Chapter 4

Potential Health Consequences from Exposure of the United States Population to Radioactive Fallout

Contents: This chapter provides a brief summary of what is currently known about the health consequences of low-level radiation exposures. The feasibility of analyzing the risk of cancer and non-cancer health outcomes resulting from fallout is discussed. Methods for estimating the number of cancers expected to occur in the United States population as a result of fallout exposure are illustrated for total cancer and leukemia using dose estimates provided in Chapter 3. Issues relating to the uncertainty in these estimates are described.

4.1 Introduction

Health effects of radiation exposure have been extensively studied and documented. These effects are diverse and vary with radiation doses. From the estimated doses presented in Chapter 3, it is clear that the health effects of interest with regard to fallout radiation are those that can be attributed to relatively low radiation exposure; the estimated thyroid dose averaged over the population of the entire country is about 10 mGy while the average bone-marrow dose is about 2 mGy. For most individuals, the doses are expected to have been less than 1,000 mGy for the thyroid gland and less than 100 mGy for bone marrow. At these dose levels the most important health effect is likely to be cancer, which typically occurs many years after the exposure. On an individual basis, the risk of developing excess cancers as a consequence of exposure to low-dose radiation is considered small. However, on a population basis, widespread exposure of large numbers of people to fallout may potentially lead to a large number of excess cancers and hence a public health problem. One goal of this chapter is to familiarize the reader with the weight of evidence linking cancer with low

radiation dose and to evaluate the magnitude of the impact of fallout radiation on the cancer burden of the United States population.

In addition to cancer, some non-cancer diseases have been reported to occur as late effects of radiation. Some of these are of neoplastic in nature, though benign in their behavior (benign tumors). Recent data from the Japanese atomic bomb survivor studies suggest that the risk of certain diseases of non-neoplastic nature such as heart diseases may also be increased after exposure to radiation; however, the magnitude of the risk is considerably uncertain, especially at low dose levels, and plausible biological mechanisms involved are unclear (Shimizu et al. 1999; Kodama et al. 1996).

Quantifying the risk of cancer and non-cancer health effects depends on the availability of information about the disease-exposure relationship from high quality observational studies (e.g., epidemiologic studies). Using this information, several standards-setting organizations and scientific committees have already developed mathematical models for estimating cancer risks to populations exposed to specified doses of radiation (NAS 1990; ICRP 1991; NRC. 1993; EPA 1994; UNSCEAR 1994, 2000). However, much less has been done to quantify non-cancer disease risk. Thus, while there is little question that estimates of the fallout-related lifetime risk of cancer for the United States population can be obtained if dose estimates are available, only a qualitative assessment of risk can be provided for non-cancer health effects. Cancer risk estimates are appropriately represented by a range of numbers in order to account for the large uncertainty in these estimates. Therefore, the question remains as to whether or not these uncertain estimates of risk will be useful for developing public health policy.

This chapter provides an overview of what is currently known about the relationship between radiation exposure and cancer and other late-occurring health effects. Two issues fundamental for understanding this relationship between radiation and health effects, dose response and time response patterns of the risk, are examined. Additionally, this chapter provides approximate estimates of cancer risk resulting from exposures from atmospheric nuclear weapons testing and indicates the degree of uncertainty in these estimates. While the main emphasis of this chapter is on cancer as a health effect of radiation exposure, non-cancer health effects are also discussed.

4.2 Health Effects of Ionizing Radiation

The most relevant sources of scientific information on the health effects of ionizing radiation are the large number of epidemiological studies that have been conducted to date. One of the most important investigations of radiation health effects is the epidemiological study of a large cohort of Japanese atomic bomb survivors. The continuing follow-up of this cohort provides information on long-term health risks associated with radiation exposure and is the major contributor to quantitative risk estimates. Others include studies of occupational groups such as uranium miners and nuclear production workers, populations exposed to radiation as a result of living in areas contaminated with fallout from nuclear weapons tests, and adults and children exposed for medical (diagnosis or treatment of diseases) and other reasons. Data on medically exposed populations have contributed substantially to estimating risks of cancers of specific sites, particularly breast and thyroid,

and data on underground miners are the main basis for estimating risks of lung cancer from exposure to radon. However, the atomic bomb data are by far the most important source of information for developing quantitative estimates of risks from radiation exposure.. Laboratory studies of animals, microorganisms, and cells grown *in vitro* also provide information helpful in understanding the mechanisms of radiation-induced diseases. The data accrued from new or continuing epidemiological and laboratory studies are regularly reviewed and updated by international and national organizations such as the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), the International Commission on Radiological Protection (ICRP), the National Academy of Sciences (NAS) and the National Council on Radiation Protection and Measurements (NCRP). Reports from these organizations provide comprehensive information on health effects of radiation. The overview presented in this chapter is largely drawn from conclusions and summaries derived by these national and international expert groups and are supplemented by additional literature considered relevant for this report.

4.2.1   Cancer (Malignant Tumors)

Before discussing radiation-induced cancer risk, a brief overview of the possible biological basis of cancer formation is relevant. It is currently thought that cancer (and possibly some other late effects) reflects DNA damage (mutations). The exact mechanisms by which radiation (or any other cancer-causing agent) leads to cancer are not completely understood. However, it is generally believed that the development of cancer requires a series of mutations accumulated over many years. Some of these mutations occur spontaneously. Others result from exposure to any of a wide range of mutagens, including radiation. Since many years may have to pass for an irradiated cell or its progeny to acquire sufficient mutations to present itself as clinical cancer, it may take years before excess cancers accountable to radiation exposure are recognized. The process of incurring DNA mutations from radiation is thought to be random in nature. Thus, the probability of cancer resulting from radiation exposure is a function of the number of affected cells and is dependent on radiation dose. The excess cancers that arise as a result of radiation exposure, with or without contributions from other agents, are not distinguishable from those occurring due to other reasons. At present there are no established biological markers that can characterize radiation-induced cancers.

As noted previously, conclusions and inferences about the cancer (and other health) effects of radiation are drawn from statistical associations obtained from epidemiological data. Results from laboratory experiments are also considered to judge the biological basis or plausibility of the epidemiological data. The principal feature of the cancer risk associated with radiation is that the probability that a person will develop cancer due to radiation exposure depends on such factors as the dose received, age at exposure, attained age (or time since exposure) and gender. The relationship of cancer risk to radiation doses (dose response) is essential in estimating the risk at low doses, and the time pattern of the risk associated with age is important in projecting the resulting cancer increase in exposed populations.

The way excess cancer risk increases with an increasing radiation dose is mathematically described by a dose response curve (dose response function or model), and

the shape of this curve is important in estimating the risk at low dose levels. There are basic limitations in estimating the cancer risk at low doses using epidemiological data. At low doses, the cancer risk becomes so small relative to the background risk that it may not be possible to find and study a large enough exposed population to detect the small risk. Furthermore, the background cancer rates often vary by amounts that are comparable to or even greater than the low-dose radiation risk that the study intends to detect. So even if a sufficiently large population were available, it would not be possible to rule out the potentiality that biases may actually explain the observed difference. Despite these limitations, much progress has been made recently in estimating the cancer risk at low doses.

Although the Japanese atomic bomb study is generally regarded as a high dose study, about 80% of the survivors in this cohort received doses that were less than 100 mSv (Pierce et al. 1996). Thus, substantial information can be obtained on low-dose risk from this study. Moreover, the atomic bomb survivor study has several important advantages over other studies including size of the cohort (about 87,000 exposed persons of both genders and all ages, who were exposed to a wide range of doses distributed throughout the body), and a follow-up period of more than 5 decades. The dose response for solid cancers (cancers excluding leukemia and other cancers of the blood and blood forming organs) obtained from this cohort data is remarkably linear. In other words, the increase in risk is directly proportional to the increase in dose. The data do not suggest the existence of a threshold below which there is no excess risk (Pierce et al. 2000). Unlike solid cancers, the relationship between radiation dose and leukemia risk is non-linear (either linear-quadratic or quadratic) indicating an increase in risk per unit dose at low dose levels that is about half that at high dose levels.

Studies of nuclear workers have a potential of providing more direct data on the cancer risk associated with protracted exposures to low doses of radiation. However, because of very low doses, most of the individual studies do not have adequate statistical power to detect small effects. To overcome this problem, the International Agency for Research on Cancer (IARC) carried out an international pooled analysis of data from studies of nuclear workers in the United States, Canada and the United Kingdom (Cardis et al. 1995). The combined cohort in this analysis includes 95,000 people with a mean dose of 40 mSv and represents over 2 million person-years of follow-up. A statistically significant dose response was found for leukemia but not for other cancers. The confidence intervals for both risks of leukemia and of cancers other than leukemia are still considerably broad but indicate consistency with risk estimates obtained from the atomic bomb survivors exposed to single doses of radiation.

In general, two distinctly different time-response patterns - one for leukemia and the other for solid cancers - are recognized. Acute exposure to radiation is followed by the excess risk of leukemia, beginning shortly after exposure, increasing with time, reaching its peak 5-10 years after initial exposure, and then declining gradually thereafter. The time-response pattern is strongly dependent on age at exposure, and generally the younger the age at exposure, the steeper the initial rise and faster the subsequent decline (Preston et al. 1994, Pierce et al. 1996). Similar time response patterns are seen in populations with protracted exposure. In contrast to leukemia, the excess risk of solid cancer, starting 5-10 years after

exposure, increases gradually and continues to rise as the background cancer rates increase with age. The latest data from the atomic bomb survivor cohort suggest that the excess solid cancer risk may be persistent for many decades after exposure and remain throughout life (Pierce et al. 1996). The excess risk of solid cancer is also dependent on age at exposure for most types of cancer; those exposed at younger ages have relatively high risk compared to those exposed at older ages. How the cancer risk behaves over time in relation to age at exposure, time after exposure, and attained age is still not completely understood. More definitive answers to this issue are expected from continued follow-up of the atomic bomb survivors. Further discussion of the relationship between radiation and some specific cancers follows. Radiation-related excess risks have been observed for cancers of many parts of the body. Since exposures to radiation from fallout result in higher doses for the thyroid glands and bone marrow, thyroid cancer and leukemia (which originates in bone marrow cells) are first discussed, followed by other cancers.

4.2.1.1 Thyroid Cancer

Thyroid cancer is one of the less fatal forms of cancer (Ries et al. 2000). The excess risk of thyroid cancer associated with exposure to external radiation (x-rays and gamma rays) has been widely studied and is well established (Ron et al. 1995). Age at exposure is the most important factor that modifies the radiation-induced risk: risk decreases dramatically with increasing age at exposure. In the atomic bomb studies, the excess thyroid cancer cases are primarily seen in those who were exposed at ages less than 20 years (Thompson et al. 1994). The carcinogenic effect of radiation is prolonged and persists at least 40 years after exposure during childhood. Although thyroid cancer occurs 2-3 times more frequently in women than in men, men and women are equally affected by radiation in terms of relative excess risks. In absolute terms, however, this means that more women are afflicted with thyroid cancer than men for a given amount of radiation.

In the case of fallout, internal exposure to ^{131}I is a major concern, but the internal exposure effect has been less extensively studied. Studies of people who received ^{131}I treatment for medical reasons (non-cancer thyroid diseases) have not shown a demonstrable excess thyroid cancer risk. However, this should not be interpreted to suggest the lack of the carcinogenic potential of ^{131}I because the large majority of the study subjects were adults at the time of ^{131}I administration, not allowing inferences on childhood exposure. The thyroid is more radiosensitive in children than in adults, possibly because the young thyroid cells are rapidly growing (Williams 2002), or because of differences in metabolism or concentration of radionuclides (Mettler and Upton 1995). It is noteworthy that following the Chernobyl accident, dramatic increases in childhood thyroid cancer cases were reported in areas heavily contaminated with radioactive fallout including ^{131}I. This has suggested a strong carcinogenic potential of ^{131}I on the thyroid in infants and children, but the presence of other radioactive contaminants and uncertain dose estimates are among the major obstacles in developing more precise risk estimates. Thus, the relative biological effectiveness of ^{131}I to induce thyroid neoplasia (malignant or benign) remains the subject of considerable uncertainty. Also, relevant for thyroid cancer risk from fallout exposure are the results from a recently completed study of people who were exposed during childhood to ^{131}I released between 1944 and 1957 from the Hanford Nuclear Site in the State of Washington ("Hanford Thyroid Disease Study") (www.cdc.gov/nceh/radiation). Compared to the

Chernobyl situation, exposure in the Hanford region lasted from months to years and was lower and almost entirely from ^{131}I. No demonstrable excess in thyroid cancer risk was found, and this suggested that, if there was an increase in risk at the range of exposure (from 0 to 400 mGy) to ^{131}I in Hanford, it was too small to detect in more than 3,000 people examined in the study.

4.2.1.2   Leukemia

Leukemia is among the rarer forms of cancer, but there is a considerable amount of epidemiological information on the risk of leukemia from radiation exposure. This may in part be due to the higher relative risk compared to other cancers and the relatively short period of time for the leukemogenic effect to be manifested. There are various sub-types of leukemia, the frequencies of which are age-dependent. Most leukemias found in childhood are acute lymphocytic types whereas chronic myeloid and chronic lymphocytic types make up a large proportion of adult leukemias. Radiation has not been found to increase the risk of chronic lymphocytic leukemia, which represents about half of adult leukemia cases in the United States and other western populations.

There are some differences in the shape of the dose response for various non-chronic lymphocytic leukemias reported from the atomic bomb survivors and other studies, but they are likely to reflect the uncertainty due to small numbers of cases or different dose distributions. As noted previously, there is clear evidence of non-linearity in the dose response that indicates the risk (per unit dose) is lower if given in a smaller dose. However, this dose response pattern is based on analyses of the total dose received. The issue regarding fallout is whether a chronic cumulative dose (from fallout) is equivalent in risk to a fractionated or acute dose. Therefore, it is of special interest to see whether chronic or fractionated exposure to radiation leads to a lower risk than expected from acute exposure (dose rate effect). As discussed earlier, a large international study of radiation workers (chronic exposure) suggests that the range for the elevated leukemia risk among workers receiving chronic low dose exposures is consistent with the risk estimates obtained from the atomic bomb survivor studies (acute exposure). A number of studies are underway to further address this issue, including updating and expanding the worker study and follow-up of exposed populations in the former Soviet Union and other countries.

4.2.1.3   Other Cancers

Excess cancers due to radiation exposure occur in a wide variety of body sites although different organs and tissues have different sensitivities to this cancer-causing agent. In addition to leukemia and thyroid cancer, cancer types for which excess risks have been reported include cancer of the salivary glands, esophagus, stomach, colon, liver, lung, bone, urinary bladder, ovary, female breast, skin, thyroid, and brain and central nervous system. Evidence is currently inconclusive for non-Hodgkin's lymphoma and multiple myeloma and is weak for establishing a radiation effect for a number of other cancer types such as Hodgkin's Disease, cancers of the pancreas, prostate, testis, uterine cervix, uterine corpus, small intestine, pharynx, larynx, and nasal cavity and certain childhood cancers such as retinoblastoma and Wilm's tumor (Boice et al. 1996; NAS 1990; UNSCEAR 1994; UNSCEAR 2000). As previously noted, the excess risk for these cancers is generally

dependent on age, time, and gender, although there is considerably variability among different cancers. For example, the dependence on age at exposure is stronger for cancers of the breast and thyroid than for other cancers. How the risk of various types of cancer is modified by gender, age, and characteristics of the exposure such as the type of radiation and the rate at which dose was received, as well as exposures to other risk factors (e.g., smoking) and susceptibility factors is the continuing subject of ongoing epidemiological research.

4.2.2   Benign Tumors

The induction of benign tumors appears to be similar to cancer induction, but benign tumors are almost always non-fatal, with the exception of brain tumors. Benign tumors are difficult to identify adequately and their diagnoses are also difficult to validate for epidemiological studies. Because the medical significance of benign tumors can be minor compared with malignant tumors, benign tumors are not routinely reported to cancer registries, do not usually require hospitalization, and are rarely the underlying cause of death listed on death certificates. Autopsy studies and screening programs are potentially useful sources of information, but the differing levels of effort in tumor diagnosis complicate these investigations and can lead to biased ascertainment of cases. These reasons make is difficult to conduct epidemiological studies of benign tumors. However, limited data available to date suggest radiation exposure is capable of causing excess benign tumors, especially of the thyroid. Information is currently insufficient for characterizing the shape of the dose-response and the magnitude of risk for most benign tumors. The risk of benign tumors following radiation exposure appears to persist for many years, but currently only limited information is available on the modifying effects of gender and age and time patterns.

Radiation-associated benign tumors tend to occur in the same organs and tissues as malignant tumors, such as the thyroid glands (Schneider et al. 1993) salivary glands (Schneider et al. 1998; Land et al. 1996; Modan et al. 1998), parathyroid glands (Fujiwara et al. 1992; Schneider et al. 1995), gastrointestinal tract (Ron et al. 1995), female breast (Tokunaga et al. 1994), and central nervous system (Ron et al. 1988; Schneider et al. 1985). For fallout exposure, tumors of the thyroid are the major concern because of the potential for relatively high exposure to radioactive iodine. Thyroid adenomas are the major benign tumor of the thyroid and present themselves as nodules. Childhood exposure to external radiation, such as from the atomic bombs or given for medical reason, has been linked to excess risk of thyroid adenomas (Ron et al. 1989; Shore et al. 1993; Yoshimoto et al. 1995). Therefore, one could expect that internal irradiation to radionuclides resulting from fallout exposure is capable of increasing the risk of benign thyroid tumors. Although the limited data currently available from Utah (based on small numbers) support this (Kerber et al. 1993), there are no fallout data that provide adequate information for quantifying risks. Studies are currently ongoing on benign thyroid tumors in other irradiated populations, such as in Chernobyl, Ozyorsk in Russia, and Kazakhstan.

4.2.3   Other Diseases (Non-Neoplastic Diseases)

Exposure to ionizing radiation can directly affect health by damaging the structure and function of various tissues and organs in the human body. Clinical manifestation of an effect is thought to occur after a sufficient proportion of cells are affected by radiation exposure (Mettler and Upton 1995). This would imply that there may be a dose level under which no health risk is observed. Most radiation-induced non-neoplastic diseases are believed to occur through this process, and the ICRP has estimated threshold dose levels for certain deterministic effects for the reproductive organs, eyes, and bone marrow (ICRP 1991). Non-neoplastic diseases do not represent a major concern for fallout exposures that usually are below threshold values. However, non-neoplastic diseases are discussed here because of new data coming out of the atomic bomb survivor study as well as studies of various exposed populations around Chernobyl. Concern has been expressed by members of the public regarding non-neoplastic diseases and radiation, particularly, non-neoplastic thyroid disease.

4.2.3.1   Thyroid Disease

Clinical experience has demonstrated that exposure to high-dose radiotherapy to the head and neck or radioiodine therapy for thyrotoxicosis causes subsequent non-neoplastic thyroid disease (IOM 1999; Maxon and Saenger 1996; Barsano 1996; UNSCEAR 1993). The response at lower levels of exposure is not well understood. Results from studies of environmental exposures have been inconsistent. The occurrence of non-neoplastic thyroid disease in relation to environmental radiation exposure has probably been best studied in the various populations near the Chernobyl nuclear power plant and in the Hanford region.   As a result of the Chernobyl accident, these populations were exposed to a mix of radioiodines, which included ^{131}I, other shorter lived radioiodines, and ^{137}Cs among others. Besides thyroid cancer, non-neoplastic thyroid conditions have been investigated in children who were exposed to fallout from the accident. The largest study reviewed, which addresses both neoplastic and non-neoplastic thyroid abnormalities, comes out of the screening program conducted by the Chernobyl Sasakawa Health and Medical Cooperation Project (Sasakawa Memorial Health Foundation 1994; Sasakawa Memorial Health Foundation 1995). In this large examination program, carried out in about 160,000 children less than 4 years of age at the time of the accident, no increased risk of hypothyroidism, hyperthyroidism or goiter related to radiation exposure was found. Reviewing these and other Chernobyl data, UNSCEAR has recently concluded that there has been no increased risk of thyroid abnormalities, with the exception of thyroid cancer in those exposed at young ages, in affected populations following the Chernobyl accident (UNSCEAR, 2000). The Hanford Thyroid Disease Study found no increase in risk of benign thyroid nodules, hypothyroidism, or hyperparathyroidism associated with exposure to ^{131}I (www.cdc.gov/nceh/radiation).

4.2.3.2   Other Non-Neoplastic Diseases

An increased risk of heart disease following high doses of radiation therapy has been reported previously (Mettler and Upton 1995; Hancock et al. 1993). More recently, the

atomic bomb survivor data have shown a small excess risk for non-neoplastic diseases, mostly heart disease and stroke (Shimizu et al 1999). The excess non-neoplastic disease in the atomic bomb survivors is seen at a level below that given for medical purposes. However, the shape of the dose response is not clear, especially at low dose levels, from the current data. A linear dose response cannot be ruled out, but the data are also consistent with the possibility of essentially zero risk below 0.5 Sv. No animal experiments have shown cardiovascular changes following this level of low-dose exposure, so the biological mechanisms for non-neoplastic disease related to low-dose exposure are currently speculative. Given the lack of a clear dose-response curve and the uncertainty of the risk at a low dose, no quantitative assertions on non-neoplastic risks relevant for fallout exposure can be made.

There has not been any demonstrable inherited adverse health effect, including untoward pregnancy outcome, birth defects, or cancer, in a cohort of over 70,000 children whose parents were exposed to radiation from atomic bombs in Hiroshima and Nagasaki (Neel and Schull 1991). This suggests that the excess health risks inherited from radiation-exposed parents are very small and much less than those found for people who were directly exposed to radiation.

4.3 Risk Analysis

The large amount of epidemiological and experimental data on the health effects of exposure to radiation, and specifically the quantitative data that relates cancer to radiation dose, makes it possible to estimate the risk as well as the likely number of people developing cancer as a result of fallout radiation exposure. As noted earlier, several national and international scientific committees periodically review the literature relevant to radiation risk assessment, and recommend models for estimating risks of several types of cancer. These models can then be used to estimate risks – or number of cases to be expected – which result from exposures of specific populations, such as those among the United States population alive during the years of fallout and exposed to its radiation. In contrast, little has been done to attempt to develop similar models to quantify non-cancer disease risk. As observed in previous sections of this chapter, a great deal is still unknown about the relationship between radiation and non-cancer health effects, particularly with regard to whether there is any risk at low doses.

Because models for estimating risks of cancer have been developed by several groups of investigators, there is little question that estimates for risk of cancer for the United States population resulting from fallout exposures could be obtained if dose estimates are computed. It must be noted, however, that the populations and exposures for which risk projections are needed nearly always differ from those for which epidemiological data are available. This means that resulting risk projections must be based on assumptions about which there is considerable uncertainty. This raises the question of whether or not uncertain estimates of risk can be useful for developing public health policy. To address this question, example estimates of cancer risks are provided later in this chapter. Additionally, the degree of uncertainty in these example estimates is evaluated. First, however, various measures of risk are defined, a description of how cancer risk models have been developed and applied is

provided, and the major sources of uncertainty in the risk estimates obtained from these models are discussed. This section on risk analysis focuses primarily on cancer as a health effect of radiation exposure; however, non-cancer health effects are also discussed. Although the discussion of risk measures, model development, and uncertainty are framed in terms of cancer risk, the concepts reviewed are applicable to non-cancer risk as well.

4.3.1   Measures of Risk

An important measure of risk that has been emphasized in most recent risk assessments is the "lifetime risk" or probability that a given radiation exposure will lead to death from cancer in the remaining lifespan of the individual. Although radiation risks have commonly been measured in terms of mortality, projections of lifetime risks of cancer incidence can also be made. Mortality and incidence are both of interest, the former because it can be considered the most serious adverse effect of exposure and the latter because it more fully reflects the public health impact. The measures of lifetime risk that are emphasized here are the risk of radiation-induced death or radiation-induced cancer incidence.

As previously noted, epidemiological data generally support the use of linear dose-response relationships for most cancers, that is, a relationship in which risk is proportional to dose. Even when the dose-response relationship is better described by a linear-quadratic function (as is the case for leukemia), at low doses the linear term dominates and the quadratic term can be ignored. For this reason, lifetime risk, at least at lower doses, is usually specified by a numerical coefficient expressing the risk per unit of radiation dose. This means that the lifetime risk resulting from a specific dose can be obtained by multiplying the 'lifetime risk coefficient' by the radiation dose.

"Lifetime risk coefficients" depend on gender and age at exposure, because both sensitivity to radiation exposure and the years of life remaining for cancer to develop depend on these factors. Lifetime risks for an entire population can be estimated by first carrying out the calculations for each age at exposure and gender and then averaging the risks according to characteristics of the population of interest. Overall risk coefficients presented in reports such as those of the National Academy of Science's BEIR V Committee (NAS 1990), the International Commission on Radiological Protection (ICRP 1991), or the U.S. Environmental Protection Agency (EPA 1994, 1999) have usually been obtained as averages reflecting the age-gender composition of a specified population. For example, the most recent EPA estimates (EPA 1999) reflect the 1990 population of the United States. Although it is recognized that there is considerable variation in risk from a given dose of radiation among individuals within any population, 'lifetime risk coefficients' are summary measures that provide information on the average risk for a group that shares common characteristics. Available epidemiological data make it possible to obtain estimates that are specific for categories defined by age at exposure and gender, but are inadequate to take account of all factors that affect risks. Hence, these average risks are useful for estimating overall public health impact, but are much poorer for estimating the likelihood of an individual developing cancer.

In evaluating risks from fallout exposure, there is interest not only in risks for the overall United States population, but also for groups of people living in certain geographic locations or for groups born near to the same time. Within those groups, there may be considerable variation in the doses that individuals have received. However, multiplying the 'lifetime risk coefficient' by the average dose for the group will yield an estimate of the average risk. Multiplying this average risk by the size of the population will then yield the estimated number of radiation-induced cancers in the population that may occur in addition to those expected without any nuclear fallout exposure.

4.3.2   Risk Model Development

The first step in developing risk estimates is to develop a model for describing the relevant epidemiological data. This means expressing age-specific cancer mortality or incidence rates as a function of baseline cancer rates and parameters that characterize the relationship between risk and radiation dose. The risk from radiation is often expressed as a function of dose, age at the time of exposure, time since exposure, gender, and sometimes other factors. A model that describes the epidemiological data can then be used to calculate the lifetime risk for a group of people with specific ages at exposure and gender. To do this, one essentially follows the group forward in time and calculates the risk of developing a radiation-induced cancer at each age subsequent to the age at exposure. This requires probabilities of survival to each subsequent age, obtained from life tables, and may also require background rates, usually obtained from cancer mortality vital statistics for the population of interest (or incidence rates if cancer incidence is to be estimated). For more detail on risk model development, the reader is referred to Bunger et al. (1981), Thomas et al. (1992), or any of several reports from international committees and agencies that provide risk models (NAS 1990; UNSCEAR 1994; ICRP 1991; UNSCEAR, 2000).

4.3.2.1   Uncertainties in quantifying risk due to radiation

As noted above, risk models cannot precisely predict risk to an individual or the number of health effects in a population; hence, all risk projections are inherently uncertain. The more important assumptions and associated uncertainties involved in estimating risks in persons exposed to doses from fallout in the United States are discussed below.

Uncertainties in the epidemiological data. Estimates obtained from epidemiological data are subject to random or chance fluctuation, which is referred to as "statistical uncertainty". This source of uncertainty can be quantified, and is often expressed by presenting 90 or 95% confidence intervals that reflect a range of values that are reasonably compatible with the data. Statistical uncertainty in estimated risk coefficients expressing the risk per unit dose tends to be larger when risks are small than when they are large, and this is the primary reason that risk estimates have been based mainly on epidemiological data from populations exposed at high doses.

Uncertainties also come about because of imperfect disease detection and diagnosis and errors in the dose estimates that are used. In particular, mortality studies often rely on death certificate information, which is often inaccurate, especially for providing information on specific types of cancer. In addition, because epidemiological studies are not controlled

experiments, estimates of risk may be biased (that is, may be too high or too low) by unknown factors that differ by level of dose. For example, if subjects with higher doses tended to smoke more than subjects with lower doses, estimates of lung cancer risks resulting from radiation exposure could be biased. This type of bias is known as confounding, and is especially problematic in studying populations where radiation risks are small. Furthermore, a selection bias may occur when exposed subjects are healthier, as often observed in studies of healthy occupational populations ("healthy worker effect"), or less healthy, as with medically irradiated populations, than the general population. In such cases, comparison of the cohort disease occurrence with that of the general population may conceal or overstate the true radiation-related risk. A surveillance bias may occur when heightened scrutiny (such as screening) is undertaken to detect diseases of interest in exposed populations. This has been an important source of concern in assessing cancer risk, especially of thyroid cancer, in studies of Chernobyl populations given medical attention.

Extrapolating to low doses and dose rates. Probably the most important source of uncertainty in risk estimates for persons exposed to fallout radiation is the extrapolation from high to low doses and high to low dose rates. Rudimentary dose estimates presented in Chapter 3 indicate that most doses from weapons testing fallout are much smaller than those that have been used to estimate risks, and in addition, they are received at low dose rates.

Estimates obtained directly from epidemiological data on populations exposed to low doses and low dose rates, such as nuclear workers, are very imprecise (Cardis et al. 1995). The few studies of persons exposed to fallout are also inadequate for estimating risks with any precision. With small doses, the increased cancer risk from radiation is very small relative to the baseline cancer risk, so that random fluctuation and the possibility of confounding make it difficult if not impossible to detect risk or to estimate it with any precision.

For this reason, it is necessary to extrapolate from risks estimated for persons exposed to much higher doses and dose rates than those received from fallout. Specifically, data on atomic bomb survivors have played an important role in developing models for risk estimation. Although the atomic bomb survivors include individuals who were exposed at low doses, risk estimates derived from these data tend to be driven by those doses exceeding 1 Gy (1000 mGy). To a lesser extent, medically exposed populations have also been used in developing risk estimates, and these also primarily involve relatively large doses. Usually, linear dose-response functions in which cancer risk is proportional to radiation dose have been used to extrapolate from high to low doses. Although most epidemiological data are compatible with such a relationship, other models such as a linear-quadratic relationship cannot be excluded. Because experimental data have suggested that risk per unit of dose is lower when radiation is received at low rates than when it is received at high rates, linear estimates of risk at low doses and dose rates are often reduced by a factor known as the dose and dose rate effectiveness factor (DDREF). A factor of 2 for the DDREF has been used in several risk assessments, but the magnitude of the factor, or whether it is needed at all, is uncertain. Some think that there may be a threshold, that is a dose below which there is no risk, though as noted previously (Section 4.2.1), for most cancer sites, this hypothesis is not supported by currently available data.

Because of the large uncertainty in the risks associated with exposures at low doses, the National Academy of Science's BEIR V committee (NAS 1990) did not publish estimates of risk for single doses below 0.1 Gy (100 mGy), and also noted the possibility of no risk at very low doses. It should be noted that with the exception of dose to the thyroid, most doses from fallout that were estimated for this feasibility report are much smaller than 0.1 Gy, and estimates of average doses tend to be in the range of 0.001 to 0.003 Gy (1-3 mGy). The relative uncertainties in estimating risks at these low doses are especially large.

Transfer from Japanese atomic bomb survivors to the United States population. Another important source of uncertainty results from applying risks estimated from studying a particular exposed population to another population that may have different genetic and lifestyle characteristics and different baseline cancer risks. Specifically, the application of risk estimates based on Japanese atomic bomb survivors to a United States population is a concern, particularly for estimating risks of specific cancers for which baseline rates differ greatly between the two populations. For example, colon cancer rates in Japan are less than half those in the United States, whereas liver cancer rates in Japan are several times as great as those in the United States; colon and liver are two of the cancer sites where fallout doses may be of concern. To address this general problem, the NAS BEIR V committee calculations were based on the assumption that relative risks resulting from radiation exposure were proportional to baseline risks, whereas the earlier NAS BEIR III committee based their estimates on the assumption that risks (on an absolute scale) did not depend on baseline risks, and thus would be similar for Japanese and United States populations. Some recent efforts have used intermediate approaches with allowance for considerable uncertainty (EPA 1999; NIH 2000).

Differences in relative biological effectiveness (RBE). Some doses from fallout involve internal exposure from ^{131}I, which primarily exposes the thyroid gland, and from other radionuclides that expose a variety of organs including colon, liver, kidney, red bone marrow, and bone surfaces. By contrast, Japanese atomic bomb survivors were primarily exposed to external gamma rays, with some exposure to neutrons. This means that both dose rate and the uniformity of the dose within the organ may be different for fallout exposures compared with doses to atomic bomb survivors. The manner in which this might affect risk is not known with certainty. The ratio of the disease risks resulting from equal doses of different types of radiation is known as the relative biological effectiveness or RBE.

Projection of risks over time. Many of the atomic bomb survivors who were young at the time of the bombings (1945) are still alive, and thus their risks at older ages – when baseline cancer risks are largest – have not yet been studied. This is also true for other exposed groups who are being studied. Thus, estimating lifetime risks for those exposed at very early ages and who have lived for decades afterwards requires assumptions about the time-response patterns of disease. Most recently developed risk models for cancers other than leukemia and bone cancer are based on the assumption that, after a minimal latent period, the risk (measured on a scale relative to the baseline cancer risk) remains constant over the entire lifespan. This could overestimate risk if the relative risk decreases over time as is suggested by some epidemiological data (Pierce et al. 1996; Thompson et al. 1994; Little et al. 1998.), especially for those who were young at exposure. For leukemia, the risk to those exposed early in life seems to have decreased to near zero by 20-30 years following

exposure (Preston et al. 1994); however, there is some uncertainty in risks for the period 2-5 years following exposure, since data on atomic bomb survivors are not available before 1950.

Quantifying uncertainties. Recently, there has been increased attention to quantifying the degree of uncertainty in risk estimates [NCRP 1997; EPA 1999; and NIH 2000]. The approach that is taken is first to quantify the uncertainty from each of several sources by specifying distributions, or the probabilities associated with a range of plausible values. For most uncertainty sources, this requires informed judgments based on the weight of available scientific evidence by those conducting the analysis.   Because these judgments are necessarily somewhat subjective, intervals reflecting uncertainty are often referred to as "credibility intervals" instead of confidence intervals (which are usually determined by more rigorous statistical procedures). In order to allow flexibility in the distributions used to indicate the uncertainties in the separate sources, computerized simulations, called Monte Carlo calculations, are often needed.

In evaluating the uncertainty in the risk estimated for a group of individuals exposed to a particular level of dose, it is necessary to include the uncertainty in the dose estimate. Dose estimates are subject to several sources of uncertainty, including those involved in the determination of: (1) the deposition densities of the various radionuclides as a function of time and space; (2) the transfer of those radionuclides in the environment; and (3) the lifestyle and dietary habits of the group of individuals that is considered. To a large extent, these uncertainties have not been quantified in this feasibility study. In principle, the uncertainty in dose can be included in risk calculations.

4.3.3   Illustrations and Discussion of Problems in Estimating Cancer Risks from Fallout Doses

In this section, the problems involved in estimating risks of several types of cancer are illustrated. With the exception of the thyroid cancer, the examples were developed using approaches that could be applied quickly, and are given for illustration only. The results presented here need careful re-evaluation if a more detailed dose and risk assessment for radioactive fallout is undertaken.

4.3.3.1   Thyroid Cancer Risks from Internal Exposure to ^{131}I

A detailed evaluation of dose to the thyroid gland from ^{131}I from tests in Nevada has already been conducted (NCI 1997). Doses to the thyroid are predicted to be much larger than those to other organs. Results of this feasibility study indicate most of the dose to the thyroid is from NTS rather than global fallout. Land (IOM 1999) has already evaluated risks of thyroid cancer from exposure to ^{131}I from the NTS, and estimated that between 11,300 and 212,000 thyroid cancers would be expected to occur among persons who were under age 20 in the period 1951-1957 with a median estimate of 49,000. The risk coefficients used in this evaluation were based on a pooled analysis of data from seven epidemiological studies of persons exposed externally (Ron et al. 1995). Because both thyroid doses and 'lifetime risk coefficients' depend strongly on age at exposure, the

calculation of Land gave separate consideration to different ages at exposure with the largest risks for the youngest age groups and with no risk for those exposed at ages 20 and older. Consideration of global fallout likely would increase the thyroid cancer estimates for the United States by about 15% (Table 3.22), although thyroid cancers resulting from global fallout would tend to occur in later birth cohorts than those resulting from NTS fallout.

The range of predicted thyroid cancer cases from NTS fallout allowed for two of the most important uncertainty sources – statistical uncertainty and uncertainty in the estimated average dose – but did not include uncertainty in the relative biological effectiveness (RBE) of ^{131}I exposure compared with external exposure, or for the possibility of reduction of thyroid cancer risk over time. Both Shore and Xue (1999) and Little et al. (1998) find evidence of such a reduction; and Shore and Xue indicate the reduction of the lifetime risk estimates of thyroid cancer after childhood exposure might be about 40-60%.

Estimates of lifetime risks for groups of individuals sharing certain characteristics could have also been made, such as groups defined by age at exposure and geography. For example, based on tables describing the Land calculations (Appendix B of the Institute of Medicine's review of NCI's fallout report), the average lifetime risk for the entire United States for persons exposed under age 5 can be estimated to be about 0.002 (or about 1 in 500), while no risk is estimated for persons exposed at ages 20 and older (IOM 1999). The uncertainty estimates for specific groups are likely to be larger than that for the population as a whole. This example for thyroid cancer illustrates the feasibility of estimating risks. In addition, the wide range in the number of thyroid cancer cases predicted (11,300-212,000) illustrates the large uncertainty that such estimates carry.

4.3.3.2   Total Cancer Risks from External Exposure to NTS and Global Fallout

For tissues other than thyroid, the crude dose estimates in Chapter 3 suggest that the contribution from external dose is larger than that from internal dose. Specifically, the per capita external dose over the period 1951-2000 from both NTS and global fallout is estimated to be about 1.2 mGy (Table 3.14), whereas, with the possible exception of bone surfaces, internal dose even to the more heavily exposed tissues is likely to be less than this. External dose can be expected to expose all tissues of the body in a reasonably uniform manner so that estimating the risk of all cancers is important. An ideal assessment would evaluate risks for each year of birth, taking account of the age at exposure in each subsequent year. An assessment for groups exposed in separate geographic areas could also be made to the extent that doses can be estimated for such groups. However, because a substantial portion of the external dose is from exposure to global fallout, geographical variability may be much less than for internal dose.

Several scientific committees and groups have provided models for estimating the risks of all fatal cancers combined. Here, we make use of the ICRP (1991) coefficient of 5% per Sv for total cancer mortality. We first evaluate risks for the 3.8 million people born in the United States in 1951 (Bogue 1985), a group that would, on average, have received larger doses at earlier ages than those born earlier or later. The average dose for this population is estimated to be about 1.2 mSv, resulting in a population dose of about 4600

113

person-Sv. If the ICRP coefficient of 5% per Sv is applied, about 230 cancers would be predicted to result from this exposure (a lifetime risk of about 1 in 16,500). However, because much of the dose would be received in childhood for this group, risks might be larger; for example, calculations shown in UNSCEAR (1994) indicate that risks for those exposed under age 20 might be 2 or 3 times risks for those exposed in adulthood. It seems unlikely, however, that consideration of age at exposure would result in an estimate of more than 1000 excess cancers in this group (about 1 in 3800). Since more than 20% of all deaths are due to cancer (Greenlee et al. 2000), this can be contrasted with about 760,000 cancer deaths that might be predicted in this group in the absence of radiation exposure from fallout. It is also noted that the average annual dose from natural background for the US population is about 1 mSv, with a total dose of 70 mSv over a 70-year lifespan. For persons born in 1951, the population dose from natural background is thus about 266,000 person-Sv. Applying the ICRP coefficient thus results in an estimated 13,300 cancer deaths from natural background, more than 13 times the estimated number from fallout.

Cancer incidence estimates (including non-fatal cases) would be about double those for cancer mortality (Ries et al. 1996), resulting in a prediction of less than 2,000 fallout-induced incident cases among persons born in 1951; about 1,520,000 incidence cancer cases would be expected to occur in this group in the absence of exposure. In this simple evaluation, we have not attempted to provide detail on the distribution of the excess deaths and cases by gender, or by age and calendar year of occurrence.

Risks for other birth cohorts could also be evaluated and would have smaller risks than those for the 1951 cohort. For example, the 1931 birth cohort would receive about the same external dose, but it would all be received in adulthood. The number of excess fatal cancers predicted in the 2.5 million persons born in 1931 (Bogue 1985) would be about 150, compared to about 500,000 fatal cancers that would be predicted in the absence of fallout exposure. This can be further contrasted to risks estimated for persons born in 1971. The average dose for this birth cohort is only about 0.23 mSv (dose received by the year 2000), with most of this dose received in childhood. The predicted number of excess fatal cancer among this cohort of 3.6 million persons is likely to be less than 100, compared with about 720,000 cancer deaths that would be predicted in the absence of fallout. Estimates for the 1931, 1951, and 1971 birth cohorts are summarized in Table 4.1. Estimates for cancer incidence (including non-fatal cases) would be about double those shown in Table 4.1.

Table 4.1. Estimates of the total number of excess cancer deaths resulting from external exposures from NTS and global fallout for persons born in 1931, 1951 or 1971.

Birth cohort (Population size)	Cancer deaths expected in the absence of fallout	Estimated excess cancer deaths.*	Risk of cancer death in the absence of fallout	Estimated excess risk of cancer death
1931 (2.5 million)	About 500,000	About 150	About 20% (1 in 5)	About 0.006% (1 in 17,000)
1951 (3.8 million)	About 760,000	Less than 1000	About 20% (1 in 5)	Less than 0.03% (1 in 3800)
1971 (3.6 million)	About 720,000	Less than 100	About 20% (1 in 5)	Less than 0.003% (1 in 36,000)

*Includes deaths from leukemia.

It would be possible to repeat this exercise for every birth year that contributed persons alive in the period 1950-2000; that is, persons born in the years 1880 through 2000. As noted above, persons born in 1951 would experience the largest risks. Persons born before 1931 would have risks that were lower than those indicated for those born in 1931, and persons born after 1971 would have risks that were lower than those indicated for 1971. Although it is not sensible to estimate an average individual risk that applies to all contributing birth years, it is possible to estimate the total number of excess cancers that might have occurred among all exposed birth-year cohorts. This can be done by considering the size of the exposed population in each of the years of fallout. The population doses given in Table 3.14 are based on the assumption that the population was 163 million (1954 population) throughout the period 1951-2000, which does not allow for increases in the United States population over time. For the purpose of this illustration, we have made a crude correction by using a population of 250 million (1990 population) for the exposure received in the years 1973-2000, resulting in a total population dose of 217,000 person-Sv. Applying the ICRP coefficient of 5%, it can be estimated that about 11,000 extra cancer deaths would be predicted to occur among the United States population alive during the years of fallout. Cancer incidence estimates (including non-fatal cases) would be about double those for cancer mortality, resulting in a prediction of about 22,000 radiation-induced incident cases. The cancer deaths (and incident cases) would be spread out over the period extending from the 1950s through much of the 21st century, and would be in addition to the far larger number of cancer deaths that occur every year in the United States; for example, about 500,000 cancer deaths occurred in 1990 (Bureau of the Census 1997). About 40 million cancer deaths and 80 million incident cases might be predicted to occur over a 75-year period. Another perspective is provided by noting that if the same methodology were applied to estimate risks from natural background exposure received during the period 1951-1972, when 80% of the fallout dose was received (Table 3.14), about 180,000 cancer deaths and 360,000 incident cases would be predicted, about 16 times the number from fallout.

The National Council on Radiation Protection and Measurements evaluated sources of uncertainty in the ICRP risk coefficient of 5% per Sv that was used to obtain the above estimates (NCRP 1997). The uncertainty sources evaluated were: statistical uncertainty,

errors in reporting of cancer deaths in atomic bomb survivors, errors in dose estimates for atomic bomb survivors, extrapolation from acute exposure at high doses and dose rates to low doses and dose rates, transfer of risk estimates from Japanese atomic bomb survivors to a US population, and projection of risks over time. Uncertainty from each source was quantified, and computer simulations were conducted to evaluate the overall uncertainty from all sources. Using that approach, the 90% credibility interval for the lifetime risk coefficients for fatal cancer covered a range from 1.2% per Sv to 8.8% per Sv. Applying that range to the total population dose from external fallout, the number of excess cancer deaths among the United States population is predicted to be from 2,600 to 19,100 The range for the number of incident cases would be about double these values.

The range for the 'lifetime risk coefficient' does not account for uncertainties in the estimated external doses from fallout. Inclusion of all sources of uncertainty could be accomplished by conducting computer simulations that used both the uncertainty distributions given by the NCRP and a distribution reflecting uncertainties in the dose estimates. Because the uncertainties in dose estimates are not provided in this feasibility study, this computer simulation has not been performed. For illustration only, it is assumed that the 90% credibility interval for dose extends from a factor of three below the estimate to a factor of three above the estimate. Under this assumption, simplified calculation incorporating all of the above uncertainties result in risk projections that range from 1,700 to 32,500 excess cancer deaths.

Although the estimates above should be regarded as illustrative only, they indicate that the total number of incident cancers from external fallout exposure (about 22,000 cancers) would be about half the estimated number of thyroid cancers from ^{131}I exposure (49,000). It is likely that the number of deaths (roughly 11,000) might exceed deaths from thyroid cancer, which generally has a low fatality rate. Doses from external exposure, especially those from global exposure, vary less than doses to the thyroid from ^{131}I by geographic location, birth cohort, and dietary habits (such as milk consumption). Risks for cancers other than thyroid cancer are also less strongly dependent on age at exposure. For these reasons, risks for all cancers from external exposure are likely to vary less by geographic location, age at exposure and other factors than risks of thyroid cancer from NTS ^{131}I exposure, which makes it much less likely that there will be groups with particularly large risks.

It should also be noted that total cancer risk from external exposure can be estimated with greater certainty than can risks of most individual types of cancers or risks from internal exposure. This is because of the relative wealth of epidemiological data on external exposure (including the atomic bomb survivors studies), and because both statistical uncertainties and uncertainties in extrapolating risks from atomic bomb survivors to a United States population are smaller. Nevertheless, the above discussion demonstrates that even estimates of total cancer risk from external exposure are accompanied by large uncertainties.

4.3.3.3   Leukemia Risks from External and Internal Exposure

Leukemia is perhaps of special interest because it has been strongly linked with radiation in several epidemiological studies, because it occurs in young people, and because of the strontium-90 component of fallout exposure. Also, increased rates of leukemia have been reported in participants in the Smoky nuclear weapons test conducted at the NTS in 1957 (Robinette et al. 1985) and an association of leukemia and fallout dose has been suggested among persons living downwind of the NTS (Stevens et al. 1990). In addition, during numerous CDC public meetings on other radiation-related issues, members of the public have consistently identified leukemia as one of their main cancer concerns.

For leukemia, the ICRP (1991) lifetime risk coefficient is 0.5% per Sv. Since this estimate was based on atomic bomb survivor data at a time when nearly all leukemias were fatal, it can appropriately be considered as an estimate of lifetime leukemia incidence as well as mortality. Actually, modern leukemia survival rates would reduce mortality, but this is seldom taken into account in estimating leukemia risks. As with other cancers, the ICRP risk coefficient includes reduction by a DDREF of 2. This is roughly equivalent to using the linear term of the linear-quadratic function that has been used to describe the dose-response relation in atomic bomb survivors.

It is noted first that the estimates for total cancer mortality from external dose given in Table 4.1 include deaths from leukemia and that roughly 10% of these deaths would be predicted to be from leukemia. (About 3% of background cancer deaths are from leukemia.) Similarly, about 1,100 of the 11,000 cancer deaths for all birth-year cohorts from external exposure might be from leukemia. As shown in Table 3.22, internal exposures would result in additional dose to the red bone marrow, mostly from global fallout. For a person born 1 January 1951, the average dose from internal sources is estimated to be 0.9 mSv, resulting in a population dose of 3420 person-Sv. If it is assumed that risk coefficients are similar for internal and external exposure, one might predict about 17 (0.5% x 3420) leukemia deaths from internal exposure, a lifetime risk of about 1 in 220,000. Lifetime risks for leukemia do not depend strongly on age at exposure (UNSCEAR 1994). Average bone marrow doses from internal exposure are not given in this report for other specific birth-year cohorts, and thus we have not attempted to estimate risks for these cohorts. However, Table 3.22 also indicates that the average dose for an adult from internal sources is estimated to be 0.7 mSv. A rough estimate of the total number of leukemia deaths from internal exposure for all birth-year cohorts can be obtained by noting that the adult internal exposure is about half of that due to external exposure. If it is again assumed that risk coefficients are similar for internal and external exposure, about 550 leukemias from internal exposure might be added to the 1,100 leukemias estimated to result from external exposure.

4.3.3.4   Risks from Internal Exposure (Other Than Thyroid and Leukemia)

Dose from internal exposure varies considerably by organ, making it important to separately consider risks of cancers in specific organs. Presently available data on NTS and global exposures indicate that the tissues or organs that can be expected to receive the largest internal doses are thyroid, colon, kidney, liver, red bone marrow, and bone surfaces.

Risks of thyroid cancer and leukemia from internal exposure were discussed earlier in this section.

Several groups of scientists have made estimates of risk coefficients for at least some of these cancers. For illustrative purposes, those lifetime risk coefficients developed by the EPA (1999) for cancer mortality are provided in Table 4.2. These risk estimates are reasonably recent and include estimates for all the tissues noted above. Estimates of cancer incidence are also available.

Table 4.2. Environmental Protection Agency's age-averaged site-specific lifetime cancer mortality risk estimates from low-dose, low-LET uniform irradiation of the body.

Site	Percent per Sv
Colon	1.04
Liver	0.15
Bone	0.01
Kidney	0.05
Leukemia	0.56
All cancer	5.75

Except for leukemia and all cancer, the EPA has not carried out a detailed analysis of the level of uncertainty in the risk coefficients listed in Table 4.2, but sources of uncertainty are discussed and approaches for evaluating them are suggested (EPA 1999). Uncertainty for specific cancers is likely to be larger than that for all cancers combined, both because statistical variation is greater, and, for estimates based on atomic bomb survivor data, differences in United States and Japanese baseline risks are greater.

Risk estimates for exposures involved in fallout could be obtained by multiplying those coefficients by the dose to the tissue or organ that was exposed. This feasibility report does not go through this exercise. However, the following observations are made. First, the rudimentary dose assessment performed indicates that most tissues received little dose from internal sources (Tables 3.10, 3.19 and 3.22). Secondly, with the exception of the thyroid, there are no organs that are likely to receive doses that are substantially larger than those from external exposure. For these reasons, the total risk of cancer (other than thyroid cancer) from internal exposure is likely to be less than that from external exposure.

4.3.4   Future Possibilities for Analyzing Cancer Risk

The examples above were intended only for illustration, hence, the methods were based on readily available "lifetime risk coefficients". If a more detailed assessment of doses from fallout is undertaken, several improvements can likely be considered. In the illustrations provided, no attempt was made to give detailed attention to developing risk estimates for specific years of birth that took account of both specific ages at exposure and specific population sizes for different exposure years. Such estimates would help to provide information on which persons were at greatest risk, and would also provide a slightly more

accurate estimate of the overall risk. In addition, risk estimates for specific geographic locations could be developed, again providing information on those at greatest risk. This latter refinement is probably of greater interest for doses from NTS fallout since these show greater geographic variation than doses from global fallout. Better information on the predicted age and calendar period of appearance of predicted cancer deaths and incident cases could also be developed.

Evaluation of uncertainty in risk estimates should include both the uncertainty in the lifetime risk coefficient and uncertainty in the estimated dose. To allow full flexibility in the distributions used to describe uncertainties, computer simulations would be needed. Although we have not used this approach in our illustrations, the feasibility of conducting such simulations has been demonstrated by the NCRP (1997), EPA (1999), and most recently by the NIH (NIH 2003) as discussed below.

The National Institutes of Health (NIH 2003) has recently updated the Radioepidemiological Tables that were published in 1985 (NIH 1985). This revision required developing risk models for more than 20 specific cancers, including those organs and tissues that are of interest following exposures to radioactive fallout. Although the tables are being developed to estimate the "probability of causation" (that is, the probability that a cancer that has been diagnosed in an individual is the result of some previous exposure to radiation), the models could be used to estimate the lifetime risk of developing cancer. The evaluation of uncertainty in the revised tables is probably the most comprehensive that has been undertaken in the field of radiation risk assessment. The overall uncertainty distributions include statistical uncertainty of parameters, as well as subjective evaluation of uncertainties in the errors related to extrapolating to low doses and dose rates, the differences between Japanese and United States populations, and uncertainties in the dosimetry of atomic bomb survivors. Software has been developed that allows a person interested in a specific "probability of causation" to specify the type of cancer and when it occurred, the age at exposure and gender, the radiation dose and when it was received, and, if desired, the uncertainties in the dose estimate. A computer calculation (simulation) is then performed, and the person is provided with a range of estimates of the probability the cancer was a result of radiation exposure (see http://www.niosh-irep.com/irep_niosh/).

Although the software is now limited to evaluating "probability of causation", it could be expanded to estimate lifetime risks – a more useful quantity for those exposed to fallout and who as yet have no observable health effects. In addition to providing a comprehensive evaluation of uncertainty, the NCI approach has the advantage that it is based primarily on atomic bomb survivor cancer incidence data from the Hiroshima and Nagasaki tumor registries. This means that diagnostic information on specific cancer types is likely to be more reliable than for the mortality data used in most other risk assessments.

In addition, the National Academy of Science's BEIR VII Committee is expected to recommend models for risk estimates of the health effects of exposure to low levels of ionizing radiation. The models to emerge from that study are likely to make use of the latest mortality and incidence data from the atomic bomb survivors as well as from other epidemiological studies that provide relevant information. Analyses of mortality data

covering 1950-1997 have recently been published (Preston et al. 2003), and analyses of updated atomic bomb survivor cancer incidence data are currently underway and will extend the period covered by eleven years (covering 1958-1998 instead of 1958-1987 as previously).

Finally, a thyroid dose and cancer risk calculator was developed by NCI to allow any individual to obtain an estimate of the risk of thyroid cancer resulting from the estimated thyroid dose from ^{131}I arising from nuclear tests conducted at the NTS. The NCI ^{131}I thyroid dose/cancer risk calculator for NTS fallout, together with educational material, can be found on the internet at http://i131.nci.nih.gov. Details are provided in Chapter 5 of this report.

Although the approaches and resources noted above are expected to provide a stronger basis for estimating risks and particularly for quantifying their uncertainties, they cannot greatly reduce some important sources of uncertainty in estimating the risks from exposures received from fallout. These include uncertainties in extrapolating from high to low doses and dose rates, uncertainties in using estimates from Japanese atomic bomb survivors for a United States population, and uncertainties in the relative biological effectiveness of some of the exposures involved in nuclear fallout.

4.3.5 Analyzing the Risk of Non-Cancer Health Effects

Data presented earlier in this chapter described the relationship between radiation and non-cancer health effects, including benign tumors of the thyroid, the salivary glands, and other sites and non-neoplastic diseases such as hypothyroidism and heart disease. While a number of epidemiologic studies have demonstrated an association between radiation and non-cancer health effects, more fundamental research is needed clarify the biological mechanisms by which low-dose, and low-dose-rate radiation exposure causes disease. Also, dose response and time response patterns of the disease-exposure relationship require further assessment before risk analyses can be performed reliably.

In considering the dose data available in this feasibility assessment, the most likely non-cancer health outcomes that may affect the American people are those involving the thyroid gland. Present estimates of dose from fallout radiation indicate that the internal organ-specific dose to the thyroid is much higher than the dose to other organs/tissue evaluated (Tables 3.10 and 3.22). Internal and external exposures (delivering a uniform dose to the whole body) to fallout radiation are unlikely to result in an increase in other non-neoplastic disease at the currently estimated dose levels. However, it is conceivable that select individuals may have much greater sensitivity to radiation than has been found on average. For example, individuals with pre-existing disease could be more radiosensitive.

4.3.5.1 Benign Tumors of the Thyroid

While considerable effort has gone into quantifying the lifetime risk of cancers, much less has been done to quantify non-malignant disease in a similar manner. Among those benign tumors that have been related to radiation exposure in various studies, lifetime projections of risk are available only for benign thyroid nodules. This lifetime risk coefficient was developed for the Nuclear Regulatory Commission (NRC 1989, 1993) for

predicting health effects from nuclear power plant accidents and has been reviewed by the NCRP (1993). The risk estimate is based on data from studies of external x-ray irradiation of children and is based on the assumptions that women are more sensitive to exposure than men are and children are more sensitive than adults are. Internal exposure to ^{131}I is assumed to be substantially less effective than external irradiation in inducing benign neoplasms in the general population (NRC 1993).

At this point in time, however, quantifying the lifetime risk of benign thyroid nodules resulting from fallout exposure is not advisable. Although risk estimates can be developed using available risk coefficients, these estimates do not take into consideration recent studies of the relationship between radiation and thyroid disease, specifically those studies conducted in populations exposed to ^{131}I from the Chernobyl accident. More importantly, existing risk coefficients do not adequately account for uncertainty. Given the important issues surrounding the detection and diagnosis of these benign nodules, the uncertainty associated with this health endpoint will likely be much greater than that seen for thyroid cancer. Additionally, issues related to the effectiveness of internal exposure to ^{131}I in inducing benign nodules, extrapolation of risk estimates from one population to another, and projection of risk over a lifetime need to be considered.

Separate from actually developing risk estimates, but, equally important in determining whether it is advisable to estimate the lifetime risk of benign thyroid nodules, is the clinical significance of these tumors. Currently, the significance of small ultrasound detected lesions remains unknown. Most thyroid nodules are benign (IOM 1999) and there is no evidence to date to suggest that radiation exposure induces adenomas that are more likely to progress to malignant disease than adenomas occurring in unexposed individuals (Wang and Crapo 1997; Mettler and Upton 1995).

4.3.5.2 Non-Neoplastic Thyroid Disease

Clinical and epidemiological data clearly indicate an association between high-dose radiotherapy and hypothyroidism; however, the association with low-dose exposures and, in particular with low doses of ^{131}I, is less clear. Hyperthyroidism after radiotherapy has also been reported (IOM 1999). The IOM, in reviewing the NCI ^{131}I report, did not consider the impact of thyroid dose from NTS fallout on other nonmalignant thyroid diseases because the review committee felt the data describing these health effects were inconclusive for the range of doses estimated for average Americans (NAS 1999). And, a recent review of the Chernobyl studies by UNSCEAR was unable to conclude that non-malignant diseases were increased as a result of low dose radiation exposure (UNSCEAR 2000). Given the current state of knowledge, a quantitative risk analysis of non-neoplastic thyroid disease from fallout is not feasible. Additional studies of exposed populations, especially those exposed from the Chernobyl accident, that have longer follow-up periods, sufficient sample size, and individual dosimetry, may be necessary to provide adequate data on which to base a risk assessment. It is likely, however, that the uncertainty associated with any future quantitative risk estimates will be quite large.

The IOM reported that the risk of non-malignant thyroid disease resulting from exposure to ionizing radiation could extend into the range of doses of less than 1 Gy (1000

mGy). Maxon and Saenger (1996) reported that hypothyroidism from radioiodine exposure is unlikely to occur at doses less than 0.1 to 0.2 Gy (100 to 200 mGy). These lower values can be used as a "threshold" to qualitatively assess the potential risk of hypothyroidism from fallout exposures. Using these values will more likely result in an overestimate than an underestimate of a health effect. Based on the data presented in Chapter 3, the average American was exposed to a significantly lower dose than the dose range described by Maxon and Saenger (1996). However, it is clear from Figure 3.17 that there may be subgroups of the population who, based on their age during the testing period and place of residence, have received doses approaching 0.2 Gy. Higher doses for some individuals would be expected if non-commercial milk sources (backyard cow or goat) and above-average milk consumption patterns were considered. Thus, this health effect is the most likely non-cancer health consequence of fallout exposure.

4.4 Conclusions

It is feasible to estimate fallout-related risks of developing cancer among population groups or for representative exposure scenarios, and to quantify the range of uncertainty in these risks. This range is likely to be large because of uncertainties in dose estimates and in the risk models that are used. In spite of the large uncertainties, it is likely that there is an increased risk of cancer from fallout, but it is also highly likely that this increase is very small relative to the usual risk of cancer in the absence of fallout exposure. For example, the 3.8 million people born in the United States in 1951 might experience a few hundred extra fatal cancers as a result of fallout exposures compared with more than a half a million fatal cancers that would be predicted in the absence of fallout. Persons born in 1951, on average, have received larger doses than those born earlier or later. Because doses from global fallout vary less by geographic location and birth cohort than do thyroid doses from NTS ^{131}I exposure, it is much less likely that there would be groups with unusually large risks. At this time, not enough information is available to perform a quantitative radiation risk analysis for non-cancer health outcomes. A crude evaluation of the doses estimated for this feasibility report and the available epidemiological literature indicate, however, the most likely non-cancer health outcomes are those affecting the thyroid gland.

With regard to the exposures of the American people from Nevada Test Site fallout, the Institute of Medicine has indicated that further epidemiologic studies could help to clarify the extent to which the Nevada tests increased the incidence of thyroid cancer. The University of Utah is currently extending the follow-up for a previous epidemiological study of children who lived in the vicinity of the Nevada Test Site in the 1950s; results are expected to be available in a few years. Outcomes evaluated will include neoplastic and non-neoplastic thyroid disease.

A number of non-United States populations have been exposed to substantially higher levels of radioiodine and other radionuclides than the United States population. These populations include the residents of the Republic of Marshall Islands; the people living near the nuclear weapons test site in Semipalatinsk, Kazakstan; those exposed in the former Soviet Union to accidental releases from the Chernobyl nuclear power station in Ukraine; and persons living near the Mayak nuclear fuel reprocessing plant in Russia.

Ongoing dosimetric and epidemiological studies of these populations are expected to provide additional data regarding the health consequences of fallout exposure. In particular, it is fairly clear from the results from the Chernobyl studies that exposure to ^{131}I in childhood can increase thyroid cancer risks, although these risks cannot yet be quantified accurately and only time will tell how long they will persist. Also, on-going studies of populations living near the Mayak nuclear fuel reprocessing plant in Russia may improve the risk estimate for leukemia at low dose rates. Expansion or enhancement of these investigations may be useful to better characterize risks. The results from these epidemiological studies should be available before further health research is considered.

References

Amemiya, T., Takano, J., and Shoshi, K. Did atomic bomb radiation influence the incidence of retinoblastoma in Nagasaki and Hiroshima? Ophthalmic Paediatr. Genet. 14(2):75-79, 1993.

Barsano, C.P. Other Forms of Primary Hypothyroidism. In: Werner and Ingbar's The Thyroid. 7th edition. Braverman, L.E., Utiger, R.D. (Editors). Lippincott-Raven Publishers, Philadelphia, PA, 1996.

Bogue, D.J. The Population of the United States: Historical Trends and Future Projections. The Free Press (A Division of Macmillan Inc.). New York, 1985.

Boice, J.D. Jr., Land, C.E., and Preston, D.L. Ionizing Radiation. In: Cancer Epidemiology and Prevention. Schottenfeld, D., Fraumeni, J.F. Jr. (Editors). Oxford University Press, New York, NY, 1996.

Bunger, B.M., Cook, J.R. and Barrick, M.K. Life table methodology for evaluating radiation risk: an application based on occupational exposures. Health Phys., 40:439-455, 1981.

Bureau of the Census, Statistical Abstract of the United States: 1997 (117th edition), Washington DC, 1997.

Cardis, E., Gilbert, E.S., Carpenter, L., Howe, G., Kato, I., Armstrong, B.K., Beral, V., Cowper, G., Douglas, A., Fix, J., et al. Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. Radiat. Res. 142:117-132, 1995.

EPA. U.S. Environmental Protection Agency. Estimating radiogenic cancer risks. EPA 402-R-93-076. Washington, DC, June 1994.

EPA. U.S. Environmental Protection Agency. Estimating radiogenic cancer risks. Addendum: uncertainty analysis. EPA 402-R-99-003. Washington, DC, May 1999.

Fujiwara, S., Sposto, R., Ezaki, H., Akiba, S., Neriishi, K., Kodama, K., Hosoda, Y., and Shimaoka, K. Hyperparathyroidism among atomic bomb survivors in Hiroshima. Radiat. Res. 130:372-378, 1992.

Greenlee, R.T., Murray, T., Bolden, S., Wingo, P.A. Cancer Statistics, 2000. CA Cancer J Clin 50:7-33, 2000.

Hancock S.L., Tucker M.A., and Hoppe R.T. Factors affecting late mortality from heart disease after treatment of Hodgkin's disease. JAMA 270:1949-55, 1993.

Kerber R.A., Till J.E., Simon S.L., Lyon J.L., Thomas D.C., Preston-Martin S., Rallison M.L., Lloyd R.D., and Stevens W. A cohort study of thyroid disease in relation to fallout from nuclear weapons testing. JAMA 270: 2076-82, 1993.

Kodama K., Fujiwara S., Yamada M., Kasagi Y., Shimizu Y., and Shigematsu I. Profiles of non-cancer diseases in atomic bomb survivors. World Health Stat Q 49:7-16, 1996.

IOM. Institute of Medicine. NRC. National Research Council. Exposure of the American people to Iodine-131 from Nevada nuclear-bomb tests. Review of the National Cancer Institute report and public health implications. National Academy Press, Washington, DC, 1999.

ICRP. International Commission on Radiological Protection. 1990 Recommendations of the International Commission on Radiological Protection. ICRP Publication 60. Ann ICRP 21(1-3). Pergamon Press, Oxford, UK, 1991.

Land, C.E., Saku, T., Hayashi, Y., Takahara, O., Matsuuma, H., Tokuoka, S., Tokunaga, M., and Mabuchi, K. Incidence of salivary gland tumors among atomic bomb survivors, 1950-1987. Evaluation of radiation-related risk. Radiat. Res. 146:28-36, 1996.

Little, M.P., De Vathaire, F., Charles, M.W., Hawkins, M.M. and Muirhead, C.R. Variations with time and age in the risks of solid cancer incidence after radiation exposure in childhood. Statist. Med. 17:1341-1355, 1998.

Maxon, H.R. and Saenger, E.L. Biologic effects of radioiodines on the human thyroid gland. In: Werner and Ingbar's The Thyroid. 7th edition. Braverman, L.E., Utiger, R.D. (Editors). Lippincott-Raven Publishers, Philadelphia, PA, 1996.

Mettler, F.A. Jr. and Upton, A.C. Medical Effects of Ionizing Radiation. 2nd edition. W.B. Saunders Company, Philadelphia, PA, 1995.

Modan B., Chetrit A., Alfandary E., et al. Increased risk of salivary gland tumors after low-dose irradiation. Laryngoscope 108:1095-7, 1998.

NAS. National Academy of Sciences. NRC. National Research Council. Committee on the Biological Effects of Ionizing Radiation. Health effects exposure to low levels of ionizing radiation (BEIR V Report). National Academy Press, Washington, DC, 1990.

NCI. National Cancer Institute. Cancer Incidence and Mortality in the United States, 1973-1977, NCI Monograph No. 57. Surveillance, Epidemiology and End Results (SEER) Program, National Institutes of Health, Bethesda, MD, 1981.

NCI. National Cancer Institute. Estimated exposures and thyroid doses received by the American people from Iodine-131 in fallout following Nevada atmospheric nuclear bomb tests. Bethesda, MD, 1997.

NCRP. National Council on Radiation Protection and Measurements. NCRP Report No. 80. Induction of thyroid cancer by ionizing radiation. Bethesda, MD, 1985.

NCRP. National Council on Radiation Protection and Measurements. NCRP Report No. 115. Risk estimates for radiation protection. Bethesda, MD, 1993.

NCRP. National Council on Radiation Protection and Measurements. NCRP Report No. 126. Uncertainties in fatal cancer risk estimates used in radiation protection. Bethesda, MD, 1997.

Neel J.V. and Schull W.J. (eds). The Children of Atomic Survivors. A Genetic Study. National Academy Press, Washington, DC, 1991.

NIH. National Institutes of Health. NIH Publication No. 85-2748. Report of the National Institutes of Health Ad Hoc Working Group to develop radioepidemiological tables. Bethesda, MD, 1985.

NIH, Land C.E., Gilbert E., Smith J., Hoffman F.O., Apostoiae I., Thomas B., Kocher D.M. Report of the NCI-CDC Working Group to revise the 1985 NIH Radioepidemiological Tables. U.S. Dept. of Health and Human Services, National Institutes of Health, National Cancer Institute, Bethesda, Maryland. NIH Publication No. 03-5387, 118 pp, 2003.

NRC. Nuclear Regulatory Commission. Health Effects Models for Nuclear Power Plant Accident Consequence Analysis. Low- LET Radiation, Part II: Scientific Bases for Health Effects Models. NUREG/CR-4214, Rev. 1, Part 2, U.S. Government Printing Office, Washington, DC, 1989.

NRC. Nuclear Regulatory Commission. Health Effects Models for Nuclear Power Plant Accident Consequence Analysis. Part I: Introduction, Integration, and Summary. NUREG/CR-4214, Rev. 2, Part 1, ITRI-141. U.S. Government Printing Office, Washington, DC, October 1993.

Pierce, D.A., Shimizu,Y., Preston, D.L., Vaeth, M., and Mabuchi, K. Studies of mortality of atomic bomb survivors. Report 12, Part I. Cancer: 1950-1990. Radiat Res 146:1-27, 1996.

Pierce D.A. and Preston D.L. Radiation-related cancer risks at low doses among atomic bomb survivors. Radiat Res 154:178-186, 2000.

Preston, D.L., Kusumi, S., Tomonaga, M., et al. Cancer incidence in atomic bomb survivors. Part III: Leukemia, lymphoma and multiple myeloma, 1950-1987. Radiat Res 137:S68-S97, 1994.

Preston, D.L., Shimizu, Y., Pierce, D.A., Suyama, A. and Mabuchi, K.. Studies of mortality of atomic bomb survivors Report 13: Solid cancer and noncancer disease mortality: 1950-1997. Radiat. Res., in press, 2003.

Ries, L.A., Hankey, F., Harras, A., and Devesa, S.S. Cancer incidence, mortality and patient survival in the United States. In: Schottenfeld D., Fraumeni, J.F. Jr., editors. Cancer Epidemiology and Prevention. Oxford University Press, New York, NY, 1996: 168-191.

Ries L.A.G., Eisner M.P., Kosary C.L., Hankey B.F., Miller B.A., and Edwards B.K. (eds). SEER Cancer Statistics Review, 1973-1997. National Cancer Institute, Bethesda, MD, 2000.

Robinette, C.D., Jablon, S., and Preston, D.L. Mortality studies in nuclear weapons tests participants. P.1-47 in: Medical Follow-up Agency, National Research Council. National Academy Press, Washington, 1985.

Ron E., Modan B., Boice J.D., et al. Tumors of the brain and nervous system after radiotherapy in childhood. New Engl J Med 319:1033-39, 1988.

Ron E., Modan B., Preston D., Alfandary E., Stovall M., and Boice J. Thyroid neoplasia following low-dose radiation in childhood. Radiat Res 120:516-531, 1989.

Ron, E., Lubin, J.H., Shore, R.E., Mabuchi, K., Modan, B., Pottern, L., Schneider, A.B., Tucker, M.A., and Boice, Jr. J.D. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res 141:259-277, 1995.

Ron, E., Wong, F,L., Mabuchi, K., et al. Incidence of benign gastrointestinal tumors among atomic bomb survivors. Am J Epidemiol 142:68-75, 1995.

Sasakawa Memorial Health Foundation. A report on the 1994 Chernobyl Sasakawa Project Workshop Moscow, 16-17, May 1994.

Sasakawa Memorial health Foundation, Tokyo, 1994, Sasakawa Memorial Health Foundation. A report on the 1995 Chernobyl Sasakawa Project Workshop, St Petersburg. 7-8July 1995. Sasakawa Memorial health Foundation, Tokyo, 1995.

Schneider A., Shore-Freedman E., Ryo U., et al. Radiation-induced tumors of the head and neck following childhood irradiation. Medicine 64:1-15, 1985.

Schneider A.B., Ron E., Lubin J., Stovall M., and Gierlowski T.C.. Dose-response relationship for radiation-induced thyroid cancer and thyroid nodules: evidence for the prolonged effects of radiation on the thyroid. J Clin Endocrinol Metab 77:362-369, 1993.

Schneider A.B., Gierlowski T.C., Shore-Freedman E., et al. Dose-response relationship for radiation-induced hyper-parathyroidism. J Clin Endocrinol Metab 80:254-7, 1995.

Schneider A.B., Lubin J., Ron E., et al: Salivary gland tumors after childhood radiation treatment for benign conditions of the head and neck: dose response relationship. Radiat Res 149:625-30, 1998.

Shimizu, Y., Pierce, D.A., Preston, D.L., and Mabuchi, K. Studies of the mortality of atomic bomb survivors. Report 12, Part II. Noncancer mortality: 1950-1990. Radiat Res 152:374-89, 1999.

Shore, R.E., Hildreth N., Dvoretsky P., and Anderson E. Benign thyroid adenomas among persons x-irradiated in infancy for enlarged thymus gland. Radiat Res 134:217-223, 1993.

Stevens, W., Thomas, D.C., Lyon, J.L. et al. Leukemia in Utah and radioactive fallout from the Nevada test site. JAMA 264: 585-591, 1990.

Thomas, D., Darby, S., Fagnani, F., Hubert, P., Vaeth, M., and Weiss, K. Definition and estimation of lifetime detriment from radiation exposures: Principles and methods. Health Phys., 63:259-272, 1992.

Thompson, D.E., Mabuchi, K., Ron, E., et al. Cancer incidence in atomic bomb survivors. Part II: solid tumors, 1958-1987. Radiat. Res. 137:S17-S67, 1994.

Tokunaga M., Land C.E., Tokuoka S., Nishimori I., Soda M., and Akiba S. Incidence of female breast cancer among atomic bomb survivors,1950-1985. Radiat Res 138:209-23, 1994.

UNSCEAR. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionizing radiation. 1993 Report to the General Assembly, with annexes. United Nations, New York, NY, 1993.

UNSCEAR. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionizing radiation. 1994 Report to the General Assembly, with annexes. United Nations, New York, NY, 1994.

UNSCEAR. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionizing radiation. 2000 Report to the General Assembly, with annexes. United Nations, New York, NY, 2000.

Wang, C. and Crapo, L.M. The epidemiology of thyroid disease and implications for screening. Endocrinology and metabolism clinics of North America. 26(1):189-218, 1997.

Williams, D. Cancer after nuclear fallout: Lessons from the Chernobyl accident. Nature Rev. Cancer 2:543-549, 2000.

Wong, F.L., Yamada, M., Sasaki, H., Kodama, K., Akida, S., Khimaoka, K., and Hosoda, Y. Noncancer disease incidence in the atomic bomb survivors: 1958-1986. Radiat. Res. 135:418-430, 1993.

Yoshimoto Y., Ezaki H., Etoh R., Hiraoka T., and Akiba S. Prevalence of thyroid diseases among autopsy cases of the atomic bomb survivors in Hiroshima, 1951-1985. Radiat Res 141:278-286, 1995.