33.	.48	5.0	47.
36	.26	2.7	32.	.48	4.9	47.
37	.25	2.6	31.	.46	4.8	46.
38	.24	2.5	30.	.46	4.7	46.
39	.23	2.4	30.	.45	4.7	46.
40	.22	2.3	29.	.45	4.6	45.
41	.21	2.2	28.	.44	4.6	45.
42	.20	2.1	27.	.44	4.5	45.
43	.20	2.1	27.	.44	4.5	45.
44	.19	2.0	26.	.44	4.5	45.
45	.19	2.0	26.	.44	4.5	45.
46	.18	1.9	25.	.44	4.6	45.
47	.18	1.9	25.	.45	4.6	45.
48	.18	1.9	25.	.45	4.7	46.
49	.18	1.9	25.	.46	4.7	46.
50	.17	1.8	24.	.47	4.8	46.

Table PC-9-B (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Nonsmokers. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.17	1.8	24.	.48	4.9	47.
52	.17	1.8	24.	.48	5.0	47.
53	.17	1.8	24.	.49	5.1	48.
54	.17	1.8	24.	.51	5.2	49.
55	.17	1.8	24.	.52	5.3	49.
56	.17	1.8	24.	.54	5.5	50.
57	.17	1.8	24.	.55	5.6	50.
58	.17	1.9	24.	.57	5.8	51.
59	.18	1.9	25.	.58	5.9	52.
60	.18	1.9	25.	.60	6.1	53.
61	.18	1.9	25.	.62	6.3	53.
62	.18	2.0	25.	.64	6.5	54.
63	.19	2.0	26.	.66	6.7	55.
64	.19	2.0	26.	.68	6.9	56.
65	.20	2.1	27.	.70	7.1	57.
66	.20	2.1	27.	.72	7.3	57.
67	.21	2.2	28.	.75	7.5	58.
68	.22	2.3	29.	.78	7.8	59.
69	.23	2.4	30.	.81	8.1	60.
70	.24	2.5	30.	.83	8.3	61.
71	.24	2.6	31.	.85	8.5	61.
72	.25	2.7	32.	.87	8.7	62.
73	.26	2.8	33.	.89	8.8	62.
74	.27	2.9	34.	.90	8.9	63.
75	.28	3.0	34.	.91	9.0	63.

Table PC-9-C. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad, for Former Smokers. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.66	6.7	55.	.65	6.6	55.
11	.60	6.1	53.	.60	6.1	53.
12	.53	5.5	50.	.55	5.6	50.
13	.47	4.9	47.	.50	5.1	48.
14	.42	4.3	44.	.45	4.6	45.
15	.37	3.8	41.	.41	4.2	43.
16	.33	3.4	38.	.37	3.9	41.
17	.29	3.0	35.	.34	3.6	39.
18	.26	2.7	32.	.32	3.3	37.
19	.23	2.5	30.	.29	3.1	35.
20	.21	2.2	28.	.27	2.8	33.
21	.19	2.0	26.	.25	2.6	32.
22	.17	1.8	24.	.23	2.5	30.
23	.16	1.7	23.	.22	2.3	29.
24	.15	1.6	21.	.20	2.2	27.
25	.13	1.4	20.	.19	2.0	26.
26	.12	1.3	19.	.18	1.9	25.
27	.11	1.2	18.	.17	1.8	24.
28	.11	1.1	16.	.16	1.7	23.
29	.099	1.1	15.	.15	1.6	22.
30	.093	.99	15.	.15	1.6	21.
31	.087	.93	14.	.14	1.5	21.
32	.081	.87	13.	.14	1.4	20.
33	.077	.82	12.	.13	1.4	19.
34	.072	.77	12.	.13	1.3	19.
35	.068	.73	11.	.12	1.3	18.
36	.065	.70	11.	.12	1.3	18.
37	.062	.66	10.	.12	1.3	18.
38	.059	.63	9.9	.12	1.2	18.
39	.057	.61	9.5	.11	1.2	17.
40	.055	.59	9.2	.11	1.2	17.
41	.053	.57	8.9	.11	1.2	17.
42	.051	.55	8.6	.11	1.2	17.
43	.050	.53	8.4	.11	1.2	17.
44	.048	.52	8.2	.11	1.2	17.
45	.047	.51	8.0	.11	1.2	17.
46	.046	.50	7.9	.11	1.2	17.
47	.045	.49	7.7	.11	1.2	17.
48	.045	.48	7.6	.11	1.2	17.
49	.044	.47	7.5	.12	1.2	18.
50	.044	.47	7.5	.12	1.3	18.

Table PC-9-C (Continued). Lung Cancer 10 or More Years After Exposure to low-LET Radiation, by Age A, at Exposure, Sex, and Dose in Rad, for Former Smokers. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.043	.47	7.4	.12	1.3	18.
52	.043	.46	7.4	.12	1.3	18.
53	.043	.46	7.4	.12	1.3	19.
54	.043	.46	7.4	.13	1.4	19.
55	.043	.46	7.4	.13	1.4	20.
56	.043	.47	7.4	.14	1.4	20.
57	.044	.47	7.5	.14	1.5	20.
58	.044	.47	7.5	.14	1.5	21.
59	.044	.48	7.6	.15	1.6	21.
60	.045	.48	7.7	.15	1.6	22.
61	.046	.49	7.8	.16	1.7	22.
62	.046	.50	7.9	.16	1.7	23.
63	.047	.51	8.0	.17	1.8	24.
64	.048	.52	8.2	.17	1.8	24.
65	.050	.53	8.4	.18	1.9	25.
66	.051	.55	8.6	.18	1.9	25.
67	.053	.57	8.9	.19	2.0	26.
68	.055	.59	9.2	.20	2.1	27.
69	.057	.61	9.5	.20	2.2	27.
70	.059	.63	9.9	.21	2.2	28.
71	.062	.66	10.	.22	2.3	29.
72	.064	.68	11.	.22	2.3	29.
73	.066	.71	11.	.22	2.4	29.
74	.069	.73	11.	.23	2.4	30.
75	.071	.76	12.	.23	2.4	30.

Table PC-9-D. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers. All PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.24	2.5	30.	.23	2.4	30.
11	.21	2.2	28.	.21	2.2	28.
12	.19	2.0	26.	.19	2.0	26.
13	.17	1.8	24.	.18	1.9	24.
14	.15	1.6	21.	.16	1.7	23.
15	.13	1.4	19.	.14	1.5	21.
16	.12	1.2	18.	.13	1.4	20.
17	.10	1.1	16.	.12	1.3	18.
18	.092	.98	15.	.11	1.2	17.
19	.083	.88	13.	.10	1.1	16.
20	.074	.79	12.	.095	1.0	15.
21	.068	.72	11.	.089	.95	14.
22	.061	.66	10.	.083	.88	13.
23	.056	.60	9.4	.077	.83	12.
24	.052	.55	8.7	.072	.77	12.
25	.048	.51	8.1	.068	.72	11.
26	.044	.47	7.5	.064	.68	11.
27	.041	.44	7.0	.060	.64	10.
28	.038	.40	6.5	.057	.61	9.6
29	.035	.38	6.1	.054	.58	9.1
30	.033	.35	5.7	.052	.56	8.8
31	.031	.33	5.4	.050	.53	8.4
32	.029	.31	5.0	.048	.51	8.1
33	.027	.29	4.8	.046	.49	7.8
34	.026	.27	4.5	.044	.48	7.6
35	.024	.26	4.3	.043	.46	7.4
36	.023	.25	4.1	.042	.45	7.3
37	.022	.23	3.9	.041	.44	7.1
38	.021	.23	3.7	.041	.44	7.0
39	.020	.22	3.6	.040	.43	6.9
40	.019	.21	3.5	.040	.43	6.8
41	.019	.20	3.3	.039	.42	6.8
42	.018	.19	3.2	.039	.42	6.8
43	.018	.19	3.1	.039	.42	6.7
44	.017	.18	3.1	.039	.42	6.7
45	.017	.18	3.0	.039	.42	6.8
46	.016	.18	2.9	.039	.42	6.8
47	.016	.17	2.9	.040	.43	6.9
48	.016	.17	2.8	.040	.43	6.9
49	.016	.17	2.8	.041	.44	7.0
50	.015	.17	2.8	.042	.45	7.1

Table PC-9-D (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁, at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, All. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
51	.015	.17	2.8	.042	.45	7.3
52	.015	.16	2.7	.043	.46	7.4
53	.015	.16	2.7	.044	.47	7.5
54	.015	.16	2.7	.045	.49	7.7
55	.015	.16	2.7	.047	.50	7.9
56	.015	.17	2.8	.048	.51	8.1
57	.015	.17	2.8	.049	.53	8.3
58	.016	.17	2.8	.051	.54	8.6
59	.016	.17	2.8	.052	.56	8.8
60	.016	.17	2.9	.054	.57	9.0
61	.016	.17	2.9	.055	.59	9.3
62	.016	.18	2.9	.057	.61	9.5
63	.017	.18	3.0	.059	.63	9.8
64	.017	.18	3.1	.061	.65	10.
65	.018	.19	3.1	.063	.67	10.
66	.018	.19	3.2	.065	.69	11.
67	.019	.20	3.3	.067	.72	11.
68	.019	.21	3.5	.070	.75	11.
69	.020	.22	3.6	.072	.77	12.
70	.021	.23	3.7	.074	.79	12.
71	.022	.23	3.9	.076	.82	12.
72	.023	.24	4.0	.078	.83	13.
73	.023	.25	4.1	.079	.85	13.
74	.024	.26	4.3	.081	.86	13.
75	.025	.27	4.4	.082	.87	13.

Table PC-9-E. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, Under 10 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.68	6.9	56.	.66	6.7	55.
11	.61	6.2	53.	.61	6.2	53.
12	.55	5.6	50.	.56	5.7	51.
13	.48	5.0	47.	.50	5.2	48.
14	.43	4.4	44.	.46	4.7	46.
15	.38	3.9	41.	.42	4.3	44.
16	.33	3.5	38.	.38	3.9	41.
17	.30	3.1	36.	.35	3.6	39.
18	.27	2.8	33.	.32	3.4	37.
19	.24	2.5	31.	.30	3.1	35.
20	.21	2.3	28.	.28	2.9	34.
21	.20	2.1	27.	.26	2.7	32.
22	.18	1.9	25.	.24	2.5	31.
23	.16	1.7	23.	.22	2.3	29.
24	.15	1.6	22.	.21	2.2	28.
25	.14	1.5	20.	.20	2.1	27.
26	.13	1.4	19.	.18	2.0	26.
27	.12	1.3	18.	.17	1.8	24.
28	.11	1.2	17.	.17	1.8	23.
29	.10	1.1	16.	.16	1.7	22.
30	.095	1.0	15.	.15	1.6	22.
31	.089	.95	14.	.14	1.5	21.
32	.083	.89	13.	.14	1.5	20.
33	.078	.84	13.	.13	1.4	20.
34	.074	.79	12.	.13	1.4	19.
35	.070	.75	11.	.12	1.3	19.
36	.066	.71	11.	.12	1.3	18.
37	.063	.68	10.	.12	1.3	18.
38	.061	.65	10.	.12	1.3	18.
39	.058	.62	9.7	.12	1.2	18.
40	.056	.60	9.4	.11	1.2	17.
41	.054	.58	9.1	.11	1.2	17.
42	.052	.56	8.8	.11	1.2	17.
43	.051	.54	8.6	.11	1.2	17.
44	.049	.53	8.4	.11	1.2	17.
45	.048	.52	8.2	.11	1.2	17.
46	.047	.51	8.0	.11	1.2	17.
47	.046	.50	7.9	.11	1.2	18.
48	.046	.49	7.8	.12	1.2	18.
49	.045	.48	7.7	.12	1.3	18.

Table PC-9-E (Continued). Lung Cancer 10 or More Years After Exposure to low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, Under 10 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.045	.48	7.6	.12	1.3	18.
51	.044	.48	7.6	.12	1.3	18.
52	.044	.47	7.6	.12	1.3	19.
53	.044	.47	7.5	.13	1.4	19.
54	.044	.47	7.5	.13	1.4	19.
55	.044	.47	7.6	.13	1.4	20.
56	.044	.48	7.6	.14	1.5	20.
57	.045	.48	7.6	.14	1.5	21.
58	.045	.48	7.7	.15	1.6	21.
59	.046	.49	7.8	.15	1.6	22.
60	.046	.49	7.8	.15	1.6	22.
61	.047	.50	7.9	.16	1.7	23.
62	.047	.51	8.1	.16	1.7	23.
63	.048	.52	8.2	.17	1.8	24.
64	.049	.53	8.4	.17	1.9	24.
65	.051	.54	8.6	.18	1.9	25.
66	.052	.56	8.8	.19	2.0	26.
67	.054	.58	9.1	.19	2.1	26.
68	.056	.60	9.4	.20	2.1	27.
69	.058	.63	9.7	.21	2.2	28.
70	.061	.65	10.	.21	2.3	28.
71	.063	.67	10.	.22	2.3	29.
72	.065	.70	11.	.23	2.4	29.
73	.068	.72	11.	.23	2.4	30.
74	.070	.75	11.	.23	2.4	30.
75	.072	.78	12.	.24	2.5	30.

Table PC-9-F. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 10 to 20 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.28	2.9	34.	.27	2.8	33.
11	.25	2.6	31.	.25	2.6	31.
12	.22	2.3	29.	.23	2.4	29.
13	.20	2.1	27.	.20	2.2	27.
14	.17	1.8	24.	.19	2.0	26.
15	.15	1.6	22.	.17	1.8	24.
16	.14	1.4	20.	.15	1.6	22.
17	.12	1.3	18.	.14	1.5	21.
18	.11	1.1	17.	.13	1.4	19.
19	.097	1.0	15.	.12	1.3	18.
20	.087	.93	14.	.11	1.2	17.
21	.079	.85	13.	.10	1.1	16.
22	.072	.77	12.	.097	1.0	15.
23	.066	.71	11.	.090	.96	14.
24	.061	.65	10.	.085	.90	14.
25	.056	.60	9.3	.079	.85	13.
26	.051	.55	8.7	.075	.80	12.
27	.048	.51	8.1	.070	.75	12.
28	.044	.47	7.5	.067	.72	11.
29	.041	.44	7.0	.064	.68	11.
30	.038	.41	6.6	.061	.65	10.
31	.036	.38	6.2	.058	.62	9.7
32	.034	.36	5.9	.056	.60	9.4
33	.032	.34	5.5	.054	.58	9.1
34	.030	.32	5.2	.052	.56	8.8
35	.028	.30	5.0	.051	.54	8.5
36	.027	.29	4.7	.050	.53	8.4
37	.026	.27	4.5	.048	.52	8.2
38	.025	.26	4.3	.048	.51	8.1
39	.024	.25	4.2	.047	.50	8.0
40	.023	.24	4.0	.047	.50	7.9
41	.022	.24	3.9	.046	.49	7.9
42	.021	.23	3.8	.046	.49	7.8
43	.021	.22	3.7	.046	.49	7.8
44	.020	.21	3.6	.046	.49	7.8
45	.020	.21	3.5	.046	.49	7.8
46	.019	.21	3.4	.046	.49	7.9
47	.019	.20	3.3	.047	.50	7.9
48	.019	.20	3.3	.047	.51	8.0
49	.018	.20	3.3	.048	.51	8.1

Table PC-9-F (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 10 to 20 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.018	.19	3.2	.049	.52	8.2
51	.018	.19	3.2	.050	.53	8.4
52	.018	.19	3.2	.051	.54	8.5
53	.018	.19	3.2	.052	.55	8.7
54	.018	.19	3.2	.053	.57	8.9
55	.018	.19	3.2	.054	.58	9.1
56	.018	.19	3.2	.056	.60	9.4
57	.018	.19	3.2	.057	.61	9.6
58	.018	.20	3.2	.059	.63	9.9
59	.018	.20	3.3	.061	.65	10.
60	.019	.20	3.3	.063	.67	10.
61	.019	.20	3.4	.065	.69	11.
62	.019	.21	3.4	.067	.71	11.
63	.020	.21	3.5	.069	.74	11.
64	.020	.21	3.6	.071	.76	12.
65	.021	.22	3.7	.073	.78	12.
66	.021	.23	3.8	.076	.81	12.
67	.022	.24	3.9	.079	.84	13.
68	.023	.24	4.0	.082	.87	13.
69	.024	.25	4.2	.085	.90	14.
70	.025	.26	4.3	.087	.93	14.
71	.025	.27	4.5	.089	.95	14.
72	.026	.28	4.6	.091	.97	14.
73	.027	.29	4.8	.093	.99	15.
74	.028	.30	5.0	.094	1.0	15.
75	.029	.31	5.1	.096	1.0	15.

Table PC-9-G. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 21 to 39 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.16	1.7	23.	.16	1.7	22.
11	.14	1.5	21.	.14	1.5	21.
12	.13	1.4	19.	.13	1.4	19.
13	.11	1.2	17.	.12	1.3	18.
14	.10	1.1	16.	.11	1.1	17.
15	.088	.94	14.	.093	1.0	15.
16	.078	.83	13.	.089	.95	14.
17	.069	.74	11.	.082	.87	13.
18	.062	.66	10.	.075	.81	12.
19	.056	.60	9.4	.069	.74	11.
20	.050	.54	8.5	.064	.69	11.
21	.046	.49	7.8	.060	.64	10.
22	.042	.45	7.1	.056	.60	9.3
23	.038	.41	6.6	.052	.56	8.8
24	.035	.37	6.1	.049	.52	8.3
25	.032	.34	5.6	.046	.49	7.8
26	.030	.32	5.2	.043	.46	7.4
27	.027	.29	4.8	.041	.44	7.0
28	.025	.27	4.5	.039	.41	6.7
29	.024	.25	4.2	.037	.39	6.4
30	.022	.24	3.9	.035	.38	6.1
31	.021	.22	3.7	.034	.36	5.8
32	.019	.21	3.5	.032	.35	5.6
33	.018	.20	3.3	.031	.33	5.4
34	.017	.19	3.1	.030	.32	5.2
35	.016	.18	2.9	.029	.31	5.1
36	.016	.17	2.8	.029	.31	5.0
37	.015	.16	2.7	.028	.30	4.9
38	.014	.15	2.5	.027	.30	4.8
39	.014	.15	2.4	.027	.29	4.8
40	.013	.14	2.4	.027	.29	4.7
41	.013	.14	2.3	.027	.29	4.7
42	.012	.13	2.2	.026	.28	4.7
43	.012	.13	2.1	.026	.28	4.6
44	.012	.12	2.1	.026	.28	4.6
45	.011	.12	2.0	.026	.28	4.7
46	.011	.12	2.0	.027	.29	4.7
47	.011	.12	2.0	.027	.29	4.7
48	.011	.12	1.9	.027	.29	4.8
49	.011	.11	1.9	.028	.30	4.9

Table PC-9-G (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 21 to 39 per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.010	.11	1.9	.028	.30	4.9
51	.010	.11	1.9	.029	.31	5.0
52	.010	.11	1.9	.029	.31	5.1
53	.010	.11	1.9	.030	.32	5.2
54	.010	.11	1.9	.031	.33	5.3
55	.010	.11	1.9	.031	.34	5.5
56	.010	.11	1.9	.032	.35	5.6
57	.010	.11	1.9	.033	.36	5.8
58	.010	.11	1.9	.034	.37	5.9
59	.011	.11	1.9	.035	.38	6.1
60	.011	.12	1.9	.036	.39	6.3
61	.011	.12	2.0	.037	.40	6.4
62	.011	.12	2.0	.038	.41	6.6
63	.011	.12	2.0	.040	.43	6.8
64	.012	.12	2.1	.041	.44	7.0
65	.012	.13	2.1	.042	.45	7.2
66	.012	.13	2.2	.044	.47	7.5
67	.013	.14	2.3	.045	.49	7.7
68	.013	.14	2.4	.047	.50	8.0
69	.014	.15	2.5	.049	.52	8.3
70	.014	.15	2.5	.050	.54	8.5
71	.015	.16	2.6	.052	.55	8.7
72	.015	.16	2.7	.053	.56	8.9
73	.016	.17	2.8	.054	.57	9.0
74	.016	.18	2.9	.054	.58	9.1
75	.017	.18	3.0	.055	.59	9.3

Table PC-9-H. Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 40 or More per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
10	.11	1.2	17.	.11	1.2	17.
11	.10	1.1	16.	.10	1.1	16.
12	.090	.96	14.	.092	.98	15.
13	.080	.85	13.	.083	.89	13.
14	.070	.75	11.	.076	.81	12.
15	.062	.66	10.	.069	.74	11.
16	.055	.59	9.2	.063	.67	10.
17	.049	.52	8.3	.058	.62	9.6
18	.044	.47	7.5	.053	.57	8.9
19	.039	.42	6.8	.049	.53	8.3
20	.035	.38	6.1	.045	.49	7.7
21	.032	.34	5.6	.042	.45	7.2
22	.029	.31	5.1	.039	.42	6.8
23	.027	.29	4.7	.037	.39	6.4
24	.025	.26	4.3	.034	.37	6.0
25	.023	.24	4.0	.032	.35	5.6
26	.021	.22	3.7	.030	.33	5.3
27	.019	.21	3.4	.029	.31	5.0
28	.018	.19	3.2	.027	.29	4.8
29	.017	.18	3.0	.026	.28	4.6
30	.016	.17	2.8	.025	.27	4.4
31	.015	.16	2.6	.024	.25	4.2
32	.014	.15	2.5	.023	.24	4.0
33	.013	.14	2.3	.022	.24	3.9
34	.012	.13	2.2	.021	.23	3.8
35	.011	.12	2.1	.021	.22	3.7
36	.011	.12	2.0	.020	.22	3.6
37	.010	.11	1.9	.020	.21	3.5
38	.010	.11	1.8	.019	.21	3.5
39	.010	.10	1.7	.019	.21	3.4
40	.009	.099	1.7	.019	.20	3.4
41	.009	.096	1.6	.019	.20	3.4
42	.009	.093	1.6	.019	.20	3.3
43	.008	.090	1.5	.019	.20	3.3
44	.008	.087	1.5	.019	.20	3.3
45	.008	.085	1.4	.019	.20	3.3
46	.008	.083	1.4	.019	.20	3.4
47	.008	.082	1.4	.019	.20	3.4
48	.008	.081	1.4	.019	.21	3.4
49	.007	.080	1.3	.019	.21	3.5

Table PC-9-H (Continued). Lung Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad, for Present Cigarette Smokers, 40 or More per Day. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
50	.007	.079	1.3	.020	.21	3.5
51	.007	.078	1.3	.020	.22	3.6
52	.007	.078	1.3	.021	.22	3.7
53	.007	.078	1.3	.021	.23	3.7
54	.007	.078	1.3	.022	.23	3.8
55	.007	.078	1.3	.022	.24	3.9
56	.007	.078	1.3	.023	.24	4.0
57	.007	.079	1.3	.023	.25	4.1
58	.007	.079	1.3	.024	.26	4.3
59	.008	.080	1.4	.025	.27	4.4
60	.008	.081	1.4	.025	.27	4.5
61	.008	.083	1.4	.026	.28	4.6
62	.008	.084	1.4	.027	.29	4.8
63	.008	.085	1.4	.028	.30	4.9
64	.008	.087	1.5	.029	.31	5.1
65	.008	.090	1.5	.030	.32	5.2
66	.009	.093	1.6	.031	.33	5.4
67	.009	.096	1.6	.032	.34	5.6
68	.009	.099	1.7	.033	.36	5.8
69	.010	.10	1.7	.034	.37	6.0
70	.010	.11	1.8	.035	.38	6.1
71	.010	.11	1.9	.036	.39	6.3
72	.011	.12	1.9	.037	.40	6.4
73	.011	.12	2.0	.038	.40	6.5
74	.012	.12	2.1	.038	.41	6.6
75	.012	.13	2.1	.039	.42	6.7

Table PC-9-I. Lung Cancer, by Cumulative Exposure to Radon Daughters, in WLM, and by Assumed Risk Factor, for Exposure 10 or More Years Before Diagnosis. PC in Percent.

WLM	Assumed Percent Excess Risk per WLM		
	0.7	1.2	1.5
1	0.7	1.2	1.5
2	1.4	2.3	2.9
3	2.1	3.5	4.3
4	2.7	4.6	5.7
5	3.4	5.7	7.0
6	4.0	6.7	8.3
7	4.7	7.7	9.5
8	5.3	8.8	11.
9	5.9	9.7	12.
10	6.5	11.	13.
11	7.1	12.	14.
12	7.7	13.	15.
13	8.3	13.	16.
14	8.9	14.	17.
15	9.5	15.	18.
16	10.	16.	19.
17	11.	17.	20.
18	11.	18.	21.
19	12.	19.	22.
20	12.	19.	23.
25	15.	23.	27.
30	17.	26.	31.
35	20.	30.	34.
40	22.	32.	38.
45	24.	35.	40.
50	26.	38.	43.
60	30.	42.	47.
70	33.	46.	51.
80	36.	49.	55.
90	39.	52.	57.
100	41.	55.	60.
120	46.	59.	64.
140	49.	63.	68.
160	53.	66.	71.
180	56.	68.	73.
200	58.	71.	75.
250	64.	75.	79.
300	68.	78.	82.
350	71.	81.	84.
400	74.	83.	86.
450	76.	84.	87.
500	78.	86.	88.
600	81.	88.	90.
700	83.	89.	91.
800	85.	91.	92.
900	86.	92.	93.
1000	88.	92.	94.

Table PC-10. Female Breast Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
0	---	---	---	2.3	19.	70.
1	---	---	---	2.3	19.	70.
2	---	---	---	2.2	19.	70.
3	---	---	---	2.2	18.	69.
4	---	---	---	2.0	17.	68.
5	---	---	---	1.9	17.	66.
6	---	---	---	1.8	16.	65.
7	---	---	---	1.7	15.	64.
8	---	---	---	1.6	14.	62.
9	---	---	---	1.5	13.	60.
10	---	---	---	1.4	13.	59.
11	---	---	---	1.3	12.	57.
12	---	---	---	1.2	11.	56.
13	---	---	---	1.2	11.	54.
14	---	---	---	1.1	10.	53.
15	---	---	---	1.1	9.7	52.
16	---	---	---	.98	9.0	50.
17	---	---	---	.89	8.2	47.
18	---	---	---	.79	7.4	44.
19	---	---	---	.69	6.5	41.
20	---	---	---	.60	5.7	38.
21	---	---	---	.52	5.0	34.
22	---	---	---	.45	4.1	31.
23	---	---	---	.39	3.3	28.
24	---	---	---	.35	3.4	26.
25	---	---	---	.35	3.2	25.
26	---	---	---	.31	3.0	24.
27	---	---	---	.30	2.9	23.
28	---	---	---	.28	2.8	22.
29	---	---	---	.28	2.7	22.
30	---	---	---	.27	2.6	21.
31	---	---	---	.26	2.5	21.
32	---	---	---	.25	2.4	20.
33	---	---	---	.24	2.4	19.
34	---	---	---	.23	2.2	19.
35	---	---	---	.21	2.1	18.
36	---	---	---	.19	1.9	16.
37	---	---	---	.17	1.7	15.
38	---	---	---	.15	1.5	13.
39	---	---	---	.13	1.2	11.
40	---	---	---	.10	1.0	9.4

Table PC-10 (Continued). Female Breast Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	---	---	---	.083	.83	7.7
42	---	---	---	.067	.66	6.3
43	---	---	---	.055	.54	5.2
44	---	---	---	.048	.48	4.6
45	---	---	---	.045	.45	4.3
46	---	---	---	.043	.43	4.1
47	---	---	---	.041	.41	3.9
48	---	---	---	.039	.39	3.8
49	---	---	---	.037	.37	3.6
50	---	---	---	.036	.36	3.5
51	---	---	---	.034	.34	3.3
52	---	---	---	.033	.33	3.2
53	---	---	---	.032	.32	3.1
54	---	---	---	.030	.30	3.0
55	---	---	---	.029	.29	2.8
56	---	---	---	.028	.28	2.7
57	---	---	---	.026	.26	2.6
58	---	---	---	.025	.25	2.4
59	---	---	---	.023	.23	2.3
60	---	---	---	.021	.21	2.1
61	---	---	---	.020	.20	2.0
62	---	---	---	.018	.18	1.8
63	---	---	---	.017	.17	1.7
64	---	---	---	.015	.15	1.5
65	---	---	---	.014	.14	1.4
66	---	---	---	.013	.13	1.3
67	---	---	---	.011	.11	1.1
68	---	---	---	.010	.10	.99
69	---	---	---	.008	.086	.85
70	---	---	---	.007	.072	.71
71	---	---	---	.005	.058	.58
72	---	---	---	.004	.044	.44
73	---	---	---	.002	.029	.29
74	---	---	---	.001	.015	.15
75	---	---	---	.000	.000	.000

Table PC-11. Kidney and Bladder Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
20	.12	1.3	19.	.30	3.2	36.
21	.12	1.2	18.	.29	3.0	35.
22	.11	1.2	17.	.27	2.9	34.
23	.10	1.1	16.	.26	2.7	33.
24	.095	1.0	15.	.25	2.6	32.
25	.089	.95	14.	.24	2.5	30.
26	.083	.89	13.	.22	2.4	29.
27	.078	.83	13.	.21	2.2	28.
28	.073	.78	12.	.20	2.1	27.
29	.069	.73	11.	.19	2.0	26.
30	.065	.69	11.	.18	1.9	25.
31	.061	.66	10.	.17	1.8	24.
32	.058	.62	9.7	.16	1.7	23.
33	.055	.59	9.2	.16	1.7	23.
34	.052	.56	8.8	.15	1.6	22.
35	.050	.53	8.4	.14	1.5	21.
36	.048	.51	8.1	.14	1.5	20.
37	.045	.49	7.7	.13	1.4	19.
38	.043	.47	7.4	.13	1.3	19.
39	.042	.45	7.1	.12	1.3	18.
40	.040	.43	6.9	.12	1.3	18.
41	.038	.41	6.6	.11	1.2	17.
42	.037	.40	6.4	.11	1.2	17.
43	.036	.38	6.2	.11	1.1	17.
44	.034	.37	6.0	.10	1.1	16.
45	.033	.36	5.8	.10	1.1	16.
46	.032	.35	5.7	.10	1.1	16.
47	.032	.34	5.5	.098	1.0	15.
48	.031	.33	5.4	.097	1.0	15.
49	.030	.32	5.3	.095	1.0	15.
50	.030	.32	5.2	.094	1.0	15.
51	.029	.31	5.1	.093	.99	15.
52	.029	.31	5.0	.092	.98	15.
53	.028	.30	5.0	.091	.97	14.
54	.028	.30	4.9	.090	.97	14.
55	.028	.30	4.9	.090	.96	14.
56	.028	.30	4.8	.090	.96	14.
57	.027	.29	4.8	.090	.96	14.
58	.027	.29	4.8	.090	.96	14.
59	.027	.29	4.8	.090	.96	14.
60	.027	.29	4.8	.090	.96	14.

Table PC-11 (Continued). Kidney and Bladder Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
61	.027	.29	4.8	.090	.96	14.
62	.027	.29	4.8	.090	.97	14.
63	.027	.29	4.8	.091	.97	14.
64	.027	.29	4.8	.091	.97	14.
65	.027	.29	4.8	.091	.98	14.
66	.028	.30	4.9	.092	.98	15.
67	.028	.30	4.9	.093	.99	15.
68	.028	.30	4.9	.093	.99	15.
69	.029	.31	5.0	.094	1.0	15.
70	.029	.31	5.1	.095	1.0	15.
71	.029	.31	5.1	.096	1.0	15.
72	.030	.32	5.2	.097	1.0	15.
73	.030	.32	5.3	.098	1.0	15.
74	.031	.33	5.3	.099	1.1	15.
75	.031	.33	5.4	.10	1.1	16.

Table PC-12. Thyroid Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A₁ at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A ₁	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
0	9.6	51.	91.	9.1	50.	91.
1	8.8	49.	91.	8.5	48.	90.
2	8.1	47.	90.	8.0	47.	90.
3	7.6	45.	89.	7.6	45.	89.
4	7.1	43.	88.	7.2	44.	89.
5	6.7	42.	88.	6.8	42.	88.
6	6.3	40.	87.	6.5	41.	88.
7	6.0	39.	86.	6.3	40.	87.
8	5.7	38.	86.	6.0	39.	86.
9	5.4	36.	85.	5.8	38.	86.
10	5.2	35.	85.	5.6	37.	86.
11	5.0	34.	84.	5.5	37.	85.
12	4.8	34.	83.	5.3	36.	85.
13	4.6	33.	83.	5.2	36.	85.
14	4.5	32.	82.	5.2	35.	84.
15	4.4	31.	82.	5.1	35.	84.
16	4.3	30.	81.	4.9	34.	84.
17	3.8	28.	80.	4.7	33.	83.
18	3.5	26.	78.	4.4	31.	82.
19	3.1	24.	76.	4.0	29.	81.
20	2.7	22.	74.	3.6	27.	79.
21	2.4	20.	71.	3.2	25.	77.
22	2.1	18.	68.	2.8	22.	74.
23	1.8	16.	65.	2.4	20.	71.
24	1.6	14.	61.	2.1	18.	68.
25	1.4	12.	58.	1.8	16.	65.
26	1.3	11.	56.	1.7	15.	63.
27	1.2	11.	55.	1.6	14.	62.
28	1.2	11.	55.	1.6	14.	63.
29	1.2	11.	55.	1.7	14.	63.
30	1.2	11.	54.	1.7	14.	63.
31	1.2	11.	54.	1.7	15.	63.
32	1.1	10.	54.	1.7	15.	63.
33	1.1	10.	53.	1.7	15.	63.
34	1.1	10.	53.	1.7	15.	64.
35	1.1	9.9	52.	1.7	15.	64.
36	1.1	9.7	52.	1.7	15.	64.
37	1.0	9.6	51.	1.7	15.	64.
38	1.0	9.4	51.	1.7	15.	64.
39	1.0	9.3	50.	1.7	15.	64.
40	1.0	9.2	50.	1.7	15.	64.

Table PC-12 (Continued). Thyroid Cancer 10 or More Years After Exposure to Low-LET Radiation, by Age A_1 at Exposure, Sex, and Dose in Rad. PC in Percent, to Two Significant Digits or Three Decimal Places.

A_1	Sex					
	Male			Female		
	Dose					
	1	10	100	1	10	100
41	.98	9.0	50.	1.7	15.	64.
42	.97	8.9	50.	1.7	15.	64.
43	.96	8.9	49.	1.7	15.	64.
44	.95	8.8	49.	1.7	15.	64.
45	.94	8.7	49.	1.7	15.	64.
46	.93	8.6	48.	1.7	15.	64.
47	.91	8.4	48.	1.7	15.	64.
48	.89	8.3	47.	1.7	15.	63.
49	.88	8.1	47.	1.7	15.	63.
50	.86	8.0	46.	1.7	15.	63.
51	.84	7.8	46.	1.7	15.	63.
52	.82	7.7	45.	1.7	14.	63.
53	.81	7.5	45.	1.7	14.	63.
54	.79	7.4	44.	1.6	14.	63.
55	.78	7.3	44.	1.6	14.	63.
56	.77	7.2	44.	1.6	14.	62.
57	.75	7.1	43.	1.6	14.	62.
58	.75	7.1	43.	1.6	14.	62.
59	.75	7.0	43.	1.6	14.	62.
60	.75	7.0	43.	1.6	14.	62.
61	.74	7.0	43.	1.6	14.	62.
62	.74	6.9	43.	1.6	14.	62.
63	.73	6.9	42.	1.6	14.	62.
64	.73	6.8	42.	1.6	14.	62.
65	.72	6.8	42.	1.6	14.	62.
66	.72	6.7	42.	1.6	14.	62.
67	.71	6.7	42.	1.6	14.	62.
68	.71	6.7	42.	1.6	14.	62.
69	.71	6.6	42.	1.7	14.	63.
70	.71	6.7	42.	1.7	14.	63.
71	.71	6.7	42.	1.7	14.	63.
72	.72	6.8	42.	1.6	14.	63.
73	.74	6.9	43.	1.6	14.	63.
74	.76	7.1	43.	1.6	14.	62.
75	.78	7.3	44.	1.6	14.	62.

APPENDIX II - STATUS OF FINAL REPORT OF THE WORKING GROUP IN RELATION
TO THE RECOMMENDATIONS OF THE NATIONAL ACADEMY OF SCIENCES (NAS)
OVERSIGHT COMMITTEE ON AN EARLIER DRAFT (JULY, 1984)

The NIH Working Group has been in close communication with the NAS Oversight Committee throughout the period during which the Radioepidemiological Tables have been in preparation. In consequence, many of the recommendations made by the Oversight Committee on the July draft have been followed in the preparation of the final draft. Others, of course, look to the future and counsel any future group that may have the task of preparing revisions. In what follows, the NAS recommendations are first reproduced individually and a statement is provided to show how that topic has been handled in the final report.

1. "The Oversight Committee recommends that the Working Group prominently indicate that the doses used in the tables are absorbed doses in organs and that use of other radiation measures, such as kerma or instrument readings, in calculating assigned shares will result in errors."

The final report should make it clear that the dose to be used for each site is the absorbed dose. Chapters IV, V, VI, and IX, in which the methodology is outlined, all refer to dose as "absorbed", "tissue", or "organ" dose, and in Chapter X the PC calculation for each site is given in terms of absorbed dose.

2. "The Oversight Committee recommends that the Working Group consider other ways of defining the category of "leukemia excluding CLL" (chronic lymphocytic leukemia)-- for example, ways that would exclude cases that should be diagnosed as CLL but are not."

The Working Group's definition of a disease that included all types of leukemia other than chronic lymphocytic leukemia (CLL) was based on the previous use of this definition by the BEIR III Committee and on the fact that CLL is the only major type of leukemia that has not been observed to increase in incidence in irradiated human populations. It is true, as stated by the Oversight Committee, that this definition can result in the inclusion of cases of CLL that are not diagnosed as such. However, no classification can protect entirely against misdiagnosis. To define the category by inclusion rather than exclusion based on current diagnostic criteria would require re-analysis of all the leukemia case material from the A-bomb survivors, ankylosing spondylitics, Thorotrast patients and other series, which is probably not feasible.

3. "The Oversight Committee recommends that the decision of whether to include specific sites of cancer in the radioepidemiologic tables be based, to the extent possible, on an evaluation of the reliability of the estimates of assigned share, rather than on a subjective judgment preceding the data analysis."

It may well be that all tissues in which cancers arise are susceptible to the carcinogenic effect of ionizing radiation, but this has not been shown. The Working Group employed three criteria in selecting sites:

- (1) The available evidence indicates that cancers of the site in question may be caused by ionizing radiation;
- (2) There are risk coefficients of sufficient specificity as to age and sex to permit the calculation of PC tables; and
- (3) The risk coefficients have sufficient stability to warrant the calculation of PC estimates.

4. "The Oversight Committee recommends that, in compiling assigned shares in the future, greater use be made of original radioepidemiologic data, including the latest updates available, and that correspondingly less use be made of derived risk coefficients, such as those from the BEIR III report."

The Working Group agrees that future revisions of the Tables should include original risk estimates from the latest available data and notes that a somewhat larger committee operating in a longer time frame would be desirable. However, care should be taken to avoid unnecessary duplication between a future committee's work and that of a new BEIR committee of the NAS.

5. "The Oversight Committee recommends that the use of mortality data be considered for improving the understanding of the baseline incidence data and for identifying the uncertainties in the trends for those data."

The Working Group examined mortality trends over time and included in Chapter VII-C remarks concerning the several sites for which such trends are most important.

6. "The Oversight Committee recommends that the Working Group explain in greater detail the consequences of different time-projection models. Different models not only distribute observed cancer risks differently over the period of observation, but also lead to different estimates or risk for longer periods after exposure. The best choice of model is still uncertain, and the users of the tables should understand their limitations."

The Working Group agrees with the Oversight Committee that the choice of a time-projection or time-to-tumor model can have profound implications for PC, or assigned share, calculations. Many pages of text have been devoted to this topic in Chapters III, V and VII, in addition to text and tables in the site-specific sections of Chapter X. Much discussion has been devoted to the fitting of lognormal time-to-tumor distributions to data for bone cancer and leukemia, and to the choice of the constant relative risk model for the other cancer sites treated. The latter choice was based on the plausibility of the model in the context of a multi-stage hypothesis for radiation carcinogenesis, in which

radiation acts at an early stage, and on analyses of data for breast, lung, and stomach cancer. For those sites, the constant relative risk model fits well. The extension of the model to other sites receives support from analyses by Kato and Schull (4, Chapter V) showing that the relative risk for all cancers other than leukemia, considered as a group, varies little over time, within age-at-exposure cohorts. Also, Darby's analyses in parallel of mortality data from the A-bomb survivor and British spondylitic series (18, Chapter V) indicates that the model holds for the group of sites heavily irradiated in the latter series. Only for thyroid cancer is there reason to believe that relative risk may vary over time; this variation may, however, merely reflect unusually thorough ascertainment in irradiated populations thought to be at elevated risk.

7. "The Oversight Committee recommends that the Working Group provide explicit guidance on projecting risks beyond the period of observed data-- e.g., how to estimate an assigned share for a person whose cancer occurs more than 35 years after exposure--or else provide an explicit statement that it cannot now be done."

The tables for leukemia and bone cancer have been carried out to 49 years, but for other sites, where the relative risk time distribution model is employed, the tables permit PC's to be estimated for any period following exposure. The user is informed as to the specific period of observation on which the underlying data for other sites are based and alerted to the additional uncertainty attending PC estimates for longer periods.

8. "The Oversight Committee recommends that full consideration be given to the possibility of reanalyzing the available statistics on excess cancer to model their time dependence without any specific assumptions about period of latency, rather than assuming a fixed minimal latent period and a prescribed form for the hazard function."

(See comment following 9 below.)

9. "The Oversight Committee recommends that, if analyses like those described in Recommendation 8 prove ineffective, consideration be given to allowing different minimal latency periods and different periods during which relative risks increase, for each specific type of cancer and age at exposure."

Minimal latent period is very difficult to investigate except when the relative excess risk is extremely high, as for bone sarcoma in patients exposed to radium-224. Another complication is that, for example in the case of breast cancer among women exposed at young ages, it would be possible for the true relative risk to be fairly high at ages of very low baseline risk, without any cancers being observed even in a large sample. The approaches recommended by the Oversight Committee are in fact no different from what actually has been

done; the discussion by the Working Group reflects the fact that these approaches seldom are successful.

10. "The Oversight Committee recommends that the assumption of constant relative risks be reassessed as new data and new methods of analysis appear."

This is for the future, but the Working Group endorses the recommendation.

11. "The Oversight Committee recommends that the method for projecting relative risk estimates among populations be reconsidered when the tables are next revised."

This is for the future, but the Working Group endorses the recommendation.

12. "The Oversight Committee recommends that each revision of the tables include a fresh appraisal of the relationship between cancer risks and radiation dose and dose rate, allowing different responses under different conditions for different tumor types."

This also is for the future, but scarcity of human data may always force reliance on experimental results with animal models.

13. "The Oversight Committee recommends that the Working Group further justify its decision on how to apply quality factors in calculating assigned shares for various high-LET radiations."

(See comment following 14 below.)

14. "The Oversight Committee recommends that a method for estimating assigned shares for persons exposed to high-LET radiation be developed that does not depend so heavily on the estimates for low-LET radiation."

In the final report, the Working Group has abandoned the use of quality factors (Q) for estimating the cancer risk from high-LET radiation. In the narrowest sense, Q for a given type of radiation may be viewed as a somewhat arbitrarily selected constant "relative biological effectiveness" (RBE) factor. The use of Q makes sense from a radiation protection standpoint, in that it enables one to express doses of radiation of different qualities on a common scale (dose equivalent in rem). In reality, the RBE of a given radiation varies with the end point studied, the energy (and hence the LET) of the radiation at the target site, the total dose and in many cases the dose rate. Therefore, it is not possible to assign a single RBE value for a given type of high-LET radiation, say, fast neutrons. For internal emitters (deposited radionuclides), dosimetry is further complicated by variations in spatial and temporal distributions of the radiation sources within the target tissues. For these reasons, the Working Group has limited its consideration of high-LET radiation to cases where data from direct observations exist, i.e., exposures of bone to radium-224 (in which case the alpha-radiation dose is measured in rad) and exposure of lung to radon daughters (radiation exposure in working level months, WLM).

15. "The Oversight Committee recommends that the current assumptions about the relationships between radiation and smoking be reviewed as new information on both low- and high-LET exposures accumulates."

The human data on the interaction between smoking and radiation leave much to be desired and the Working Group can only endorse this recommendation.

16. "The Oversight Committee recommends that the Working Group provide sufficient further documentation of its approach to handling dose rate for the calculations to be reproduced independently. Graphic displays showing the distribution of dose over time may be useful."

The handling of dose-rate effect has been discussed in Chapter V, Section B. Specific examples are provided in Chapter IX, Example 5, and in examples for the specific sites in Chapter X.

17. "The Oversight Committee recommends investigation of the possibility of modeling the response to radiation to include a variable for dose rate as well as dose, age at exposure, and age at diagnosis, with a smooth variation in response to changes in any variable."

The Oversight Committee's recommendation suggests that there is some intrinsic advantage in using smooth models to analyze data as opposed to smoothing estimates derived from partitioned data. This seems debatable in the absence of theoretical models specifying the dependence of risk on various factors used to define the partition. Such models do exist for dose response, and the Working Group's calculations and those of the BEIR Committee incorporate them. Such models do not exist for the effect of age at exposure, on the other hand, and it seems reasonable to base the method of smoothing, if any is to be employed, at least partly on the way in which risk is observed to vary with exposure age.

18. "The Oversight Committee recommends that the Working Group discuss in detail the methods, data, assumptions, and calculations that need to be made to estimate assigned shares for radiation as a cause of cancer. Such a discussion would be useful to the users, as well as in the production of improved versions of the tables."

The Working Group believes that it has performed this necessary task in a way that will aid in the use as well as the revision of the tables.

19. "The Oversight Committee recommends that, before the Working Group disbands, it document completely the derivation of the factors used in the calculation of an assigned share."

The Working Group believes that it has provided adequate documentation.

20. "The Oversight Committee recommends that a well-documented set of computer programs be developed to facilitate both tabulation of the

factors used in the formulas and unambiguous application of the assigned-share formulas."

The Working Group has prepared a documented version of the programs used in its calculations. There should be little difficulty in adapting these programs, which are written in MLAB, to other programming languages.

21. "The Oversight Committee recommends that an alternative expression be considered for 'probability of causation,' such as 'assigned share,' that more accurately reflects what is being estimated."

The Working Group preferred to use the language of the enabling Orphan Drug Act.

22. "The Oversight Committee recommends that the possibility of using a different partition of the populations be kept in mind when new versions of the tables are being produced, to be consistent with relevant newly available information."

This recommendation also is for the future and one the Working Group can endorse.

23. "The Oversight Committee recommends that the available radioepidemiologic data be analyzed with techniques that exploit the inherent smoothness of the relevant biologic processes."

See response to recommendation no. 17.

24. "The Oversight Committee recommends that the Working Group conduct a quantitative appraisal, such as a sensitivity analysis, to evaluate the uncertainties in the assumptions, data, and methods used in constructing the tables; their influence on the reliability of the tables of assigned shares; and their implications for possible uses of the tables."

The Working Group has included a discussion of the elements that contribute to uncertainty in Chapter VII. A quantitative analysis of the influence of these elements on the reliability of the estimates of the tables of Probability of Causation has been included as Chapter VII, Section O.

25. "The Oversight Committee recommends that the tables of assigned shares be updated promptly after the revised atomic-bomb dosimetry is released, with cancer data through 1982 or later if available and analysis with improved techniques if possible."

In Chapter VIII the Working Group has taken this position.

APPENDIX III - GLOSSARY

Absolute risk -

an expression of excess risk based on the assumption that the excess risk from radiation exposure adds to the underlying (baseline) risk, by a constant increment dependent on dose; an absolute risk time-response model distributes the radiogenic risk after exposure independently of the underlying natural risk.

Additive interaction model (AIM) -

the assumption that the total excess risk from exposures to radiation and to another risk factor is equal to the sum of the excess risks from the two taken separately.

Alpha particle -

a charged particle emitted from certain unstable atomic nuclei (radioactive elements), having the physical characteristics of a helium nucleus (mass 4, charge 2+).

Ankylosing spondylitis -

arthritis of the spine.

Assigned share -

a number that expresses the probability that a given cancer is caused by a previous exposure to a carcinogenic agent, such as radiation; here synonymous with "probability of causation" (PC).

Ataxia telangiectasia (AT)

an inherited disorder associated with an increased risk of cancer, lymphoma in particular, and characterized by immunologic, chromosomal, and DNA defects.

ATB -

at the time of the bomb; referring to the dropping of the atomic bombs at Hiroshima and Nagasaki in 1945.

Background radiation -

the amount of radiation to which a member of the population is exposed from natural sources, such as terrestrial radiation from naturally occurring radionuclides in the soil, cosmic radiation originating in outer space, and naturally occurring radionuclides deposited in the human body. The natural background radiation received by an individual depends on geographic location and living habits. In the U.S., the background radiation is on the order of 100-200 mrem per year.

Baseline rate -

the cancer experience observed in a population in the absence of the specific agent being studied; the baseline rate might, however, include cancers from a number of other causes, such as smoking, background radiation, etc. The Working Group has used data from the SEER program (see this) as baseline rates for the present report.

BEIR III -

refers to the third National Academy of Sciences' Committee on Biological Effects of Ionizing Radiation, as well as to the report published by this committee in 1980; the 1972 BEIR I report was also used by the Working Group.

Beta particle -

a charged particle emitted from the nucleus of certain unstable atomic nuclei (radioactive elements), having the charge (+ 1 or -1) and mass of an electron.

Biologically equivalent dose (BED) -

for a given dose and quality of radiation, and for a given cancer site, the BED is the dose of 250 kVp X rays required to produce the same increase in cancer risk.

Cancer -

a malignant tumor of potentially unlimited growth, capable of invading surrounding tissue or spreading to other parts of the body by metastasis.

Carcinogen -

an agent that may cause cancer. Ionizing radiations are physical carcinogens; there are also chemical and biologic carcinogens and biologic carcinogens may be external (e.g., viruses) or internal (genetic defects).

Carcinoma -

a malignant tumor (cancer) of epithelial origin.

Case-control study -

an epidemiological study in which people with disease are compared with a similarly composed group of people without disease and the histories of exposures to a putative causative agent are compared.

Cohort study -

or follow-up study; an epidemiological study in which groups of people are identified with respect to the presence or absence of exposure to a disease-causing agent and the outcomes in terms of disease rates are compared.

Confidence interval -

an interval estimate of a statistical parameter, obtained as a particular function of observed values of one or more random variables whose joint distribution depends upon that parameter. The interval-valued function is so defined that, in an infinitely increasing number of independent replications of the experiment yielding the observed values of the random variables, the proportion of times that the interval contains the (unknown) parameter value converges to a number at least as large as some preset value, called the confidence level of the interval.

Credibility interval -

an analogue of confidence interval, in terms of subjective probability. If one's information about the true value of an unknown parameter can be summarized by a probability distribution for that value, a credibility interval of a given probability level for the parameter is an interval such that the subjective probability distribution, integrated over the interval, is not less than the given probability level.

Crossover dose -

that value of the radiation dose for which the contributions of the linear and quadratic components of the linear-quadratic dose-response function are equal. A crossover dose of zero corresponds to a pure quadratic dose-effect function, and an infinite crossover dose corresponds to a pure linear dose-effect function.

DNA -

deoxyribonucleic acid; the genetic material of cells.

Dose = absorbed radiation dose -

see: rad.

Dose-effect (dose-response) model -

a mathematical formulation of the way in which the effect, or response, depends on dose.

Dose equivalent -

a quantity that expresses all radiations on a common scale for calculating the effective absorbed dose. Dose equivalent is defined as the product of the absorbed dose in rad and certain modifying factors (the most important being the so-called quality factor, Q) and is expressed in units of "rem" (see this).

Dose rate -

the quantity of absorbed dose delivered per unit time.

Epidemiology -

the study of the determinants of the frequency of disease in man. The two main types of epidemiological studies of chronic disease are cohort (or follow-up) studies and case-control (or retrospective) studies.

Etiology -

the science or description of cause(s) of disease.

Fallout -

radioactive debris from a nuclear detonation or other source, usually deposited from air-borne particulates.

Fluoroscopy -

a method of visualizing internal structures by directing X rays through an object (e.g., part of the body) onto a fluorescent screen.

Fractionation -

the delivery of a given total dose of radiation as several smaller doses, separated by intervals of time.

Gamma radiation -

also gamma rays; short wavelength electromagnetic radiation of nuclear origin, similar to X rays but usually of higher energy (10 keV to 9 MeV).

Geometric mean -

the geometric mean of a set of positive numbers is the exponential of the arithmetic mean of their logarithms. The geometric mean of a lognormal distribution is the exponential of the mean of the associated normal distribution.

Geometric standard deviation (GSD) -

the geometric standard deviation of a lognormal distribution is the exponential of the standard deviation of the associated normal distribution. The geometric standard deviation is not standard for statistical terminology but is more commonly used by physicists.

Half-life -

(physical); the time required for a radioactive element to lose 50% of its activity by decay.

High-LET radiation -

radiation producing high ionization density along its track; includes neutrons, protons, alpha particles, and the charged nuclei of higher atomic-weight elements (see LET).

ICDA -

the International Classification of Diseases Adapted for use in the U.S. The ICD is periodically revised by the World Health Organization; the 8th ICDA is adapted from the 8th ICD and was issued in 1972.

ICRP -

International Commission on Radiological Protection.

Incidence -

or incidence rate; the rate of occurrence of a disease within a specified period of time, often expressed as number of cases per 100,000 individuals per year.

In utero -

in the womb, i.e., before birth.

In vitro -

(literally, in glass), in culture or in the test-tube (as opposed to in vivo, in the living individual).

In vivo -

in the living individual.

Ionizing radiation -

radiation sufficiently energetic to dislodge electrons from an atom. Ionizing radiation includes X and gamma radiation, electrons (beta radiation), alpha particles (helium nuclei), and heavier charged atomic nuclei. Neutrons ionize indirectly by colliding with atomic nuclei.

Kerma -

Kinetic Energy Released in Material. A unit of exposure, expressed in rad, that represents the kinetic energy transferred to charged particles per unit mass of irradiated medium when indirectly ionizing (uncharged) particles, such as photons or neutrons, traverse the medium.

kVp -

"kilovolt peak", a measure of the energy of the X-ray tube-voltage and hence of the maximum energy of the X-ray photons produced.

Latent period -

also time to response, induction period; the period of seeming inactivity between the time of exposure of a tissue to an injurious agent (e.g., radiation) and observed response (e.g., diagnosis of cancer).

LET = linear energy transfer -

a measure of ionization density of a given radiation. LET is the average loss in energy per unit length of path of the incident radiation. See high-LET and low-LET radiation.

Linear energy transfer

see LET.

Life Span Study -

see LSS.

Life Table -

a table showing the number of persons who, of a given number born or living at a specified age, live to attain successive higher ages, together with the numbers who die in the intervals.

Linear (L) model -

also, linear dose-effect relationship; expresses the effect (e.g., mutation or cancer) as a direct (linear) function of dose.

Linear-quadratic (LQ) model -

also, linear-quadratic dose-effect relationship; expresses the effect (e.g., mutation or cancer) as partly directly proportional to the dose (linear term) and partly proportional to the square of the dose (quadratic term). The linear term will predominate at lower doses, the quadratic term at higher doses (see crossover dose).

Lognormal distribution -

if the logarithms of a set of values are distributed according to a normal distribution they are said to have a lognormal distribution, or be distributed "lognormally."

Low-LET radiation -

radiation producing low ionization density, such as X and gamma radiation, and accelerated electrons (see LET).

LSS -

Life Span Study, refers to the study of a population of Japanese atomic-bomb survivors selected for lifetime follow-up study.

Millirad (mrad) -

1/1000 of a "rad."

Millirem

1/1000 of a "rem."

Mortality (rate) -

the rate at which people die from a disease, e.g., a specific type of cancer, often expressed as number of deaths per 100,000 per year.

Multiplicative interaction model (MIM) -

the assumption that the relative risk (= the relative excess risk plus one) resulting from the exposure to two risk factors is the product of the relative risks from the two factors taken separately.

NAS -

National Academy of Sciences.

NCRP -

National Council on Radiation Protection and Measurements.

Neutron -

uncharged subatomic particle capable of producing free radicals in matter by indirect ionization.

Normal distribution -

a random variable X is said to be normally distributed if, for some number μ and some positive number σ , $Y = (X - \mu)/\sigma$ has a standard normal distribution with probability density function

$$\phi(y) = (2\pi)^{-1/2} \exp(-y^2/2).$$

NRC -

National Research Council (in this report); a unit of the NAS.

PC = probability of causation -

a number that expresses the probability that a given cancer, in a specific tissue, has been caused by a previous exposure to a carcinogenic agent, such as radiation; essentially synonymous with "assigned share."

Probability of causation -

see PC.

Projection model -

a mathematical model that simultaneously describes the excess cancer

risk at different levels of some factor such as dose, time after exposure, or baseline level of risk, in terms of a parametric function of that factor. It becomes a projection model when data in a particular range of factor values are used to assign values to the parameters in order to estimate (or project) excess risk for factor values outside that range.

Promoter -

an agent which is not by itself carcinogenic, but which can amplify the effect of a true carcinogen by increasing the probability of late-stage cellular changes needed to complete the carcinogenic process.

Protraction -

the spreading out of a radiation dose over time by continuous delivery at a lower dose rate.

PY = person-years -

a unit used in epidemiological analyses, obtained by adding the numbers of years of observation for all members of the group studied. The number of PY may be used to predict the number of baseline cancers expected in the population group studied.

Quality factor -

also QF or Q, the LET-dependent factor by which absorbed doses are multiplied to obtain (for radiation protection purposes) a quantity that expresses the effectiveness of an absorbed dose on a common scale for all kinds of ionizing radiations. X rays at 250 kVp are usually used as reference radiation ($Q = 1$).

Rad -

unit of absorbed dose of ionizing radiation = 100 erg/g mass; a newer unit of absorbed radiation dose is the gray (Gy): 1 gray = 1 joule absorbed energy per kg mass; thus 1 gray = 100 rad. (Average background radiation in the U.S. is on the order of 0.1 - 0.2 rad annually.)

Radiation quality -

a general term referring to the spatial distribution of absorbed dose in extremely small volumes of target tissue. For example, an exposure to neutron radiation may be quantitatively the same as an exposure to gamma ray, in the sense that, for volumes of tissue on the order of one cubic centimeter, the absorbed energy is the same. Yet at resolutions of a few microns the ionizing events will be more uniformly dispersed for the gamma ray radiation than for the neutron radiation (see LET), producing quantitatively different biological effects (see (RBE)).

Radiogenic -

caused by radiation.

Radionuclide -

a radioactive atomic species.

Radon daughters -

(radioactive) decay products from the radioactive gas, radon (itself a decay product from radium).

RBE = relative biologic effectiveness -

a factor used in comparing ionizing radiation of different types, generally by measuring the effectiveness relative to 250 kVp X radiation. For a given dose of given type of radiation, the RBE is the ratio of the dose of 250-kVp X rays to the dose of the given radiation that will produce the same biological effect. For a given type of radiation, RBE varies with the energy, the magnitude of the dose, and with the end point studied.

Relative risk -

an expression of excess risk relative to the underlying (baseline) risk; if the excess equals the baseline risk the relative risk is 2.

Rem -

(rad equivalent, man); unit of dose equivalent. The dose equivalent in "rem" is numerically equal to the absorbed dose in "rad" multiplied by the "quality factor" (see this), the distribution factor and any other necessary modifying factor.

RERF -

Radiation Effects Research Foundation; a Japanese foundation chartered by the Japanese Welfare Ministry under an agreement between the U.S.A and Japan. The RERF is the successor to the ABCC (Atomic Bomb Casualty Commission).

Risk coefficient -

a fitted constant in an equation that describes how an effect depends on dose.

Sarcoma -

a malignant growth arising in tissue of mesodermal origin (connective tissue, bone, cartilage or striated muscle).

SEER program -

Surveillance, Epidemiology and End Results, a nationwide system of population-based cancer registries supported by the National Cancer Institute to provide systematic cancer incidence data for the U.S. Approximately 10 percent of the U.S. population is covered; data for 1973-1977 are published, data are otherwise available through 1981. (The Working Group has used SEER data for base-line cancer incidence rates in the present report.)

Stochastic -

a stochastic process is one in which the system incorporates an element of randomness, as opposed to a deterministic system. As used in this report (following ICRP), stochastic effects are those in which the probability of an effect occurring rather than its severity is a function of dose, without threshold.

Thorotrast -

a contrast agent used earlier (1928-1955) for X ray diagnostic procedures; Thorotrast contains radioactive thorium-232 dioxide.

Threshold (dose) -

a specified level of dose below which, it is assumed, no radiation injury of a specified type occurs.

Time-response model -

a mathematical model expressing the conditional probability distribution of the time from exposure to a carcinogen until diagnosis of a cancer caused by that exposure.

Tinea capitis -

ringworm of the scalp.

UNSCEAR -

United Nations Scientific Committee on the Effects of Atomic Radiation; publishes periodic reports on sources and effects of ionizing radiation.

WL = Working Level -

any combination of short-lived radon daughters in one liter of air that will result in the ultimate emission of 1.3×10^5 MeV of potential alpha particle energy.

WLM = Working Level Month

exposure resulting from the inhalation of air with a concentration of 1 WL of radon daughter for 170 working hours. One WLM corresponds to a dose of approximately 6 rem.

X radiation -

also X rays; penetrating electromagnetic radiation, usually produced by bombarding a metallic target with fast electrons in a high vacuum.

Xeroderma pigmentosum (XP) -

an inherited disease in which skin cells are highly susceptible to sun-induced cancer; XP cells have a defect in DNA repair after ultraviolet irradiation which apparently accounts for the propensity for this neoplasm.

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