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REVIEW

The Million Person Study, whence it came and why

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ABSTRACT

Purpose: The study of low dose and low-dose rate exposure is of immeasurable value in understanding the possible range of health effects from prolonged exposures to radiation. The Million Person Study (MPS) of low-dose health effects was designed to evaluate radiation risks among healthy American workers and veterans who are more representative of today's populations than are the Japanese atomic bomb survivors exposed briefly to high-dose radiation in 1945. A million persons were needed for statistical reasons to evaluate low-dose and dose-rate effects, rare cancers, intakes of radioactive elements, and differences in risks between women and men.

Methods and materials: The MPS consists of five categories of workers and veterans exposed to radiation from 1939 to the present. The U.S. Department of Energy (DOE) Health and Mortality study began over 40 years ago and is the source of ∼360,000 workers. Over 25 years ago, the National Cancer Institute (NCI) collaborated with the U.S. Nuclear Regulatory Commission (NRC) to effectively create a cohort of nuclear power plant workers (∼150,000) and industrial radiographers (∼130,000). For over 30 years, the Department of Defense (DoD) collected data on aboveground nuclear weapons test participants (∼115,000). At the request of NCI in 1978, Landauer, Inc., (Glenwood, IL) saved their dosimetry databases which became the source of a cohort of ∼250,000 medical and other workers.

Results: Overall, 29 individual cohorts comprise the MPS of which 21 have been or are under active study (∼810,000 persons). The remaining eight cohorts (∼190,000 persons) will be studied as resources become available. The MPS is a national effort with critical support from the NRC, DOE, National Aeronautics and Space Administration (NASA), DoD, NCI, the Centers for Disease Control and Prevention (CDC), the Environmental Protection Agency (EPA), Landauer, Inc., and national laboratories.

Conclusions: The MPS is designed to address the major unanswered question in radiation risk understanding: What is the level of health effects when exposure is gradual over time and not delivered briefly. The MPS will provide scientific understandings of prolonged exposure which will improve guidelines to protect workers and the public; improve compensation schemes for workers, veterans and the public; provide guidance for policy and decision makers; and provide evidence for or against the continued use of the linear nonthreshold dose-response model in radiation protection.

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Introduction

The Million Person Study (MPS) of low-dose health effects of radiation-exposed workers and veterans was designed to evaluate the health consequences of exposure to radiation received gradually over time and not acutely (Boice 2015). The MPS (Boice 2012a; NCRP 2018a) was conceived over 25 years ago following a National Cancer Institute (NCI) request to the U.S. Nuclear Regulatory Commission (NRC) to consider creating a radiation worker registry by modifying the NRC requirement as to how licensees report radiation doses received by individual workers (Muirhead et al. 1996; Boice 2012a; Hagemeyer et al. 2018). Over time, the MPS (Boice 2015; NCRP 2018a) was formed with the inclusion of 115,000 atomic veterans who participated in above-ground nuclear weapons testing (Boice 2012b; Till et al. 2014; Till, Beck, Aanenson, et al. 2018; Till, Beck, Boice et al. 2018; Beck et al. 2017; Boice, 2014b, 2014c; Caldwell et al. 2016), 360,000 Department of Energy (DOE) workers employed during and after the Manhattan Project (Boice, Cohen, et al. 2006, 2014; Boice 2013a; Ellis and Girardi et al. 2018), 250,000 early radiologists and other medical workers (Yoder et al. 2018), 150,000 nuclear power plant (NPP) workers (Boice 2013b, 2016a; Golden et al. 2018; Boice et al. 2018; NCRP 2018b; Boice, Ellis et al. 2019), and 130,000 industrial radiographers (NCRP 2018a, 2018b; Boice, Ellis et al. 2019). The follow-up started as early as 1939 for industrial radiographers.

The overriding goal of the MPS is to estimate the risk of organ-specific cancers from radiation doses received at low dose rates over the course of years, for which there is much

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interest and much uncertainty (Jacob et al. 2009). These risk estimates from healthy American workers and veterans are deemed more valid for American workers and populations than those from the atomic bomb survivor study which involved a brief, acute exposure in a Japanese population in 1945 with a profile of cancer types and other health conditions that differ from the U.S. population. Initial MPS publications stressed the importance of dosimetry for the DOE facility workers (Leggett et al. 2005; Boice, Cohen, et al. 2006; Ellis, Boice, et al. 2018), the atomic veterans (Till et al. 2014; Till, Beck, Aanenson, et al. 2018; Beck et al. 2017), and for all cohorts studied (Boice, 2013c, 2014b, 2016a; Bouville et al. 2015; NCRP 2018a). It is a credit to the Atomic Energy Commission (now the DOE) for having industrial hygiene programs in the 1940s for worker protection and the foresight to archive the comprehensive records that could be used for research applicable to problems faced today and will be faced tomorrow (Ellis, Girardi, et al. 2018). Statistical issues of the uncertainties in estimating radiation doses and risks are being addressed (NCRP 2012, 2018a; UNSCEAR 2014; Stram et al. 2015).

The MPS is poised to address the public health issues on radiation facing the nation today. Ever-increasing population exposures are accompanied by public concerns about medical exposures (e.g. computed tomography (CT) imaging), nuclear waste and facility cleanups, nuclear power generation, certain occupations (e.g. interventional radiologists), increased air travel and cosmic-ray exposures, technologically enhanced naturally occurring radioactive materials (TENORM) in the environment from hydraulic fracturing, reactor accidents (e.g. at the Daiichi facilities in Fukushima, Japan; O'Brien 2012), and the possibility of terrorist events with dirty bombs or improvised nuclear devises. The MPS will inform regulations (ICRP 2007; NCRP 2018c), improve methods of dose reconstruction, provide emergency response guidance, address medical radiation uses, help set clean up levels after a major nuclear incident, support TENORM recommendations, contribute to compensation schemes (NRC/NA 2003; Neton et al. 2008; Neton 2014), guide occupational and environmental limits, and support radiation guidance for astronauts embarking to Mars (Boice 2017a, 2017c, 2019; NCRP 2014, 2016). Further, differences between men and women in their response to radiation can be fully examined (Boice, Ellis et al. 2019), and noncancer outcomes such as cardiovascular disease (NCRP 2018b) and neurological disorders (NCRP 2016; Boice 2017c) can be examined comprehensively.

Publications to date have included evaluations of Rocketdyne (Atomics International) workers (Boice et al. 2011), Mound workers (Boice et al. 2014; Boice 2017a; NCRP 2018b; Boice, Ellis et al. 2019), Mallinckrodt workers (Boice et al. 2018; Ellis, Boice, et al. 2018; Boice, Ellis et al. 2019; Golden et al. 2019), atomic veterans (Caldwell et al. 2016; Boice et al. 2017a; Till, Beck, Aanenson, et al. 2018; NCRP 2018b; Boice, Ellis et al. 2019), nuclear power plant workers (Golden et al. 2018; NCRP 2018b; Boice, Ellis et al. 2019; Boice et al. 2019a), and industrial radiographers (NCRP 2018b; Boice, Ellis et al. 2019; Boice et al. 2019b). The necessary statistical power to obtain precise risk estimates over a range of low dose exposures, particularly for many cancer sites that are relatively rare, will come from the combination of the study cohorts, similar to the large-scale INWORKS study of nuclear workers from three countries: France, the United Kingdom and the U.S.A (Laurier et al. 2017). The earlier MPS publications, while informative, were not sufficiently powerful to address radiation risks in the low-dose domain or evaluate the consistency or lack of consistency with the LNT model[1] used for radiation protection (NCRP 2001, 2018b, 2018c; ICRP 2007; Boice 2017b; Shore et al. 2018). In contrast, the great statistical power, precision, and validity of the risk estimates within the complete MPS will be due to: the large numbers, the broad dose distribution, standard methods for population selection, thorough vital status tracing (Mumma et al. 2018), and comprehensive dose reconstruction applied across all exposed cohorts (Dauer, Bouville, et al. 2018; NCRP 2018a). The dose distribution is broader than for most occupational studies, with more workers with cumulative doses >50 mGy than reported among atomic bomb survivors. Brief descriptions of the five major components of the MPS are provided below: DOE workers, nuclear weapons test participants,

Table 1. Summary of the epidemiologic cohorts and main sources of exposure for the five major categories of workers within the Million Person Study (as of April 2017)[a].

MPS Cohort	Main sources of exposure
NPP workers first employed from 1957 through 1984 (∼145,000)	External: gamma-ray-emitting fission products (e.g. ^{137}Cs) and activation products (e.g. ^{58}Co, ^{60}Co); in some cases, neutrons Internal: few documented cases of ingestion or inhalation of radionuclides
Industrial radiographers/nondestructive testing (∼126,000)	External: 192Ir, 60Co and 75Se systems; x-ray units Internal: none
Nuclear weapons test participants (∼115,000 atomic veterans)	External: gamma-ray-emitting fission products (e.g. 140Ba-140La, 95Zr-95Nb) Internal: some intakes of radionuclides (e.g. 131I, 133I; 239Pu)
DOE workers (∼360,000, many last followed 15–20 years ago)	External: gamma-ray-emitting radioactive materials; in some cases, neutrons Internal: intakes of uranium and plutonium isotopes (e.g. Rocketdyne workers); intakes of ^{210}Po, ^{238}Pu, ^{3}H (tritium) (e.g. Mound workers); intakes of ^{235}U and ^{226}Ra (e.g. Mallinckrodt workers)
Medical workers (∼170,000) (includes early radiologists, radiologic technologists, nuclear medicine technologists, radiation oncologists, cardiologists, interventional radiologists, and other medical specialties with potential for relatively high doses)	External: diagnostic x-ray production devices, x-ray or gamma-ray teletherapy units, ^{99m}Tc and other medical radiopharmaceuticals, brachytherapy sources such as radium Internal: possible inadvertent intakes of radionuclides may occur during nuclear-medicine procedures

[a]Adapted from Table 2.1 in NCRP (2018a). Note that because of the dynamic nature of epidemiologic research for the Million Person Study over the years, the population numbers throughout may differ but were current at the time of the specific publication or report.

nuclear power plant workers, industrial radiographers and medical, and other radiation workers (Table 1).

The five major components of the MPS include a total of 29 individual cohorts. Some of the individual cohorts, such as the study of nuclear weapons test participants, include multiple sub-cohorts. The status of the 29 cohorts under study is summarized in Table 2. Each study cohort is placed into one of five categories: completed ($n = 127{,}000$), completed with additional analyses ongoing ($n = 271{,}000$), ongoing and to complete in 1–3 years ($n = 193{,}000$), recently begun and to complete in 2–3 years ($n = 70{,}000$), to begin in stepwise approach as resources become available ($n = 122{,}000$). Our goal is to complete all cohort studies within the next 3–4 years. If resources are not sufficient, the first mortality follow-up for the MPS will include at a minimum ~810,000 workers and veterans, and the second mortality follow-up would include all 29 individual cohorts and over 1,000,000 persons.

Study populations of workers and veterans

The sources of population and dosimetry data and how they were incorporated into the MPS are described in detail in NCRP Report 178 (2018a) and elsewhere (Till et al. 2014; Hagemeyer et al. 2018; Dauer, Bouville, et al. 2018; Ellis, Boice, et al. 2018; Yoder et al. 2018). Briefly, the DOE Health and Mortality study began over 40 years and is the source of ~360,000 DOE workers (Ellis, Girardi, et al. 2018). Over 25 years ago, the NCI collaborated with the U.S. NRC to change their reporting requirements and effectively created a database to study nuclear power plant workers ($n = \sim150{,}000$) and industrial radiographers ($n = \sim130{,}000$) (Hagemeyer et al. 2018). For over 30 years, the Department of Defense (DoD) collected data that facilitated studies of aboveground nuclear weapons test participants (~115,000) (Till et al. 2014). At the request of NCI in 1978, Landauer, Inc. saved their dosimetry databases which became the source to study ~170,000 medical and other workers (Yoder et al. 2018).

DOE workers

The U.S.A. was one of the first countries to develop both nuclear weapons and nuclear power reactors to generate electricity and to fuel military ships and submarines. Within the MPS, epidemiologic studies are being conducted or are planned of ~360,000 workers employed by DOE and its contractors since 1940. While there are many DOE facilities, the MPS focuses on the larger and previously studied DOE facilities for both efficiency and cost savings. The MPS has followed the same classification scheme used by the DOE Health and Mortality Studies program of defining facilities as to uranium or plutonium activities (Shy 1982; Lushbaugh et al. 1983; Fry et al. 1985; CEDR 2018; Ellis, Girardi, et al. 2018). About 400,000 workers in the DOE worker database could conceivably be studied; the MPS focuses on ~360,000 workers: ~240,000 uranium workers (Table 3), and ~120,000 plutonium workers (Table 4). Sites that had not been comprehensively studied are excluded, such as the Sandia National Laboratory, for which a follow-up would be both challenging and expensive. Because of unique exposure or worker characteristics, some facilities not previously studied were purposely included: the Tennessee Eastman Corporation (TEC) female workers employed in Oak Ridge

Table 2. Status of the epidemiologic cohorts under study in the Million Person Study as of October 2018 and updated.

Cohort	Relevant references	Approximate number of workers
Completed		
Rocketdyne	Boice et al. (2011)	5801
Mound	Boice et al. (2014), (2017), NCRP (2018b), Boice, Ellis et al. (2019)	4101
Mallinckrodt	Golden et al. (2019)	2514
Atomic Veterans (8 Series)	Caldwell et al. (2016), NCRP 2018b; Boice, Ellis et al. 2019; Boice, Mumma, et al. (2019)	115,000
Completed with additional analyses ongoing		
Nuclear power plant workers	Golden et al. (2018), NCRP (2018b); Boice, Ellis et al. (2019); Boice et al. (2019a)	145,000
Industrial radiographers	NCRP (2018b), Boice, Ellis et al. (2019), Boice et al. (2019b)	126,000
Ongoing to complete in 1–3 years		
Middlesex		700
Los Alamos National Laboratory		15,727
Fernald		6000
Medical radiation workers		170,000
Recently begun		
Rocky Flats		17,000
Linde		1500
Hanford		32,643
Tennessee Eastman Corporation (Y-12) – women		20,423
Planned to begin shortly		
Oak Ridge Gaseous Diffusion Plant (K-25)		49,749
Portsmouth Gaseous Diffusion Plant		9215
Planned to begin as resources become available		
Tennessee Eastman Corporation (Y-12) – men		41,107
Savannah River Site		18,883
Oak Ridge National Laboratory, X-10 Graphite Reactor		28,528
Union Carbide Corporation Nuclear Division, Oak Ridge (Y-12)		26,059
Paducah		6526
Pantex		1031
Total planned		122,134
Overall total		1,028,301

Table 3. Prior studies of workers at DOE uranium facilities[a].

Worker Cohort	Number in previous studies	Relevant publications	Last follow-up	Total dead	Comment	Total in database
Oak Ridge segment	106,020	Frome et al. (1997)	2005	27,982	All Oak Ridge	
K-25	35,712	Dupree et al. (1994)	1989	12,848	White males	49,794
X-10	6348	Gilbert, Cragle, et al. (1993), Schubauer-Berigan et al. (2015)	1984	1246	Recent follow-up combined	28,528
Y-12 (TEC)[b] (males)	18,348	Polednak and Frome (1981)	1977	5394	White males	41,107
Y-12 (TEC) (females)	N/A	None, first time studied	N/A	15,429	Females, white and black; never studied, in process	20,423
Y-12 (Union Carbide Corporation Nuclear Division)	8116	Loomis and Wolf (1996)	1990	1861	Electromagnetic enrichment	26,059
Portsmouth Gaseous Diffusion	9215	NIOSH (2001), Yiin et al. (2017)	1991	1275	Enriched uranium	9308
Paducah	6759	Chan et al. (2010)	2003	1638	Gaseous diffusion	5731
Manhattan Engineer District (uranium)						
Niagara Frontier						
Harshaw, ElectroMet, Bethlehem	N/A	None	N/A	N/A	N/A	1144
Linde	995	Dupree et al. (1987)	1979	429	Employed 1943–1949	1551
Middlesex	N/A	None, first time studied	N/A	N/A	Never studied, in process	670
Fernald Feed Materials Production Center	4014	Cragle et al. (1995), Ritz (1999), Silver et al. (2013)	1989	1064	White males	7337
Mallinckrodt Chemical Works	2514	Dupree-Ellis et al. (2000)	1993	1013	White males, in process	3272
Savannah River Site (uranium processing)	18,883	Cragle et al. (1988), Richardson et al. (2007)	2002	5096	Internal exposure to uranium, tritium	21,509
Pantex (weapons assembly)	4668	Acquavella et al. (1985), Silver et al. (2005)	1995	1031	Minimum uranium, possible control	12,670
Rocketdyne (Atomics International)	5801	Boice, Cohen, et al. (2006), Boice, Leggett, et al. (2006), Boice et al. (2011)	1999	1468	Comprehensive dosimetry	46,970
Sum of unique workers				62,379		240,000[c]

[a]Adapted from Table 4.1 in NCRP (2018a).
[b]TEC: Tennessee Eastman Corporation
[c]Because workers may be in more than one cohort, the individual sites sum to more than the total which is for unique workers; 240,000 is an approximate figure.

1943–1947 [the so-called girls of the atomic city (Kiernan 2013)] and the workers at the Middlesex Sampling Plant (Middlesex, New Jersey) with unique exposures to pitchblende dust (Eisenbud 1975).

Atomic veterans

Approximately 250,000 U.S. military personnel participated in aboveground nuclear weapons testing between 1945 and 1962. Previous studies were conducted on participants at seven of the test series. An eighth series, TRINITY, was added to these previous seven making up the Eight Series Study. The study population was obtained from databases within the DoD Nuclear Test Personnel Review (NTPR) program (NRC/NA 2003) coupled with epidemiologic research investigations conducted by the Medical Follow Up Agency (Johnson et al. 1996, 1997; Thaul et al. 2000) and the Veterans Affairs (VA) (Watanabe et al. 1995; Dalager et al. 2000). These test series were selected because of the availability of high-quality records of personnel and radiation dosimetry and indications that radiation exposures were higher than at other tests series. Notable scientists in the study include J. Robert Oppenheimer, Enrico Fermi, and Hans Bethe, who were at the first nuclear test (TRINITY) in 1945 at Alamogordo, New Mexico.

There were 98 weapon detonations (or shots) within the eight test series (DOE 2000). The estimation of radiation was facilitated by the Nuclear Test Review Information System (*NuTRIS*) maintained by the U.S. Defense Threat Reduction Agency (DTRA), DoD which included film badge readings (Till et al. 2014; Till, Beck, Aanenson, et al. 2018; Beck et al. 2017). Table 5 shows the number of participants at each of the eight nuclear weapons test series, the number from each military service, and other demographic characteristics.

The tracing and determination of vital status among these veterans were challenging because the social security number was not used as the military identification number until 1968 and thus was not readily available. We relied heavily on mortality linkages based on military identification number and name and date of birth. The Department of VA BIRLS system (Beneficiary Identification Record Location Subsystem) was a primary source of vital status information (Fisher et al. 1995), supplemented with other sources such as the Social Security Administration records and the National Death Index (NDI) (Mumma et al. 2018). The VA Patient Treatment File was also of value (Fisher et al. 1995; Boyko et al. 2000).

Publications to date include a second follow-up, with collaborators at the Centers for Disease Control and Prevention (CDC), of the 1979 SMOKY shot within the PLUMBBOB test series where an excess of leukemia had led to future studies and compensation programs (Caldwell et al. 1983, 2016); detailed dose reconstructions (Till et al. 2014; Till, Beck, Aanenson, et al. 2018; Beck et al. 2017); an evaluation

Table 4. Studies of workers at DOE plutonium facilities[a].

Worker cohort	Number in previous studies	Relevant Publications	Last follow-up	Number dead	Total in database[b]
Hanford	32,643	Peterson et al. (1990), Gilbert, Cragle, et al. (1993), Gilbert, Omohundro, et al. (1993), Wing et al. (2004), Wing and Richardson (2005)	1986	9452	56,688
Los Alamos	15,727	Gilbert, Cragle, et al. (1993), Wiggs et al. (1994), Wilkinson et al. (1987)	1990	3196	23,288
Mound	4101	Boice et al. (2014), Wiggs, Cox-DeVore, Voelz, et al. (1991), Wiggs, Cox-DeVore CA, Wilkinson (1991); Boice et al. (2017), NCRP (2018b); Boice, Ellis et al. 2019)	2009	3686	7270
Rocky Flats	5413	Brown et al. (2004), Gilbert, Cragle, et al. (1993)	1979	409	53,033
Sandia National Lab	N/A	None	N/A	N/A	24,685
Total	–	–	–	55,000[c]	120,000

[a]Adapted from Table 4.2 in NCRP (2018a).
[b]Because workers may be in more than one cohort, the individual sites sum to more than the total which is for unique workers; 120,000 is an approximate number.
[c]Number found to have died during the pilot and previous investigations.

of mesothelioma among sailors at the Pacific Proving Grounds linked to work in boiler rooms and other areas with high likelihood of asbestos exposures (Till, Beck, Boice, et al. 2018); and an evaluation of ischemic heart disease (Boice 2017a; NCRP 2018b).

Also, not all exposures were low; e.g. exposures greater than 300 mSv occurred during the 1954 Bravo test at Operation Castle, where the wind blew the wrong way, and personnel stationed at Rongerik Atoll were exposed to direct fallout before they were evacuated (DTRA 2015). A special study was conducted by the NCI that focused on the living high-dose servicemen (>200 mSv) at the Bravo test or the Nevada test site to compare three forms of dose estimation: (1) historical personnel monitoring data; (2) dose reconstruction based on detailed scenarios; and (3) two chromosome aberration assays and a telomere length assay (Simon et al. 2019).

Rarely can an occupational study address personal medical x-ray procedures, such as CT that are so frequent today (although much less so in the years covered by this study). We were able to link to the electronic records of the VA medical care system and evaluated radiological procedures for all veterans with leukemia and lung cancer and a sample of the cohort (Fisher et al. 1995; Boyko et al. 2000). Preliminary findings indicated that the frequency of CT examinations was the same between leukemia cases with the cohort sample and did not differ by years prior to death. Atomic veterans who died of lung cancer, however, had more CT examinations than the cohort sample, but the increased numbers were entirely due to procedures performed within 1–2 years of death, indicating that they were conducted for the purposes of diagnosis and treatment planning.

A unique population of 37,000 military personnel who participated in the underground nuclear weapons tests from 1962 to 1992 could be studied where the potential for exposure includes radioactive dust and gas venting such as occurred at the Baneberry test in 1970. Cancer incidence and noncancer diseases could also be evaluated for all atomic veterans who reach the age of 65 and were eligible for Medicare (Rector et al. 2004). A feasibility effort was conducted but at this time there are no plans to initiate a follow-up of this population.

The study of atomic veterans provides a service to the veterans and their families in obtaining sound information on the possible health risks related to service to our country. It also is relevant to understanding the consequences of possible terrorist attacks with dirty bombs or improvised nuclear devices, since the nuclear exposures in these circumstances are similar to those from weapons testing. It is the relevant population for evaluating compensation claims and radiation risks among atomic veterans.

Nuclear power plant workers

By law, NRC is required to record radiation dosimetry information from its licensees to assure that they are in compliance with existing regulations. These data have been collected since the late 1950s, but it was not until 1994 that the reporting requirements changed and it was possible to make these data available for epidemiologic study (Hagemeyer et al. 2018; NCRP 2018a). In 1986, Drs. Gilbert Beebe and John Boice, both at the NCI, composed a letter that was sent by NCI Director Vincent DeVita, MD, to NRC Chairman Lando Zech requesting the changing of the reporting requirements in order to develop a registry that would be valuable for health studies. In 1991, a positive response was received from NRC Chairman Kenneth Carr to NCI Director Samuel Broder. In 1994, as part of the implementation of the 1991 revisions of 10 CFR 20 'Standards for Protection Against Radiation,' the NRC began requiring annual radiation exposure records for every monitored worker (NRC 1992). In 1994 Dr. Boice urged the voluntary reporting of additional occupational radiation exposure data so that a high-quality radiation worker registry might be created for epidemiologic studies. In 1994 NRC (1994) sent a 'generic letter' to licensed utilities requesting that they report voluntarily the career doses of current and past employees; the utilities responded favorably, and a registry of radiation workers suitable for epidemiologic study was created. Twenty years later, the REIRS registry (ORISE 2011; REIRS 2018) became the cornerstone for identifying the ∼150,000 early nuclear utility workers (1957–1984) being studied today as part of the MPS (Boice, 2013b, 2016a, 2017a; Boice et al. 2018, 2019a; Dauer, Bouville, et al. 2018; NCRP 2018a).

In 1957 the town of Moorpark, California, became the first in the country to be powered (briefly) by electricity produced from a nuclear reactor. Later that year, the Shippingport Atomic Power Plant became the first commercial nuclear power plant in the U.S.A. There have been over 600,000 nuclear power plant workers over the years, of which ∼150,000 were selected for study on the basis of NRC REIRS files, supplemented by dosimetry records from Landauer, Inc. Feasibility studies were conducted utilizing NRC, Landauer, Inc., and utility records (Jablon and Boice 1993; Muirhead et al. 1996), but the current REIRS database now supersedes all previous approaches to conduct research studies (NCRP 2018a, 2018b; Boice, Ellis et al. 2019). Additional records from Landauer include 2880 rolls of microfilm of early workers (1954–1979) which have been used in validation studies (see below) and could be tapped to expand and enhance the early worker data if resources became available.

Early regulations allowed workers to receive up to 30 mSv per quarter (120 mSv y^{-1}), and although rare, some workers did receive high cumulative exposures (Hall et al. 2009). A broad distribution of cumulative radiation doses found that 28% of the workers in the current study have cumulative doses >50 mSv which will enhance the statistical power of the study to detect any associated increases in cancer or other causes of mortality should they have occurred (NCRP 2018a). A study of current workers in the nuclear industry would not be informative because the individual doses are so low; indeed they are lower than doses received from ubiquitous natural background radiation and lower than those received from medical radiation exposures. From 1973 to 2006, the average annual measurable dose per worker was reduced from 6.6 to 1.4 mSv (Blevins and Andersen 2011).

To verify the accuracy of the reported film badge doses for workers monitored 1950–1979, 27 workers were selected, and their film dosimeters (commercial product name: Gardray) were retrieved from archive storage in salt mines in Hutchinson, Kansas (Underground Vaults & Storage, Salt Mine). Twenty-seven dosimeters (and control dosimeters which were stored alongside the worker film badges) were reanalyzed using current Macbeth TD 931 reader and compared with their past recorded film badge doses. The actual reports were found by searching 2880 rolls of microfilm from 1954 to 1979. Overall, for film badge readings in the MPS sample, the accuracy of the historical measurement data and dose calculation to current readings was within 10% thus verifying the accuracy of the reported doses used for early workers understudy (Kirr et al. 2016; Kirr and Passmore 2016).

Industrial radiographers

Industrial radiographic nondestructive testing typically utilizes ^{192}Ir and ^{60}Co sources (Bouville et al. 2015; NRC 2017; NCRP 2018a), and thus radiographers receive external irradiation, generally in an anterior-posterior geometry. Similar to the cohort of nuclear power plant workers described above, information on annual recorded dose was collected for ∼130,000 industrial radiographers within the NRC Radiation Exposure Information and Reporting System (REIRS 2018) and the Landauer, Inc. dosimetry database (NRC 1992, 1994, 2018; Muirhead et al. 1996; Anzenberg et al. 2010). The average cumulative recorded dose for these industrial radiographers is ∼20 mGy, with 10% receiving a cumulative recorded dose >50 mGy (NCRP 2018a). Over 32,000 of the industrial radiographers are currently known to have worked in naval shipyards and analyses suggest a high risk for mesothelioma likely attributable to asbestos exposure (Mumma et al. 2019). Approaches to follow-up, dose reconstruction, mortality ascertainment, and analyses were equivalent to those for the study of NPP workers. A unique feature of the MPS being utilized in the NPP and industrial radiographer studies is the use of census block group data for education as a proxy measure of socioeconomic status which is included in the statistical models to control for potential confounding by smoking or other lifestyle factors (Cohen et al. 2018). Preliminary analyses for leukemia, other than chronic lymphocytic leukemia, and lung cancer have been conducted (NCRP 2018b; Boice, Ellis et al. 2019; Boice et al. 2019b). The industrial radiographers include nearly 200 leukemia cases, in comparison with the 98 cases among adult male atomic bomb survivors.

Medical radiation workers

The Medical Radiation Workers in the MPS include radiologists, radiologic technologists, radiopharmaceutical workers, interventionalists, cardiologists, nuclear medicine workers, physicists, and nurses (Bouville et al. 2015; NCRP 2018a; Yoder et al. 2018). Approximately 170,000 persons were selected from an eligible population of 1.71 million medical workers identified within the Landauer, Inc. dosimetry database. The database was created in the 1980s to assist with an epidemiology study of radiological technologists being conducted by the Radiation Epidemiology Branch of the NCI (Boice et al. 1992; Simon et al. 2006). The database contains annual doses for the years 1977 and later; cumulative doses up to 1977 for workers who had coverage with Landauer before 1977; and annual doses for the years 1960–1976 can be obtained through manual examination of copies of dosimetry reports for many workers available on 2880 rolls of microfilm. The estimation of radiation doses among medical workers over the years has been challenging but improving (Linet et al. 2010). NCRP has convened Scientific Committee 6–11 to comprehensively address the dosimetry issues associated with the medical radiation workers in the MPS (Yoder et al. 2018; NCRP 2018a).

The medical radiation workers represent the largest occupational cohort in the MPS and include large numbers of women that will allow a statistically powerful evaluation of any sex-specific radiation risks. Studies of Japanese atomic bomb survivors report an approximately three times greater radiation risk of lung cancer among females compared with males (Ozasa et al. 2012; NCRP 2014; Cahoon et al. 2017; Boice 2019; Boice, Ellis, et al. 2019). The National Aeronautics and Space Administration (NASA) provides

Table 5. Number of nuclear weapons test participants at each of the eight test series by military service. These tests involved 98 bomb detonations[a].

Test series	Year	Test site	No. of tests	Air force	Army	Marine corps	Navy	Total
CROSSROADS	1946	Pacific	2	0	3395	551	39,188	43,134
GREENHOUSE	1951	Pacific	4	2442	1548	70	3854	7914
UPSHOT-KNOTHOLE	1953	Nevada	11	2175	13,401	2256	886	18,718
CASTLE	1954	Pacific	6	2763	1644	306	11,918	16,631
REDWING	1956	Pacific	17	2976	1708	250	6993	11,927
PLUMBBOB	1957	Nevada	23	2216	7052	2,120	601	11,989
HARDTACK	1968	Nevada	34	3476	1535	187	9487	14,685
TRINITY	1945	New Mexico	1		726			726
Total	–	–	98	16,048	31,009	5740	72,927	125,724

[a]Seven military cohorts (test series) had been carefully constructed and studied by the Medical Follow-Up Agency (MFUA) (Robinette et al. 1985; Johnson et al. 1996, 1997; Thaul et al. 2000) and the U.S. Department of Veterans Affairs (VA) (Watanabe et al. 1995; Dalager et al. 2000). These cohorts, along with the TRINTY test, formed the basis of the study population.

support for the medical worker study because 1) they are interested in protracted rather than acute radiation and 2) since the NASA protection standards for astronauts are based on individual lifetime risk projections, sex-specific differences limit the time women can spend in space, including on long-term missions to Mars (NCRP 2014; Boice 2016b, 2017a, 2017c, 2019; Boice et al. 2018; Boice, Ellis, et al. 2019).

Landauer, Inc. has provided radiation dosimetry services since 1953 for U.S. medical, nuclear, and other facilities. A computerized database of millions of workers is maintained which formed the source of the medical radiation worker cohort. An initial cohort of 1.71 million workers first monitored before 1995 was assembled. To reduce this size to a more cost-efficient design without losing statistical power, a 50% random sample of workers with cumulative recorded doses between 10 and 50 mSv and a 2% random sample of workers with doses less than 10 mSv were taken. All workers having cumulative recorded doses equal to or greater than 50 mSv were selected (Table 6). The broad dose distribution is seen in Table 6 with 36% ($n\sim$62,000) of the cohort having cumulative recorded doses over 50 mSv, 16% ($n\sim$27,000) over 100 mSv, and 4% ($n\sim$6,600) over 250 mSv. For comparison, there were 18,443 Japanese survivors of the atomic bombings with exposures $>$100 mSv. The large numbers and broad range of doses in the MPS indicate substantial statistical power to detect any late-occurring health effects and to distinguish any differences associated with radiation exposures experienced gradually over time compared with acute exposures for individual cancer sites.

Other – U.S. Navy submariners

Navy personnel who served on nuclear submarines are the most important population currently not included in the MPS. A third follow-up could be conducted of 85,498 nuclear submariners who were previously studied by Yale University (Charpentier et al. 1993) and New York University (Shore et al. 2001; Friedman-Jimenez 2003a, 2003b; Mueller et al. 2018). In this study, Navy enlisted men who served on nuclear submarines sometime between 1969 and 1982 were followed through 1995. The average lifetime badge reading was 5.2 mSv with 1.4% over 50 mSv. Most sailors were alive at last follow-up and only 3263 (3.8%) had died. The follow-up was too short to provide a powerful evaluation of possible effects. An extended follow-up of 22 years, through 2018, would increase the statistical ability to detect a radiation effect, had there been one. To further increase statistical power and to improve the study design, the study could be expanded to include submariners who served prior to 1969 (the Nautilus was commissioned in 1954) and to include officers. To date, over 100,000 submariners have been identified who served from 1954 through 1984. Between 10-15% were officers. Discussions are ongoing with U.S. Navy personnel concerning permission to conduct a new follow-up of the submariner population and, if permitted, we would include it within the MPS program of studies.

National effort

The DOE had for many years supported low-dose radiation research (Hall et al. 2009). The DOE funded an important pilot study that proved the feasibility of conducting the MPS (Boice 2012a); it provided additional support with interagency collaborations (NASA, NRC, Environmental Protection Agency (EPA)) and has recently renewed its support for the DOE worker studies with a 5-year grant to the NCRP. Further, the DOE provided access to the databases essential for study conduct. The vision to conduct a study of the early U.S. radiation workers began 30 years ago with requests to the U.S. NRC to change its reporting requirements to facilitate possible future study of licensee workers. These changes were made and the NRC remains one of the major supporters of the study. NASA also is a strong supporter of the MPS, first through an interagency agreement with DOE and now directly to National Council on Radiation Protection and Measurements (NCRP). Over the years, the CDC continued to provide foundational support essential for the study conduct. The U.S. EPA provided support through the DOE interagency agreement as well as indirect support via the Oak Ridge National Laboratory (ORNL). The NCI awarded a five-year grant to Vanderbilt University for the study of atomic veterans, with support and cooperation from the U.S. DoD, the Defense Threat Reduction Agency (DTRA), and VA. Recently the Naval Sea Systems Command awarded a five year contract for research focusing on naval personnel. National laboratory collaborators include ORNL, the Los Alamos National Laboratory (LANL) as well as the Oak Ridge Institute for Science and Education (ORISE). Other academic involvement comes from Vanderbilt University, the University of Southern California, Harvard University, and the Fred Hutchison Cancer Research Center. Private-sector contributors and collaborators are from the

International Epidemiology Institute, the Risk Assessment Corporation, Landauer, Inc., and Oak Ridge Associated Universities (ORAU).

The importance of the MPS and the continued funding for research in the U.S.A. was covered in the recent U.S. Government Accountability Office (GAO) Report on Low Dose Radiation: Interagency Collaboration on Planning Research Could Improve Information on Health Effects (GAO 2017; Davis et al. 2019). This Report highlighted the need for federal funding of low-level radiation research, extensively described the funding history of the MPS, and reported discussions with various government agencies on the value of ongoing MPS research to their missions. Congress recently supported the MPS by directing the DOE to provide research funds for the MPS of workers and veterans in recent appropriation bills.

The scientific understandings obtained also will be used in setting standards to protect workers and the public, and in improving compensation schemes for workers (Neton 2014), veterans (NRC/NA 2003) and civilians who were on-site participants at above-ground nuclear weapons tests, down-winders who lived in proximity to the weapons testing, and underground miners who worked in uranium mines (NA/NRC 2005).

In brief, for claimants requesting compensation for cancer and diseases they believe were linked to their prior radiation exposure, extensive dose reconstructions are often required. The estimated radiation doses and characteristics of each claimant are then evaluated as to whether or not the dose was the contributing cause, i.e. more likely than not. The procedures to estimate individual risk and a so-called 'probability of causation' (more correctly 'assigned share') were developed by law to maximize the likelihood of an award. However, the major source of information on cancer or disease risks used in these computations comes from the study of Japanese atomic bomb survivors. This database is based on a single exposure in 1945 to an Asian population and the risks are then modified, often appreciably, to be made appropriate for a U.S. population of healthy workers or civilians. The numbers of cancers for specific sites, when broken down by sex, age, and follow-up after exposure, can be quite small with risk coefficients having great uncertainty. All compensation schemes could be improved by the results from the MPS because the numbers will be much larger than from the atomic bomb survivors so the estimates will have more precision; they are more representative of healthy Americans than the Japanese population; and they do not require challenging procedures that attempt to convert a single exposure to a Japanese population with different disease rates and make it appropriate to American populations with chronic or prolonged exposures. The MPS also will be able to provide precise estimates for rare cancer sites that cannot be determined among the Japanese atomic bomb survivor population except by assumption. The MPS then will provide a high-quality assessment of cancer risks among healthy men and women that could be incorporated into the 'probability of causation' computations and thus contribute to enhancing the quality of information needed for these three different, but similar, compensation programs for workers and veterans and civilians who were exposed to radiation in the service of their country. Congress has passed laws that address these compensation issues.

Dosimetry

Good dosimetry is the key to good epidemiology (NCRP 2018b, UNSCEAR 2018). NCRP Report 178 (NCRP 2018a) entitled '*Deriving organ doses and their uncertainty for epidemiologic studies* (*With a focus on the one million U.S. workers and veterans study of low-dose radiation health effects*' guides the overall dose reconstruction process. The approach to estimating occupational doses received by individuals has also been described in several publications: Rocketdyne workers (Leggett et al. 2005; Boice, Cohen, et al. 2006, 2011); Mound workers (Boice et al. 2014); atomic veterans (Till et al. 2014; Till, Beck, Aanenson, et al. 2018; Caldwell et al. 2016; Beck et al. 2017); Mallinckrodt workers (Ellis, Boice, et al. 2018; Golden et al. 2019); and all workers (Bouville et al. 2015; NCRP 2018a). Six manuscripts in this special issue are focused on the complexities of dose reconstructions: all workers (Dauer, Bouville, et al. 2018); atomic veterans (Till, Beck, Aanenson, et al. 2018); internal emitters (Leggett, Eckerman, et al. 2018); brain dosimetry (Leggett, Tolmachev, et al. 2018); and medical radiation workers (Yoder et al. 2018; Dauer, Woods, et al. 2019). Dosimetry improvements are to continue, with more emphasis on handling the uncertainties and possible biases in studies (UNSCEAR 2008, 2014, 2018; Boice 2010; NCRP 2012) and in measurements and dose estimation, especially in the early years of monitoring (Gilbert et al. 1996; Gilbert 1998; Wakeford 2018; NCRP 2018a).

Table 7 provides a comparison between an early combined dose distribution of all MPS workers as of about 5 years ago with that of the Japanese atomic bomb survivors (Ozasa et al. 2012). The numbers of workers in the MPS study cohorts and the radiation dose distributions change during active follow-up as new personnel information is incorporated from employment or other records and as dose information is obtained and refined. For example, dose

Table 6. Distribution of the cumulative recorded doses of 168,565 medical radiation workers as of April 2015 (NCRP 2018a)[a,b].

Cumulative recorded dose (mSv)[c]	Number of workers[d]	Percentage of workers
<10	29,902[d]	17.7
10–<25	50,464[d]	30.0
25–<50	26,673[d]	15.8
50–<100	34,410	20.4
100–<250	20,512	12.1
250–<500	4842	2.87
500–<1000	1247	0.74
≥1000	515	0.31
All	168,565	100.0

[a]Adapted from Table B.5 in NCRP (2018a).
[b]This distribution was based on the information available at the time NCRP Report No. 178 (2018a) was prepared and has changed somewhat during the course of the study.
[c]The doses are expressed in terms of $H_p(10)$.
[d]The initial selection of workers eligible for study was those first monitored before 1995 ($n = 1,710,951$). To reduce the population to a more manageable and cost-effective size, without reducing statistical power, a 2% sample of the ~1,500,000 eligible workers with <10 mSv, and a 50% sample of the ~160,000 eligible workers with 10–49 mSv were selected for study.

Table 7. Distribution of the accumulated recorded doses, for the Million Person Study (MPS)[a] and for the study of Japanese atomic bomb survivors (Ozasa et al. 2012).

Cumulative recorded dose[b,c] (mSv)	Number of MPS workers and veterans	Cumulative number starting >50 mSv[d]	Number of atomic bomb survivors	Cumulative number starting >50 mSv
<10	6,874,268	–	43,361	–
10–	510,719	–	18,215	–
50–	104,395	104,395	6894	6894
100–	77,670	182,065	12,330	19,224
500–	4121	186,186	3424	22,648
≥1000	1217	187,403	2387	25,035
All	7,572,390	–	86,611	–

[a]Extracted from the NRC REIRS, DOE REMS, DoD NTP, historical DOE databases, and Landauer, Inc. dosimetry databases. All subjects >50 mSv were initially included for study. The numbers of low-dose subjects were so large, that only samples were taken which reduced the total population study to about a million workers and veterans.
[b]Dose categories for the MPS are expressed in terms of $H_p(10)$ primarily low-LET radiation. Absorbed doses from intakes of radionuclides are being estimated and not included in this table.
[c]Dose categories for the Japanese atomic bomb survivors are weighted absorbed colon dose. The absorbed dose from neutrons was weighted by a factor of 10.
[d]Cumulative doses from 50 mSv to indicate the differences in study size for relatively high-dose subjects.

reconstructions for individual workers will change to reflect the incorporation of organ doses from intakes of radionuclides, adding doses from work at other facilities, and converting personal dose equivalent [Hp(10)] (the film badge or personnel dosimeter measurement) to organ dose. The doses for the MPS were initially expressed in terms of personal dose equivalent [Hp(10)] and thus not strictly comparable with the absorbed dose to colon displayed for the atomic bomb survivors. On the other hand, the MPS tabulations in Table 7 do not include doses received at other facilities (see for example the influence of such doses on cumulative individual dose in Boice, Leggett, et al. 2006); nor does it include the doses from intakes of radionuclides, which can be substantial for some organs in several studies (Boice, Leggett, et al. 2006, 2014). Nonetheless, the distribution supports the tenet that the MPS has sufficient numbers and a broad dose distribution to provide new information on the effects of radiation when dose is delivered in a chronic or fractionated manner over a period of years.

Estimates of risks from gradual exposure over years will be substantially improved by the MPS (Boice 2014a). Radiation risk estimates will be precise having 20 times the number of adults than the atomic bomb survivor study (86,000 total and 54,000 adults), as broad a dose range (>100 mSv), as long a follow-up (>70 years), and based on U.S. radiation workers and veterans for whom the follow-up for vital status and death information and dose reconstruction (external and internal) are done in the same manner for all cohorts within the MPS (Mumma et al. 2018; Dauer, Bouville, et al. 2018; NCRP 2018a).

Summary

The MPS of U.S. radiation workers and veterans has been ongoing for over 15 years. The MPS will fill a critically important gap in knowledge by answering the question: what are the health consequences of exposure to radiation received gradually over time? The size of the MPS and range of radiation doses will provide substantial understanding as to the adequacy of the LNT model as used today in radiation protection (not for risk assessment) (ICRP 2007; Boice 2017b; NCRP 2018b; Shore et al. 2018). Approximately 810,000 workers and veterans within 21 of 29 MPS cohorts are currently under study to fill this need, with the remaining 8 cohorts to be incorporated once funds become available. The MPS is relevant today to federal agencies (GAO 2017; Davis et al. 2019) and the public: NRC will obtain information on the worker populations they regulate and set standards for; DoD and the DTRA will learn the extent to which atomic veterans have developed diseases related to their service for the nation; EPA has interest in accurate risks related to environmental exposures, especially to radionuclides; CDC's mission includes emergency response, environmental and medical exposures; and NASA requires more precise information on risks following gradual exposures and high-LET exposures to provide protection guidance for astronauts on long-duration missions such as to Mars. The scientific understandings obtained will be used in setting standards to protect workers and the public, in improving compensation schemes for workers, veterans, and the public, and in providing guidance for policy and decision makers.

Note

1. LNT refers to the linear-nonthreshold (LNT) dose-response model as used in radiation protection. Its purpose is to give regulators an approach to manage the potential risk of low-dose radiation exposures where radiation epidemiology is incapable of providing clear or convincing evidence or risk. It is inappropriate to use the LNT model in risk assessment for individuals or populations since it incorporates many assumptions and judgments that are not related to radiation risk (ICRP 2007; Boice 2017b; Shore et al. 2018; NCRP 2018b).

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