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Effects of Low Level Radiation—What's New?

Henry D. Royal, MD

A comprehensive review of the effects of exposure to low levels of ionizing radiation, BEIR VII–Phase 2: Health Risks From Exposure to Low Levels of Ionizing Radiation, was published in 2006. The BEIR (Biological Effects of Ionizing Radiation) reports are a series of publications by the National Academy of Sciences. The last BEIR report on the effects of low level radiation, BEIR V, was published in 1990. To update the risk estimates for exposure to low levels of ionizing radiation, the BEIR committee reviewed recent epidemiologic studies of the atomic bomb survivors, as well as recent studies of populations exposed to radiation from diagnostic and therapeutic medical studies, from occupational exposures and from exposure due to releases of radioactive materials into the environment. Additional increasingly sophisticated epidemiologic studies continue to be published. BEIR VII reconfirmed that the linear no threshold model is the most practical model to estimate radiation risks, especially for radiation protection purposes. The updated risk estimates have not changed significantly from the BEIR V estimates, but the confidence intervals have narrowed as the result of the availability of additional data. The effects of low doses of radiation should be of particular interest to medical professionals because radiation exposure from diagnostic medical studies is, by far, the largest source of radiation exposure from human activity. One recommendation of the BEIR VII report is to perform epidemiologic studies of patients, especially children, who have been exposed to radiation as part of their care. A large, sophisticated epidemiologic study will likely be able to detect an increase in cancer risk. The purpose of this article is to highlight the contents of this important publication with particular emphasis on what is new.
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Biological Effects of Ionizing Radiation (BEIR) VII[1,2] is the most recent in a series of publications from the National Academy of Sciences that reviews the health risks from exposure to low levels of ionizing radiation. The previous comparable report, BEIR V[2], was published 16 years ago. The purpose of this review is to highlight some of the new data that were available to the committee and to summarize their major findings. In addition, important selected data on radiation effects published after the BEIR VII report are reviewed.

The primary objective of the BEIR VII Committee was to develop the best possible risk estimate for exposure to low-dose, low-linear energy transfer (LET) radiation in human subjects. The committee (1) conducted a comprehensive review of all relevant epidemiologic data related to the risk from exposure to low-dose, low-LET radiation; (2) defined and established principles on which quantitative analyses of low-dose and low dose rate effects can be based; (3) considered relevant biologic factors (such as the dose- and dose-rate effectiveness factor, relative biologic effectiveness, genomic instability, and adaptive responses); (4) developed etiologic models to estimate population detriment; (5) assessed the current status and relevance to risk models of biologic data and models of carcinogenesis, including a critical assessment of all data that might affect the shape of the response curve at low doses (evidence for or against adaptive responses and radiation hormesis); (6) considered when appropriate potential target cells and problems that might exist in determining dose to the target cell; and (7) considered any recent evidence regarding genetic effects not related to cancer.

This 500-plus page report provides a comprehensive review of our current state of knowledge regarding the effects of low dose LET radiation. Low dose was defined as less than 100 mSv by the committee. Chapters 1 to 4 discuss basic aspects of radiation physics and radiation biology, including the known interaction between radiation exposure and genetic material, cellular structures, and whole organisms. Chapters 5 to 9 discuss basic principles of epidemiology and include substantive data relating to exposure from the atomic bombs, medical radiation, occupational radiation, and environmental radiation. Chapters 10 to 12 integrate information

Division of Nuclear Medicine, Mallinckrodt Institute of Radiology, Washington University School of Medicine, St. Louis, MO.

Address reprint requests to Henry D. Royal, MD, Division of Nuclear Medicine, Mallinckrodt Institute of Radiology, 510 S. Kingshighway Boulevard, St. Louis, MO 63110. E-mail: royalh@mir.wustl.edu

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from biology and epidemiology, and the authors develop risk estimates based on this information. Chapter 13 is an overall scientific summary and lays out the research needs that the Committee has identified.

Dose–Effect Models

Before reviewing the epidemiologic data, a brief discussion of radiation dose-effect models is needed. Historically, epidemiologic data on radiation-induced cancers have been analyzed with 2 simple dose response models, excess absolute risk (EAR) and excess relative risk (ERR). These are models are empirical rather than biologically based. The values for the relevant biological parameters used in biologically based models are too uncertain for these more complex models to be of any practical use.

The EAR model assumes that the risk caused by the exposure is independent of the baseline risk and is proportional to the dose. The simplest formula for EAR is:

$$R = a + bD$$

where R = total risk, a = baseline risk, b = risk coefficient, and D = dose. Because the risk from the exposure is simply added to the baseline risk, the EAR model is commonly referred to as the additive model.

The ERR model assumes that the risk caused by the exposure is proportional to the baseline risk as well as to the exposure. The simplest formula for ERR is:

$$R = a(1 + bD)$$

where R = total risk, a = baseline risk, b = risk coefficient, and D = dose.

In this model, the risk from the exposure is a product of both the baseline risk and the dose. For this reason, this model is often referred to as the multiplicative model.

More sophisticated EAR and ERR models would account for variation in excess rates by sex, age, time since exposure, etc. Other modifications to these models also are possible, eg, a term can be added to the model that increases or decreases the risk with time since exposure, and with attained age. The ERR model with some modifications was favored by the BEIR VII committee.

Evidence from Epidemiology

Animal and cellular data have been very useful to elucidate the biological mechanism of carcinogenesis, but cancer risk estimates have primarily been derived from epidemiologic studies of human subjects. To derive its cancer risk estimates, the BEIR committee reviewed epidemiologic data from the (1) atomic bomb survivor studies, (2) medical radiation studies, (3) occupational radiation studies, and (4) environmental studies.

Atomic Bomb Survivors (ABS) Studies

Much of what is known about the carcinogenic effects of radiation is derived from studies of ABS.[3] Half of the survivors were still alive in 2000, so continued follow-up of this population is very informative. The BEIR VII committee was able to evaluate 13,000 incidence cancers and approximately 10,000 cancer deaths in the ABS in contrast to the fewer than 6000 cancer deaths available to the BEIR V committee. In addition, a major re-evaluation of dosimetry referred to as dosimetry system 2002 or DS2002[4] was completed, increasing the certainty in the relationship between radiation exposures and health effects.

Although the relevance of epidemiologic data from Hiroshima and Nagasaki to the effects of radiation at low doses has been questioned by some, 65% of the ABS were exposed to 100 mSv or less. Organ doses in the tens of mSv range have become commonplace with the advent of multidetector spiral computed tomography and positron emission tomography/computed tomography procedures, and organ doses for studies involving multiple diagnostic positron emission tomography and computed tomography images[5] and/or therapeutic interventions done with imaging guidance may result in doses approaching levels for which there is direct epidemiologic evidence for increased cancer.

The advantages of studies of the ABS include the large size of the population, inclusion of both sexes and all ages, wide range of individual doses that are well known, long follow-up, and high-quality mortality and cancer incidence data. In addition, the whole-body exposure received by this cohort offers the opportunity to assess risks for cancers of a large number of specific sites and to evaluate the comparability of site-specific risks. Special studies of subgroups of the ABS

Table 1 Solid Cancers Cases by Dose Category (Modified From Preston et al[3])

Dose Category*	Subjects	Observed	Expected	Observed − Expected	Attributable Fraction (%)
<0.005	60,792	9597	9537	3	0.0
0.005 to 0.1	27,789	4406	4374	81	1.8
0.1 to 0.2	5527	968	910	75	7.6
0.2 to 0.5	5935	1144	963	179	15.7
0.5 to 1	3173	688	493	206	29.5
1 to 2	1647	460	248	196	44.2
2 to 4	564	185	71	111	61.0
Total	105,427	17,448	16,595	853	10.7

*Weighted colon dose in Gy.

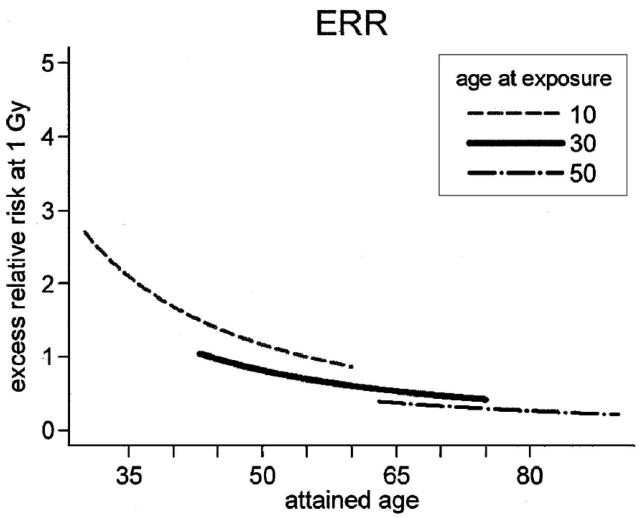


Figure 1 ERR as a function of age at exposure and attained age is shown. (Reprinted with permission from Preston et al.[3])

have provided clinical data, biological measurements, and information on potential confounders or modifiers.

The most recent major report of the ABS was published after the BEIR VII report. Table 1 lists the number of ABS in each dose category, the observed and expected numbers of cancers, the excess number of cancers, and the percent of cancers that can be attributed to radiation exposure (attributable fraction). In more than 50 years of follow-up of the 105,427 atomic bomb survivors, percent of cancers attributed to their radiation exposure is 10.7%. The cancer prevalence in the unexposed population was approximately 15.8% (9597/60,792), whereas the cancer prevalence in the population exposed to greater than 5 mGy (0.5 rad) was approximately 17.6% ([17,448 − 9597]/[105,427 − 60,792]). Because the lifetime incidence of solid cancers in the United States is 45% for men and 38% for women, further follow-up of the aging ABS will identify many more cancers because cancer is predominantly a disease of the elderly. In the future, the larger number of cancer cases for analysis should further reduce the uncertainty regarding radiation risks and will provide important information about whether the risk following radiation exposure decreases with time since exposure.

One important variable that determines the risk of radiation exposure is the age at exposure. Because the studies of the ABS included persons of all ages and have long follow-up, the effects of age at exposure and attained age on excess relative risk can be studied. As shown in Fig. 1, the ERR is greater at younger ages and decreases with time since exposure.[3]

Because the radiation exposure of ABS included the whole body, analysis of these studies provide risk estimates for cancers of specific organs. Given that there are only 853 total excess solid cancers in the ABS (Table 1), risk estimates based on small subsets of these cancers are much more uncertain (Table 2). In adults, a radiation dose of 1 Gy, increases the lifetime solid cancer risk by about 40%. In young children, the risk is twice as great.

Medical Radiation Studies

Medical radiation studies have been the second most useful source of data on radiation effects but analysis of this data are often complicated by the presence of confounding factors such as the presence of disease. In addition, the dose that is most useful to epidemiologists (the organ dose) is often much more uncertain than the organ doses for the atomic bomb survivors. The dose to the ABS was more uniform and could be reasonably estimated by knowing where the survivor was the instant that the atomic bombs exploded. In contrast, medical doses were much less uniform and are very dependent on technical factors that may not have been recorded and preserved. The age ranges and dose ranges in medical studies are usually less than for the atomic bomb survivors. Despite these limitations, data from medical studies have been very useful in generally confirming the results of the analysis of ABS studies.

Occupational Studies

Nuclear workers are chronically exposed to low doses of ionizing radiation. Because radiation is only a weak carcinogen, directly demonstrating a dose response relationship between cancer and these low doses of radiation has been difficult. To have sufficient power to detect the small expected effects, very large populations would need to be studied for many years. This need has led to the collaboration of many countries to pool their data so that meaningful analyses could be done.[6]

Table 2 Age-at-Exposure Category Specific ERR Estimates* for All Solid Cancers and Selected Sites (Modified from Preston et al[3])

	Age-at-Exposure Group			
Site	**0 to 9**	**10 to 19**	**20 to 39**	**40+**
All solid	0.72 (0.52; 0.98)	0.64 (0.51; 0.79)	0.41 (0.33; 0.50)	0.41 (0.29; 0.53)
Stomach	0.63 (0.23; 1.4)	0.38 (0.19; 0.68)	0.38 (0.22; 0.56)	0.23 (0.06; 0.42)
Colon	0.45 (0.13; 1.3)	0.54 (0.25; 1.0)	0.54 (0.23; 0.92)	0.51 (−0.06; 1.3)
Liver	0.06 (<−0.1; 0.63)	0.61 (0.18; 1.3)	0.18 (<−0.07; 0.44)	0.44 (<−0.14; 1.1)
Lung	0.66 (<−0.02; 2.0)	0.57 (0.23; 1.1)	0.79 (0.48; 1.2)	1.2 (0.71; 1.7)
Breast	0.78 (0.38; 1.5)	1.2 (0.69; 1.9)	0.83 (0.48; 1.3)	0.54 (−0.02; 1.4)
Bladder	−0.09 (<−0.1; 5.1)	1.3 (0.16; 3.9)	1.1 (0.33; 2.2)	1.4 (0.47; 2.8)
Thyroid	1.5 (0.47; 3.9)	1.2 (0.50; 2.5)	0.46 (0.11; 1.1)	0.31 (−0.1; 0.92)

*Sex-averaged ERR estimates at 1 Gy in age-at-exposure categories.

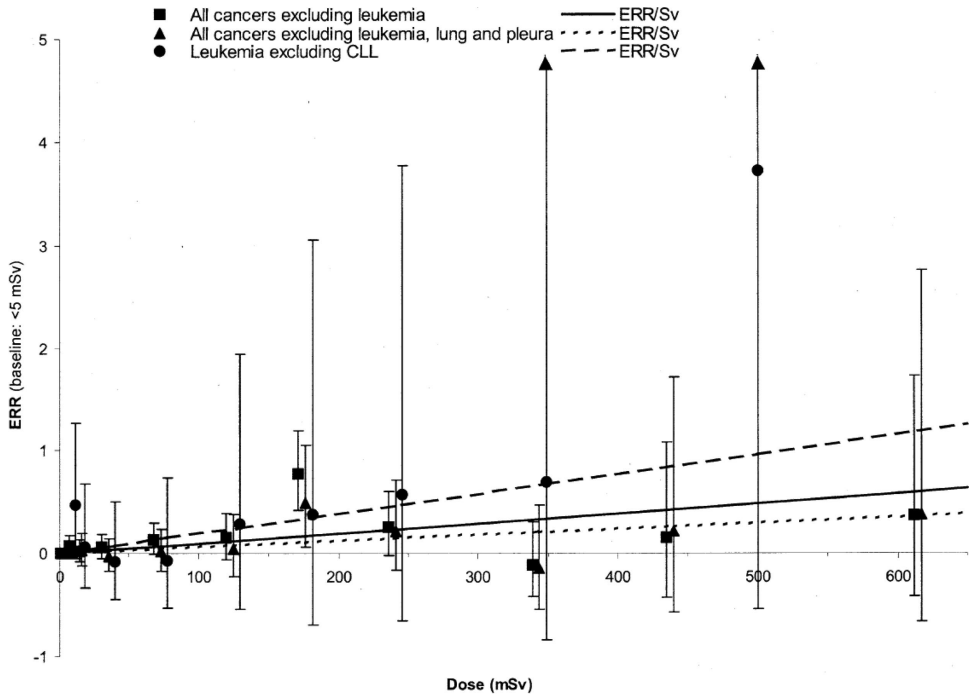


Figure 2 Excess relative risk by dose category (relative to 5 mSv category) and 90% CI: all cancers excluding leukemia, all cancers excluding leukemia, lung and pleural cancers; leukemia excluding CLL. (Reprinted with permission from Cardis et al.[7])

Since the publication of BEIR VII, the largest collaborative study of cancer risk among radiation workers in the nuclear industry has been published.[7] For this study, 15 countries pooled data on 407,391 nuclear workers to provide direct estimates of cancer risk following protracted low doses of ionizing radiation. A significant association was seen between radiation dose and all-cause mortality (ERR 0.42 per Sv, 90% CI 0.07, 0.79). This was mainly attributable to a dose-related increase in all cancer mortality (ERR/Sv 0.97, 90% CI 0.28-1.77; Fig. 2). Among 31 specific types of malignancies studied, a significant association was found for lung cancer (ERR/Sv 1.86, 90% CI 0.49-3.63). Further studies will be important to better assess the role that tobacco and other occupational exposures play in these risk estimates.

Environmental Studies

A considerable number of epidemiologic studies have attempted to determine whether persons exposed to ionizing radiation from environmental sources are at an increased risk of developing cancer. In evaluating the evidence, it is important to consider carefully the specific methodological features of the study designs employed. Studies of environmental radiation exposure are of 3 basic designs: (1) descriptive studies, often referred to as ecologic; (2) case-control studies; and (3) cohort or follow-up studies. The existing published literature consists primarily of reports that are descriptive in nature and ecologic in design. The preponderance of this type of study is due to the fact that they are relatively easy to carry out and are usually based on existing data. However, ecologic studies based on average population doses and average cancer rates often are associated with considerable biases.[8] Most often, geopolitical boundaries or distance from a source of radiation are used as surrogate means to define radiation exposure.

Recently published epidemiologic studies of populations exposed because of the Chernobyl nuclear accident[9-14] are listed in Table 3. The endpoint of greatest interest has been thyroid cancer in children exposed to radioiodines, predominantly I-131, because this is the only carcinogenic effect that has been scientifically documented in studies of the exposed population 20 years after the accident. These studies have caused scientists to re-evaluate the carcinogenic effects of I-131 in children. Before the results of these studies, most experts had concluded that I-131 was, at most, one-third as effective at causing thyroid cancer as was external radiation exposure.[15] The ERR per Gy listed in Table 3 are similar to the ERR per Gy (7.7) estimated for children after external exposure.[16]

Two other contradictory studies on the carcinogenic effects of radioiodine exposure on the thyroid have been recently published. In a comprehensive study of downwinders exposed caused by the releases of I-131 from the Hanford Nuclear site,[17] no radiation associated thyroid effects were observed (Fig. 3). In contrast, reanalysis of data on downwinders from the Nevada test site reported a radiation related increase in thyroiditis.[18]

The Preferred Dose Response Model

The BEIR committee reiterated that the linear no-threshold (LNT) model was the most computationally conve-

Table 3 Results From Major Studies of Thyroid Cancer in Relation to Exposure Due to the Chernobyl Accident

Author	Type of Study	Number of Subjects	Thyroid Cancers	Mean Dose (cGy) (Range)	ERR Gy^{-1} (95% CI)	EAR/10^4 PY Gy (95% CI)
Cardis et al[9]	Case–control	Cases: 276 Controls: 1300	276	Belarus 36.5 (0.7 to 310.9) Russian Federation 4 (0.3 to 169.1)	4.5 (2.1 to 8.5)	Not calculated
Tronko et al[14]	Cohort	13,127	45	200 (0->400)	5.25 (1.70 to 27.5)	Not calculated
Likhtarov et al[13]	Ecological	301,907	32	35.3 (<2.0->200)	8.0	1.5 (1.2 to 1.9)
Kopecky et al[12]	Case–control	Cases: 66 Controls: 132	66 Not calculated	4.35 (0.014 to 164)	48.7 (4.8 to 1151)	Not calculated
Jacob et al[11]	Ecological	1,620,000	1089	7 (1.8 to 65)	18.9 (11.1 to 26.7)	2.66 (2.19 to 3.13)
Ivanov et al[19]	Ecological	375,000	199	8 (0 to 20)	Girls: age (years)—0 to 4, 45.3; 5 to 9, 10.1; 10 to 14, 1.0; 15 to 17, <0; Boys: age (years)—0 to 9, 68.6; 10 to 17, <0	Not calculated

nient starting point for the estimation of radiation risks, especially when used for radiation protection purposes.[19] Unless the repair of DNA damage is perfect, there is unlikely to be a threshold. Most radiation biologists recognize that the complex biological events needed for a cancer to develop cannot be described by a simple LNT model. However, an alternative model would be impractical for the purposes of radiation protection. The data available from epidemiological studies are associated with enough uncertainty that use of more complicated dose response models cannot be justified.

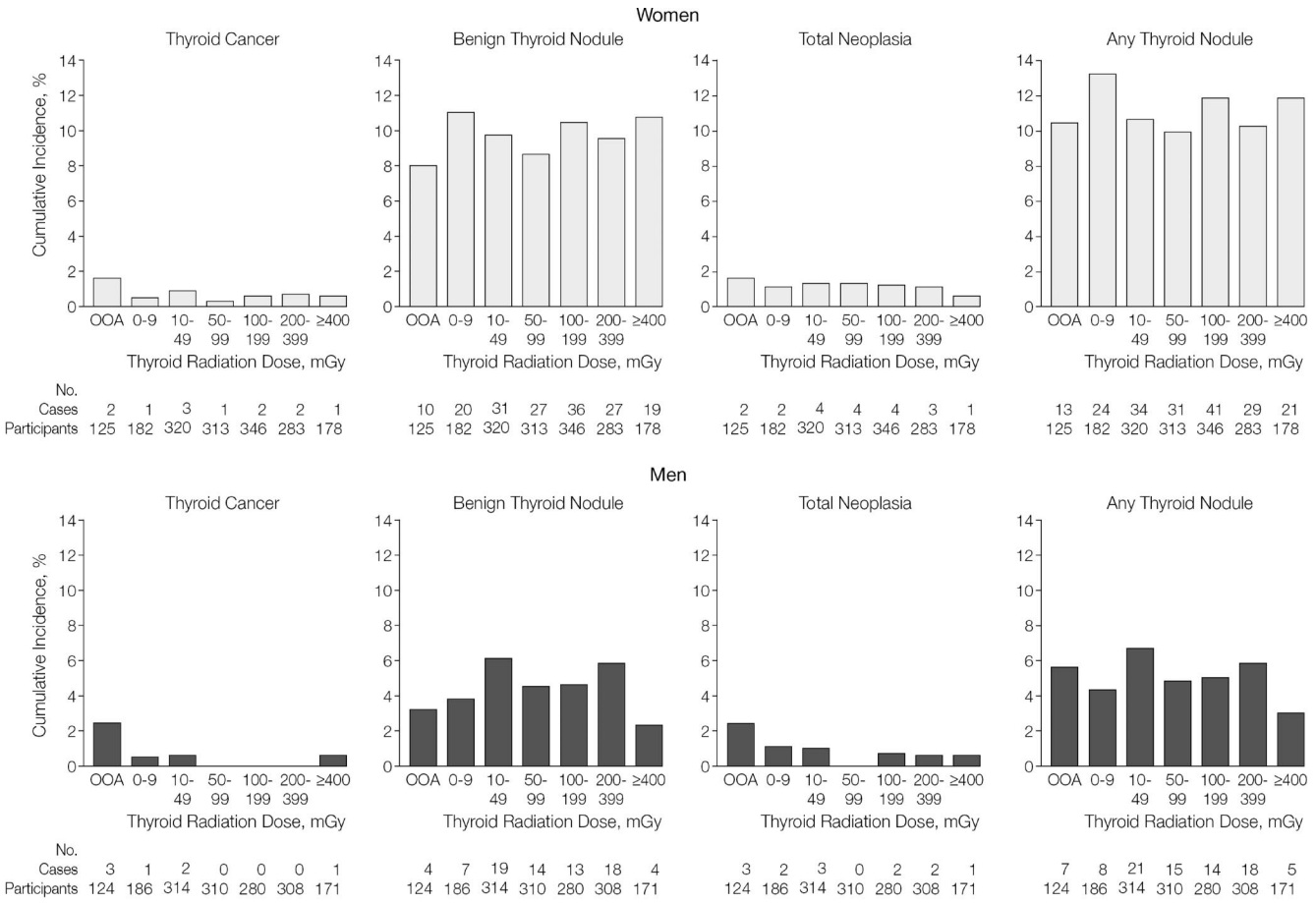
Critics of the use of the LNT model often react to the fact that some use the LNT model as a way to imply that radiation is a unique hazard. We have all heard the expression, "there is no safe level of radiation" based on the "no-threshold" part of the LNT hypothesis, but there is no threshold for any chance (stochastic) event. The risk of crossing the street (an activity that most would agree is safe) has no threshold. There is a very small chance that something bad will happen if you are not paying attention or if a driver is not paying attention. There are many chance events in life.

Even when risk is predicted using the LNT hypothesis, radiation is a weak carcinogen. In Table 4, the risk of smoking is compared with the risk from smoking.[20] There is no radiation dose that could increase a person's lung cancer risk to a similar degree as the risk of smoking 20+ cigarettes a day. Radiation doses similar to the risk of 1+ cigarettes a day would be extraordinary. It is important to recognize that the acceptability of a risk has little to do with the magnitude of the risk. Understandably, acceptability of a risk is determined by the perceived risk benefit ratio. Why accept even a small risk if there is little or no benefit to the activity? Risk benefit ratio helps explain why the public accepts the much larger radiation doses associated with medical uses of radiation and often rejects very small doses related to environmental contamination.

Cancer Risks Estimates

Although the cancer risk estimates in BEIR VII have not changed greatly since the 1990 report, confidence in the estimates has increased because of the increase in epidemiologic and biological data available to the committee. Table 5 lists BEIR VII's estimates of the solid cancer incidence and mortality (and the 95% confidence intervals) for men and women who are exposed to different levels of radiation at different ages. Note that cancer incidence and cancer mortality attributed to radiation exposure is higher in woman than in men.

Table 6 compares BEIR VII's lifetime cancer mortality estimates with those of other scientific bodies. The numbers in parenthesis is the estimate for chronic exposures. BEIR VII recommends the use of a dose and dose rate effectiveness factor (DDREF) of 1.5. This means chronic exposures are 1.5 times less carcinogenic than acute exposures. BEIR V had recommended a DDREF of 2.[12] Risk estimates from all of the organizations listed in table 6 are in good agreement espe-



OOA indicates out of area.

Figure 3 Cumulative incidence of thyroid neoplasia outcomes by sex and estimated dose category. (Reprinted with permission from Davis et al.[17] Copyright © 2004, American Medical Association. All rights reserved.)

cially when the 95% confidence intervals in table 5 are considered.

The expected number of radiation induced cancer from an exposure to 0.1 Gy is compared with the number of "naturally occurring" cancers in Table 7. In men, the 900 (800 + 100) extra cancers would be dwarfed by 46,330 (45,500 + 830) cases that would occur in the absence of exposure. Detecting this small number of excess cancers over the lifetime of 100,000 males would not be possible. Table 7 also lists the expected excess cancer deaths (480 and 660 respectively for males and females) as well as the expected cancer deaths (22,810 and 18,210 respectively for males and females). The number of radiation induced cancers is very small compared with the number of naturally occurring cancers making detection of this excess very difficult.

The BEIR VII committee also estimated the lifetime radiation cancer risks for specific organs as a function of age at the time of exposure and gender. Table 8 lists the number of cancers expected from a single exposure to 0.1 Gy at various ages. Note that that the lifetime cancer risk is about 3 times greater in early childhood than it is after the age of 35 (Fig. 4).

Noncancer Effects

Studies of the ABS have detected radiation-related increases in a diverse group of noncancer diseases (Fig. 5).[21-23] It is unclear how radiation can cause or facilitate such a diverse group of diseases. These non cancer effects have also been seen following therapeutic radiation studies. Most likely, these effects have a threshold and are only seen after large (>1 Sv) doses of radiation. The BEIR VII committee has concluded that there is insufficient data to estimate the risk, if

Table 4 Risk of Lung Cancer From Smoking or Radiation (Adapted from Boice and Lubin[20])

Relative Risk for Lung Cancer	Cigarettes Per Day	A-Bomb Dose (rad)
1.0	0	0
4.6	1 to 9	3.4
7.5	10 to 19	6.1
13.1	20 to 39	(11.4)*
16.6	40+	(14.1)*

*Unrealistic dose since it would be lethal if it was an acute exposure.

Table 5 BEIR VII Preferred Estimates of Lifetime Attributable Risk of Solid Cancer Incidence and Mortality With 95% Subjective Confidence Intervals

Exposure Scenario	Incidence		Morality	
	Men	Women	Men	Women
0.1 Gy to population of mixed ages	800 (400, 1590)	1310 (690, 2490)	410 (200, 830)	610 (300, 1230)
0.1 Gy at age 10	1330 (660, 2660)	2530 (1290, 4930)	640 (300, 1390)	1050 (470, 2330)
0.1 Gy at age 30	600 (290, 1290)	1000 (500, 2020)	320 (150, 650)	490 (250, 950)
0.1 Gy at age 50	510 (240, 1100)	680 (350, 1320)	290 (140, 600)	420 (210, 810)
1 mGy per year throughout life	550 (280, 1100)	970 (510, 1840)	290 (140, 580)	460 (230, 920)
10 mGy per year from ages 18 to 65	2600 (1250, 5410)	4030 (2070, 7840)	1410 (700, 2860)	2170 (1130, 4200)

Number of cases or deaths per 100,000 exposed persons is shown.

any, of noncancer disease (including the risk of benign tumors) at low doses.

The mutagenic effects of radiation are poorly understood by many for 2 reasons. First, early experiments used radiation to induce genetic effects in plants and animals, especially drosophila. In the 1950s, it was assumed that a major effect of radiation exposure would be a significant increase in genetic diseases. Second, there has been confusion about the difference between mutations in somatic cells versus mutations in germ cells. There is ample evidence that radiation causes measurable increases in mutations in somatic cells. Karyotyping has been used for many years to detect chromosomal abnormalities in lymphocytes following acute radiation exposures of more than 100 mSv. More recently, much more sensitive techniques (eg, fluorescent in situ hybridization), have been developed to study somatic mutations, including

Table 6 Comparison of BEIR VII Lifetime Cancer Mortality Estimates With Those From Other Reports

Cancer Category	BEIR V (1990)*	ICRP (1991)†	EPA (1999)†	UNSCEAR (2000)‡	BEIR VII
Leukemia§	95 (50)	56	50		61
All cancer except leukemia (Sum)	700 (460)	450	520		
All solid cancers (Sum)				1150, 780 (520) 1400,¶ 1100¶	510
Digestive cancers	230 (150)				
Esophagus		30	12	30, 60 (25)	
Stomach		110	41	15, 120 (18)	22
Colon		85	100	160, 50 (75)	61
Liver		15	15	20, 85 (20)	16
Respiratory cancer	170 (110)				
Lung		85	99	340, 210 (160)	210
Female breast‖	35 (23)	20	51	280, 65 (43)	37
Bone		5	1	—	
Skin		2	1	—	
Prostate‖					5
Uterus‖					3
Ovary‖		10	15		12
Bladder		30	24	40, 20 (22)	25
Kidney		—	5	—	
Thyroid		8	3	—	
Other cancers of other solid cancers**	260 (170)	50	150	280, 180 (160)	130

Excess deaths for population of 100,000 of all ages and both sexes exposed to 0.1 Gy.

*These estimates are the average of estimates for males and females. The measure used was the excess lifetime risk (ELR); unlike other estimates in this table, radiation-induced deaths in persons who would have died from the same cause at a later time in the absence of radiation exposure are excluded. The estimates are not reduced by a DDREF, but we have shown in parentheses the result that would be obtained if the DDREF of 1.5, used by the BEIR VII Committee had been employed.

†Except for the EPA breast and thyroid cancer estimates, the solid cancer estimates are linear estimates reduced by a DDREF of two.

‡These estimates are the average of estimates for males and females. Except where noted otherwise, estimates are based on the attained-age model. The first estimate is based on relative risk transportation; the second on absolute risk transportation. The estimate in parentheses is a combined estimate (using the same weights as used by the BEIR VII Committee applied on a logarithmic scale) reduced by a DDREF of 1.5, although these were not recommendations of the UNSCEAR Committee.

§These estimates are based on a linear-quadratic model.

¶Estimates based on age-at-exposure model.

‖These estimates are half those for females only.

**These estimates are for the remaining solid cancers.

Table 7 The Committee's Preferred Estimates of the Lifetime Attributable Risk of Incidence and Mortality for All Solid Cancers and for Leukemia With 95% Subjective Confidence Intervals

	All Solid Cancer		Leukemia	
	Males	Females	Males	Females
Excess cases (including nonfatal cases) from exposure to 0.1 Gy	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 0.1 Gy	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

Number of cases or deaths per 100,000 exposed persons.

those induced by radiation, in more detail. This has lead to the widespread belief that an important effect of radiation exposure is an increase in genetic diseases. The BEIR VII committee re-iterated that radiation related inherited diseases have not been observed in humans and concluded that, at low or chronic doses of low LET irradiation, the genetic risks are very small compared with the baseline frequencies of genetic diseases in the population.

Research Needs

The BEIR VII committee identified 12 research needs. A few of these needs will be highlighted here.

Determination of the Level of Various Molecular Markers of DNA Damage as a Function of Low-Dose Ionizing Radiation

Better understanding of the DNA damage caused by low-dose radiation exposure will likely increase our understanding of the biological events that lead to the formation of cancers. It is likely that many of these events are not specifically related to radiation induced carcinogenesis so a better understanding of these events will lead to a better understanding of the biological events that lead to the development of most cancers. If some events prove to be

Table 8 Lifetime Attributable Risk of Site-Specific Solid Cancer Incidence

	Number of Cases per 100,000 Persons Exposed to a Single Dose of 0.1 Gy										
	Age at Exposure (Years)										
Cancer Site	0	5	10	15	20	30	40	50	60	70	80
Men											
Stomach	76	65	55	46	40	28	27	25	20	14	7
Colon	336	285	241	204	173	125	122	113	94	65	30
Liver	61	50	43	36	30	22	21	19	14	8	3
Lung	314	261	216	180	149	105	104	101	89	65	34
Prostate	93	80	67	57	48	35	35	33	26	14	5
Bladder	209	177	150	127	108	79	79	76	66	47	23
Other	1123	672	503	394	312	198	172	140	98	57	23
Thyroid	115	76	50	33	21	9	3	1	0.3	0.1	0.0
All solid	2326	1667	1325	1076	881	602	564	507	407	270	126
Leukemia	237	149	120	105	96	84	84	84	82	73	48
All cancers	2563	1816	1445	1182	977	686	648	591	489	343	174
Women											
Stomach	101	85	72	61	52	36	35	32	27	19	11
Colon	220	187	158	134	114	82	79	73	62	45	23
Liver	28	23	20	16	14	10	10	9	7	5	2
Lung	733	608	504	417	346	242	240	230	201	147	77
Breast	1171	914	712	553	429	253	141	70	31	12	4
Uterus	50	42	36	30	26	18	16	13	9	5	2
Ovary	104	87	73	60	50	34	31	25	18	11	5
Bladder	212	180	152	129	109	79	78	74	64	47	24
Other	1339	719	523	409	323	207	181	148	109	68	30
Thyroid	634	419	275	178	113	41	14	4	1	0.3	0.0
All solid	4592	3265	2525	1988	1575	1002	824	678	529	358	177
Leukemia	185	112	86	76	71	63	62	62	57	51	37
All cancers	4777	3377	2611	2064	1646	1065	886	740	586	409	214

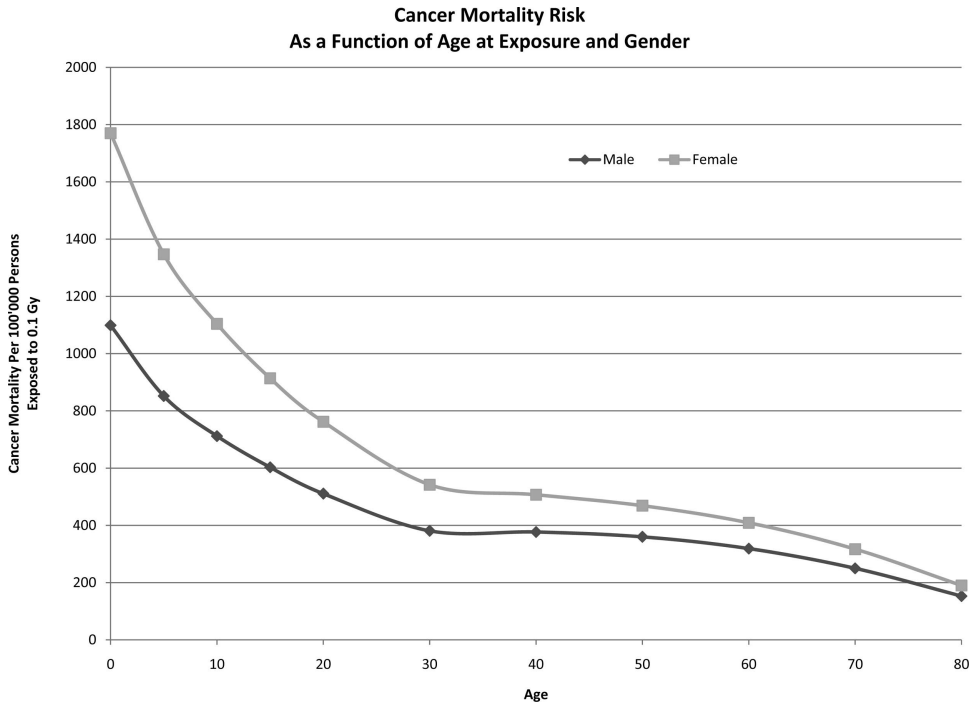


Figure 4 Number of excess cancer deaths caused by a single radiation exposure of 0.1 Gy as a function of age at the time of exposure and gender. (Based on Table 12-D2 in the BEIR VII report.[1])

specific for radiation-induced cancers, these events can be used as markers for radiation-induced cancers. Having markers for radiation-induced cancers could have a significant impact on our ability to detect radiation-induced cancers in epidemiologic studies and would have an impact on compensation for radiation-induced cancers.

Evaluation of the Relevance of Adaptation, Low-Dose Hypersensitivity, Bystander Effect, and Genomic Instability for Radiation Carcinogenesis

In recent years, 2 opposing concepts regarding DNA repair have emerged. Some have argued that small amount of radiation stimulate DNA repair mechanisms and thus result in a protective effect. The concept that small doses of a toxic have a beneficial effect (hormesis)[24] is not new but experiments that show that small doses of radiation have a protective effect (also known as an adaptive response) are frequently published. On the other hand, the bystander effect[25] has been observed where damage occurs not to the cell that was exposed to radiation but also to surrounding cells. Some would claim that this means that radiation is more damaging than previously thought. Although adaptive responses and bystander effects may provide important insights into how radiation causes disease, these mechanisms do not change the results of epidemiologic studies from which risk estimates are derived.

Future Medical Radiation Studies

Exposure to medical radiation is now, by far, the greatest manmade source of radiation exposure to the general population. It has been estimated that the per capita radiation dose for medical exposures in the United States has increased from about 0.67 mSv per year in 1980 to more than 3 mSv in 2008. This dramatic increase has occurred largely due to the introduction of CT and estimates of the number of cancers caused by these radiation exposures have become common.[5]

The BEIR VII committee has recommended that epidemiologic studies be conducted of patients, particularly children, who have had a significant medical radiation exposure to better estimate the risk from these exposures. Due to the lack of centralization of medical data, it is unlikely that these studies will be conducted in the United States but it is very likely that such studies will be feasible in other countries.

Conclusions

Epidemiologic studies of the atomic bomb survivors continue to provide valuable epidemiologic data to better assess the risk from radiation exposure. This knowledge is supplemented and affirmed by studies of populations exposed as the result of medical, occupational and environmental exposures. Although BEIR VII's cancer risk estimates have not changed greatly since the 1990 BEIR V report, confidence in the estimates has risen because of the increase in epidemiologic and biological data available to

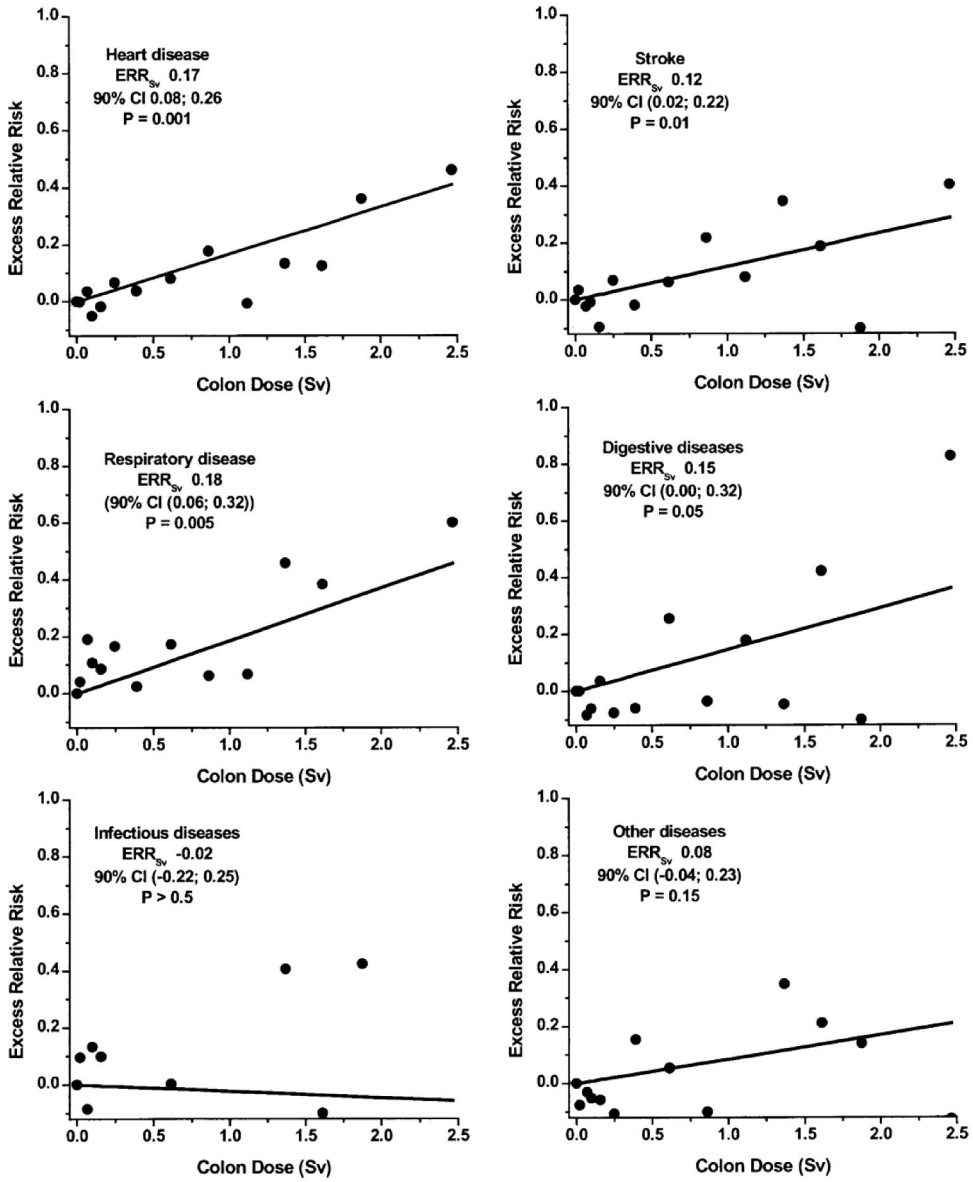


Figure 5 Cause-specific dose–response functions for noncancer deaths. The plots display the best-fitting linear ERR models together with nonparametric ERR estimates for 20 dose categories. (Reprinted with permission form Preston et al.[21])

the committee. Finally, additional research is needed to better understand the underlying biological mechanism by which radiation causes cancer and to better determine the risk for medical exposures since these exposures are, by far, the greatest manmade exposures.

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