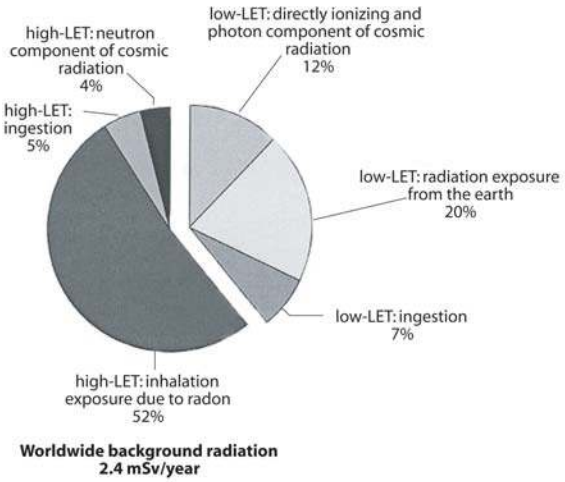
BEIR VII: HEALTH RISKS FROM EXPOSURE TO LOW LEVELS OF IONIZING RADIATION

BEIR VII develops the most up-to-date and comprehensive risk estimates for cancer and other health effects from exposure to low-level ionizing radiation. It is among the first reports of its kind to include detailed estimates for cancer incidence in addition to cancer mortality. In general, BEIR VII supports previously reported risk estimates for cancer and leukemia, but the availability of new and more extensive data have strengthened confidence in these estimates. A comprehensive review of available biological and biophysical data supports a "linear-no-threshold" (LNT) risk model—that the risk of cancer proceeds in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans.

This report is the seventh in a series of publications from the National Academies concerning radiation health effects called the Biologic Effects of Ionizing Radiation (BEIR) reports. BEIR VII focuses on the health effects of low levels of low linear energy transfer (low-LET) ionizing radiation such as x-rays and gamma rays. The most recent BEIR report to address low level low-LET radiation was the BEIR V report published in 1990. Humans are exposed to ionizing radiation from both natural and man-made sources (see Figure 1). Very high doses can produce damaging effects in tissues that can be evident within days after exposure. Late effects such as cancer, which can occur after more modest doses including the low-dose exposures that are the subject of this report, may take many years to develop.

Most radiation sources have a mixture of high- and low-LET radiation. Compared to high-LET radiation, low-LET radiation deposits less energy in the cell along the radiation path and is considered less destructive per radiation track. The BEIR VII report defines low doses as those in the range of near zero up to about 100 mSv (0.1 Sv) of low-LET radiation. People in the United States are exposed to average annual background radiation levels of about 3 mSv; exposure from a chest X-ray is about 0.1 mSv and exposure from a whole body computerized tomography (CT) scan is about 10 mSv.

There are many challenges associated with understanding the health effects of low doses of low-LET radiation, but current knowledge allows several conclusions. The BEIR VII report concludes that the current scientific evidence is consistent with the hypothesis that, at the low doses of interest in this report, there is a linear dose-response relationship between exposure to ionizing radiation and the development of



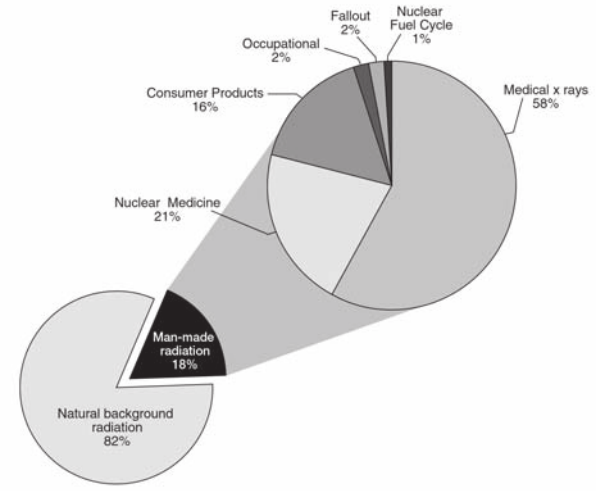


Figure 1. The chart on the left shows the sources of global "background" radiation of both high- and low-LET radiation. The figure at right shows the relative contributions of the various types of man-made radiation to the US population.[1] Medical x rays and nuclear medicine account for about 79% of the man-made radiation exposure in the United States. Substances in consumer products such as tobacco, the domestic water supply, building materials, and to a lesser extent, smoke detectors, televisions, and computer screens, account for another 16%. Occupational exposures, fallout, and the nuclear fuel cycle comprise about 5% of the man-made component.

[1]Figures based on data from Ionizing Radiation Exposure of the Population of the United States, National Council on Radiation Protection and Measurements, No.93, 1987.

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solid cancers in humans. It is unlikely that there is a threshold below which cancers are not induced, but at low doses the number of radiation-induced cancers will be small. Other health effects (such as heart disease and stroke) occur at higher radiation doses, but additional data must be gathered before an assessment of any possible dose response can be made between low doses of radiation and non-cancer health effects. The report also concludes that with low dose or chronic exposures to low-LET irradiation, the risk of adverse heritable health effects to children conceived after their parents have been exposed is very small compared to baseline frequencies of genetic diseases in the population.

Radiation Exposure and Health Effects

The mechanisms that lead to adverse health effects after ionizing radiation exposure are not fully understood. Ionizing radiation has sufficient energy to change the structure of molecules, including DNA, within the cells of the body. Some of these molecular changes are so complex that it may be difficult for the body's repair mechanisms to mend them correctly. However, the evidence is that only a small fraction of such changes would be expected to result in cancer or other health effects.

The most thoroughly studied individuals for the evaluation of health effects of ionizing radiation are the survivors of the Hiroshima and Nagasaki atomic bombings, a large population that includes all ages and both sexes. The Radiation Effects Research Foundation (RERF) in Japan has conducted follow-up studies on these survivors for more than 50 years. An important finding from these studies is that the occurrence of solid cancers increases in proportion to radiation dose. More than 60% of exposed survivors received a dose of radiation of less than 100 mSv (the definition of low dose used by the BEIR VII report).

Risk Models for Cancer

An important task of the BEIR VII committee was to develop "risk models" for estimating the risk that an exposed individual will develop cancer. This task requires expressing the dependence of risk on radiation dose and also on sex and age at exposure. Data from epidemiologic studies were used to accomplish this task. The Japanese atomic bomb survivors were the primary source of data for estimating risks of most solid cancers and leukemia. For 2 of the 11 specific cancers evaluated, breast and thyroid cancer, atomic bomb survivor data were combined with data on medically exposed persons to estimate risks. Data from additional medical studies and from studies of nuclear workers were evaluated and found to be compatible with BEIR VII models.

Since the publication of BEIR V in 1990, more comprehensive data on cancer incidence (including non-fatal diseases) in atomic bomb survivors have become available, mortality follow-up has been extended for 15 years nearly doubling the number of deaths from solid cancer, and an improved dosimetry system (DS02) has been implemented. In addition, new data have become available from studies of persons exposed to radiation for medical reasons and from studies of nuclear workers exposed at low doses and dose rates. These developments have strengthened the epidemiologic data that are used to develop risk estimates. Box 1 lists some of the new epidemiologic information and approaches that have become available since BEIR V.

On average, assuming a sex and age distribution similar to that of the entire U.S. population, the BEIR VII lifetime risk model predicts that approximately one

Box 1. New epidemiologic information and approaches used in BEIR VII risk models

1) The information available from epidemiologic studies has been greatly increased.
   a. For the A-bomb survivors, cancer incidence data from the Hiroshima and Nagasaki tumor registries have become available (13,000 cases of solid cancer), and the number of solid cancer deaths available for analysis has nearly doubled (10,000 deaths).
   b. There are new data from many studies of persons exposed for medical reasons. These data have been incorporated in estimating risks of female breast cancer and thyroid cancer.
   c. There are new data from studies of nuclear workers exposed at low doses and dose rates, including results of analyses that combine data from many studies. These data were evaluated and found to be compatible with BEIR VII risk estimates.
2) BEIR VII provides estimates of both cancer incidence (including non-fatal cancer) and cancer mortality, whereas previous reports focused on mortality data.
3) The availability of cancer incidence data on A-bomb survivors has made it possible to develop estimates for eleven specific cancer sites.
4) The newly implemented DS02 dosimetry system for A-bomb survivors provides a more accurate basis for evaluating the dependence of risk on dose.

individual in 100 persons would be expected to develop cancer (solid cancer or leukemia) from a dose of 100 mSv while approximately 42 of the 100 individuals would be expected to develop solid cancer or leukemia from other causes (see Figure 2). Lower doses would produce proportionally lower risks. For example, it is predicted that approximately one individual in 1000 would develop cancer from an exposure to 10 mSv. Table 1 shows BEIR VII's best estimates of the lifetime attributable risk (LAR) of incidence and mortality for all solid cancers and for leukemia per 100,000 persons exposed to 100 mSv. The report also provides estimates for cancers of several specific sites.

Risk Estimates at Very Low Doses

At doses of 100 mSv or less, statistical limitations make it difficult to evaluate cancer risk in humans. A comprehensive review of available biological and biophysical data led the committee to conclude that the risk would continue in a linear fashion at lower doses without a threshold and that the smallest dose has the potential to cause a small increase in risk to humans.[3] This assumption is termed the "linear-no-threshold" (LNT) model.

There are two competing hypotheses to the linear no-threshold model. One is that low doses of radiation are more harmful than a linear, no-threshold model of effects would suggest. BEIR VII finds that the radiation health effects research, taken as a whole, does not support this hypothesis. The other hypothesis suggests that risks are smaller than predicted by the linear no-threshold model are nonexistent, or that low doses of radiation may even be beneficial. The report concludes that the preponderance of information indicates that there will be some risk, even at low doses, although the risk is small.

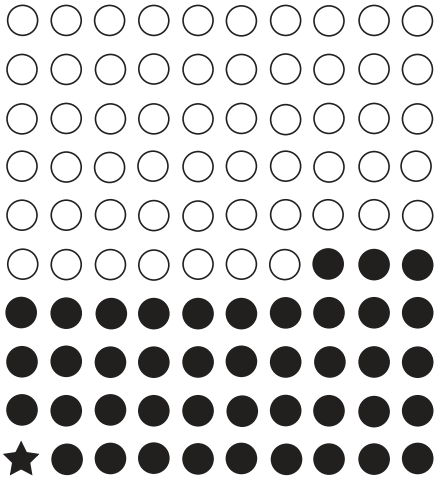

Figure 2. In a lifetime, approximately 42 (solid circles) of 100 people will be diagnosed with cancer[2] from causes unrelated to radiation. The calculations in this report suggest approximately one cancer (star) in 100 people could result from a single exposure 100 mSv of low-LET radiation.

Health Effects Other than Cancer

Radiation exposure has been demonstrated to increase the risk of diseases other than cancer, particularly cardiovascular disease, in persons exposed to high therapeutic doses and also in A-bomb survivors exposed to more modest doses. However, there is no direct evidence of increased risk of non-cancer diseases at low doses, and data are inadequate to quantify this risk if it exists. Radiation exposure has also been shown to increase risks of some benign tumors, but data are inadequate to quantify this risk.

	All solid cancer		**Leukemia**	
	Males	Females	Males	Females
Excess cases (including non-fatal cases) from exposure to 100 mSv	800 (400–1600)	1300 (690–2500)	100 (30–300)	70 (20–250)
Number of cases in the absence of exposure	45,500	36,900	830	590
Excess deaths from exposure to 100 mSv	410 (200–830)	610 (300–1200)	70 (20–220)	50 (10–190)
Number of deaths in the absence of exposure	22,100	17,500	710	530

Table 1. The table shows the estimated number of cancer cases and deaths expected to result in 100,000 persons (with an age distribution similar to that of the entire U.S. population) exposed to 100 mSv. The estimates are accompanied by 95% subjective confidence intervals shown in parentheses that reflect the most important uncertainty sources including statistical variation, uncertainty in adjusting risk for exposure at low doses and dose rates, and uncertainty in the method of transporting data from a Japanese to a U.S. population. For comparison, the number of expected cases and deaths in the absence of exposure is listed.

[2]Approximately 42 cancers per 100 individuals calculated from Table 12-4 in Chapter 12 of the BEIR VII report.

[3] In special cases, such as *in utero* exposure, some evidence suggests excess cancers can be detected as low as 10 mSv.

Estimating Risks to Children of Parents Exposed to Ionizing Radiation

Naturally-occurring genetic (i.e., hereditary) diseases arise as a result of alterations (mutations) occurring in the genetic material (DNA) contained in the germ cells (sperm and eggs) and are heritable (i.e., they can be transmitted to the offspring and subsequent generations). The concern over whether exposure to ionizing radiation would cause an increase in the frequencies of genetic diseases launched extensive research programs to examine the adverse genetic effects of radiation in the children of A-bomb survivors and other studies focusing on mammals that could be bred in the laboratory, primarily the mouse.

Studies of 30,000 children of exposed A-bomb survivors show a lack of significant adverse genetic effects. During the past 10 years, major advances have occurred in our understanding of the molecular nature and mechanisms underlying naturally occurring genetic diseases and radiation-induced mutations in experimental organisms including the mouse. The risk estimates presented in this report have incorporated all these advances. They show that, at low or chronic doses of low-LET irradiation, the genetic risks are very small compared to the baseline frequencies of genetic diseases in the population.

Given BEIR VII estimates, one would not expect to see an excess in adverse hereditary effects in a sample of about 30,000 children (the number of children evaluated in Hiroshima and Nagasaki). One reason that genetic risks are low is that only those genetic changes compatible with embryonic development and viability will be recovered in live births.

Research Needs

Continued research is needed to further increase our understanding of the health risks of low levels of ionizing radiation. BEIR VII identifies the following top research needs:

- Determination of the level of various molecular markers of DNA damage as a function of low dose ionizing radiation.
- Determination of DNA repair fidelity, especially double and multiple strand breaks at low doses, and whether repair capacity is independent of dose.
- Evaluation of the relevance of adaptation, low-dose hypersensitivity, bystander effect, hormesis, and genomic instability for radiation carcinogenesis.
- Identification of molecular mechanisms for postulated hormetic effects at low doses.
- Reduction of current uncertainties on the specific role of radiation in how tumors form.
- Studies on the genetic factors that influence radiation response and cancer risk.
- Studies on the heritable genetic effects of radiation.
- Continued medical radiation and occupational radiation studies.
- Continued follow-up health studies of the Japanese atomic-bomb survivors, 45% of whom were still alive in 2000.
- Epidemiologic studies to supplement studies of atomic-bomb survivors, for example studies of nuclear industry workers and persons exposed in countries of the former Soviet Union.

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This brief was prepared by the National Research Council based on the committee's report. For more information, contact the Nuclear and Radiation Studies Board at 202-334-3066. *BEIR VII: Health Risks from Exposure to Low Levels of Ionizing Radiation* is available from the National Academies Press, 500 Fifth Street, NW, Washington, DC 20001; 800-624-6242; www.nap.edu. This report is sponsored by the U.S. Department of Defense, U.S. Department of Energy, U.S. Nuclear Regulatory Commission, U.S. Environmental Protection Agency, and U.S. Department of Homeland Security.