RADIATION-EXPOSED POPULATIONS: WHO, WHY, AND HOW TO STUDY

Steven L. Simon and Martha S. Linet*

Abstract—Everyone is exposed to natural and manmade ionizing radiation that can originate from sources in the environment and in medical and occupational settings. There is notable variation, however, among individuals and across populations in the types of sources of radiation and in the frequency, level, and duration of exposure. Adverse health effects associated with radiation exposure have been known for decades, and ionizing radiation exposure has been linked with a broad range of different types of cancer and benign neoplasms as well as birth defects, reproductive effects, and diseases of the circulatory, hematologic, and neurologic systems. Our present understanding of radiation-related health risks derives primarily from multidisciplinary health risk (epidemiologic) studies that provide the key information on radiation-associated health outcomes, quantify radiation-related disease risks, and enhance understanding of mechanisms of radiation-related disease pathogenesis. Such information is central to quantifying risks in relation to benefits; addressing public concerns, including societal and clinical needs in relation to radiation exposure; and providing the database needed for establishing recommendations for radiation protection. Because of the importance of determining risks compared to benefits for all situations where exposure to ionizing radiation might result, it is useful for planning new health risks studies to categorize exposed populations according to the sources and types of radiation. This paper describes a wide range of populations exposed to radiation and the motivation and key methodological criteria that drive the rationale and priority of studying such populations. Also, discussed are alternative methods for evaluating radiation-related health risks in these populations, with a major focus on epidemiologic approaches. This paper concludes with a short summary of major highlights from radiation epidemiologic research and important unanswered questions.

INTRODUCTION

Everyone is exposed to natural and manmade ionizing radiation that can originate from sources in the environment and in medical and occupational settings. The use of radiation in evolving technologies for diagnosis and treatment of many diseases has revolutionized medical care, but it also exacts a cost in subsequent radiation-related secondary disease risks. Occupational radiation exposures of medical and nuclear power plant workers (as well as astronauts, industrial radiographers, and those working in the aviation and other industries) must be considered when determining radiation protection measures, given the significant societal benefits provided by these workers. Natural background radiation (terrestrial gamma rays, cosmic rays, radon) is ubiquitous and exposes everyone regardless of country of residence. On a much smaller scale, there are a few populations that have been exposed to undesirable events involving radiation in the context of warfare and industrial accidents. Intermediate in numbers are the populations exposed to fallout from nuclear testing. Collectively, radiation exposure affects potentially all people everywhere on earth, and for that reason, it is imperative to understand the associated risks.

There has been limited cataloging of radiation-exposed populations in the literature that enumerates the numbers of persons exposed, typical radiation doses received by members of the population, and for some populations, quantitative measures of disease risks to address public health and radiation protection considerations (e.g., UNSCEAR 2008). Such listings, however, have rarely considered other attributes of radiation-exposed populations and how those attributes may be used to set priorities for conducting studies of health risks that can address public health, clinical, and societal concerns about radiation exposure.

While adverse health effects from ionizing radiation have been known for >100 y, it has taken decades of health risk (epidemiologic) and clinical studies to link radiation exposure quantitatively with several types of cancer.
and other nonmalignant disorders. The process of quantification of radiation-related disease risks has been derived primarily from analytic epidemiologic studies, while epidemiologic, animal, molecular, functional biomarker, and genetic studies have increased understanding of radiation-related pathogenesis.

This paper describes a broad range of radiation-exposed populations and discusses their key population and radiation exposure attributes. The rationale for studying radiation-related health risks is described, and alternative approaches for evaluating radiation-related health risks are discussed. This paper identifies important population, exposure, and methodological issues that must be weighed when determining feasibility and priority of studying radiation-exposed populations. The paper concludes with a brief list of important unanswered questions.

DISCUSSION

Who are the radiation-exposed populations?

Definitions. To identify “radiation-exposed populations,” key terms of reference must be defined. “Exposure” within the radiation sciences has a long history because the term has been used as a quantifiable index of ionization in air (ICRU 1980). More generally, radiation exposure means being subjected to an ionizing radiation hazard, either by irradiation or contamination. In the context of radiation safety and protection, “exposed population” means any identifiable group of persons that has received a radiation dose. The dose is generally associated with emissions from a specific, identifiable radiation source. While it is reasonably simple to identify populations likely to have been exposed (e.g., persons living in the vicinity of a nuclear power plant accident), it is more difficult to determine whether specific individuals were exposed or not. This difficulty is related, in part, to the ambiguity of determining, specifying, or measuring “exposure.”

To ascertain whether a specific person was exposed to radiation, evidence of exposure can be derived from several types of measurements, including a dosimeter that a person might have worn, radiant emissions from a person’s body reflecting internal or surface contamination, or observations of specific biological changes consistent with exposure to ionizing radiation (e.g., changes in chromosomes, tooth enamel, or other tissues) (ICRU 2002). Determining exposure on an individual level is further complicated because all types of measurements have minimum limits of detection that prohibit ascertainment of exposures lower than the minimum limits of detection of the device. Fortunately, however, in the context of learning about health risks, determination of “who is exposed” is less important than identifying a target population in which all members may have been exposed. Within the target population, individuals may have received doses at levels that are quite similar or highly variable, ranging from very low (e.g., nearly indistinguishable from zero) to very high, depending on the exposure conditions. Identification of populations exposed to radiation is but the first step in determining which populations may be useful to consider for epidemiologic studies.

Sources of radiation exposure. Cataloging of radiation-exposed populations requires recognition of sources of exposure and populations that are proximate to the sources or to the emanations from the source in the case of releases of radioactive material to the environment. Exposed populations may include:

1. persons exposed to natural background sources of radiation (e.g., radon, terrestrial gamma, or cosmic radiation) (Table 1);
2. patients who have undergone diagnostic image-guided, interventional procedures, radiotherapy, or other medical procedures involving ionizing radiation (Table 2);
3. persons exposed as a consequence of their occupation (e.g., those employed as medical radiation workers or in the aviation or nuclear energy industries) (Table 3); and
4. persons exposed to radiation or radioactive releases from wartime events, from nuclear accidents and nuclear testing, or for security reasons including airport security screening (Table 4).

Identification of radiation-exposed populations generally requires recognition of the source of radiation as well as recognition of a population that was likely to have been in contact with the radiation source or emissions from the source.

Sources of information about radiation exposure. An exposed population, by definition, is composed of individuals who have been or are likely to have been exposed, a condition often assumed based on proximity to the source. While identification of exposed populations is sometimes based on proximity (i.e., not based on evidence of individual exposures) for some populations (e.g., nuclear workers or radiologists), radiation exposure of members of the population may be verified by individual exposure records. Occupational doses can often be verified on an individual level more easily and reliably than in many other exposure situations because of the monitoring and recording requirements imposed by regulation. In contrast, patients exposed to radiation therapy do not have individual exposure measurements, though often doses to individuals can be determined retrospectively from records of the “administered radiation dose” (e.g., for external beam radiotherapy) or from the description of the medical protocol used (e.g., the “administered activity” in the case...
of nuclear medicine). In turn, the exposure data allows estimation of doses to the treatment field or targeted organ as well as to organs and tissues outside the field or targeted organ. Both estimates may be valuable for health risk studies, depending on the purpose and design of such studies.

In contrast to radiotherapy, exposure records are almost never available from diagnostic radiologic imaging. Medical records do not provide information on dose from diagnostic imaging examinations, nor is such information available from radiology department records. However, data on the number of examinations received by the individual as derived from their medical record and from questionnaires and interviews, as well as hospital imaging protocols, can be useful in deducing a patient’s individual radiation exposure. In all of these examples, which include workers in nuclear facilities and patients undergoing radiotherapy, computed tomography (CT), or other diagnostic imaging procedures, the population of potentially exposed persons can be identified even if individual exposure data are limited.

There are numerous sources of information on radiation exposures in a variety of populations and contexts (e.g., NA/NRC 2006; Simon et al. 2006a and b; UNSCEAR 2008; NCRP 2009; Wakeford 2009).

Uncertainty of exposure of populations. Within an exposed population, there is a true, often unknown, dose received by each person and sometimes a known, but fallible, estimate of dose. How close the estimated dose is to the true dose is often difficult to ascertain without empirical validation measurements, though contemporary uncertainty analysis strategies (e.g., Monte-Carlo modeling) can often bound the possible values of the true dose by a confidence or credibility interval (e.g., NCRP 2009).

Recognizing that true doses for individuals cannot be known with certainty, one other uncertain attribute of exposed populations is the range of true doses received. The importance of understanding the range of doses received in the population is related to the need for deriving a meaningful dose-response over a wide range of doses.

Radiation risk: The basis and reasons for study

The findings and quantitative assessment of health risks in humans derive primarily from epidemiologic studies. Many, but not all, of the findings in humans have been confirmed in animal studies (UNSCEAR 1988; NA/NRC 2006; Dupont et al. 2012). Radiobiology studies, in conjunction with epidemiologic and experimental animal investigations, have provided data critical to the understanding of radiation-related disease pathogenesis (UNSCEAR 2006, 2012; Little et al. 2013).
Table 2. Populations exposed to radiation in medical care: Attributes and feasibility for study.\(^{a}\)

<table>
<thead>
<tr>
<th>Populations according to listed medical procedures</th>
<th>Sources of exposure / Type of radiation</th>
<th>Reliability of exposure estimates for individuals in population(^{b})</th>
<th>Variation of level of exposure in population</th>
<th>Existing population size in relation to statistical power requirements</th>
<th>Public health value</th>
<th>Clinical importance</th>
<th>Societal &amp; public concern</th>
<th>Potential for successful epidemiologic study (feasibility)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone mineral densitometry patients</td>
<td>Gamma radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Unclear, perhaps hundreds of thousands</td>
<td>Low(^{c})</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Brachytherapy patients</td>
<td>Gamma radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Low to moderate</td>
<td>High</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Computed tomography (CT) patients</td>
<td>Bremsstrahlung radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Millions</td>
<td>High(^{d})</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Diagnostic radiology patients other than CT</td>
<td>Bremsstrahlung radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Millions</td>
<td>Moderate(^{e})</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Dental radiography patients</td>
<td>Bremsstrahlung radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Millions</td>
<td>Low to moderate(^{f})</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>External beam radiation therapy patients</td>
<td>Orthovoltage x-rays to high energy gamma radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Moderate(^{g})</td>
<td>High</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Fluoroscopically guided interventional procedures</td>
<td>Bremsstrahlung radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Low(^{h})</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate(^{g})</td>
</tr>
<tr>
<td>Mammography patients</td>
<td>Bremsstrahlung radiation</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Millions</td>
<td>Low</td>
<td>Moderate</td>
<td>High</td>
<td>Moderate</td>
</tr>
<tr>
<td>Nuclear medicine patients (diagnostic procedures with conventional isotopes)</td>
<td>Gamma radiation from isotopes</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate(^{i})</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Nuclear medicine patients (therapeutic procedures with conventional isotopes)</td>
<td>Gamma radiation from isotopes</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Hundreds of thousands</td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate to High</td>
</tr>
<tr>
<td>Positron emission tomography (PET) patients with or without CT</td>
<td>Gamma radiation from isotopes</td>
<td>Low to high</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Low to moderate(^{j})</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

\(^{a}\) Difficult to identify populations with single types of radiologic imaging or radiation therapy procedures since most patients undergo multiple types of different procedures. It is important to capture the cumulative history of specific procedures, both diagnostic and therapeutic.

\(^{b}\) Estimation of dose is highly dependent on the availability and quality of medical records. Records are more likely to be missing or incomplete for procedures carried out in earlier years. The accuracy of dose estimation will also vary depending upon whether the exposure assessment is for in-field or out-of-field doses.

\(^{c}\) Dosimetry studies might be useful.

\(^{d}\) Dosimetry and epidemiologic studies are ongoing.

\(^{e}\) Dosimetry and epidemiologic studies have been done for monitored tuberculosis patients.

\(^{f}\) Dosimetry and epidemiologic studies have been done.

\(^{g}\) Depends on availability of detailed treatment records.

\(^{h}\) Dosimetry studies have been carried out for workers but would be useful for patients; epidemiologic studies are ongoing.

\(^{i}\) Dosimetry studies have been conducted.

\(^{j}\) Dosimetry studies would be useful for technologists.
Table 3. Populations occupationally exposed: Attributes and potential for study.

<table>
<thead>
<tr>
<th>Populations according to listed source</th>
<th>Sources of exposure / type of radiation</th>
<th>Reliability of exposure estimates for individuals in population</th>
<th>Variation of level of exposure in population</th>
<th>Existing population size in relation to statistical power requirements</th>
<th>Public health value</th>
<th>Clinical importance</th>
<th>Societal &amp; public concern</th>
<th>Potential for successful epidemiologic study (feasibility)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airline transportation screening staff</td>
<td>Bremsstrahlung radiation</td>
<td>Low</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Aircrew members (pilots and flight attendants)</td>
<td>Cosmic radiation</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Many thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Astronauts, including shuttle and space station crews</td>
<td>Extra-galactic cosmic rays, of solar particles</td>
<td>Moderate</td>
<td>High</td>
<td>Available: A few hundred</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Energy and nuclear fuel cycle employees (historical)</td>
<td>Gamma radiation, occasional low intakes of radionuclides Bremsstrahlung radiation</td>
<td>Low to moderate</td>
<td>High</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Physicians/technologists performing fluoroscopically guided interventional procedures</td>
<td>Gamma radiation</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Hundreds</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Industrial radiographers</td>
<td>Gamma radiation and occasional intakes of I-131 and other isotopes</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: Thousands to hundreds of thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Irradiated nuclear fuel handlers</td>
<td>Gamma radiation</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: All available</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Liquidators (Chernobyl)</td>
<td>Gamma radiation and occasional intakes of isotopes</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: Hundreds</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>National laboratory workers (Los Alamos, Oak Ridge, and others)</td>
<td>Gamma radiation and occasional intakes of isotopes</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Luminers (radium dial painters)</td>
<td>Ra-226</td>
<td>Low to moderate</td>
<td>High</td>
<td>Available: Hundreds</td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Miners: underground and quarry (coal, gold, phosphates, misc. minerals, rare earths, uranium)</td>
<td>Terrestrial gamma radiation, radon, thoron, and progeny</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Nuclear medicine technologists</td>
<td>Gamma radiation</td>
<td>Low to high</td>
<td>Low to Moderate</td>
<td>Available: Hundreds of thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Nuclear power reactor personnel</td>
<td>Intakes of Pu</td>
<td>Moderate</td>
<td>Low to Moderate</td>
<td>Available: Thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Plutonium (Pu) workers (historical), including those from the Mayak facility in the Southern Urals</td>
<td>Intakes of Pu</td>
<td>Low to moderate</td>
<td>Low to Moderate</td>
<td>Available: Thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Radiologic Technologists</td>
<td>Bremsstrahlung radiation + occasional gamma radiation</td>
<td>Moderate</td>
<td>Low to Moderate</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Radiologists</td>
<td>Bremsstrahlung radiation primarily</td>
<td>Moderate</td>
<td>High</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Uranium processors and millers</td>
<td>Gamma radiation + radon</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Veterinarians, Veterinary Assistants</td>
<td>Bremsstrahlung radiation</td>
<td>Moderate</td>
<td>Low to Moderate</td>
<td>Available: Thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Welders</td>
<td>Bremsstrahlung radiation</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: Unknown</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

Notes:
- aDosimetry studies would be useful.
- bEpidemiologic and dosimetry studies have been conducted.
- cDosimetry studies are being conducted.
- dEpidemiologic and dosimetry studies are ongoing.
- eNot feasible to conduct epidemiologic or dosimetry studies since most workers are deceased.
- fUranium miners: epidemiologic and dosimetry studies have been conducted.
- gEpidemiologic studies are ongoing.
<table>
<thead>
<tr>
<th>Populations according to listed source</th>
<th>Sources of exposure/ type of radiation</th>
<th>Reliability of exposure estimates for individuals in population</th>
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<th>Public health value</th>
<th>Clinical importance</th>
<th>Societal &amp; public concern</th>
<th>Potential for successful epidemiologic study (feasibility)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air travelers undergoing security checks from backscatter x-ray</td>
<td>Bremsstrahlung radiation</td>
<td>Low</td>
<td>Low</td>
<td>Available: Millions</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Atomic veterans: military nuclear test observers and participants</td>
<td>Prompt gamma radiation, fallout</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: &gt;100,000</td>
<td>High</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Chernobyl residents proximate to the nuclear plant at the time of the accident</td>
<td>Gamma radiation + radionuclides (primarily radioiodines and radionuclides)</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Hundreds of thousands</td>
<td>High</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Moderate to high</td>
</tr>
<tr>
<td>Downwinders (public living downwind from any nuclear weapons testing sites exposed to local and regional fallout)</td>
<td>Gamma radiation from fallout + internal radionuclides (primarily 131I, 137Cs)</td>
<td>Low</td>
<td>Low to Moderate</td>
<td>Available: Hundreds of thousands</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Low to moderate</td>
</tr>
<tr>
<td>Fukushima workers/residents</td>
<td>Gamma radiation, low internal radionuclides (primarily radioiodines, low radionuclides)</td>
<td>Low</td>
<td>Low</td>
<td>Available: Hundreds of thousands</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Global fallout exposed persons</td>
<td>Gamma radiation, primarily from 137Cs</td>
<td>Low</td>
<td>Low</td>
<td>Available: Hundreds of thousands</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Hanford area residents</td>
<td>Primarily 137I (residents)</td>
<td>Moderate</td>
<td>Low</td>
<td>Available: Thousands</td>
<td>Low</td>
<td>Moderate</td>
<td>Low to moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Japanese atomic bomb survivors</td>
<td>Prompt gamma radiation, delayed gamma radiation</td>
<td>Moderate</td>
<td>Low to High</td>
<td>Available: More than 100,000</td>
<td>High</td>
<td>High</td>
<td>High</td>
<td>High</td>
</tr>
<tr>
<td>Semipalatinsk (Kazakhstan) nuclear test site: nearby residents</td>
<td>Gamma radiation from fallout and internal radionuclides (primarily 131I)</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: 3,000 young persons</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate</td>
</tr>
<tr>
<td>Marshall Islands residents (Bikini, Enewetak, Rongelap, Utirik, other atoll groups)</td>
<td>Gamma radiation from fallout, internal radionuclides</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: All available</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Moderate (depending on population subgroups studied)</td>
</tr>
<tr>
<td>Nuclear test site workers including clean-up workers (Nevada Test Site, Johnston Atoll, Enewetak Atoll)</td>
<td>Occasional low internal intakes to residual radionuclides including 137Cs, Pu</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: All available</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Techa River and Southern Urals residents</td>
<td>Gamma radiation, low internal radionuclides, e.g., 90Sr, 137Cs</td>
<td>Low to moderate</td>
<td>Moderate</td>
<td>Available: Thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Moderate</td>
</tr>
<tr>
<td>Three Mile Island workers or nearby residents</td>
<td>Gamma radiation (workers), very low 131I to public</td>
<td>Low to moderate</td>
<td>Low</td>
<td>Available: Hundreds of thousands</td>
<td>Moderate</td>
<td>Low</td>
<td>Moderate</td>
<td>Low</td>
</tr>
<tr>
<td>Taiwan 60Co contaminated apartment dwellers</td>
<td>High energy gamma radiation from 60Co</td>
<td>Moderate</td>
<td>Low</td>
<td>Available: Unknown</td>
<td>Moderate</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
</tbody>
</table>

*aEpidemiologic studies are ongoing.
*bSome epidemiologic studies have been completed.
*cDosimetry work is ongoing.
*dDosimetry and risk projection studies have been completed.
*eEpidemiologic and dosimetry studies have been completed.
*fDosimetry and epidemiologic studies are ongoing.
The history of understanding radiation risks has evolved continually, at least from the early part of the 20th century. Within a few years after the initial use of x-rays for radiologic imaging, clinical reports described skin carcinomas, leukemia, dermatitis, cataracts, and other serious conditions associated with radiation exposures of physicians, other health workers, and patients (Frieben 1902; Scott 1911). From decades of research, data from studies of humans have consistently linked moderate to high doses of ionizing radiation exposure with increased risk of many different forms of cancer (Boice 2006), certain benign neoplasms (Neglia et al. 2006), radiation-induced dermatitis (Hymes et al. 2006), cataracts (Ainsbury et al. 2009), and diseases of the circulatory (Little et al. 2012; Darby et al. 2013), hematologic (Ichimaru et al. 1972; Iwanaga et al. 2011), and neurologic systems (Boice 2006; UNSCEAR 1994, 2000, 2006, 2008; NCRP 2013). High radiation doses to pregnant women during weeks 10–27 of gestation may cause severe mental retardation and decrease in the intelligent quotient of offspring (NCRP 2013).

Modification of health effects by individual characteristics, lifestyle, and other factors. Increasingly, epidemiologic and, to a lesser extent, animal studies have demonstrated differences in radiation-related disease risks according to age at initial exposure, gender, ethnicity, and genetic factors within and across populations (Allan 2008). Patients with certain hereditary cancer syndromes can experience increased cancer risks when undergoing radiotherapy (Kleinerman 2009). Accumulating data, however, point to other potential modifiers of radiation-related disease risks, including cigarette smoking, reproductive factors, specific chemotherapy drugs, and possibly other factors (Travis et al. 2003; Cardis et al. 2005; Karagas et al. 2007; Furukawa et al. 2010; Egawa et al. 2012). Improvements in radiation dose measurement in the past few decades have been notable, but increasing knowledge about the long latency of many radiation-related late health effects motivates the need for high-quality historical dose reconstruction along with identification and incorporation of quantitative measures of uncertainty in dose. With growing recognition of the sensitivity of the fetus, young children, and adolescents to radiation-related carcinogenesis (ICRP 2003; Ronckers et al. 2008; NCRP 2013), the dramatic growth in medical radiation exposures to the general population since 1980 (NCRP 2009), and the lifetime nature of radiation-related risks, increasing emphasis has been placed on estimating future radiation-related disease risks using accurate risk projection statistical models. In estimating risks for sensitive population subgroups. These models can account for potential confounding and measures of uncertainty in dose.

Public health value of radiation epidemiologic studies. From the public health perspective, there are several important reasons why quantification of health risks from radiation exposure is important. First and foremost is society’s responsibility to use radiation for greater benefit than harm. Equally important, however, is the large number of persons exposed each year either for intended or unintended reasons. Because of the widespread use of radiation in medicine and industry, the potential benefit to society is great, but similarly, the potential for harm is substantial. Public health studies, by definition, are designed to prevent disease and promote health. The continuous evolution of medical imaging and other devices involving ionizing radiation necessitates timely reviews of the risks and benefits of each new generation of technology.

In addition to the fundamental purpose of establishing a net benefit for the use of devices that emit ionizing radiation, it is important to determine whether radiation exposure is associated with health outcomes for which the evidence is limited, such as chronic lymphocytic leukemia, prostate cancer, or uterine myomata (Boice 2006). For that purpose in particular, epidemiologic studies with high-quality exposure assessment and adequate statistical power are needed to quantify health risks to estimate the disease burden associated with radiation exposure. Such studies are crucial for quantifying the response (health outcome) per unit dose and for providing insight into disease pathogenesis to clarify whether a statistical association is etiologic.

The presence of a statistically significant dose response in epidemiologic studies is useful, at least in a conceptual framework, for establishing appropriate radiation protection guidelines. The dose response provides the incremental risk for incremental additions in exposure. This information is needed for devising appropriate risk protection measures. To characterize the dose-response relationship, reasonably accurate estimates of past radiation doses are needed, along with quantification of potentially important modifiers of dose, and the information to adjust for possible confounding factors (e.g., socioeconomic status, environmental or behavioral factors linked with both the radiation exposure and the disease outcome under study).

For public health reasons, there is a particularly great value to initiate high-quality radiation epidemiologic studies to ascertain and monitor health risks of patients undergoing radiologic imaging procedures that are carried out in large numbers. Such procedures include, but are not limited to, CT, repeated fluoroscopic procedures for patients with inflammatory bowel disease, children with repeated urinary tract problems, and many others. Moreover, it is important to consider conducting epidemiologic studies of patients (Table 2) exposed to newer radiographic procedures with potentially high doses (e.g., certain types
of fluoroscopically-guided procedures, repeated administration of radionuclides for cardiac screening, and repeated positron emission tomography for patients at low risk of developing cancer recurrence or metastasis). There may also be public health value in conducting dosimetry evaluation in patients to develop clinical protocols for optimizing dose levels for most of the examinations listed immediately above and for some additional common examinations (e.g., bone mineral densitometry).

For medical radiation and nuclear energy workers who received continuous exposure to radiation over long periods of time (Table 3), public health needs continue to be served with careful dose monitoring and radiation epidemiologic studies of those workers with the highest doses (e.g., medical radiation workers who perform fluoroscopically guided procedures and those who mix or administer radionuclides in medicine, plutonium workers, uranium miners, and nuclear power plant accident cleanup workers). Conducting such studies provides empirical evidence to ensure that radiation protection standards are adequate. One area of indeterminate risks is for commercial aircrew. Epidemiologic studies have not shown consistent radiation-related risks for aircrew (UNSCEAR 2006). However, dose and risk estimation should be carried out for astronauts because of their potential to receive much greater doses.

Radiation doses to populations exposed to atomic bombs in warfare (Cullings et al. 2006; Egbert 2012), releases from nuclear accidents (Bouville et al. 2006; Gilbert et al. 2006), or nuclear testing have been reconstructed (Beck et al. 2006; Simon et al. 2010) (Table 4). In more limited cases, the populations have been followed up to evaluate health risks. Such studies are inherently difficult to conduct due to the challenge of tracing persons exposed decades ago. This information, however, can provide insights into the best approaches for estimating doses if such events occur in the future and to determine the public health burden of disease from past and future events, as well as provide useful data for policy recommendations about dose mitigation strategies.

The ubiquity of exposure to natural sources of radiation motivates the public health value of estimating doses for most of these populations, but the low level of radiation exposures complicates efforts to undertake epidemiologic studies (Table 1) (Hendry et al. 2009; Kendall et al. 2011). One important exception has been the completed epidemiologic studies of lung cancer associated with residential radon exposure (Field et al. 2006; WHO 2009).

Clinical importance of epidemiologic studies of radiation-exposed populations. There are at least three important reasons from the clinical perspective for studying radiation-exposed populations. The first is in common with all radiation protection-based studies; i.e., to ensure that a net benefit in health is achieved by the process of acquiring diagnostic information using ionizing radiation. A second reason is for clinical monitoring of persons who are at high risk of developing serious diseases for which early diagnosis or treatment can improve survival and/or quality of life. The third reason is to provide the scientific basis for educating physicians to enable them to counsel their patients about health risks associated with radiation exposures and for incorporating evidence-based justifications for ordering radiologic imaging procedures more fully in their medical practice.

For patients who have undergone radiation treatments via brachytherapy or external beam radiotherapy, follow-up studies are useful to ascertain acute and long-term health effects (the latter including second cancers and adverse functional effects due to tissue damage to critical organs such as the heart, lungs, thyroid, rectum, or other anatomic sites) (Table 2). In general, physicians need to learn more about the value of lifetime monitoring of their patients for late effects from radiotherapy. Patients undergoing one or more fluoroscopically guided interventional procedures should be evaluated for evidence of both early and late deterministic effects, such as tissue damage, and they should receive as much detailed dose information as possible about the need for repeated procedures of this type for chronic health conditions (Table 2). Appropriate information should be conveyed to primary care physicians about the need to maintain appropriate distances between family members and friends of those patients who have undergone thyroid ablation with $^{131}$I. Physicians also need to receive updated information about radiation doses and health risks to children and adolescents who are prescribed CT examinations. They also need to be familiar with the results of randomized trials of alternative approaches for evaluation of patients following head injury (Kuppermann et al. 2009), alternative approaches to CT for monitoring patients at increased risk of radiation-related second tumors (de Graaf et al. 2012), the American College of Radiology Appropriateness Criteria for choosing the appropriate type of imaging examination (Cascade 2000), and other strategies to incorporate an evidence-based approach that are particularly important when using repeated higher-dose imaging procedures to monitor patients with chronic diseases (Voss et al. 2009; Linet et al. 2012).

Clinicians should incorporate assessment of their patients’ job history to identify those with potentially serious exposures to ionizing radiation. Medical radiation workers (particularly those first employed prior to 1960, those performing or assisting with fluoroscopically guided procedures, and those mixing or handling radionuclides), as well as other medical professionals repeatedly involved in conducting fluoroscopic examinations, should be monitored for radiation-related health outcomes. These include certain
types of cancer (thyroid cancer, breast cancer in women, brain tumors, and leukemia), nonmalignant thyroid diseases, circulatory diseases, and cataracts (Table 2). Underground miners (particularly those mining uranium, rare earths, coal, gold, and phosphates) should be monitored for lung cancer.

In the context of environmental exposures (Table 4), with a few exceptions, the evidence for significant health risks is generally weak. Some exceptions to this are Chernobyl residents living in proximity to the nuclear plant at the time of the accident (Cardis and Hatch 2011), Japanese atomic bomb survivors (Ozasa et al. 2012), persons living in proximity to nuclear testing sites (Lyon et al. 2006; Land et al. 2008), and residents living near the Techa River in the southern Ural mountains (Schonfeld et al. 2013). Where environmental exposures have a higher probability of inducing a cancer (e.g., for exposure to radon), physicians should encourage their patients to have their homes tested (Table 1).

Societal and public concern as motivators for undertaking epidemiologic studies of radiation-exposed populations. Public health and clinical considerations serve as the key motivators that determine whether an ongoing epidemiologic study of radiation-exposed populations should be continued or a new study launched, though sometimes the major rationale for a new study is societal or public concern. Most of the examples of radiation exposures in this category are included in the list in Table 4 primarily because the public is most concerned about exposures that are perceived as “involuntary.” The general public considers the great benefit of most diagnostic imaging and therapeutic procedures involving radiation to greatly outweigh the small risk. For workers in occupations involving exposure to radiation, the public considers those workers to have voluntarily chosen to work in such jobs. Ubiquitous natural background exposures are considered to be unavoidable or, through voluntary radon testing, the resident can identify and then mitigate such exposures.

In contrast, the general public has no control over nuclear accidents, nuclear testing, use of radiation for military or wartime purposes, or exposure to radiation at airports for security purposes. Although choosing to live near a nuclear plant can be argued to be voluntary, the construction of a new nuclear plant near one’s residence would be considered “involuntary.” These types of exposures have generated strong community pressure to undertake epidemiologic studies to evaluate health risks of sources noted in Table 4.

How to quantify health risks in radiation-exposed populations

Epidemiologic studies. The basis of most of our understanding of quantitative health risks of radiation in humans derives primarily from epidemiologic studies. Descriptive epidemiologic studies examine the occurrence and distribution of disease in populations, while analytic epidemiologic studies assess the statistical relationship between an exposure and a disease outcome.

Two attributes of exposed populations worthy of mention in relation to assessing feasibility of conducting new studies are average population dose and number of subjects available for study (Land 1980; Brenner et al. 2003). These attributes are important because of the inherent difficulties in assessing causal relationships (e.g., between disease endpoints and radiation exposure) in the presence of confounding variables. While data is limited in many cases on absolute population sizes and average doses received, Tables 1–4 present a qualitative assessment of these variables and our general assessment of the feasibility of studying a variety of potentially exposed populations.

A small proportion of the epidemiologic studies evaluating the relationship between radiation exposure and disease outcomes have used the ecological approach, in which the population rather than individuals is the primary unit evaluated. Examples of ecological studies of radiation exposures include investigations of natural background gamma radiation (Evrard et al. 2006) and radon exposures (Evrard et al. 2005) in relation to childhood leukemia and exposures to fallout from the Chernobyl nuclear reactor accident and risk of thyroid cancer risk in populations residing in regions within Ukraine (Jacob et al. 2006). Ecological studies can often be carried out quickly and inexpensively and are helpful if they suggest strong statistical associations, but the lack of information available on individuals may lead to false results.

The two major types of analytic observational epidemiologic studies are case-control studies and cohort studies. The case-control study design is used widely and compares the frequency of past occurrence of a given exposure or other attribute between cases of persons with a disease and a comparison group of persons without that disease. If a larger proportion of cases than the proportion of the comparison group have been exposed to a specific form of radiation, this statistical association may suggest an etiologic relationship. Examples of important case-control studies of radiation exposure include assessment of the risks of leukemia, non-Hodgkin lymphoma, and multiple myeloma in relation to diagnostic x-ray exposures in a U.S. health maintenance organization (Boice et al. 1991) and a nested case-control study of chronic lymphocytic leukemia and other forms of leukemia in relation to occupational exposure to radiation among Chernobyl cleanup workers in Ukraine (Zablotska et al. 2013).

In the cohort study design, an exposed population is followed up prospectively or retrospectively, and incidence and/or mortality from specific outcomes are compared with occurrence in an unexposed population followed up in
a similar fashion. Examples of key cohort studies of radiation exposure include follow-up to assess incidence of solid tumors in relation to exposures from the atomic bombings among the Japanese atomic-bomb survivors (Preston et al. 2007), thyroid cancer in relation to fallout exposure among young persons residing in Ukraine in proximity to Chernobyl at the time of the accident (Tronko et al. 2006), and incidence of leukemia and brain tumors in relation to CT scans during childhood and adolescence among persons living in the United Kingdom (Pearce et al. 2012).

Increasingly important approaches for clarifying results of multiple epidemiologic studies of a given relationship are meta-analysis and pooled analysis. Meta-analysis involves use of statistical methods to compare and combine results of published data from different studies to reveal patterns, sources of variation, and other relationships. Meta-analysis, which requires only the published reports from studies, often accompanies a systematic review of studies on a given topic. Examples of important meta-analyses of radiation epidemiologic studies include assessment of lung cancer mortality from residential radon exposure (Lubin and Boice 1997) and examination of radiation-related circulatory disease risks (Little et al. 2012). Pooled analysis involves combining primary data from individual subjects across studies and requires common definitions, coding, and cut-points for variables and adjustment for the same confounders. An example of a well known pooled analysis of radiation epidemiologic studies is the 15-country study of cancer risks in nuclear industry workers (Cardis et al. 2007).

**Risk projection studies.** When risks to individuals from radiation are small, it may be difficult to study such risks directly. If the radiation exposure is common in the population, even small risks on an individual level can have a substantial public health impact. Methods and statistical models have been developed to estimate future cancer risks from low-dose radiation exposures (UNSCEAR 2000; NA/NRC 2006). Risk projection models use the extensive existing information on long-term cancer risks following radiation exposure to provide a timely and cost-effective estimate of the magnitude of the cancer or disease burden.

Examples of risk projection studies are numerous and include most all sources of exposure. For example, risks have been projected for medical imaging (Linet et al. 2012), for cancers in the United States that can be related to diagnostic x-rays and CT scans (Berrington de Gonzalez et al. 2009), and CT scans in children under 15 y of age (Miglioretti et al. 2013). From environmental exposures, the risks have been projected for exposures to radon (Pawel and Puskin 2004) and those due to exposure to nuclear testing fallout [e.g., for the residents of the Marshall Islands (Land et al. 2010) and those downwind of the Nevada Test Site (NA/NRC 1999)]. For occupational exposures, radiation-related health risks to astronauts have been projected (Cucinotta and Durante 2006). Software exists to project the potential magnitude of radiation-related cancer risks following low-dose radiation exposures based on dose, age at exposure, and age at disease expression (Berrington de Gonzalez et al. 2012).

**Experimental studies.** Questions about health risks associated with radiation exposure that require experimental manipulation can be addressed in animal studies. For example, the relation between the precise timing of a radiation exposure in relation to gestational period and a specific health outcome would be very difficult to study in observational studies in humans. A body of work in various animal models has identified excess risks of various tumors after in utero radiation (NCRP 2013). Investigations of very low dose and low dose-rate effects may be hampered by limited statistical power at low cumulative radiation doses. Results for rare outcomes from individual large and pooled studies may provide risk estimates, albeit with wide confidence intervals, but understanding of the shape of the dose-response relationship and of mechanisms of radiation pathogenesis will require research on radiobiological effects (Dauer et al. 2010).

**CONCLUSION**

Herein, many of the populations known and often assumed to be exposed to ionizing radiation have been identified, along with their unique attributes. Many of the populations are identified by proximity to the radiation source, while in fewer instances populations are identified by personnel monitoring data or empirical measurements on individuals. For the purposes of designing health risk studies, it is important to identify the target population whose members would have likely been exposed and to understand the extent to which radiation exposure can be estimated reliably, the variation in the radiation exposure of the population, the size of the target population in relation to statistical power requirements, and other key methodological features related to the potential for conducting a high-quality epidemiologic study. Determination of the priority for epidemiologic studies is also strongly related to the public health value, clinical appropriateness, and societal and public concerns about the radiation exposure of a population.

In this discussion, exposed populations have been categorized according to the sources or circumstances of their exposure (i.e., from naturally occurring radiation; as patients intentionally exposed for beneficial medical purposes; as workers who receive exposure in the course of occupations; and due to the combined circumstances of
national security, warfare, nuclear testing, and military activities). While there may be further unidentified exposed populations, one of these categories will likely apply to the source or circumstance.

As presented in a series of tables, attributes of the exposed populations are important to take into account when considering or designing new epidemiologic studies. Quantifying these attributes is based on a degree of subjectivity but is still useful in the study of these populations. The following four attributes are particularly important:

1. Population size adequate to meet statistical power considerations (Land 1980; Brenner et al. 2003);
2. Large enough average dose and a wide enough dose range to derive a dose-response relationship;
3. Understanding and capability to determine or reliably estimate individual doses—usually required for specific organs (Simon et al. 2006a); and
4. Potential value of the study as determined by public health, clinical, or societal concerns.

At least the first two of these attributes have a synergistic relationship; hence, no absolute numbers for either can be given in the absence of the other. The sum of these four attributes, while not necessarily requiring equal weighting, provides much of the information needed to assess the feasibility or the likelihood of a successful health risk study. These tables may be useful in consideration of future possible studies.

Despite the large number of radiation-exposed populations and accumulation of knowledge on radiation-related health risks in humans from decades of epidemiologic studies, gaps in understanding remain. Further understanding is needed of the specific types of cancer, circulatory diseases, and cataracts associated with cumulative radiation doses <200 mGy and, for those medical conditions statistically associated with low-dose radiation exposure, the pattern of the dose response. The attributable risk of radiation to occurrence of disease is not well quantified for radiation exposures at all dose levels for either individuals or populations, in part due to the absence of specific radiation molecular signatures and to lack of comprehensive data on how to transport estimation of disease risks across populations or population subgroups. Knowledge is not well developed on health risks associated with internal emitters, and much more work is needed to clarify health risks from a wide group of radionuclides. Health risks associated with a broad range of radiation exposures of children require additional study, as do studies of other sensitive populations (e.g., pregnant women). There is very limited information on health risks to patients associated with radiation from diagnostic and therapeutic radiation procedures of all types. Information is limited on estimates of organ doses and radiation-related health risks of medical radiation and other medical workers with protracted exposures to radiation sources, particularly for workers exposed to higher doses from fluoroscopically guided interventional procedures or administration of radionuclides for diagnostic or treatment purposes. Further work is needed to clarify radiation-related late health effects and dose-response for the broad range of workers in the nuclear energy industry. Although the lifespan study of Japanese atomic bomb survivors is continuing, data are limited on long-term health effects from an acute single dose exposure during childhood or adolescence. Similarly, while the dosimetry and health risks studies of young persons living near Chernobyl and of the Chernobyl cleanup workers have been extensive, questions remain about long-term health effects for persons in these populations. A small number of populations and persons with genetically mediated radiation sensitivity have been identified, but the mechanisms of this sensitivity are not all understood. Genetic variants that may be linked with small risks have not been identified, although it is hypothesized that such variants might be important in explaining risks in general populations.

In summary, studies of radiation-exposed populations are a fundamental responsibility of a society that, by design, uses ionizing radiation in technological applications designed to either improve or better living conditions, health, or security. The individual and societal benefits derived from the use of radiation in medical diagnostic and therapeutic procedures, energy production and numerous other technologies must be weighed in relation to the possibility of causing adverse health effects. The need for society to make these comparisons is served by epidemiologic studies from which the risks can be deduced and compared to the benefits.

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REFERENCES


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risk in areas of Ukraine and Belarus affected by the Chernobyl accident. Radiat Res 165:1–3; 2006.
Kuppermann N, Land CE, Bouville A, Apostoaei I, Simon SL. Projected lifetime risk in areas of Ukraine and Belarus affected by the Chernobyl accident. Radiat Res 165:1
Little MP, Goodhead DT, Bridges BA, Bouffler SD. Evidence relevant to untargeted and transgenenral effects in the offspring of irradiated parents. Mutat Res 614; 2006.


