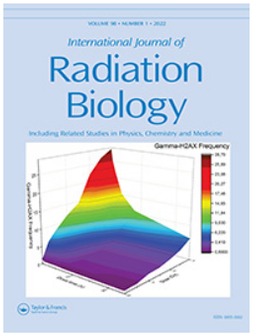

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ORIGINAL ARTICLE

Mortality from leukemia, cancer and heart disease among U.S. nuclear power plant workers, 1957–2011

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ABSTRACT

Background: The aim of the Million Person Study of Low-Dose Health Effects (MPS) is to examine the level of radiation risk for chronic exposures received gradually over time and not acutely as was the case for the Japanese atomic bomb survivors. Nuclear power plant (NPP) workers comprise nearly 15 percent of the MPS. Leukemia, selected cancers, Parkinson's disease, ischemic heart disease (IHD) and other causes of death are evaluated.

Methods and material: The U.S. Nuclear Regulatory Commission's Radiation Exposure Information and Reporting System (REIRS) and the Landauer, Inc. dosimetry databases identified 135,193 NPP workers first monitored 1957–1984. Annual personal dose equivalents [*Hp(10)*] were available for each worker. Radiation records from all places of employment were sought. Vital status was determined through 2011. Mean absorbed doses to red bone marrow (RBM), esophagus, lung, colon, brain and heart were estimated by adjusting the recorded *Hp(10)* for each worker by scaling factors, accounting for exposure geometry and energy of the incident gamma radiation. Standardized mortality ratios (SMR) were calculated. Radiation risks were estimated using Cox proportional hazards models.

Results: Nearly 50% of workers were employed for more than 20 years. The mean duration of follow-up was 30.2 y. Overall, 29,124 total deaths occurred, 296 from leukemia other than chronic lymphocytic leukemia (CLL), 3382 from lung cancer, 140 from Parkinson's disease and 5410 from IHD. The mean dose to RBM was 37.9 mGy (maximum 1.0 Gy; percent >100 mGy was 9.2%), 43.2 mGy to lung, 43.7 mGy to colon, 33.2 mGy to brain, and 43.9 mGy to heart. The SMRs (95% CI) were 1.06 (0.94; 1.19) for leukemia other than CLL, 1.10 (1.07; 1.14) for lung cancer, 0.90 (0.76; 1.06) for Parkinson's disease, and 0.80 (0.78; 0.82) for IHD. The excess relative risk (ERR) per 100 mGy for leukemia other than CLL was 0.15 (90% CI −0.001; 0.31). For all solid cancers the ERR per 100 mGy (95% CI) was 0.01 (–0.03; 0.05), for lung cancer −0.04 (–0.11; 0.02), for Parkinson's disease 0.24 (–0.02; 0.50), and for IHD −0.01 (–0.06; 0.04).

Conclusion: Prolonged exposure to radiation increased the risk of leukemia other than CLL among NPP workers. There was little evidence for a radiation association for all solid cancers, lung cancer or ischemic heart disease. Increased precision will be forthcoming as the different cohorts within the MPS are combined, such as industrial radiographers and medical radiation workers who were assembled and evaluated in like manner.

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Introduction

The study of a *Million U.S. Radiation Workers and Veterans* (also known as the Million Person Study of Low-Dose Health Effects (MPS)) is designed to examine the level of radiation risk for chronic exposures that are received gradually over time (Boice, Cohen et al. 2019) and not acutely, as occurred for the Japanese atomic bomb survivors (Ozasa et al. 2012; Grant et al. 2015; McLean et al. 2017). Individualized and annualized dosimetry is an essential aspect of the MPS (Boice et al. 2006; Till et al. 2014; Bouville et al. 2015; Beck 2017; Dauer et al. 2018; Leggett et al. 2018; Ellis, Boice et al. 2018; NCRP 2018a, 2020; Yoder et al. 2021). Previous studies have been published on workers at U.S. Department of Energy (DOE) facilities (Boice et al. 2011, 2014; Boice, Cohen, Mumma, Golden et al. 2021; Boice 2017a; Boice 2017b; Golden et al. 2019) and veterans who participated in above-ground nuclear weapons tests (Boice 2014; Till et al. 2014; Caldwell et al. 2016; Boice et al. 2020).

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Supplemental data for this article can be accessed here.

Workers in the nuclear power plant industry comprise nearly 15% of the MPS population. The consistent reporting of annual worker doses required by the U.S. Nuclear Regulatory Commission (NRC) for their licensees provided a high-quality dosimetry database that was redesigned in 1994 to facilitate epidemiologic study (Hagemeyer et al. 2018). The number of nuclear power plant workers under study ($n = 135,193$) is nearly three times the number of adults over age 20 years at exposure ($n = 51,215$) in the study of Japanese atomic bomb survivors (Ozasa et al. 2012), and over seven times the number of adult males ($n = 18,860$). Herein we report cause-specific analyses for over 40 causes of death and dose-response analyses for leukemia, myelodysplastic disease, all solid cancers, esophageal cancer, lung cancer, Parkinson's disease, and ischemic heart disease (IHD) among early workers in the nuclear power industry first monitored between 1957 and 1984 in the United States and followed through 2011.

Methods

Human subjects research approval for the study was received from Vanderbilt University.

Cohort definition

A cohort of 1,065,703 workers employed at nuclear power plants in the United States in 1957 through 2011 was available for study: 1,001,958 workers within the Radiation Exposure Information and Reporting System (REIRS) maintained by the NRC (Anzenberg et al. 2010; Hagemeyer et al. 2018; USNRC 2021) and 63,745 workers within the Landauer, Inc. dosimetry database (NCRP 2018a, 2020; Yoder et al. 2021) (Figure 1). Workers were excluded if the date of first monitoring was after 1984 ($n = 592,935$) or if personal identifiers needed for tracing, specifically a Social Security Number ($n = 5738$) were absent. Workers first monitored before 1985 were selected on the basis of cost and information value. Workers employed after 1984 were less likely to receive moderate to high cumulative doses compared with workers employed earlier, and were younger and less likely to have died. The choice of 1985 rather than 1980 was because the Three Mile Island reactor accident in 1979 led to new NRC safety requirements involving reactor modifications that increased workers' exposures until about 1985 (Anzenberg et al. 2010; Blevins and Andersen 2011; NCRP 2018a). There were 307,553 workers with cumulative

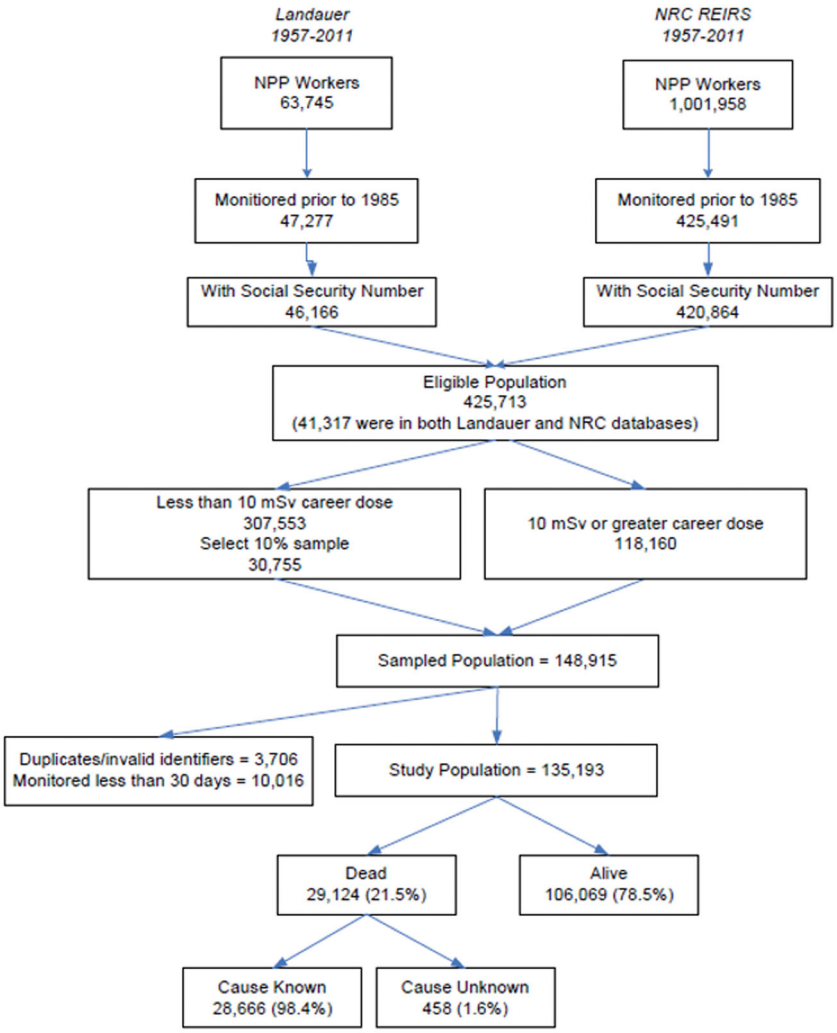

Figure 1. Schematic of the selection and vital status of the 135,193 nuclear power plant workers first monitored between 1957 and 1984 in the United States and followed through 2011.

doses <10 mSv, and it would have been prohibitively expensive to trace and collect death information on them all. A 10% sampling of these very low dose workers was for cost savings without a noticeable diminution of statistical power for dose-response analyses. Short-term workers monitored for less than 30 days ($n = 10{,}016$), duplicate records and those with invalid identifiers ($n = 3706$) were removed. The final study population of 135,193 consisted of all workers with a cumulative dose ≥10 mSv and a 10% sample of workers with a cumulative dose <10 mSv (Table 1). The short-term workers monitored for less than 30 days were traced and the cause of death determined in the same manner as the final study population and evaluated separately.

Just over 15% of the cohort had dosimetry records in both REIRS and Landauer files. The final cohort was comprised almost entirely of workers identified within REIRS (99.2%) with supplemental information from Landauer files (Table 1). In the past, the REIRS and Landauer databases have been used in the planning and conduct of epidemiologic studies (Goldsmith et al. 1989; Jablon and Boice 1993; Muirhead et al. 1996; Boice et al. 2006) but not in defining a cohort for study.

Although first monitoring at a nuclear power plant could begin as early as 1957 (Supplement Table 2), follow-up started in 1969 for the 14% of workers who were identified within the REIRS database as being monitored before 1970. The Atomic Energy Act of 1969 provided the legal requirements for NRC licensees to record and report worker doses. However, these reports to the NRC were not optimal for epidemiologic study (Goldsmith et al. 1989; Jablon and Boice 1993; Muirhead et al. 1996) until 1994 when reporting requirements changed and near complete voluntary reporting back to 1969 essentially created a system of records with personal identifiers and annual doses that could be used for health studies (USNRC 1994; Oak Ridge Institute for Science and Education (ORISE) 2011; Hagemeyer et al. 2018). Follow-up started in 1977 for the 0.8% of workers who were identified only from the Landauer files. Although Landauer has microfiche records dating back to the 1950s, they are not easily accessible. Electronic files suitable for epidemiologic studies were first available in 1977 and included cumulative exposures before 1977 if the worker had been employed as a Landauer client. After removing 3706 workers with invalid identifiers or who were duplicates and 10,016 workers who were monitored for less than 30 d, the cohort was reduced from the sampled population of 148,915 workers to the final study cohort of 135,193 workers (Figure 1).

Landauer developed a special database of annual and lifetime personal monitoring results in response to a mid-1980s request from the Radiation Epidemiology Branch of the National Institutes of Health as an ongoing tool to support their study of registered radiologic technologists (Villoing et al. 2021). The expanded and extensive nature of the database has allowed its use as a confirmatory and supplemental source of dose information residing in other governmental dose registers or worker records (Ellis, Girardi et al. 2018; Yoder et al. 2021; Boice, Cohen, Mumma, Howard et al. 2021).

Table 1. Demographic and occupational characteristics of 135,193 nuclear power plant workers first monitored for radiation between 1957 and 1984 and followed through 2011 in the United States.

Characteristic	*N*	%
Source of the population		
NRC REIRS only	111,681	82.6
Landauer only	1123	0.8
Both REIRS and Landauer	22,389	16.6
Sex		
Female	4420	3.3
Male	130,773	96.7
Year of birth (YOB)		
1902–	2529	1.9
1920–	9906	7.3
1930–	18,941	14.0
1940–	42,026	31.1
1950–	52,990	39.2
1960–1966	8801	6.5
Mean YOB = 1946		
Year first monitored for occupational radiation at an NPP		
1957–	1823	1.4
1970–	17,649	13.1
1975–	46,821	34.6
1980–1984	68,900	51.0
Mean year of first NPP monitoring = 1978		
Number of nuclear power plants at which a worker was monitored		
1	64,241	47.4
2	27,351	20.2
3	13,256	9.8
4	7417	5.5
5–9	13,773	10.2
10 or more facilities	9155	6.8
Years monitored for radiation at a nuclear power plant		
<1	20,569	15.2
1–	28,881	21.4
5–	19,201	14.2
10–	27,331	20.2
20–	25,241	18.7
30–47	13,970	10.3
Mean number of years monitored at a NPP = 12.8		
Years of follow-up		
<1	118	0.1
1–	3092	2.3
10–	7303	5.4
20–	46,473	34.4
30–	74,711	55.3
40–42	3496	2.6
Mean duration of follow-up (years) = 30.2		
Mean age at start of follow-up (years) = 32.0		
Career cumulative radiation dose, personal dose equivalent		
< 5 mSv	21,048	15.6
5–	72,085	53.3
50–	13,786	10.2
75–	8293	6.1
100–	13,659	10.1
200–	4024	3.0
300 mSv or greater	2298	1.7
Mean career dose = 52.6 mSv		
Vital status as of 12/31/2011		
Alive/assumed alive	106,069	78.5
Dead	29,124[a]	21.5
Mean age at end of follow-up (years) = 62.2		

[a]29,076 deaths occurred in the US and were eligible for the SMR analyses. 13 deaths occurred outside the US, and 35 deaths occurred after age 94 y.

NRC: U.S. Nuclear Regulatory Commission; REIRS: Radiation Exposure Information and Reporting System; NPP: Nuclear Power Plant; SMR: Standardized Mortality Ratio.

Vital status and outcome determination

Vital status was determined through 2011. The Social Security Administration (SSA) Service for Epidemiological Researchers (https://www.ssa.gov/policy/about/epidemiology.html) was relied upon to determine alive status. This service

Table 2. Standardized mortality ratios (SMR) and 95% confidence intervals (CI) for 135,193 Nuclear Power Plant Workers, first monitored for radiation 1957–1984 with follow-up through 2011 in the United States.

	Males		Females		Total		
Persons-at-risk	130,773		4420		135,193		
Person-years-at-risk	3,947,966		131,654		4,079,620		
Cause of death (ICD9)[a]	Obs	SMR	Obs	SMR	Obs	SMR	95% CI
All causes of death (001–999)	28,646	0.88*	430	1.00	29,076	0.89*	0.88–0.90
All malignant neoplasms (140–208)	9157	1.03*	172	1.12	9329	1.03*	1.01–1.05
All solid cancers (140–199)	8287	1.04*	158	1.12	8445	1.04*	1.01–1.06
Buccal cavity & pharynx (140–149)	163	0.82*	3	2.11	166	0.83*	0.71–0.96
Esophagus (150)	351	1.07	4	3.13	355	1.07	0.96–1.19
Stomach (151)	216	1.01	0	0.00	216	1.00	0.87–1.14
Colon (153)	629	0.94	16	1.64	645	0.95	0.88–1.03
Rectum (154)	131	0.96	1	0.54	132	0.95	0.80–1.13
Biliary passages & liver (155,156)	253	0.81*	4	1.32	257	0.81*	0.72–0.92
Pancreas (157)	498	1.01	10	1.40	508	1.01	0.92–1.10
Pleura & peritoneum (158.8, 158.9, 163) & mesothelioma (ICD10 C45)[b]	251	5.69*	0	0.00	251	5.66*	4.98–6.40
Larynx (161)	97	0.96	0	0.00	97	0.96	0.78–1.17
Bronchus, trachea & lung (162)	3334	1.10*	48	1.27	3382	1.10*	1.07–1.14
Bone (170)	8	0.40*	0	0.00	8	0.39*	0.17–0.77
Connective & other soft tissue (171)	63	1.00	2	1.44	65	1.01	0.78–1.29
Female breast (174)	n/a	n/a	37	1.15	37	1.15	0.81–1.58
Male breast (175)	4	0.35*	n/a	n/a	4	0.35*	0.09–0.89
All uterine (females) (179–182)	n/a	n/a	3	0.37	3	0.37	0.07–1.08
Cervix uteri (180)	n/a	n/a	1	0.23	1	0.23	0.00–1.26
Ovary and other female genital organs (183–184)	n/a	n/a	7	0.67	7	0.67	0.27–1.38
Prostate (185)	527	0.99	n/a	n/a	527	0.99	0.91–1.08
Testes & other male genital organs (186, 187)	19	0.72	n/a	n/a	19	0.72	0.43–1.12
Kidney (189.0–189.2)	229	0.86*	3	1.21	232	0.87*	0.76–0.99
Bladder & other urinary (188, 189.3–189.9)	209	0.92	0	0.00	209	0.91	0.79–1.05
Melanoma of skin (172)	217	1.01	3	1.08	220	1.01	0.88–1.15
Other malignant neoplasm of skin (173)	41	0.73*	0	0.00	41	0.73*	0.52–0.99
Eye (190)	6	1.25	0	0.00	6	1.23	0.45–2.67
Brain & central nervous system (191–192)	267	0.90	7	1.41	274	0.90	0.80–1.02
Thyroid & other endocrine glands (193–194)	31	1.04	1	1.57	32	1.06	0.72–1.49
All lymphatic, hematopoietic tissue (200–208)	870	0.96	14	1.15	884	0.96	0.90–1.03
Non–Hodgkin lymphoma (200, 202)	316	0.86*	3	0.64	319	0.86*	0.77–0.96
Hodgkin lymphoma (201)	24	0.65*	0	0.00	24	0.63*	0.41–0.94
Multiple myeloma (203)	166	1.09	4	2.01	170	1.11	0.95–1.29
Leukemia (202.4, 204–208)	360	1.03	6	1.26	366	1.04	0.93–1.15
Acute lymphocytic leukemia (204.0)	21	0.99	0	0.00	21	0.97	0.60–1.49
Acute myeloid leukemia (205.0, 205.3, 206.0, 207.0, 207.2)	159	1.12	2	0.88	161	1.12	0.95–1.30
Chronic myeloid leukemia (205.1, 206.1)	37	1.08	0	0.00	37	1.06	0.75–1.47
Chronic lymphocytic leukemia (CLL) (202.4, 204.1, 204.9)	67	0.95	0	0.00	67	0.95	0.73–1.20
Leukemia other than CLL	290	1.05	6	1.41	296	1.06	0.94–1.19
Smoking-related cancers (140–150, 157, 161–162, 188–189)	4881	1.05*	68	1.31*	4949	1.05*	1.02–1.08
Nonsmoking-related cancers	4276	1.00	104	1.02	4380	1.00	0.97–1.03
Polycythemia vera (238.4)	1	0.27	0	0.00	1	0.27	0.00–1.49
Myelodysplastic syndrome (238.7)	48	1.09	0	0.00	48	1.08	0.80–1.43
Diabetes (250)	578	0.68*	13	1.00	591	0.68*	0.63–0.74
Mental and behavioral disorders (290–319)	419	0.77*	6	0.84	425	0.77*	0.70–0.85
Dementia, Alzheimer's, Parkinson's & motor neuron disease (290.0–290.4, 331.0, 332, 335.2)	651	0.93	6	0.55	657	0.93	0.86–1.00
Dementia and Alzheimer's (290.0–290.4, 331.0)	405	0.93	6	0.74	411	0.92	0.84–1.02
Parkinson's disease (332)	140	0.91	0	0.00	140	0.90	0.76–1.06
Diseases of the nervous system (320–389)	664	0.83*	9	0.63	673	0.82*	0.76–0.89
All heart disease (390–398, 404, 410–429)	7497	0.82*	64	0.81	7561	0.82*	0.80–0.84
Ischemic heart disease (410–414)	5372	0.80*	38	0.77	5410	0.80*	0.78–0.82
Cerebrovascular disease (430–438)	1056	0.88*	22	1.12	1,078	0.88*	0.83–0.94
Nonmalignant Respiratory Disease (460–519)	2155	0.89*	25	0.72	2,180	0.89*	0.85–0.92
Bronchitis, emphysema, asthma (490–493)	1080	0.97	15	0.80	1,095	0.96	0.91–1.02
Asbestosis (501)	87	9.15*	0	0.00	87	9.15*	7.33–11.3
Cirrhosis of liver (571)	714	0.81*	4	0.42	718	0.81*	0.75–0.87
AIDS (042–044, 795.8)	144	0.29*	1	0.44	145	0.29*	0.24–0.34
Nephritis & nephrosis (580–589)	281	0.78*	5	0.96	286	0.78*	0.69–0.88
All external causes of death (800–999)	3076	0.84*	53	1.25	3,129	0.85*	0.82–0.88
Accidents (850–949)	1960	0.91*	37	1.42	1,997	0.92*	0.88–0.96
Suicides (950–959)	817	0.79*	10	1.00	827	0.79*	0.74–0.85
Unknown causes of death	446	–	12	–	458	–	

[a]ICD = International classification of disease. Revision 9 codes are shown. n/a denotes not applicable.
[b]Mesothelioma did not have an explicit code in ICD9 but did in ICD10 as denoted.
*Indicates SMR is significantly different from 1.0.

accesses the Internal Revenue Service records of persons who recently filed a tax return, Medicare beneficiaries for those 65 y of age or older, and other sources of vital status. Death notifications relied upon the National Death Index (NDI) which began in 1979, the SSA Death Master File which began in 1960, and state mortality files available from 33 states (Mumma et al. 2018). A matching algorithm that uses a probabilistic scoring system for all matching variables, e.g. date of birth, was used to confirm the fact of death (Campbell et al. 2008). The NDI, state mortality data files, and death certificates obtained from state departments of health identified both the underlying and contributing causes of death. Information from LexisNexis (www.lexisnexis.com) and/or credit bureaus was employed to validate or correct key matching variables.

Overall, 106,069 workers (78.5%) were confirmed or assumed to be alive, and 29,124 workers (21.5%) were found to have died. Cause of death was obtained for all but 458 (1.6%) of those who died. Of the 106,069 workers confirmed or assumed alive at the end of follow-up (Table 1), 90.0% were confirmed alive by the SSA Service for Epidemiological Researchers. The remaining workers were presumed alive based on the absence of a match against the NDI, the SSA Death Master File, and 33 state mortality files. The over 11,000 workers known to be alive after 1978, based on dates recorded on dosimetry records, were submitted to the NDI for a full search of death records from 1979 through 2011. Further, a 1% sample of workers presumed to be alive was intensely searched through credit bureaus and LexisNexis and 94% were confirmed alive as of the end of follow-up and no deaths were found.

Of the 29,124 deaths overall, only 370 (1.3%) occurred before 1979 when the NDI began. Of these 370 deaths, a cause of death was obtained for 281 (76.0%) from state mortality files or from a death certificate. For 89 pre-NDI deaths (0.3% of all deaths), a death certificate or cause of death could not be determined.

Radiation dose estimation

Most radiation exposures received by nuclear power plant workers were from penetrating external gamma radiation with only a negligible contribution coming from neutrons or intakes of radioactive material (Bouville et al. 2015; Dauer et al. 2018; NCRP 2018a). Annual personal dose equivalents, *Hp(10)*, were available from the REIRS and Landauer files. Radiation doses from all places of employment were sought by linking the study roster to the Radiation Exposure Monitoring System (REMS) maintained by the U.S. Department of Energy (DOE) (DOE 2021), other DOE dosimetry databases, and U.S. military service dosimetry databases. All doses were combined to create annual dose estimates for each worker following methods previously described (Boice et al. 2006; Ellis, Boice et al. 2018). Overall, the mean cumulative *Hp(10)* was estimated as 19.5 mSv for all 425,713 workers eligible for the study, 52.6 mSv for the study cohort of 135,193 workers, and 61.3 mSv for the 115,288 workers with cumulative doses >10 mSv (maximum 1.32 Sv).

Practically all recorded doses were from external exposures to high-energy low-LET photons, predominantly from ^{58}Co, ^{60}Co and ^{137}Cs. As in previous MPS studies (Boice et al. 2006), a workshop was held with former nuclear power radiation workers, dosimetrists, and health physicists to learn firsthand about exposure circumstances, monitoring practices, and work conditions (Boice 2016). Most exposures were received during maintenance, modification, and repair work during outages where the external exposure photon fields were generally anterior to posterior (AP) and with degraded energy through piping, valves or tank steel. The methods employed to estimate organ doses for the NPP cohort are described in NCRP Report 178 (NCRP 2018a). Mean absorbed doses (mGy) to red bone marrow (RBM), lung, esophagus, colon, brain and heart were estimated by adjusting the recorded *Hp(10)* for each worker by scaling factors (conversion coefficients), accounting for exposure geometry and energy of the incident gamma radiation (ICRP 2010). The conversion coefficients were assumed to be stable and not variable over time or with exposure circumstances following the recommendation in NCRP Report 178 (NCRP 2018a) when only annual dosimetry results are available. The activity-weighted average photon energy was typically around 0.7 MeV, ranging from about 0.6 to 1.5 MeV (NCRP 2018a). The associated scaling factors were 0.72 for RBM, 0.81 for lung, 0.79 for esophagus, 0.83 for colon, 0.63 for brain, and 0.83 for heart. The mean cumulative absorbed dose to RBM in the study cohort was 37.9 mGy (maximum 1.0 Gy; percent >100 mGy was 9.2%); 43.2 mGy to lung (maximum 1.1 Gy; percent >100 mGy was 11.3%); 41.6 mGy to esophagus (maximum 1.05 Gy; percent > 100 mGy was 10.7%); 43.7 mGy to colon (maximum 1.1 Gy; percent > 100 mGy was 11.5%); 33.2 mGy to brain (maximum 0.83 Gy; percent >100 mGy was 7.4%); and 43.9 mGy to heart (maximum 1.1 Gy; percent >100 mGy was 11.6%).

Outcome classification for leukemias

The classifications for the leukemia subtypes used in the analyses are based on the International Classification of Diseases (ICD) codes for leukemia over three ICD Revisions: ICD-8, ICD-9 and ICD-10 (Supplement Table 1). The specific categories were selected to be consistent with the incident study of Japanese atomic bomb survivors (Hsu et al. 2013). The Japanese investigators reclassified early leukemia diagnoses using the French–American–British (FAB) classification system and subsequently coded leukemia diagnoses using the ICD for Oncology (ICD-O) codes that were current at the time of diagnosis. The specific analyses conducted are 'leukemia other than CLL', CLL, acute myelogenous leukemia (AML), acute lymphocytic leukemia (ALL), chronic myelogenous leukemia (CML) and myelodysplastic syndrome (MDS). While up to a third of the cases of MDS may progress to AML, it appears that MDS is biologically and clinically different from AML and should be considered

separately (Albitar et al 2002; Komrokji et al. 2019; Zeidan et al. 2019), noting also that its association with radiation exposure appears uncertain (UNSCEAR 2020).

Analytic methods

Standardized mortality ratio (SMR) analyses were employed to compare the observed number of deaths from specific causes with the number expected based on general population rates in the United States for persons of the same age and sex over the same calendar years. Rates for white males and females were used in the SMR analysis since the most common ethnicity among nuclear power plant workers over the years of study was white. Follow-up started on the date of first radiation monitoring at a nuclear power facility or 1 January 1969 (if the worker was identified in REIRS) or 1 January 1977 (if the worker was identified only from Landauer records), whichever was earlier. The end of the follow-up was the date of death, 95th birthday, or 31 December 2011, whichever came first. Of the 29,124 deaths overall, 29,076 occurred in the US and were eligible for the SMR analyses which are based on mortality rates for the US. Excluded from the SMR analyses were 13 deaths that occurred outside the US and 35 deaths that occurred after age 94 y.

Internal (within-cohort) analyses were conducted to account in part for the healthy worker effect that is often present in occupational studies when comparisons are made with the general population (Monson 1986; Howe et al. 1988; Checkoway et al. 1989; Buckley et al. 2015). Internal analyses were conducted using Cox proportional hazards models (Cox 1972) to compute the risks of leukemia, all solid cancers, lung cancer, esophageal cancer, non-Hodgkin lymphoma, multiple myeloma, MDS, Parkinson's disease, and IHD across categories of radiation dose. The Cox models included adjustment for sex, year of birth, and socioeconomic status (SES) (categorized as a low, medium, high based on census block group mean education levels) (Cohen et al. 2018). Age was used as the timescale for the hazard function. The primary analysis used categories of radiation exposure as the primary exposure. Dose-response functions for continuous measurement of radiation exposure were additionally modeled as linear functions. Cox analyses were conducted using SAS/STAT software (version 9.4 of the SAS System for Windows, SAS Institute Inc., Cary, NC).

Cox and Poisson excess relative risk (ERR) models were constructed using EPICURE software (Preston et al. 2015). The PEANUTS model for ERRs included the same covariates as the final Cox models (sex, year of birth, and SES). Akaike Information Criterion (AIC) values were used during some analyses to compare different regression models (Akaike 1974). Poisson regression models were also used. For each individual worker, the personal dose equivalents in mSv were all converted to organ-specific mGy doses. The dose-response models were all based on the estimated organ-specific absorbed doses in mGy. The dose-response graphics presented are based on a linear model with 95% confidence bands about the regression line representing the range of *true* regression lines at 95% confidence.

Adjustment for SES is frequently done in occupational studies to control for possible confounding factors that are not available on an individual basis, such as tobacco use and other lifestyle factors that may influence mortality and disease occurrence. Estimates of SES for each nuclear power plant worker were obtained by geocoding residential histories and acquiring area-wide estimates of education based on census-block group data (Cohen et al. 2018; Mumma et al. 2018). LexisNexis provided residential histories for the over 130,000 workers in our cohort. Then, based on the geocoded address, each worker was placed into a census-block group with an estimate of mean educational attainment characterized as low, medium or high.

To account for the possibility that workers who frequently worked at different utilities each year, i.e. so called transient workers, differed from workers who remained most of their career at a single facility, an adjustment for mobility was made. Worker mobility was classified into two categories: high mobility (workers who were monitored at 2 to >10 facilities) and low mobility (workers monitored at a single facility) (Table 1). The adjustment for mobility did not significantly change the estimates of risk so was not retained in the final models (Supplement Table 4). Analyses with and without an adjustment for the duration of radiation monitoring were performed. To adjust for the duration of radiation monitoring, workers were classified into one of six categories of years monitored (<1, 1–4, 5–10, 10–19, 20–29, >30). Because time must elapse between exposure and the appearance of a consequent health event, radiation doses were lagged in the analysis. For leukemia other than CLL and for MDS, the dose lagging was 2 years; for CLL all solid cancers, lung cancer, esophageal cancer, non-Hodgkin lymphoma, multiple myeloma, Parkinson's disease and IHD, doses were lagged 10 years. A 5-year lag was also evaluated for lung cancer.

For the leukemia internal analyses, the underlying cause of death and most contributing causes of death were included to increase statistical precision. Leukemia as a contributing cause of death, however, was not included if the underlying cause was cancer. This was done to reduce the likelihood that the leukemia was secondary to any treatment for the initial primary cancer. Including contributing causes of death in studies of occupational cohorts has been recognized as providing additional information on risk assessment (Steenland et al. 1992; Rushton 1994).

All exposure estimates were based on recorded personal dosimeter measurements. There was no imputation of missing dosimetric data which were judged to be minimal among employees at nuclear power facilities (Bouville et al. 2015; NCRP 2018a). The classical (Berkson) error structure of the individual worker data dose estimates indicates little sharing of errors, and, accordingly, accounting for this type of dosimetric uncertainty in the dose-response analyses does not have a meaningful effect (Stram et al. 2015). To address the influence of unshared dosimetric errors (NCRP 2008), the procedures outlined in NCRP Report 178 (NCRP 2018a)

Table 3. Observed and expected deaths due to leukemia other than chronic lymphocytic leukemia and risk estimates by radiation dose to red bone marrow (RBM) among 135,193 nuclear power plant workers, first monitored for radiation 1957–1984 and followed through 2011 in the United States.

	Radiation dose to RBM (mGy)							
	<5	5–	50–	75–	100–	200–	≥300	Total
No. of workers	22,968	81,739	11,710	6466	9519	2078	713	135,193
Mean dose (mGy)	0.88	21.0	61.1	86.6	136.7	238.5	377.8	37.6
Leukemia deaths[a]								
Observed	58	176	27	13	13	6	3	296
Expected	60.5	166.3	20.6	11.0	15.4	3.8	1.7	279.5
O/E (SMR)	0.96	1.06	1.31	1.18	0.84	1.58	1.73	1.06
Leukemia cases[b]	62	182	28	14	14	7	4	311
Hazards Ratio[c]	1.0 (R)	1.20	1.51	1.43	1.01	2.05	2.52	1.16[d]
90% Confidence intervals	–	0.93; 1.53	1.03; 2.21	0.87; 2.34	0.62; 1.66	1.06; 3.97	1.08; 5.91	0.99; 1.36

[a]Number of leukemia deaths other than chronic lymphocytic leukemia recorded as the underlying cause of death on the death certificate
[b]Number of leukemia deaths other than chronic lymphocytic leukemia recorded on the death certificate as either the underlying cause of death or the contributing cause of death, excluding contributing causes where the underlying cause was recorded as a cancer
[c]Doses lagged by 2 years. Cox proportional hazards models adjusted for sex, year of birth, and area-level education. Age used as underlying timescale. HR denotes hazards ratio.
[d]Model estimate of HR (90% CI) at 100 mGy = 1.16 (90% CI 0.999; 1.36), one-sided p for trend = 0.051 (+). The ERR per 100 m Gy = 0.15 (90% CI −0.001; 0.31).

Table 4. Observed and expected deaths due to chronic lymphocytic leukemia (CLL) and risk estimates by radiation dose to red bone marrow (RBM) among 135,193 nuclear power plant workers first monitored for radiation 1957–1984 and followed through 2011 in the United States.

	Radiation dose to RBM (mGy)				
	<5	5–	50–	≥100	Total
No. of workers	26,027	80,273	17,604	11,289	135,193
Mean dose (mGy)	0.83	20.9	70.2	165.9	35.6
CLL deaths					
Observed[a]	12	49	4	2	67
Expected	15.5	42.2	7.8	5.3	70.9
O/E (SMR)	0.84	1.12	0.39	0.38	0.92
CLL cases[b]	17	52	3	2	74
Hazards ratio[c]	1.0 (R)	1.68	0.53	0.54	0.46[d]
95% Confidence intervals	–	0.94; 3.00	0.15; 1.86	0.12; 2.36	0.21; 1.05

[a]Number of CLL deaths recorded as the underlying cause of death on the death certificate
[b]Number of CLL deaths recorded on the death certificate as either the underlying cause of death or the contributing cause of death, excluding contributing causes where the underlying cause was recorded as a cancer
[c]Doses lagged by 10 years. Cox proportional hazards models adjusted for year of birth and area-level education. Sex was not included as an adjustment factor due to the small numbers of female cases. Age used as underlying timescale. HR denotes hazards ratio.
[d]Model estimate of HR at 100 mGy = 0.46 (95% CI 0.21; 1.05), two-sided p for trend = 0.066 (–). ERR per 100 mGy = –0.77 (95% CI –1.59; 0.05).

are being followed as are additional analyses explicitly addressing issues of undetected dose-related in part to the minimum detectable response of the dosimeters in use during the study period. Compared with other occupational dose reconstruction circumstances (Gilbert 1998), the NPP industry is required to provide precise dosimetry data that are collected under strict criteria in compliance with legal regulations (USNRC 2021).

Results

Most of the 135,193 NPP workers were male (96.7%), born before 1950 (54.3%), and followed for more than 30 years (57.9%). The date of first radiation monitoring at an NPP was before 1975 for 14.5% of the workers, and 25.3% of workers were under the age of 25 years at first monitoring. The mean number of years monitored was 12.8 years. Because of the completeness of the personal identifiers used in the matching procedures, vital status was obtained essentially for all workers. Overall, 29,076 workers (21.5%) had died before 2012 (SMR 0.89; 95% CI 0.88; 0.90). The average follow-up was 30.2 years. The mean cumulative personal dose equivalent from external radiation was 52.6 mSv (maximum 1.32 Sv; percent workers >100 mSv, 14.8%). There were 27,518 workers (20.4%) who received occupational exposures at other facilities before ($n = 10,592$) or after leaving ($n = 16,926$) employment at a nuclear power facility. The mean personal dose equivalent received elsewhere was 20.4 mSv.

The observed and expected deaths for over 50 specific and grouped causes of death are shown in Table 2 by sex. For all causes of death, the SMR was 0.89 (95% CI 0.88; 0.90) and significantly low based on 29,076 deaths, related in part to the deficit observed for ischemic heart disease (SMR 0.80; 95% CI 0.78; 0.82; $n = 5,410$). In contrast, all cancer deaths were significantly increased (SMR 1.03; 95% CI 1.01; 1.05; $n = 9,329$), related in part to the excess observed for lung cancer (SMR 1.10; 95% CI 1.07; 1.14; $n = 3,382$). Cancers of the pleura, peritoneum and mesothelioma were significantly increased (SMR 5.66; 95% CI 4.98; 6.40; $n = 251$) as were deaths due to asbestosis (SMR 9.15; 95% CI 7.33; 11.3; $n = 87$). There were 296 deaths from leukemia other than CLL (SMR 1.06; 95% CI 0.94; 1.19), and 67 deaths from CLL (SMR 0.95; 95% CI 0.73;

1.20). Hodgkin lymphoma (SMR 0.63; 95% CI 0.41; 0.94; $n = 24$) and non-Hodgkin lymphoma (SMR 0.86; 95% CI 0.77; 0.96; $n = 319$) were significantly below expectation. Multiple myeloma (SMR 1.11; 95% CI 0.95; 1.29; $n = 170$) and MDS (SMR 1.08; 95% CI 0.80; 1.43; $n = 48$) were elevated but the increases were not statistically meaningful. The SMR for Parkinson's disease was 0.90 (95% CI 0.76; 1.09; $n = 140$), and the SMR for prostate cancer was 0.99 (95% CI 0.91; 1.08; $n = 527$).

For females, the only statistically significant SMR was for all smoking-related cancers SMR 1.31 (95% CI 1.02;1.66; $n = 68$). Cancers of the female breast (SMR 1.15; 95% CI 0.81; 1.59; $n = 37$) and lung (SMR 1.27; 95%CI 0.94; 1.68; $n = 48$), and leukemia other than CLL (SMR 1.41; 95%CI 0.51; 3.07; $n = 6$) were increased but not significantly. There were no deaths due to mesothelioma or asbestosis among female workers.

The 10,043 workers monitored for <30 d had 298,458 person-years of observation (29.7 y on average). For all causes of death, the SMR was 0.98 (95% CI 0.95; 1.02) based on 2820 deaths. The site-specific SMRs for most causes of death were compatible with workers who were monitored for longer times, including all cancers (SMR 1.05; 95% CI 0.98; 1.13; $n = 832$), lung cancer (SMR 1.14; 95% CI 1.02; 1.28; $n = 305$), smoking-related cancers (SMR 1.13; 95% CI 1.02; 1.123; $n = 455$), ischemic heart disease (SMR 0.85; 95% CI 0.78; 0.93; $n = 531$), and all external causes of death (SMR 1.15; 95% CI 1.02; 1.28; $n = 303$). There were 23 deaths from leukemia other than CLL (SMR 0.97; 95% CI 0.67; 1.45).

The internal analyses included an additional 15 cases of non-CLL and an additional 7 cases of CLL that were recorded on the death certificate as a contributing, but not underlying, cause of death. The internal analyses were thus based on a total of 311 cases of non-CLL (using a 2-year dose lag) and 74 cases of CLL (using a 10-year dose lag). For leukemia other than CLL (Table 3, Figure 2), the ERR at 100 mGy was 0.15 (90% CI −0.001; 0.31). Both linear and linear-quadratic ERR models fit the data equally well, i.e. the Akaike Information Criteria (AIC) values of 600.19 and 601.85, respectively, were very similar.

The SMR for CLL was not elevated and there was no evidence of a dose-response (Table 4). Based on a linear model, the ERR at 100 mGy was −0.77 (95% CI −1.59; 0.05).

The SMRs for subtypes of leukemia were: 0.97 (95% CI 0.60; 1.49) for ALL, 1.12 (95% CI 0.95; 1.30) for AML, and 1.06 (95% CI 0.75; 1.47) for CML (Table 2). The patterns of risk over categories of dose showed increasing trends for each subtype (Table 5). For ALL the estimate of HR at 100 mGy was 1.59 (90% CI 1.10; 2.30; p for trend <0.01); for AML it was 1.27 (90% CI 1.06; 2.53; p for trend 0.046); and for CML it was 1.21 (90% CI 0.79; 1.85; p for trend 0.45). Standard Cox proportional hazards models (HR-1) and Cox proportional hazards regression models to estimate ERRs (Preston et al. 2015) provided equivalent results (Table 5). There was no significant trend over categories of RBM dose for MDS alone (ERR per 100 mGy −0.34 (95% CI −1.11; 0.42) $n = 48$) or in combination with leukemia other than CLL (data not shown). For multiple myeloma and non-Hodgkin lymphoma the comparable ERRs (95% CI) at 100 mGy were 0.01 (−0.29; 0.31; $n = 170$) and −0.09 (−0.34; 0.16; $n = 319$), respectively.

The SMR for all solid cancers, excluding leukemias and lymphomas, was significantly increased [SMR 1.04 (95%CI 1.01; 1.06; $n = 8,445$)] and this increase was due almost entirely to increases in smoking-related cancers. Internal dose-response analyses for all solid cancers found no evidence for an increase in risk over categories of absorbed dose to the colon, taken as an estimate of whole-body dose [ERR (95% CI) at 100 mGy was 0.01 (–0.03; 0.05); $n = 8,445$].

The SMR for lung cancer was significantly increased [SMR 1.10 (95% CI 1.07; 1.14; $n = 3,382$)] as was the SMR for cancers of the pleura and mesothelioma [SMR 5.66 (95% CI 4.98; 6.40; $n = 251$)] (Table 2). The highest SMR for any cause of death was for asbestosis [SMR 9.15 (95% CI 7.33; 11.3; $n = 87$)]. Internal dose-response analyses for lung cancer found no evidence for an increase in risk over categories of absorbed dose to the lung: ERR (95% CI) at 100 mGy was −0.04 (–0.11; 0.02) (Table 6, Figure 3). The sex-specific ERRs (95% CI) at 100 mGy were −0.06 (–0.11; 0.01; $n = 3334$) among the 130,773 male workers and 0.63 (–0.91; 2.17; $n = 48$) among the 4420 female workers; a difference that was not statistically significance (p-value for heterogeneity = 0.37). The mean lung dose was 44.0 mGy (max 1.08 Gy) for males and 19.3 mGy (max 0.47 Gy) for females.

Cancer of the esophagus was elevated in comparison with the general population although the increase was not statistically significant (SMR 1.07, 95% CI 0.96; 1.19, $n = 355$).

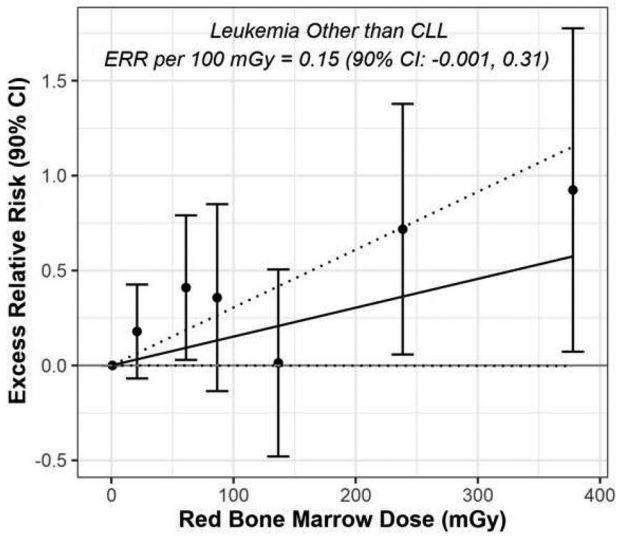

Figure 2. Excess Relative Risk (ERR) of leukemia other than chronic lymphocytic leukemia (CLL) by radiation dose to red bone marrow among 135,193 workers at U.S. nuclear power plants first monitored between 1957–1984 and followed through 2011. Linear model presented (solid line) based on a continuous measure of dose, and 95% confidence bands (dotted lines) presented about the regression line. Doses were lagged by 2 years and adjustments were made for sex, year of birth, and socioeconomic status. ERRs and 90% confidence limits are calculated for selected categories of dose to the red bone marrow and displayed at the mean dose in each category (categories <5 (referent), 5-, 50-, 75-, 100-, 200-, ≥300 with respective mean doses of 0.88, 21.0, 61.1, 86.6, 136.6, 238.5, and 377.8 mGy (see Table 3)).

Table 5. Excess relative risk (ERR) estimates at 100 mGy for leukemia subtypes by analytical method among 135,193 nuclear power plant workers, first monitored for radiation 1957–1984 and followed through 2011 in the United States.

		Standard cox model		EPICURE[d]	
Leukemia subtypes[a]	Number of cases	HR-1 at 100 mGy	90% CI	ERR per 100 mGy	90% CI
Acute lymphocytic leukemia (ALL)	25	0.59	0.10; 1.30	0.44	0.07; 0.81
Acute myeloid leukemia (AML)	165	0.27	0.06; 1.53	0.24	0.06; 0.42
Chronic myeloid leukemia (CML)	40	0.21	−0.21; 0.85	0.18	−0.25; 0.61
Chronic lymphocytic leukemia (CLL)	74	−0.54	−0.79; 0.05[b]	−0.77	−1.59; 0.05[b]
Leukemia other than CLL[c]	311	0.16	−0.001; 0.36	0.15	−0.001; 0.31

[a]ICD definitions and numbers found in Supplement Table 1. Counts include underlying and contributing causes of death. Doses are lagged two years in models for all subtypes except CLL. CLL model uses doses with 10-year lagging. All models adjusted for sex, year of birth, and area-level education except CLL which was not adjusted for sex due to small numbers of cases among female workers. Age used as underlying timescale in Cox models. HR denotes hazards ratio.
[b]95% Confidence intervals are provided for CLL because it is not seen to be consistently increased following radiation (UNSCEAR 2008).
[c]The counts for leukemia other than CLL include acute leukemias of unspecified cell type as listed in Supplement Table 1.
[d]Cox proportional hazards regression model results obtained using the PEANUTS program within EPICURE (Preston et al. 2015).

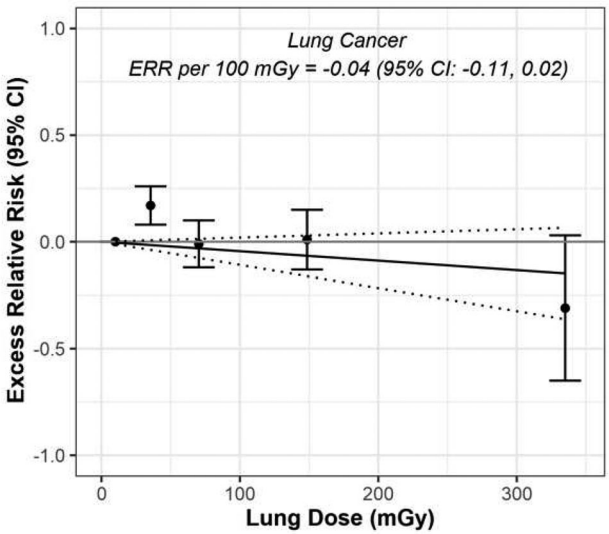

Figure 3. Excess Relative Risk (ERR) of lung cancer by radiation dose to lung among 135,193 workers at U.S. nuclear power plants first monitored between 1957–1984 and followed through 2011. Linear model presented (solid line) based on a continuous measure of dose, and 95% confidence bands (dotted lines) presented about the regression line. Doses were lagged by 10 years and adjustments were made for sex, year of birth, and socioeconomic status. ERRs and 95% confidence limits are calculated for selected categories of dose to the lung and displayed at the mean dose in each category (categories <25 (referent), 25-, 50-, 100-, and >250 with respective mean doses of 10.1, 35.5, 70.3, 148.5, and 335.0 mGy).

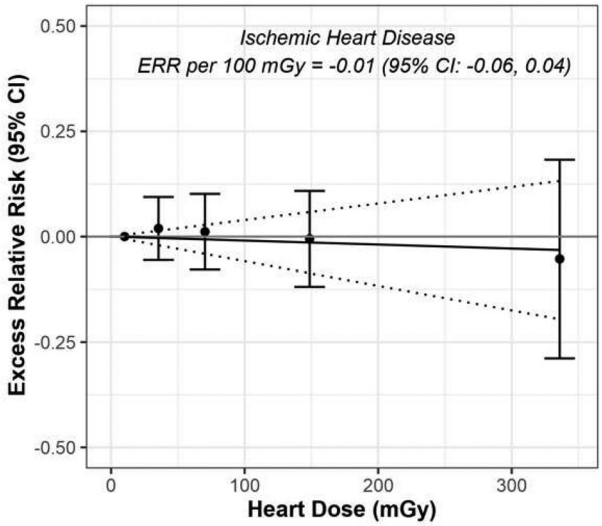

Figure 4. Excess Relative Risk (ERR) of ischemic heart disease by radiation dose to heart among 135,193 workers at U.S. nuclear power plants first monitored between 1957–1984 and followed through 2011. Linear model presented (solid line) based on a continuous measure of dose, and 95% confidence bands (dotted lines) presented about the regression line. Doses were lagged by 10 years and adjustments were made for sex, year of birth, and socioeconomic status. ERRs and 95% confidence limits are calculated for selected categories of dose to the heart and displayed at the mean dose in each category (categories <25 (referent), 25-, 50-, 100- and >250 with respective mean doses of 10.1, 35.5, 70.3, 148.7, and 335.9 mGy).

Internal dose-response analyses for esophageal cancer showed the ERR (95% CI) at 100 mGy to be 0.11 (−0.05; 0.28) (Table 6). The SMR for all heart disease was significantly low at 0.82 (95% CI 0.80; 0.84, $n = 7{,}561$). Similarly, death from IHD occurred significantly below expectation [SMR 0.80 (95% CI 0.78; 0.82, $n = 5{,}410$)]. Internal dose-response analyses found no evidence for an increase in IHD over categories of absorbed dose to the heart. Over 14,000 workers had heart doses in excess of 100 mGy and nearly 2000 had doses in excess of 250 mGy. The ERR (95% CI) at 100 mGy was −0.01 (−0.06; 0.04) (Table 6, Figure 4).

The SMRs for non-Hodgkin lymphoma (NHL), multiple myeloma, and myelodysplastic syndrome (MDS) were 0.86 (95% CI 0.77, 0.96; n = 319), 1.11 (95% CI 0.95; 1.29; n = 170), and 1.08 (95% CI 0.80, 1.43; n = 48), respectively (Table 2). The ERRs (95% CI at 100 mGy) for NHL, multiple myeloma, and MDS were −0.09 (−0.34; 0.16), 0.01 (−0.29; 0.31), and −0.34 (−1.11; 0.42), respectively (analyses not presented).

The adjustment for duration of monitoring in our study of NPP workers was found to increase both the estimate of risk and the significance of the dose-response for leukemia other than CLL (Supplement Tables 3 and 4). Without an adjustment for the duration of monitoring, the ERR at 100 mGy was 0.15 (90% CI −0.001, 0.31), whereas with an adjustment it was increased to 0.32 (90% CI 0.17, 0.46). Although the risk estimates are statistically indistinguishable, the risk estimate with adjustment for the duration of monitoring was double the estimate without such an adjustment. The choice of the number of duration categories used for adjustment did not make a difference. If two categories were used, less than or more than 10 y duration, the estimate of

Table 6. Internal cohort dose-response analyses for all solid cancers, cancers of the lung and esophagus, Parkinson's disease, and ischemic heart disease by organ-specific dose among 135,193 nuclear power plant workers first monitored for radiation 1957–1984 and followed through 2011 in the United States[a].

Dose (mGy)	Workers	Cases	HR	95% CI
All solid cancers excluding leukemias and lymphomas (ICD-9 140–199)				
<25[b]	74,707	5275	1.0	REF
25–<50	27,084	1,591	1.16	1.09; 1.23
50–<100	19,145	904	1.00	0.93; 1.08
100–<250	12,335	569	1.06	0.97; 1.15
≥250	1,922	106	0.90	0.74; 1.09
Totals and *p* for trend	135,193	8445		*0.60 (+)*
HR (95% CI) at 100 mGy			1.01	0.97; 1.05
ERR (95% CI) at 100 mGy			0.01	−0.03; 0.05
Lung cancer (total)				
<25[c]	75,217	2131	1.0	REF
25–<50	26,985	648	1.18	1.08; 1.29
50–<100	18,990	353	0.99	0.88; 1.11
100–<250	12,161	216	1.01	0.88; 1.17
≥250	1840	34	0.73	0.52; 1.03
Totals and *p* for trend	135,193	3382		0.17 (–)
HR (95% CI) at 100 mGy			0.96	0.90; 1.02
ERR (95% CI) at 100 mGy			−0.04	−0.11; 0.02
Lung cancer (males)				
<25[c]	71,784	2091	1.0	REF
25–<50	26,442	645	1.19	1.09; 1.30
50–<100	18,675	351	0.99	0.88; 1.11
100–<250	12,036	213	1.00	0.87; 1.16
≥250	1836	34	0.73	0.52; 1.03
Totals and *p* for trend	130,773	3334		0.15 (–)
HR (95% CI) at 100 mGy			0.96	0.90; 1.02
ERR (95% CI) at 100 mGy			−0.06	−0.11; 0.01
Lung cancer (females)				
<25[c]	3433	40	1.0	REF
25–<50	543	3	0.64	0.19; 2.08
50–<100	315	2	1.11	0.26; 4.66
≥100	129	3	3.59	1.09; 11.8
Totals and *p* for trend	4420	48		0.12 (+)
HR (95% CI) at 100 mGy			1.80	0.86; 3.78
ERR (95% CI) at 100 mGy			0.59	−0.16; 1.33
Esophageal cancer				
<25[d]	76,799	205	1.0	REF
25–<50	26,681	71	1.31	0.99; 1.72
50–<100	18,491	46	1.30	0.94; 1.80
100–<250	11,564	29	1.39	0.94; 2.06
≥250	1658	4	0.97	0.36; 2.61
Totals and *p* for trend	135,193	355		0.17 (+)
HR (95% CI) at 100 mGy			1.12	0.95; 1.32
ERR (95% CI) at 100 mGy			0.11	−0.05; 0.28
Parkinson's disease				
<25[e]	86,335	97	1.0	REF
25–<50	24,048	21	1.03	0.64; 1.65
50–<100	15,909	8	0.71	0.34; 1.46
100–<250	8175	11	1.74	0.93; 3.25
≥250	726	3	2.35	0.75; 7.44
Totals and *p* for trend	135,193	140		0.07 (+)
HR (95% CI) at 100 mGy			1.27	0.98; 1.65
ERR (95% CI) at 100 mGy			0.24	−0.02; 0.50
Ischemic heart disease				
<25[f]	74,427	3535	1.0	REF
25–<50	27,149	896	1.02	0.95; 1.10
50–<100	19,215	574	1.01	0.93; 1.11
100–<250	12,448	334	1.00	0.89; 1.12
≥250	1954	71	0.95	0.75; 1.20
Totals and *p* for trend	135,193	5410		0.70 (–)
HR (95% CI) at 100 mGy			0.99	0.94; 1.04
ERR (95% CI) at 100 mGy			−0.01	−0.06; 0.04

[a]Models utilize radiation doses lagged by 10 years. Outcomes include deaths from underlying causes of death only. Cox proportional hazards models adjusted for sex, year of birth, and area-level education. Age used as underlying timescale. HR denotes hazards ratio. CI denotes confidence interval. ERR denotes excess relative risk.

[b]Model utilizes dose to the colon.

[c]Model utilizes dose to the lungs. The p-value for heterogeneity was 0.37 for the difference in lung cancer sex-specific risk estimates.

[d]Model utilizes dose to the esophagus.

[e]Model utilizes dose to the brain.

[f]Model utilizes dose to the heart.

Table 7. Excess relative risk (ERR) estimates per 100 mGy for leukemia other than chronic lymphocytic leukemia for selected studies of radiation-exposed populations.

Study[a]	Persons	Cases	ERR per 100 mGy	Confidence intervals	Reference
U.S. nuclear power plant workers	135,193	311	0.15	0.00; 0.31[b]	Current study
U.S. industrial radiographers	123,556	173	0.17	−0.02; 0.35[b]	NCRP (2018b)
U.S. medical radiation workers	109,019	126	0.10	−0.34; 0.54[c]	Boice, Cohen, Mumma, Howard et al. (2021)
Mallinckrodt uranium processing	2514	18	0.14	−0.60; 0.33[c]	Golden, Ellis, et al. (2019)
Mound	4954	21	0.04	−0.37; 0.71[b]	Boice et al. (2014)
Atomic veterans	113,807	710	−0.37	−1.08; 0.33[b]	Boice et al. (2020)
Atomic bomb survivors (adult males)[d]	24,845	98	0.09	−0.16; 0.37[b]	Preston[d]
INWORKS	308,297	531	0.30	0.12; 0.52[b]	Leuraud (2015), Hamra et al. (2016)
IARC 15-country	407,391	198	0.19	<0; 0.85[c]	Cardis et al. (2005, 2007)
IARC 3-country	95,673	119	0.22	0.01; 0.57[b]	Cardis et al. (1995)
UK National Registry of Radiation Workers	174,541	198	0.17	0.01; 0.43[c]	Muirhead et al. (2009)[e]
NIOSH U.S. case-control	NR	369	0.09	−0.17; 0.65[c]	Daniels et al. (2013)
French nuclear workers	59,021	60	0.40	<0; 1.68[b]	Metz-Flamant et al. (2013)
U.S. 15-utilities	53,698	26	0.57	−0.26; 3.04[c]	Howe (2004)
U.S. radiologic technologists	110,297	155	0.05	< −0.09; 0.24[c]	Linet et al. (2020)
Mayak Production Association	22,373	56	0.36	0.16; 0.82[c]	Kuznetsova et al. (2016)

[a]Studies are not all independent. The INWORKS study, for example, contains workers in the IARC 3-country, IARC 15-country, UK NRRW and NIOSH U.S. case-control studies.
[b]90% CI; also cases include underlying and contributing causes.
[c]95% CI.
[d]Dale Preston (Personal Communication, 31 May 2016).
[e]A recent update with 269 deaths from leukemia other than CLL is generally consistent with the earlier reports [ERR per 100 mGy 0.10 (90%CI −0.23 to 2.90)] (Gillies et al. 2019).
NR denotes not reported.

Table 8. Excess relative risk (ERR) estimates per 100 mGy for subtypes of leukemia for selected studies of radiation-exposed populations.

Study[a,b] (reference)	ALL (*n*) (90% CI)	AML (*n*) (90% CI)	CML (*n*) (90% CI)	CLL (*n*) (90% CI)
Current study – U.S. nuclear power plant workers	0.44 (25) (0.07; 0.81)	0.24 (165) (0.06; 0.42)	0.18 (40) (−0.25; 0.61)	−0.77 (74) (−1.59; 0.05)
INWORKS (Leuraud et al. 2015; Hamra et al. 2016)	0.58 (30) (<0; 3.16)	0.13 (254) (−0.08; 0.43)	1.05 (100) (0.45; 2.00)	−0.11 (138) (<0; 0.18)
IARC 15-country (Cardis et al. 2007)	<0.0 (19) NR	−0.41 (81) (−0.76; 0.17)	1.0 (45) (−0.09; 4.02)	−0.17 (47) (−0.89; 0.40)
IARC 3-country (Cardis et al. 1995)	−0.89 (11) (<0; 7.3)	0.34 (32) (<0; 1.49)	1.1 (28) (0.29; 3.09)	−0.09 (27) (<0; 0.73)
UK NRRW (Muirhead et al. 2009)	0.78 (15) (<0.19; 8.95)	0.12 (102) −0.12; 0.57	0.33 (44) (0.04; 0.93)	<−0.19 (69)[d] (<−0.l9; 0.12)
NIOSH U.S. case-control (Daniels et al. 2013)	NR	0.22 (150) (−0.l9; 1.2)	0.29 (52) (<0; 2.6)	−0.032 (74) −0.16; 0.74)
French nuclear workers (Metz-Flamant et al. 2013)	NR	1.58 (35) (0.15; 4.61)	NR[c]	−0.14 (NR) (<0; 1.49)
U.S. radiologic technologists (Linet et al. 2020)	0.058 (15) (<−0.02; 1.03)	0.00 (85) (<−0.02; 0.24)	−0.02 (9) (<−0.02; >10)	<−0.02 (23) (<−0.03; 0.18)
Mayak Production Association (Kuznetsova et al. 2016)	NR	1.32 (24) (0.43; 4.9)	0.14 (13) (−0.02; 0.73)	−0.02 (21) NR

[a]Acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic myeloid leukemia (CML), chronic lymphocytic leukemia (CLL), not reported (NR). Current study includes underlying and contributing causes of death. Note that Linet and colleagues (Linet et al. 2020, Table 4) prepared an informative and detailed comprehensive summary of leukemia subtype ERRs for radiation-exposed populations.
[b]Studies are not independent. The INWORKS study, for example, contains workers in the IARC 3-country, IARC 15-country, UK NRRW and the NIOSH case-control studies.
[c]Estimates are presented only for myeloid leukemia and not separately for AML or CML. ALL not presented ($n \leq 7$).
[d]Using a 10-year lag, the ERR per 100 mSv was −0.03 (90% CI −0.17; 0.31).

risk was similar to the estimate using six categories: the HR at 100 mGy was 1.28 (95% 1.10; 1.48) based on 2 category adjustment whereas it was 1.37 (90% CI 1.19;1.59) based on a finer 6 category adjustment.

Sensitivity analyses were conducted to evaluate the choice of referent group, adjustment factors, and the effect of including contributing causes of death. Excluding all workers with zero recorded dose and using the <10 mGy category as referent had little effect on the dose-response analysis for leukemia other than CLL with the HR at 100 mGy estimated to be 1.17 (95% CI 1.02; 1.34; trend $p = 0.03$). Adjusting for mobility and year of hire increased the estimates of risk slightly but the increase was not statistically significant (Supplement Table 4). Removing adjustments for sex and SES also had minimal effect on the estimates of radiation risk. Using a 2-year lag for CLL rather than a 10-year lag, did not affect the dose-response which remained significantly negative. Using a 5-year lag for lung

cancer rather than a 10-year lag, also did not affect the dose response.

Discussion

Previous studies of nuclear power plant workers in the US were limited by low statistical power. An early study of nearly 9000 workers at a single nuclear power facility demonstrated the feasibility of linking together company dosimetry records with NRC REIRS and Landauer data to obtain complete dosimetry information on workers (Goldsmith et al. 1989; Jablon and Boice 1993; Muirhead et al. 1996). A larger study of 53,698 workers was carefully conducted but limited in design (Howe et al. 2004). Workers had to be alive in 1979 and employed at a nuclear power plant operated by one of 15 utilities in the United States. A radiation association for leukemia was not found but statistical power was limited due to small numbers. The 1979 restrictions were for ease of tracing since 1979 is the year when the NDI began, but this restriction resulted in few leukemia deaths, only 26, low cumulative doses (mean 25.7 mSv), and few career doses >100 mSv (about 5%). The current study of 135,193 early NPP workers monitored as early as 1957 is larger, with longer follow-up and a broader range of radiation doses than previous investigations. Consistent with current understanding (Daniels and Schubauer-Berigan 2011; McLean et al. 2017; Gilbert et al. 2020; Hauptmann et al. 2020) (Table 7), prolonged exposure to occupational radiation was seen to increase the mortality risk of leukemia other than CLL among NPP workers.

International occupational studies

Large international occupational studies have been coordinated by the International Agency for Research on Cancer (IARC) (Cardis et al. 1995, 2005, 2007). Results compared with other studies are not independent because of overlapping facilities included in each analysis, e.g. the British Nuclear Fuels plc (BNFL) facility at Sellafield contributed many workers and leukemia cases among those who received doses >200 mSv. A significant risk of leukemia other than CLL was reported in the IARC 3-country study (Cardis et al. 1995), primarily due to relatively high occupational doses (>200 mSv) seen at the Sellafield plant (Douglas et al. 1994). A significant leukemia risk was not observed in the subsequent IARC 15-country study which excluded workers who were monitored for internal intakes of radioactive material and other factors (Cardis et al. 2007). Among the over 49,346 U.S. nuclear power plant (NPP) workers in the 15-country study, leukemia excluding CLL also was not significantly increased (ERR per 100 mSv 0.13; 90% CI <0.00, 0.18; n = 65). It is not entirely clear, but this U.S. NPP cohort of 15 facilities (Vrijheid et al. 2008) apparently derived from the larger study conducted by Howe et al. (2004).

The latest and largest international investigation is the International Nuclear Workers Study (INWORKS), which includes 308,297 radiation workers from France, the United Kingdom, and the United States (Leuraud et al. 2015; Richardson et al. 2015, 2018; Thierry-Chef et al. 2015; Hamra et al. 2016; Daniels et al. 2017; Laurier et al. 2017; Haylock et al. 2018). In contrast to the 15-country study, U.S. NPPs were not included. INWORKS reported an association between the cumulative external photon dose to the RBM and mortality from leukemia other than CLL: ERR per 100 mGy = 0.30 (90% CI: 0.17; 0.52). These data are not independent of other studies and include radiation workers from the UK National Registry for Radiation Workers (NRRW) (Muirhead et al. 2009), nuclear industry workers in France (Metz-Flamant et al. 2013), and five nuclear facilities in the United States (Schubauer-Berigan et al. 2015). Despite the many strengths of the INWORKS investigation, possible confounding tempers interpretations (NCRP 2018b). Statistically significant risks were reported for cancers of the testis, rectum and peritoneum, sites not convincingly linked to ionizing radiation (UNSCEAR 2008), and positive dose responses were reported for cancers of the pleura and mesothelioma which are caused by asbestos and not radiation (Mumma et al. 2019). Removing France in a sensitivity analysis resulted in statistical non-significance, even though the French data were the smallest component of INWORKS, and there were rather puzzling results regarding neutron exposures (NCRP 2018b). That is, neutron doses were not computed but adjustment based upon a neutron monitoring flag was made. If no adjustment for neutron monitoring is made the ERR per Gy estimate for solid cancers was reduced from 0.48 (95% CI 0.20; 0.79) to 0.20 (90% CI −0.03; 0.46) (Richardson et al. 2015). The reasons behind this large drop in the ERR estimate, and from statistical significance to nonsignificance, are unclear, 'but may relate to some confounding, especially since one might expect missing neutron doses in the risk modeling to cause overestimation, rather than underestimation' (NCRP 2018b).

The UK National Registry for Radiation Workers (NRRW) study of 174,541 workers found a significant risk of leukemia other than CLL, based on 198 deaths, mean dose 25.5 mSv and with 6.2% of workers with occupational doses >100 mSv (excess relative risk (ERR) per Sv = 1.38; 90% CI 0.08; 3.24) (Muirhead et al. 2009; Gillies and Haylock 2014; Gillies et al. 2019). More than half of the workers with high cumulative doses came from the Sellafield facility. A study of 64,956 workers at four BNFL facilities, again with nearly 50% of workers coming from Sellafield, reported a significant risk of leukemia other than CLL (ERR per Sv = 2.60; 90% CI 0.28; 7.01) based on 85 deaths and mean dose of 53.0 mSv among the 42,431 radiation workers (Gillies and Haylock 2014). The mortality analysis based on 269 deaths from leukemia other than CLL is consistent with earlier reports [ERR per 100 mGy 0.10 (90%CI −0.23; 2.90)] (Gillies et al. 2019).

A study of 45,468 Canadian nuclear power industry workers and workers at Atomic Energy of Canada Limited (a research facility) failed to observe a significant association between occupational dose and leukemia but analyses were based on only 17 leukemia deaths (Zablotska et al. 2014). A study of 59,021 French nuclear workers reported a

nonsignificant association between occupational exposure and leukemia other than CLL based on 60 deaths and a mean dose of 22.5 mSv (Metz-Flamant et al. 2013). A study of 200,583 Japanese nuclear workers reported a nonsignificant negative association with cumulative dose and leukemia based on 80 deaths and mean dose of 12.2 mSv (with 2.6% of the workers > 100 mSv) (Akiba and Mizuno 2012; Akiba 2018).

Combined U.S. occupational studies

One of the first combined mortality analyses of U.S. worker studies was conducted by Gilbert and colleagues in 1993 of 44,943 workers at three weapons facilities (Gilbert et al. 1993). There were 67 deaths due to leukemia other than CLL, the mean dose was <50 mSv and the correlation between radiation was negative (ERR per Sv = −1.0; 90% CI <0.0; 2.2). A later combined case-control study of leukemia among workers in the United States involved six facilities (including the Portsmouth Naval Shipyard) and 105,245 workers (Daniels et al. 2013). There were 264 deaths due to leukemia other than CLL, the mean dose was 26.5 mSv, and the association between radiation was positive but not statistically significant (ERR per 100 mSv = 0.09 (95% CI −0.17; 0.65). There were 74 deaths due to CLL and similar to the current study, there was a negative association with radiation (ERR per 100 mSv = −0.032 (95% CI −0.16; 0.74)). A recent cohort evaluation of workers at five U.S. facilities ($n = 119{,}195$), excluded the Los Alamos National Laboratory, changed the eligibility criteria for inclusion, included contributing causes of CLL (total cases 128) and confirmed the previous findings based on 369 deaths from leukemia other than CLL and a mean external dose of 20.2 mS (Schubauer-Berigan et al. 2015).

A feasibility study at the Calvert Cliffs Nuclear Power Plant published in 1993 envisioned the creation of a radiation registry of workers which might form the basis of a comprehensive study of over 100,000 NPP workers in the United States (Jablon and Boice 1993). This vision became a reality (Hagemeyer et al. 2018) as demonstrated by the current study. The pilot study at the Calvert Cliffs facility included 9132 workers, of whom 5093 were plant employees and 4093 were contract workers. The contract workers experienced the higher cumulative doses (Goldsmith et al. 1989). No significant findings were reported. However, in the current follow-up of 6264 plant employees at Calvert Cliffs (Supplement Table 2), a significant SMR of mesothelioma was observed based on 5 deaths (SMR 3.19; 95% CI 1.03; 7.44), and similar to the asbestos-related risk reported for all workers in the current study.

Leukemia other than CLL

Most occupational studies of combined facilities discussed above are characterized as having well-defined populations, good occupational records, comprehensive follow-up procedures, nearly complete ascertainment of deaths and causes of death, individual personal dosimetry measurements to estimate cumulative occupational dose, and careful and complete statistical analyses (NCRP 2018b; UNSCEAR 2018). There is a consistency in the presence of a positive correlation between radiation and death due to leukemia other than CLL (Table 7), and the absence of a correlation between radiation and death due to CLL (Table 8).

Leukemia other than CLL is found to be increased in studies of Japanese atomic bomb survivors (Hsu et al. 2013), patients receiving high-dose radiation procedures (Boice et al. 1987; Curtis et al. 1994; Little et al. 1999), pioneering radiologists (Matanoski et al 1975; NA/NRC 2006; UNSCEAR 2008), populations exposed to environmental contamination (Krestinina et al. 2010; Preston et al. 2017; NCRP 2018b) and more recently in large occupational studies (NCRP 2018b; Linet et al. 2020) (Table 7). The current study of nuclear power plant workers in the United States adds to this evidence. The numbers of cases of leukemia subtypes, ALL, AML and CML, also were sufficient to compute estimates of mortality risk that were generally consistent with those reported in other studies although the confidence intervals about the risk estimates were broad (Table 8).

Among Japanese atomic bomb survivors, linear-quadratic and purely quadratic dose-response models provided better fits to the non-CLL data than a linear model (UNSCEAR 2008; Hsu et al. 2013). Among bomb survivors over the age 20 years when exposed in 1945, there were 121 deaths due to leukemia other than CLL; the ERR per Sv was approximately 3.1 (95% CI 1.7; 5.0) (UNSCEAR 2008) or about twice the estimate of the current study. In the most recent incidence study of atomic bomb survivors (Hsu et al. 2013), there were 98 incident leukemia cases other than CLL or adult T-cell leukemia (ATL) among 24,845 adult males, the mean dose was about 10 mGy, and the estimate of ERR per 100 mGy was 0.09 (95% CI −0.16; 0.37) (Table 7). Although the confidence intervals overlap for the risk estimates in the current study, the acute exposure of atomic bomb survivors may carry a somewhat higher risk of radiation-induced leukemia than the study of NPP workers who received prolonged exposures over many years. This lower risk following protracted exposures is consistent with chromosome aberration data comparing atomic bomb survivors with Sellafield workers (Tucker et al. 1997). A more statistically powerful evaluation of the risk of leukemia following prolonged radiation exposure will come within the MPS when large cohorts are combined, including industrial radiographers (NCRP 2018b), medical radiation workers (Boice, Cohen, Mumma, Howard et al. 2021), above-ground nuclear weapons test participants (Boice et al. 2020) and DOE radiation workers (Boice, Cohen et al. 2019; Boice, Cohen, Mumma, Golden 2021). A study of 112,726 nuclear submariners, including the 1954 Nautilus crew, has begun that increases the study size of previous investigations by including officers and by extending the years of follow-up by 18 years, from 1982 to 2020 (Charpentier et al. 1993; Mueller et al. 2020; NDC 2021; Friedman-Jimenez et al. 2021). The study of nuclear submariners will provide additional statistical power

for future pooled analyses of comparable populations within the MPS.

CLL

For NPP workers in the U.S., the dose-response for CLL was negative based on either a 10-year dose lag or a 2-year dose lag. CLL is not generally considered to be caused by ionizing radiation (UNSCEAR 2008). Practically all studies fail to find positive correlations, including patients treated with radiation (Boice et al. 1987; Curtis et al. 1994) and occupationally exposed workers (Cardis et al. 2007; Schubauer-Berigan et al. 2007, 2015; Vrijheid et al. 2008; Muirhead et al. 2009; Daniels et al. 2013; Leuraud et al. 2015; Kuznetsova et al. 2016; Linet et al. 2020). Negative dose-response relationships for CLL are seen for most occupational studies (Table 8).

A significant correlation between radiation and CLL was reported in the study of Japanese atomic bomb survivors (Hsu et al. 2013) based on only 12 cases. Results are uncertain because 2 of the 12 cases (16.7%) were hairy cell leukemias, which should be classified as non-Hodgkin lymphoma (NHL) and not CLL (Linet et al. 2020). In comparison with the current study, 2 of the 74 cases (2.7%) of CLL among NPP workers were hairy cell leukemias; the population expected value was 2.7 and excluding the 2 cases did not affect the negative dose-response. Further, NHL is not seen to be a consistent consequence following radiation exposure (UNSCEAR 2008), and we found no evidence for a dose response (ERR per 100 mGy −0.09; 95% CI −0.34; 0.16; n = 319). Some reports of increases in CLL (Zablotska et al. 2013) are not consistent with previous studies and may reflect peculiarities in the dose reconstruction (based on worker interviews), case ascertainment and diagnostic criteria.

MDS

Radiation has been associated with MDS among long-term atomic bomb survivors at Nagasaki (Iwanaga et al. 2011). Neither MDS nor MDS in combination with AML were found to be correlated with radiation dose in the current study, similar to three other MPS studies, i.e. for medical radiation workers, workers at the Los Alamos National Laboratory, and military participants at above-ground nuclear weapons tests (Boice et al. 2020; Boice, Cohen, Mumma, Golden 2021; Boice, Cohen, Mumma, Howard 2021). Studies of U.S. radiologic technologists (Linet et al. 2020) also report no association between MDS and radiation exposures. High dose radiotherapy, as well as chemotherapy, are major risk factors for MDS (Komrokji et al. 2019). MDS appears to be distinct from AML (Albitar et al. 2002; Zeidan et al. 2019), and it has been questioned recently whether MDS should be included in the assessment of leukemia risk following radiation (UNSCEAR 2020). MDS is a grouping of heterogeneous diseases, and its classification has evolved over the years (Komrokji et al. 2019). It was not uncommon for MDS cases to be misclassified as AML which might affect mortality evaluations. Whether low doses of radiation can cause MDS is an area of scientific interest, and will be addressed further in combined studies within the MPS.

Lung cancer

The SMR for lung cancer was significantly elevated in comparison with the general population, reflecting perhaps residual confounding due to cigarette smoking or to intakes of asbestos from thermal insulation received by many of the workers. The NPP workers had previously been found to be at high risk of asbestos-related diseases including mesothelioma and asbestosis (Mumma et al. 2019). Further, it has been estimated that up to 12% of lung cancers might be related to occupational levels of exposure to asbestos and that up to 20–25% of workers with heavy exposure to asbestos might develop lung cancer (Agency for Toxic Substances and Disease Registry (ATSDR) 2013). Given the substantial excesses of deaths from mesothelioma and asbestosis among these NPP workers, it is possible that some lung cancer deaths were similarly related to asbestos exposure. Unfortunately, job classification was not available to separate NPP workers with likely exposure to asbestos as was possible in several other MPS investigations, i.e. industrial radiographers, shipyard workers and atomic veterans (Till et al. 2018; Mumma et al. 2019).

There was little evidence for a radiation dose response for lung cancer nor was there any discernible difference between men and women and radiation risk, (p for heterogeneity 0.37), consistent with eight other MPS cohorts (Boice 2019; Boice, Ellis et al. 2019; Boice et al. 2020; Boice, Cohen, Mumma, Golden et al. 2021; Boice, Cohen, Mumma, Howard et al. 2021; Boice, Quinn et al. 2021; NASEM 2021a). These findings of healthy populations who experienced chronic exposures during employment are relevant to understanding and assessing the radiation risks faced by astronauts on long-term missions beyond Earth orbit. The lung cancer risk estimates and standards currently used by NASA to protect flight crew are based on the Japanese atomic bomb survivor study that indicates that women are at 2-3 times higher lifetime risk of lung cancer than are men on a relative scale (NCRP 2014; Boice 2019). The current radiation standard for astronauts limits the time women are allowed in space compared with men, although these standards are being reviewed (NASEM 2021a).

Other studies of occupationally exposed workers that failed to find a significant radiation association for lung cancer include the Hanford workers (Petersen et al. 1990), medical radiologic technicians (Velazquez-Kronen et al. 2020), and the UK National Registry of Radiation Workers (Muirhead et al. 2009; Haylock et al. 2018). Increases in lung cancer have been reported among atomic bomb survivors acutely exposed to radiation in 1945 (Ozasa et al. 2012); workers in the 15-country study, although a negative dose response was seen for the subcohort of NPP workers (ERR per 100 mSv −0.12; 90% CI <0.00, 0.05; n = 316) (Cardis et al. 2007); Mayak workers in Russia (Gillies et al. 2017), and the INWORKS occupationally-exposed workers (Richardson et al. 2018). Differences in results might be

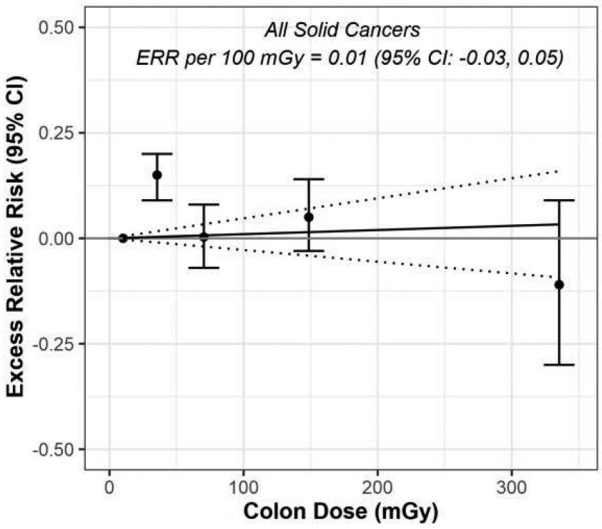

Figure 5. Excess Relative Risk (ERR) of all solid cancers by radiation dose to colon among 135,193 workers at U.S. nuclear power plants first monitored between 1957–1984 and followed through 2011. Linear model presented (solid line) based on a continuous measure of dose, and 95% confidence bands (dotted lines) presented about the regression line. Doses were lagged by 10 years and adjustments were made for sex, year of birth, and socioeconomic status. ERRs and 95% confidence limits are calculated for selected categories of dose to the colon and displayed at the mean dose in each category (categories <25 (referent), 25-, 50-, 100-, and >250 with respective mean doses to the colon of 10.1, 35.5, 70.3, 148.6, and 335.3 mGy).

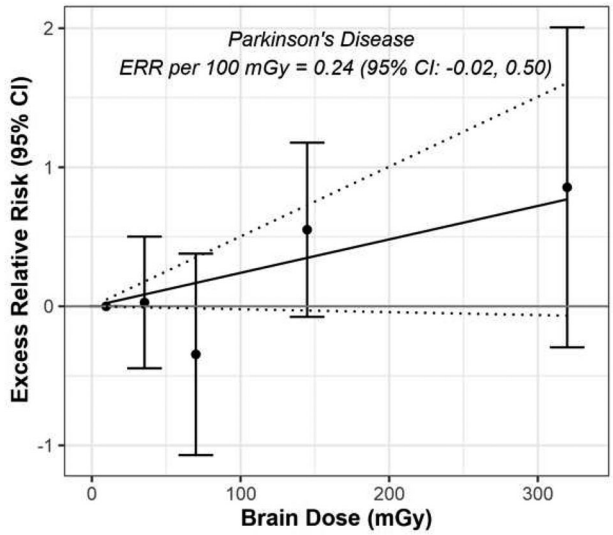

Figure 6. Excess Relative Risk (ERR) of Parkinson's disease by radiation dose to brain among 135,193 workers at U.S. nuclear power plants first monitored between 1957–1984 and followed through 2011. Linear model presented (solid line) based on a continuous measure of dose, and 95% confidence bands (dotted lines) presented about the regression line. Doses were lagged by 10 years and adjustments were made for sex, year of birth, and socioeconomic status. ERRs and 95% confidence limits are calculated for selected categories of dose to the brain and displayed at the mean dose in each category (categories <25 (referent), 25-, 50-, 100-, and >250 with respective mean doses to the brain of 9.6, 35.4, 69.9, 144.8, and 319.7 mGy).

related to characteristics of exposure such as brief compared with prolonged; the quality of the radiation such as low-LET compared with high-LET; uncontrolled confounding related to tobacco use or asbestos exposure; or possible biases in dosimetry, including the manner in which intakes of radionuclides and exposure to neutrons were handled.

All solid cancers

For completion, an analysis of all solid cancers was conducted and found little evidence for a dose-response relationship (Figure 5). Sampling variability was such, however, that ERRs per 100 mGy higher than 0.05 could be excluded with 95% confidence. Thus, the data are not inconsistent, in a statistical sense, with the Japanese atomic bomb survivor ERR per 100 mGy estimate of 0.042 (95% CI 0.032; 0.053) for all solid cancer based on a linear model (Ozasa et al. 2012). Estimation of radiation associations for all solid cancers is frequently done in epidemiologic studies to increase statistical precision, has value for purposes of radiation protection, but lacks biological plausibility (NCRP 2012). The value of combining all solid cancers as a single outcome has been recently questioned given the heterogeneity of background rates for individual cancers and the differences that arise when selected cancers are removed from the combined cancer dose-response relationship (Cologne et al. 2019). NCRP (2012) recommended caution in interpreting radiation associations, either positive or negative, based on combining all cancers: 'Clearly, there are differences in the etiologies and the radiation responses between lung cancer (caused by smoking), breast cancer (influenced by hormonal factors), cervical cancer (caused by human papillomavirus), rectal cancer (seen in excess only following radiation therapy), bone cancer (a high-dose effect), and brain cancer (nondividing neural cells, where the association is seen primarily among children)…' The different shapes of the dose-response curves for individual cancer sites, e.g. linearity for breast and thyroid cancer, nonlinearity for nonmelanoma skin and lung cancer, and a flat response (no risk) for cervical cancer and other cancers, tempers a biologically meaningful interpretation of the shape of the dose-response relationship when all cancers are taken together.

Ischemic heart disease

Nuclear power plant workers were significantly less likely to die than comparable persons in the general population. This is not unexpected because there are selection factors related to health that influence a person's ability to work, the so-called 'healthy worker effect' (Monson 1986; Checkoway et al. 1989). Internal dose-response comparisons are conducted to minimize this bias. Based on 5410 deaths from IHD, there was no evidence for a radiation association. The ERR at 100 mGy was slightly negative, −0.01; and was influenced by the lower risk apparent among the over 14,000 workers who received >100 mGy dose to the heart. The absence of a radiation association for IHD has been seen in all MPS cohorts reported to date (Boice, Quinn et al. 2021), including Rocketdyne (Boice et al. 2006, 2011), Mound (Boice et al. 2014), Mallinckrodt (Ellis, Boice et al. 2018; Golden et al. 2019), Los Alamos National Laboratory (Boice et al. 2021a), medical radiation workers (Boice, Cohen, Mumma, Howard et al. 2021), and industrial radiographers (NCRP 2018b). Significant radiation associations for heart

disease have been found among the Japanese atomic bomb survivors (Ozasa et al. 2012), although a recent report focusing on IHD failed to confirm a radiation association (Takahashi et al. 2017). It remains of great scientific and radiation protection interest to learn whether doses below 0.5 Gy can result in increased deaths due to heart disease (Tran et al. 2017; NCRP 2018b; Wakeford 2019, Boice, Held et al. 2019; Electric Power Research Institute (EPRI) 2020; Richardson et al. 2020; Anderson et al. 2021; Tapio et al. 2021). Because heart disease occurs so frequently in the population, even a small risk related to radiation exposure at low doses would equate to a meaningful excess. Nonetheless, it is not clear why there are inconsistencies among the various epidemiologic studies reported to date but reasons likely include: the epidemiologic challenges in detecting a very small excess risk at low doses; confounding effects of uncontrolled cigarette smoking or other health conditions related to heart disease such as high blood pressure, diabetes, and obesity; radiation effects on the heart related to any concomitant kidney exposure; and changes in the coding of death certificates over time or misclassification of causes of death (Ozasa et al. 2017; de Vocht et al. 2020).

Other sites

Cancer of the esophagus was elevated and there was a suggestion of a dose-response consistent with several of the other studies within the MPS including Mound (Boice et al. 2014), atomic veterans (Boice et al. 2020), and Los Alamos National Laboratory (Boice, Cohen, Mumma, Golden et al. 2021). Cancer of the prostate was not elevated: the SMR based on 527 deaths was 0.99 (95% CI 0.91, 1.08). Previous MPS studies have not revealed significant dose- response relationships for prostate cancer (Boice et al. 2020; Boice, Cohen, Mumma, Golden et al. 2021; Boice, Cohen, Mumma, Howard 2021), in contrast to a recent publication on the Japanese atomic bomb survivors (Mabuchi et al. 2021). Dementia, Alzheimer's, Parkinson's, and motor neuron diseases were not increased. However, a nonsignificant dose-response for Parkinson's was seen (ERR per 100 mGy 0.24; 95% CI −0.02, 0.50; n = 140) (Figure 6) similar to those reported in other large MPS studies, notably for medical radiation workers (ERR per 100 mGy 0.07; 95% CI −0.20, 0.54; n = 87), industrial radiographers (ERR per 100 mGy 0.24; 95% CI −0.02, 0.50; n = 128), and workers at the Los Alamos National Laboratory (ERR per 100 mGy 0.16; 95% CI −0.17, 0.40; n = 193) (Boice and Dauer 2021; Boice, Cohen, Mumma, Golden et al. 2021; Boice, Cohen, Mumma, Howard 2021; Boice, Quinn et al. 2021). These estimates are broadly consistent with the association recently reported among Mayak workers for a cumulative gamma-ray dose to the brain (ERR per Gy 1.02; 95% CI 0.59, 1.63; n = 300 diagnoses) (Azizova et al. 2020). Improved estimates of radiation risk following prolonged exposures are anticipated from the future pooling of MPS cohorts for Parkinson's disease, leukemia and cancers of the lung, stomach, bladder, brain, thyroid, kidney and other causes of death, including those from nonmalignant conditions such as IHD and cerebrovascular disease.

Strengths and limitations

The strengths of the study of nuclear power plant workers include the cohort design; large numbers of over 135,000 healthy workers; complete and long follow-up of up to 60 years (mean 30.2 years); accurate and unbiased ascertainment of causes of death from the NDI and state mortality indices; near complete determination of all occupational doses from all places of employment; precise dosimetry data collected under strict criteria in compliance with legal regulations; a comprehensive approach to estimating organ doses for the NPP cohort was followed as detailed in NCRP Report 178 (Dauer et al. 2018; NCRP 2018a); minimal exposures to neutrons or intakes of radioactive materials a large number of cause-specific deaths available for analysis (e.g. 311 deaths from leukemia other than CLL compared with 121 among atomic bomb survivors exposed over age 19 (UNSCEAR 2008)); a large number of workers exposed to over 100 mSv (e.g. 19,981 compared with 4097 adult male atomic bomb survivors over age 19 years); sufficient numbers of the four subtypes of leukemia for statistical analyses of risk; and substantial statistical power to evaluate a radiation effect following chronic exposures over many years. Limitations include the small number of female workers such that sex-specific differences could not be thoroughly evaluated; the relatively small number of excess leukemia cases that precluded clear differentiation between various dose-response models; reliance on death certificate information; the possibility of missed doses, although the legal requirements to report worker doses at nuclear power plants might mitigate somewhat this concern as does the multiple independent sources of dosimetry information available; and limited evaluation of uncertainty in the analyses to date (Ron and Hoffman 1999; Schafer and Gilbert 2006; NCRP 2008, 2018a; UNSCEAR 2014). Most of these limitations will be met in the larger context of the MPS and the pooling of all cohorts, i.e. up to a million radiation workers and veterans.

Cigarette smoking causes lung cancer, heart disease, leukemia and many other diseases (USDHSS 2010). In the absence of individual information on tobacco use or other lifestyle behaviors that may influence mortality, adjustment for SES is frequently done as a way to account for such potentially confounding factors. For the over 130,000 NPP workers, individual SES adjustment was based on area-wide educational levels obtained from small-scale census-block group residential histories (Cohen et al. 2018; Mumma et al. 2018). While individual-level SES variables are preferred over area-level variables (Steenland et al. 2004), area-level variables have been shown to be adequate correlates of SES in occupational and other studies of cancer, heart disease and overall mortality (Anderson 1997; Waitzman and Smith 1998; Yen and Kaplan 1999; Diez Roux 2001). Further, it is of note that education level has been strongly correlated with tobacco use among early DOE radiation workers in

interview studies (Mahoney and Wilkinson 1987). Nonetheless, despite our best efforts to adjust for correlates of smoking, the possibility of residual confounding is recognized as a limitation.

Other uncertainties include the choice of analytical strategies such as whether adjustments for the duration of monitoring should be made. In addition to conducting internal cohort analyses as a way to minimize the selection bias associated with having to be healthy in order to work, i.e. the 'healthy worker effect' (Monson 1986; Howe et al. 1988; Checkoway et al. 1989), adjusting for duration of employment is often done to account for any 'healthy worker survivor effect' (Buckley et al. 2015). Duration of employment can be correlated, however, with cumulative exposures, length of follow-up and other factors that might affect risk estimates (Boice 2010; Golden et al. 2018). In some radiation studies, the adjustment led to sizeable increases in the estimates of risk (Cardis et al. 2007), while in others, the effect of adjustment tended to reduce estimates of risk (Muirhead et al. 2009). It is also of interest that early departure from employment is not always an indicator of poor health, e.g. for early radiation workers it was not uncommon for many healthy workers to leave employment at a radiation facility for employment elsewhere (Boice et al. 2006). The over 10,000 NPP workers monitored for <30 d, evaluated separately, appeared as healthy as the longer-termed worker. Although the length of follow-up was similar, the workers monitored for <30 d may have been visitors or managers and not comparable to other workers. Nonetheless, they do not provide strong support for the notion that those who continued to work were especially healthy compared with shorter-term NPP workers. Further, the NPP workers who moved from plant to plant, presumably because of unique skills or the desire for improved positions, had slightly higher radiation risks (related to higher exposures) than those who remained at a single plant, although the differences were not statistically meaningful.

A recent Government Accountability Office report endorsed the MPS and stressed the need for enhanced scientific understanding in order to reduce uncertainties of the health consequences of low-dose radiation received by the public and workers (USGAO 2017). There is broad consensus support by national and international radiation research and radiation protection communities for the renewal and reinvigoration of low-dose radiation research (NASEM 2019, 2021b). Acts passed by the U.S. Congress and appropriation bills signed by the President of the U.S. have supported the MPS and confirmed the need for scientific research that will inform decision-makers and improve risk-management strategies (Boice, Held et al. 2019).

Conclusions

The study of nuclear power plant workers employed 1957–1984 provides convincing confirmatory evidence that low-dose and low-dose-rate exposures over time significantly increase the risk of leukemia other than CLL. A negative association between radiation and CLL is consistent with most radiation studies and indicates that this type of leukemia should not be considered highly sensitive to radiation exposures. Consistent with MPS cohort studies completed to date, there was little evidence for a radiation association with lung cancer or ischemic heart disease. In contrast, associations between radiation and Parkinson's disease are seen in most MPS cohort studies. More statistically precise estimates will be forthcoming when other cohorts within the MPS are combined, in particular the studies of 123,000 industrial radiographers, 114,000 nuclear weapons test participants, 109,000 medical radiation workers, 112,000 nuclear submariners, and the over 150,000 workers at the Department of Energy nuclear facilities.

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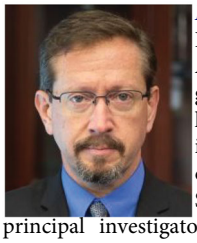

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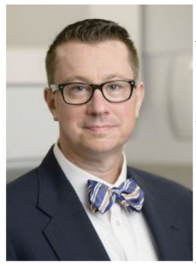

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References

Agency for Toxic Substances and Disease Registry (ATSDR). 2013. Case studies in environmental medicine: asbestos toxicity. Atlanta (GA): ATSDR, Public Health Service, US Department of Health and Human Services. [accessed 2021 January 16]. https://www.atsdr.cdc.gov/csem/asbestos_2014/docs/asbestos.pdf

Akaike H. 1974. A new look at the statistical model identification. IEEE Trans Automat Contr. 19(6):716–723.

Akiba S. 2018. The latest study of Japanese nuclear workers. J Radiol Prot. 38(2):E26–E28.

Akiba S, Mizuno S. 2012. The third analysis of cancer mortality among Japanese nuclear workers, 1991–2002: estimation of excess relative risk per radiation dose. J Radiol Prot. 32(1):73–83.

Albitar M, Manshouri T, Shen Y, Liu D, Beran M, Kantarjian HM, Rogers A, Jilani I, Lin CW, Pierce S, et al. 2002. Myelodysplastic syndrome is not merely "preleukemia." Blood. 100(3):791–798.

Anderson JL, Bertke SJ, Yiin J, Kelly-Reif K, Daniels RD. 2021. Ischaemic heart and cerebrovascular disease mortality in uranium enrichment workers. Occup Environ Med. 78(2):105–111.

Anderson RT, Sorlie P, Backlund E, Johnson N, Kaplan GA. 1997. Mortality effects of community socioeconomic status. Epidemiology. 8(1):42–47.

Anzenberg V, Lewis DE, Dickson ED, Bush-Goddard SP. 2010. The U.S. Nuclear Regulatory Commission Radiation Exposure Information Reporting System (REIRS). Radiat Res. 173(2):254–255.

Azizova TV, Bannikova MV, Grigoryeva ES, Rybkina VL, Hamada N. 2020. Occupational exposure to chronic ionizing radiation increases

risk of Parkinson's disease incidence in Russian Mayak workers. Int J Epidemiol. 49(2):435–447.
Beck HL, Till JE, Grogan HA, Aanenson JW, Mohler HJ, Mohler SS, Voillequé PG. 2017. Red bone marrow and male breast doses for a cohort of atomic veterans. Radiat Res. 187(2):221–228.
Blevins MR, Andersen RL. 2011. Radiation protection at U.S. nuclear power plants – today and tomorrow. Health Phys. 100(1):35–38.
Boice JD. 2010. Uncertainties in studies of low statistical power (editorial). J Radiol Prot. 30(2):115–120.
Boice JD, Jr. 2014. The importance of radiation worker studies (editorial). J Radiol Prot. 34(3):E7–E12.
Boice JD, Jr. 2016. From Oak Ridge to Indian Point Studying workers at nuclear power plants. Health Physics News. 44:23–24. [accessed 2021 November 12]. https://ncrponline.org/wp-content/themes/ncrp/PDFs/BOICE-HPnews/45-From-Oak-Ridge-to-Indian-Point-Feb-2016.pdf
Boice JD, Jr. 2017a. The linear nonthreshold (LNT) model as used in radiation protection: an NCRP update. Int J Radiat Biol. 93(10):1079–1092.
Boice JD, Jr. 2017b. Space: the final frontier–research relevant to Mars. Health Phys. 112(4):392–397.
Boice JD, Jr. 2019. The Million Person Study relevance to space exploration and Mars. Int J Radiat Biol. DOI:10.1080/09553002.2019.1589020
Boice JD, Jr, Blettner M, Kleinerman RA, Stovall M, Moloney WC, Engholm G, Austin DF, Bosch A, Cookfair DL, Krementz ET, et al. 1987. Radiation dose and leukemia risk in patients treated for cancer of the cervix. J Natl Cancer Inst. 79(6):1295–1311.
Boice JD, Jr, Cohen SS, Mumma MT, Chen H, Golden AP, Beck HL, Till JE. 2020. Mortality among US military participants at eight above ground nuclear weapons test series. Int J Radiat Biol. DOI:10.1080/09553002.2020.1787543
Boice JD, Jr, Cohen SS, Mumma MT, Ellis ED, Cragle DL, Eckerman KF, Wallace PW, Chadda B, Sonderman JS, Wiggs LD, et al. 2014. Mortality among Mound workers exposed to polonium-210 and other sources of radiation, 1944–1979. Radiat Res. 181(2):208–228.
Boice JD, Jr, Cohen SS, Mumma MT, Ellis ED, Eckerman KF, Leggett RW, Boecker BB, Brill AB, Henderson BE. 2011. Updated mortality analysis of radiation workers at Rocketdyne (Atomics International), 1948–2008. Radiat Res. 176(2):244–258.
Boice JD, Jr, Cohen SS, Mumma MT, Ellis ED. 2019. The Million Person Study, whence it came and why. Int J Radiat Biol. DOI:10.1080/09553002.2019.1589015
Boice JD, Jr, Cohen SS, Mumma MT, Golden AP, Howard S, Girardi DJ, Ellis ED, Bellamy M, Dauer LT, Samuels C, et al. 2021. Mortality among workers at the Los Alamos National Laboratory, 1943–2017. Int J Radiat Biol. DOI:10.1080/09553002.2021.1917784
Boice JD, Jr, Cohen SS, Mumma MT, Howard SC, Yoder C, Dauer LT. 2021. Mortality among medical radiation workers in the United States, 1965–2016. Int J Radiat Biol. DOI:10.1080/09553002.2021.1967508.
Boice JD, Jr, Dauer LT. 2021. Million Person study of low-dose radiation health effects. Trans Am Nucl Soc. (in press)
Boice JD, Jr, Ellis ED, Golden AP, Zablotska LB, Mumma MT, Cohen SS. 2019. Sex-specific lung cancer risk among radiation workers in the Million-Person Study and among TB-fluoroscopy patients. Int J Radiat Biol. DOI:10.1080/09553002.2018.1547441
Boice JD, Held KD, Shore RE. 2019. Radiation epidemiology and health effects following low-level radiation exposure. J Radiol Prot. 39(4):S14–S27.
Boice JD, Jr, Leggett RW, Ellis ED, Wallace PW, Mumma M, Cohen SS, Brill AB, Chadda B, Boecker BB, Yoder RC, et al. 2006. A comprehensive dose reconstruction methodology for former Rocketdyne/Atomics International radiation workers. Health Phys. 90(5):409–430.
Boice JD, Jr, Quinn B, Al-Nabulsi I, Ansari A, Blake PK, Blattnig SR, Caffrey EA, Cohen SS, Golden AP, Held KD, et al. 2021. A million persons, a million dreams: a vision for a National Center of Radiation Epidemiology and Biology. Int J Radiat Biol. DOI:10.1080/09553002.2021.1988183.
Bouville A, Toohey RE, Boice JD, Jr, Beck HL, Dauer LT, Eckerman KF, Hagemeyer D, Leggett RW, Mumma MT, Napier B, et al. 2015. Dose reconstruction for the million worker study: status and guidelines. Health Phys. 108(2):206–220.
Buckley JP, Keil AP, McGrath LJ, Edwards JK. 2015. Evolving methods for inference in the presence of healthy worker survivor bias. Epidemiology. 26(2):204–212.
Caldwell GG, Zack MM, Mumma MT, Falk H, Heath CW, Till JE, Chen H, Boice JD. 2016. Mortality among military participants at the 1957 PLUMBBOB nuclear weapons test series and from leukemia among participants at the SMOKY test. J Radiol Prot. 36(3):474–489.
Campbell KM, Deck D, Krupski A. 2008. Record linkage software in the public domain: a comparison of Link Plus, The Link King, and a 'basic' deterministic algorithm. Health Informatics J. 14(1):5–15.
Cardis E, Gilbert ES, Carpenter L, Howe G, Kato I, Armstrong BK, Beral V, Cowper G, Douglas A, Fix J. 1995. Effects of low doses and low dose rates of external ionizing radiation: cancer mortality among nuclear industry workers in three countries. Radiat Res. 142(2):117–132.
Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, Howe G, Kaldor J, Muirhead CR, Schubauer-Berigan M, et al. 2005. Risk of cancer after low doses of ionising radiation: retrospective cohort study in 15 countries. BMJ. 331(7508):77. DOI:10.1136/bmj.38499.599861.E0
Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, Howe G, Kaldor J, Muirhead CR, Schubauer-Berigan M, et al. 2007. The 15-country collaborative study of cancer risk among radiation workers in the nuclear industry: estimates of radiation-related cancer risks. Radiat Res. 167(4):396–416.
Charpentier P, Ostfeld AM, Hadjimichael OC, Hester R. 1993. The mortality of US nuclear submariners, 1969–1982. J Occup Med. 35(5):501–509.
Checkoway H, Pearce N, Crawford-Brown DJ. 1989. Research Methods in Occupational Epidemiology. New York (NY): Oxford University Press.
Cohen SS, Mumma MT, Ellis ED, Boice JD, Jr. 2018. Validating the use of census data on education as a measure of socioeconomic status in an occupational cohort. Int J Radiat Biol. DOI:10.1080/09553002.2018.1549758
Cologne J, Kim J, Sugiyama H, French B, Cullings HM, Preston DL, Mabuchi K, Ozasa K. 2019. Effect of heterogeneity in background incidence on inference about the solid-cancer radiation dose response in atomic bomb survivors. Radiat Res. 192(4):388–398.
Cox DR. 1972. Regression models and life-tables. J R Stat Soc B. 34(2):187–220.
Curtis RE, Boice JD, Jr, Stovall M, Bernstein L, Holowaty E, Karjalainen S, Langmark F, Nasca PC, Schwartz AG, Schymura MJ. 1994. Relationship of leukemia risk to radiation dose following cancer of the uterine corpus. J Natl Cancer Inst. 86(17):1315–1324.
Daniels RD, Bertke S, Waters KM, Schubauer-Berigan MK. 2013. Risk of leukaemia mortality from exposure to ionising radiation in US nuclear workers: a pooled case-control study. Occup Environ Med. 70(1):41–48.
Daniels RD, Bertke SJ, Richardson DB, Cardis E, Gillies M, O'Hagan JA, Haylock R, Laurier D, Leuraud K, Moissonnier M, et al. 2017. Examining temporal effects on cancer risk in the international nuclear workers' study. Int J Cancer. 140(6):1260–1269.
Daniels RD, Schubauer-Berigan MK. 2011. A meta-analysis of leukaemia risk from protracted exposure to low-dose gamma radiation. Occup Environ Med. 68(6):457–464.
Dauer LT, Bouville A, Toohey RE, Boice JD, Jr, Beck HL, Eckerman KF, Hagemeyer D, Leggett RW, Mumma MT, Napier B, et al. 2018. Dosimetry and uncertainty approaches for the million-person study of low-dose radiation health effects: overview of the recommendations in NCRP Report No. 178. Int J Radiat Biol. DOI:10.1080/09553002.2018.1536299
de Vocht F, Hidajat M, Martin RM, Agius R, Wakeford R. 2020. Ischemic heart disease mortality and occupational radiation exposure in a nested matched case-control study of British nuclear fuel cycle workers: investigation of confounding by lifestyle, physiological traits and occupational exposures. Radiat Res. 194(4):431–444.

Diez Roux AV, Merkin SS, Arnett D, Chambless L, Massing M, Nieto FJ, Sorlie P, Szklo M, Tyroler HA, Watson RL. 2001. Neighborhood of residence and incidence of coronary heart disease. N Engl J Med. 345(2):99–106.

Douglas AJ, Omar RZ, Smith PG. 1994. Cancer mortality and morbidity among workers at the Sellafield plant of British Nuclear Fuels. Br J Cancer. 70(6):1232–1243.

Electric Power Research Institute (EPRI). 2020. Cardiovascular risks from low dose radiation exposure: review and scientific appraisal of the literature. 3002018408. Palo Alto (CA): EPRI. [accessed 2021 January 12]. https://www.epri.com/research/products/000000003002018408

Ellis ED, Boice JD, Golden AP, Girardi DJ, Cohen SS, Mumma MT, Shore RE, Leggett RW, Kerr GD. 2018. Dosimetry is key to good epidemiology: workers at Mallinckrodt Chemical Works had seven different source exposures. Health Phys. 114(4):386–397.

Ellis ED, Girardi D, Golden AP, Wallace PW, Phillips J, Cragle DL. 2018. Historical perspective on the Department of Energy mortality studies: focus on the collection and storage of individual worker data. Int J Radiat Biol. DOI:10.1080/09553002.2018.1547851

Friedman-Jimenez G, Kato I, Factor-Litvak P, Shore R. 2021. Mortality of enlisted men who served on nuclear-powered submarines in the United States Navy. J Occup Environ Med. DOI: 10.1097/JOM.0000000000002364.

Gilbert ES. 1998. Accounting for errors in dose estimates used in studies of workers exposed to external radiation. Health Phys. 74(1): 22–29.

Gilbert ES, Cragle DL, Wiggs LD. 1993. Updated analyses of combined mortality data for workers at the Hanford Site, Oak Ridge National Laboratory, and Rocky Flats Weapons Plant. Radiat Res. 136(3): 408–421.

Gilbert ES, Little MP, Preston DL, Stram DO. 2020. Issues in interpreting epidemiologic studies of populations exposed to low-dose, high-energy photon radiation. J Natl Cancer Inst Monogr. 2020(56):176-187.

Gillies M, Haylock R, Hunter N, Zhang W. 2019. Risk of leukemia associated with protracted low-dose radiation exposure: updated results from the National Registry for Radiation Workers Study. Radiat Res. 192(5):527–537.

Gillies M, Haylock R. 2014. The cancer mortality and incidence experience of workers at British Nuclear Fuels plc, 1946–2005. J Radiol Prot. 34(3):595–623.

Gillies M, Kuznetsova I, Sokolnikov M, Haylock R, O'Hagan J, Tsareva Y, Labutina E. 2017. Lung cancer risk from plutonium: a pooled analysis of the Mayak and Sellafield worker cohorts. Radiat Res. 188(6):645–660.

Golden AP, Cohen SS, Chen H, Ellis ED, Boice JD, Jr. 2018. Evaluation of statistical modeling approaches for epidemiologic studies of low dose radiation health effects. Int J Radiat Biol. DOI: 10.1080/09553002.2018.1554924

Golden AP, Ellis ED, Cohen SS, Mumma MT, Leggett RW, Wallace PW, Girardi DJ, Watkins JP, Shore RE, Boice JD, Jr. 2019. Updated mortality analysis of the Mallinckrodt uranium processing workers, 1942–2012. Int J Radiat Biol. DOI:10.1080/09553002.2019.1569773

Goldsmith R, Boice JD, Jr, Hrubec Z, Hurwitz PE, Goff TE, Wilson J. 1989. Mortality and career radiation doses for workers at a commercial nuclear power plant: feasibility study. Health Phys. 56(2): 139–150.

Grant EJ, Ozasa K, Ban N, de González AB, Cologne J, Cullings HM, Doi K, Furukawa K, Imaoka T, Kodama K, et al. 2015. A report from the 2013 international symposium: the evaluation of the effects of low-dose radiation exposure in the life span study of atomic bomb survivors and other similar studies. Health Phys. 108(5): 551–556.

Hagemeyer D, Nichols G, Mumma MT, Boice JD, Brock TA. 2018. 50 Years of the Radiation exposure information and reporting system. Int J Radiat Biol. DOI:10.1080/09553002.2018.1540896

Hamra GB, Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Haylock R, Laurier D, Leuraud K, Moissonnier M, et al. 2016. Cohort profile: the International Nuclear Workers Study (INWORKS). Int J Epidemiol. 45(3):693–699.

Hauptmann M, Daniels RD, Cardis E, Cullings HM, Kendall G, Laurier D, Linet MS, Little MP, Lubin JH, Preston DL, et al. 2020. Epidemiological studies of low-dose ionizing radiation and cancer: summary bias assessment and meta-analysis. J Natl Cancer Inst Monogr. 2020(56):188–200.

Haylock RGE, Gillies M, Hunter N, Zhang W, Phillipson M. 2018. Cancer mortality and incidence following external occupational radiation exposure: an update of the 3rd analysis of the UK National Registry for Radiation Workers. Br J Cancer. 119(5):631–637.

Howe GR, Chiarelli AM, Lindsay JP. 1988. Components and modifiers of the healthy worker effect: evidence from three occupational cohorts and implications for industrial compensation. Am J Epidemiol. 128(6):1364–1375.

Howe GR, Zablotska LB, Fix JJ, Egel J, Buchanan J. 2004. Analysis of the mortality experience amongst U.S. nuclear power industry workers after chronic low-dose exposure to ionizing radiation. Radiat Res. 162(5):517–526.

Hsu WL, Preston DL, Soda M, Sugiyama H, Funamoto S, Kodama K, Kimura A, Kamada N, Dohy H, Tomonaga M, et al. 2013. The incidence of leukemia, lymphoma and multiple myeloma among atomic bomb survivors: 1950–2001. Radiat Res. 179(3):361–382.

International Commission on Radiological Protection (ICRP). 2010. Conversion coefficients for radiological protection quantities for external radiation exposures. ICRP Publication 116. Ann ICRP. 40(2–5):1–257.

Iwanaga M, Hsu WL, Soda M, Takasaki Y, Tawara M, Joh T, Amenomori T, Yamamura M, Yoshida Y, Koba T, et al. 2011. Risk of myelodysplastic syndromes in people exposed to ionizing radiation: a retrospective cohort study of Nagasaki atomic bomb survivors. J Clin Oncol. 29(4):428–434.

Jablon S, Boice JD, Jr. 1993. Mortality among workers at a nuclear power plant in the United States. Cancer Causes Control. 4(5): 427–430.

Komrokji RS, Padron E, List AF. 2019. Chapter 106: Myelodysplastic syndromes. In: DeVita VT, Lawrence TS, Rosenberg SA, editors. DeVita, Hellman, and Rosenberg's Cancer: Principles and Practice of Oncology. 11th ed. Philadelphia (PA): Wolters Kluwer; p. 1802–1817.

Krestinina L, Preston DL, Davis FG, Epifanova S, Ostroumova E, Ron E, Akleyev A. 2010. Leukemia incidence among people exposed to chronic radiation from the contaminated Techa River, 1953–2005. Radiat Environ Biophys. 49(2):195–201.

Kuznetsova IS, Labutina EV, Hunter N. 2016. Radiation risks of leukemia, lymphoma and multiple myeloma incidence in the Mayak cohort: 1948–2004. PLoS One. 11(9):e0162710.

Laurier D, Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan J, Hamra GB, Haylock R, Leuraud K, Moissonnier M, et al. 2017. The International Nuclear Workers Study (Inworks): a collaborative epidemiological study to improve knowledge about health effects of protracted low-dose exposure. Radiat Prot Dosimetry. 173(1–3): 21–25.

Leggett RW, Eckerman KF, Bellamy M. 2018. MPS dose reconstruction for internal emitters: some site-specific issues and approaches. Int J Radiat Biol. DOI:10.1080/09553002.2018.1558302

Leuraud K, Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, Haylock R, Laurier D, Moissonnier M, et al. 2015. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. Lancet Haematol. 2(7):e276–e281.

Linet MS, Little MP, Kitahara CM, Cahoon EK, Doody MM, Simon SL, Alexander BH, Preston DL. 2020. Occupational radiation and haematopoietic malignancy mortality in the retrospective cohort study of US radiologic technologists, 1983–2012. Occup Environ Med. 77(12):822–831.

Little MP, Weiss HA, Boice JD, Jr, Darby SC, Day NE, Muirhead CR. 1999. Risks of leukemia in Japanese atomic bomb survivors, in women treated for cervical cancer, and in patients treated for ankylosing spondylitis. Radiat Res. 152(3):280–292.

Mabuchi K, Preston DL, Brenner AV, Sugiyama H, Utada M, Sakata R, Sadakane A, Grant EJ, French B, Cahoon EK, et al. 2021. Risk of

prostate cancer incidence among atomic bomb survivors: 1958–2009. Radiat Res. 195(1):60–65.
Mahoney MC, Wilkinson GS. 1987. Smoking patterns among Los Alamos National Laboratory employees. Report LA-10650. Los Alamos (NM): Los Alamos National Laboratory. [accessed 2021 July 16]. https://www.osti.gov/biblio/6403953-smoking-patterns-among-los-alamos-national-laboratory-employees
Matanoski GM, Seltser R, Sartwell PE, Diamond EL, Elliott EA. 1975. The current mortality rates of radiologists and other physician specialists: specific causes of death. Am J Epidemiol. 101(3):199–210.
McLean AR, Adlen EK, Cardis E, Elliott A, Goodhead DT, Harms-Ringdahl M, Hendry JH, Hoskin P, Jeggo PA, Mackay DJC, et al. 2017. A restatement of the natural science evidence base concerning the health effects of low-level ionizing radiation. Proc Biol Sci. 284(1862):20171070.
Metz-Flamant C, Laurent O, Samson E, Caër-Lorho S, Acker A, Hubert E, Richardson DB, Laurier D. 2013. Mortality associated with chronic external radiation exposure in the French combined cohort of nuclear workers. Occup Environ Med. 70(9):630–638.
Monson RR. 1986. Observations on the healthy worker effect. J Occup Med. 28(6):425–433.
Mueller TJ, Weishar TM, Hallworth JM, Draper DA. 2020. Occupational radiation exposure from U.S. Naval nuclear plants and their support facilities. NT-20-2. Washington (DC): Naval Nuclear Propulsion Program. [accessed 2021 January 18]. https://www.energy.gov/sites/prod/files/2020/07/f77/NT-20-2.pdf
Muirhead CR, Boice JD, Jr, Raddatz CT, Yoder RC. 1996. Comparison of dose histories for U.S. nuclear power plant workers, based on records held by a major dosimetry service company and on the NRC REIRS database. Health Phys. 70(5):645–650.
Muirhead CR, O'Hagan JA, Haylock RG, Phillipson MA, Willcock T, Berridge GL, Zhang W. 2009. Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers. Br J Cancer. 100(1):206–212.
Mumma MT, Cohen SS, Sirko SS, Ellis ED, Boice JD, Jr. 2018. Obtaining vital status and cause of death on a million persons. Int J Radiat Biol. DOI:10.1080/09553002.2018.1539884
Mumma MT, Sirko JL, Boice JD, Blot WJ. 2019. Mesothelioma mortality within two radiation monitored occupational cohorts. Int J Radiat Biol. DOI:10.1080/09553002.2019.1642540
National Academies of Sciences, Engineering, and Medicine (NASEM). 2019. The future of low dose radiation research in the United States. Proceedings of a Symposium. Washington (DC): National Academies Press. https://doi.org/10.17226/25578
National Academies of Sciences, Engineering, and Medicine (NASEM). 2021a. Space radiation and astronaut health: managing and communicating cancer risks. Washington (DC): The National Academies Press. https://doi.org/10.17226/26155
National Academies of Sciences, Engineering, and Medicine (NASEM). 2021b. Developing a long-term strategy for low-dose radiation research in the United States. https://www.nationalacademies.org/our-work/developing-a-long-term-strategy-for-low-dose-radiation-research-in-the-united-states
National Academies/National Research Council (NA/NRC). 2006. Health risks from exposure to low levels of ionizing radiation (BEIR VII phase 2). Washington (DC): National Academies Press.
National Council on Radiation Protection and Measurements (NCRP). 2008. Uncertainties in the measurement and dosimetry of external radiation. NCRP Report No. 158. Bethesda (MD): NCRP.
National Council on Radiation Protection and Measurements (NCRP). 2012. Uncertainties in the estimation of radiation risks and probability of disease causation. NCRP Report No. 171. Bethesda (MD): NCRP.
National Council on Radiation Protection and Measurements (NCRP). 2014. Radiation protection for space activities: supplement to previous recommendations. NCRP Commentary No. 23. Bethesda (MD): NCRP.
National Council on Radiation Protection and Measurements (NCRP). 2018a. 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). NCRP Report 178. Bethesda (MD): NCRP.
National Council on Radiation Protection and Measurements (NCRP). 2018b. Implications of recent epidemiologic studies for the linear-nonthreshold model and radiation protection. NCRP Commentary 27. Bethesda (MD): NCRP.
National Council on Radiation Protection and Measurements (NCRP). 2020. Dosimetry guidance for medical radiation workers with a focus on lung dose reconstruction. NCRP Commentary 30. Bethesda (MD): NCRP.
Naval Dosimetry Center (NDC). 2021. Lifetime exposure history repository for the U.S. Navy's nuclear-powered fleet personnel. [accessed 2021 January 12]. https://www.cnic.navy.mil/regions/ndw/installations/nsa_bethesda/about/tenant_orgs/ndc.html
Oak Ridge Institute for Science and Education (ORISE). 2011. Establishing a U.S. Nuclear Regulatory Commission worker registry for epidemiologic investigations. A feasibility study using the Radiation Exposure Information and Reporting System. Submitted to the Nuclear Regulatory Commission. [accessed 2021 January 12]. http://www.anewstudy.org/2012NovNPP/REIRS%20Feasibility%20Study-FINAL_01142011%20%282%29.pdf
Ozasa K, Shimizu Y, Suyama A, Kasagi F, Soda M, Grant EJ, Sakata R, Sugiyama H, Kodama K. 2012. Studies of the mortality of atomic bomb survivors, Report 14, 1950–2003: an overview of cancer and noncancer diseases. Radiat Res. 177(3):229–243.
Ozasa K, Takahashi I, Grant EJ, Kodama K. 2017. Cardiovascular disease among atomic bomb survivors. Int J Radiat Biol. 93(10):1145–1150.
Petersen GR, Gilbert ES, Buchanan JA, Stevens RG. 1990. A case-cohort study of lung cancer, ionizing radiation, and tobacco smoking among males at the Hanford Site. Health Phys. 58(1):3–11.
Preston DL, Lubin J, Pierce D, McConney M, Shilnikova N. 2015. Epicure risk regression and person-year computation software: command summary and user guide. Ottawa (CA): Risk Sciences International.
Preston DL, Sokolnikov ME, Krestinina LY, Stram DO. 2017. Estimates of radiation effects on cancer risks in the Mayak Worker, Techa River and atomic bomb survivor studies. Radiat Prot Dosimetry. 173(1–3):26–31.
Richardson DB, Abalo K, Bernier MO, Rage E, Leuraud K, Laurier D, Keil AP, Little MP. 2020. Meta-analysis of published excess relative risk estimates. Radiat Environ Biophys. 59(4):631–641.
Richardson DB, Cardis E, Daniels RD, Gillies M, Haylock R, Leuraud K, Laurier D, Moissonnier M, Schubauer-Berigan MK, Thierry-Chef I, et al. 2018. Site-specific solid cancer mortality after exposure to ionizing radiation: a cohort study of workers (INWORKS). Epidemiology. 29(1):31–40.
Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, Haylock R, Laurier D, Leuraud K, Moissonnier M, et al. 2015. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). BMJ. 351:h5359.
Ron E, Hoffman O. 1999. Uncertainties in radiation dosimetry and their impact on dose-response analyses. Publication No. 99-4541. Bethesda (MD): National Cancer Institute.
Rushton L. 1994. Use of multiple causes of death in the analysis of occupational cohorts-an example from the oil industry. Occup Environ Med. 51(11):722–729.
Schafer DW, Gilbert ES. 2006. Some statistical implications of dose uncertainty in radiation dose-response analyses. Radiat Res. 166(1 Pt 2):303–312.
Schubauer-Berigan MK, Daniels RD, Bertke SJ, Tseng CY, Richardson DB. 2015. Cancer mortality through 2005 among a pooled cohort of U.S. nuclear workers exposed to external ionizing radiation. Radiat Res. 183(6):620–631.
Schubauer-Berigan MK, Daniels RD, Fleming DA, Markey AM, Couch JR, Ahrenholz SH, Burphy JS, Anderson JL, Tseng CY. 2007. Chronic lymphocytic leukaemia and radiation: findings among workers at five US nuclear facilities and a review of the recent literature. Br J Haematol. 139(5):799–808.

Steenland K, Henley J, Calle E, Thun M. 2004. Individual- and area-level socioeconomic status variables as predictors of mortality in a cohort of 179,383 persons. Am J Epidemiol. 159(11):1047–1056.

Steenland K, Nowlin S, Ryan B, Adams S. 1992. Use of multiple-cause mortality data in epidemiologic analyses: US rate and proportion files developed by the National Institute for Occupational Safety and Health and the National Cancer Institute. Am J Epidemiol. 136(7): 855–862.

Stram DO, Preston DL, Sokolnikov M, Napier B, Kopecky KJ, Boice J, Beck H, Till J, Bouville A. 2015. Shared dosimetry error in epidemiological dose-response analyses. PLOS One. 10(3):e0119418.

Takahashi I, Shimizu Y, Grant EJ, Cologne J, Ozasa K, Kodama K. 2017. Heart disease mortality in the life span study, 1950–2008. Radiat Res. 187(3):319–332.

Tapio S, Little MP, Kaiser JC, Impens N, Hamada N, Georgakilas AG, Simar D, Salomaa S. 2021. Ionizing radiation-induced circulatory and metabolic diseases. Environ Int. 146:106235.

Thierry-Chef I, Richardson DB, Daniels RD, Gillies M, Hamra GB, Haylock R, Kesminiene A, Laurier D, Leuraud K, Moissonnier M, et al. 2015. Dose estimation for a study of nuclear workers in France, the United Kingdom and the United States of America: methods for the International Nuclear Workers Study (INWORKS). Radiat Res. 183(6):632–642.

Till JE, Beck HL, Aanenson JW, Grogan HA, Mohler HJ, Mohler SS, Voillequé PG. 2014. Military participants at U.S. atmospheric nuclear weapons testing-methodology for estimating dose and uncertainty. Radiat Res. 181(5):471–484.

Till JE, Beck HL, Boice JD, Jr, Mohler HJ, Mumma MT, Aanenson JW, Grogan HA. 2018. Asbestos exposure and mesothelioma mortality among atomic veterans. Int J Rad Biol. DOI:10.1080/09553002.2018.1551641.

Tran V, Zablotska LB, Brenner AV, Little MP. 2017. Radiation-associated circulatory disease mortality in a pooled analysis of 77,275 patients from the Massachusetts and Canadian tuberculosis fluoroscopy cohorts. Sci Rep. 7(1):44147.

Tucker JD, Tawn EJ, Holdsworth D, Morris S, Langlois R, Ramsey MJ, Kato P, Boice JD, Jr, Tarone RE, Jensen RH. 1997. Biological dosimetry of radiation workers at the Sellafield nuclear facility. Radiat Res. 148(3):216–226.

U.S. Department of Energy (DOE). 2021. DOE 2019 Occupational radiation exposure. Washington (DC): US Department of Energy, Office of Environment, Health, Safety and Security, The Radiation Exposure Monitoring System (REMS). [accessed 2021 April 29]. http://energy.gov/ehss/occupational-radiation-exposure

U.S. Department of Health and Human Services (USDHHS). 2010. How tobacco smoke causes disease: the biology and behavioral basis for smoking-attributable disease: a report of the Surgeon General. Atlanta (GA): U.S. Department of Health and Human Services.

U.S. Government Accountability Office (USGAO). 2017. Low-dose radiation: interagency collaboration on planning research could improve information on health effects. GAO-17-546. Washington (DC): GAO. [accessed 2021 January 12]. https://www.gao.gov/products/GAO-17-546

U.S. Nuclear Regulatory Commission (USNRC). 1994. Voluntary reporting of additional occupational radiation of exposure data (generic letter 94-04). [accessed 2021 January 12]. https://www.nrc.gov/docs/ML1204/ML12047A243.pdf

U.S. Nuclear Regulatory Commission (USNRC). 2021. Radiation exposure information and reporting system (REIRS). [accessed 2021 January 19]. https://www.reirs.com/ and http://www.nrc.gov/reading-rm/doc-collections/gils/rad-exp.html

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 2008. Effects of ionizing radiation. UNSCEAR 2006 report. Report to the general assembly. Volume 1. Scientific annex A. Epidemiological studies of radiation and cancer. Publication E.08.IX.6. New York (NY): United Nations.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 2014. UNSCEAR 2012 Report to the General Assembly with Scientific Annexes. Scientific annex B. Uncertainties in risk estimates for radiation-induced cancer. New York (NY): United Nations.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 2018. UNSCEAR 2017 report. Principles and criteria for ensuring the quality of the committee's reviews of epidemiological studies of radiation exposure. Scientific annex A. New York (NY): United Nations. [accessed 2021 January 15]. https://www.unscear.org/docs/publications/2017/UNSCEAR_2017_Annex-A.pdf

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). 2020. Sources, effects and risks of ionizing radiation. UNSCEAR 2019 Report to the General Assembly. Scientific Annex A: evaluation of selected health effects and inference of risk due to radiation exposure. New York (NY): UNSCEAR. [accessed 2021 April 29]. https://www.unscear.org/docs/publications/2019/UNSCEAR_2019_Annex-A.pdf

Velazquez-Kronen R, Gilbert ES, Linet MS, Moysich KB, Freudenheim JL, Wactawski-Wende J, Simon SL, Cahoon EK, Alexander BH, Doody MM, et al. 2020. Lung cancer mortality associated with protracted low-dose occupational radiation exposures and smoking behaviors in U.S. radiologic technologists, 1983–2012. Int J Cancer. 147(11):3130–3138.

Villoing D, Borrego D, Preston DL, Alexander BH, Rose A, Salasky M, Linet MS, Lee C, Kitahara CM. 2021. Trends in occupational radiation doses for U.S. radiologic technologists performing general radiologic and nuclear medicine procedures, 1980-2015. Radiology. 300(3):605–612.

Vrijheid M, Cardis E, Ashmore P, Auvinen A, Gilbert E, Habib RR, Malker H, Muirhead CR, Richardson DB, Rogel A, et al. 2008. Ionizing radiation and risk of chronic lymphocytic leukemia in the 15-country study of nuclear industry workers. Radiat Res. 170(5): 661–665.

Waitzman NJ, Smith KR. 1998. Phantom of the area: poverty-area residence and mortality in the United States. Am J Public Health. 88(6): 973–976.

Wakeford R. 2019. Does low-level exposure to ionizing radiation increase the risk of cardiovascular disease? Hypertension. 73(6): 1170–1171.

Yen IH, Kaplan GA. 1999. Neighborhood social environment and risk of death: multilevel evidence from the Alameda County Study. Am J Epidemiol. 149(10):898–907.

Yoder RC, Balter S, Boice JD, Jr, Grogan H, Mumma M, Rothenberg L, Passmore C, Vetter R, Dauer L. 2021. Using personal monitoring data to derive organ doses for medical radiation workers in the Million Person Study – considerations regarding NCRP Commentary No. 30. J Radiol Prot. DOI:10.1088/1361-6498/abcfcb

Zablotska LB, Bazyka D, Lubin JH, Gudzenko N, Little MP, Hatch M, Finch S, Dyagil I, Reiss RF, Chumak VV, et al. 2013. Radiation and the risk of chronic lymphocytic and other leukemias among Chornobyl cleanup workers. Environ Health Perspect. 121(1):59–65.

Zablotska LB, Lane RS, Thompson PA. 2014. A reanalysis of cancer mortality in Canadian nuclear workers (1956–1994) based on revised exposure and cohort data. Br J Cancer. 110(1):214–223.

Zeidan AM, Shallis RM, Wang R, Davidoff A, Ma X. 2019. Epidemiology of myelodysplastic syndromes: why characterizing the beast is a prerequisite to taming it. Blood Rev. 34:1–15.