Mortality Among Workers at Oak Ridge National Laboratory

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Background *Workers employed at the Oak Ridge National Laboratory (ORNL) were potentially exposed to a range of chemical and physical hazards, many of which are poorly characterized. We compared the observed deaths among workers to expectations based upon US mortality rates.*
Methods *The cohort included 22,831 workers hired between January 1, 1943 and December 31, 1984. Vital status and cause of death information were ascertained through December 31, 2008. Standardized mortality ratios (SMRs) were computed separately for males and females using US and Tennessee mortality rates; SMRs for men were tabulated separately for monthly-, weekly-, and hourly-paid workers.*
Results *Hourly-paid males had more deaths due to cancer of the pleura (SMR = 12.09, 95% CI: 4.44, 26.32), cancer of the bladder (SMR = 1.89, 95% CI: 1.26, 2.71), and leukemia (SMR = 1.33, 95% CI: 0.87, 1.93) than expected based on US mortality rates. Female workers also had more deaths than expected from cancer of the bladder (SMR = 2.20, 95% CI: 1.20, 3.69) and leukemia (SMR = 1.64, 95% CI: 1.09, 2.36). The pleural cancer excess has only appeared since the 1980s, approximately 40 years after the start of operations. The bladder cancer excess was larger among workers who also had worked at other Oak Ridge nuclear weapons facilities, while the leukemia excess was among people who had not worked at other DOE facilities.*
Conclusions *Occupational hazards including asbestos and ionizing radiation may contribute to these excesses.* Am. J. Ind. Med. *© 2013 Wiley Periodicals, Inc.*

KEY WORDS: cohort studies; mortality study; occupational diseases

INTRODUCTION

The Oak Ridge National Laboratory (ORNL) is a US Department of Energy research and development facility located in Oak Ridge, Tennessee. ORNL, also known as X-10, was constructed as part of the government's top secret program to develop an atomic weapon during World War II. During the war, ORNL developed and operated the original plutonium production reactor and chemical separations facility that served as a pilot plant for the larger production facilities built at the Hanford Site. After the war, activities at ORNL included development and testing of reactor technologies, chemical separations of radioisotopes for government and commercial use, and basic research in engineering and the physical and biological sciences [Checkoway et al., 1985; Burns, 2007].

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Although there are historical records of occupational exposures to ionizing radiation at ORNL, there is little information with which to classify workers according to levels of exposure to non-radiological hazards, such as asbestos, solvents, and metals [Wing et al., 1993]. In the absence of reliable exposure information, effects of workplace hazards can be investigated by comparing mortality rates for an occupational cohort with mortality rates for an external reference population. Previous investigators compared cause-specific mortality in a cohort of white male ORNL workers hired prior to 1973 who had vital status and cause of death information ascertained through 1984 with expectations based upon mortality rates for white males in the US population [Wing et al., 1991]. They found that this group of ORNL workers had fewer deaths due to all causes [standardized mortality ratio (SMR = 0.74, 95% CI: 0.71, 0.78)], all cancers (SMR = 0.79, 95% CI: 0.71, 0.88), and lung cancer (SMR = 0.65, 95% CI: 0.52, 0.79) than expected, but this group had more deaths than expected due to leukemia (SMR = 1.63, 95% CI: 1.08, 2.35). Consequently, leukemia mortality was of a priori interest in this updated analysis.

In this article, we report on cause-specific mortality in an expanded cohort of ORNL workers for whom vital status and cause of death information has been ascertained through 2008. Mortality rates in the study population are compared with mortality rates for the US and Tennessee.

MATERIALS AND METHODS

We report on a cohort of 22,831 ORNL workers who were hired prior to 1985 and who worked at least 30 days. Seventeen workers with incomplete information on name, Social Security number, date of birth, or date of first hire were excluded from this cohort. During World War II, the facility was operated by the E.I. DuPont de Nemours Corporation; and, afterwards it was operated briefly by Monsanto Chemical Company and the Atomic Energy Commission. From March 1948 through March 1984, ORNL was operated by Union Carbide Corporation (and its predecessor, Carbide and Carbon Chemical Company). The employment records of these prime operations contractors were used to construct this cohort. A previous analysis of mortality among ORNL workers examined a cohort of workers who were hired prior to 1973, and who worked at least 30 days [Richardson and Wing, 1999]. We have expanded the cohort to include workers hired prior to 1985. The study protocol was reviewed and approved by the Institutional Review Board of the University of North Carolina.

The names and Social Security numbers of cohort members who had not been identified previously as deceased were submitted to the Social Security Administration (SSA) and the National Death Index (NDI) for determination of vital status through December 31, 2008. We used the NDI-Plus service to obtain underlying cause of death for deceased workers identified by the NDI. For deaths prior to 1979, cause of death information was coded according to the Eighth revision of the International Classification of Diseases (ICD); for deaths occurring in 1979 and later, cause of death information was coded to the ICD revision in effect at the time of death. If they were not identified by NDI, workers confirmed to be alive on January 1, 1979 or later by the SSA or by the Site's employment records were assumed to be alive as of December 31, 2008. Those lost to follow-up before January 1, 1979 were only considered alive until the date last observed. With updated follow-up, eight workers who were previously classified as white have been reclassified as non-white.

The mortality experience of the cohort was analyzed using the NIOSH modified Life Table Analysis System (LTAS.NET) [Steenland et al., 1990; Robinson et al., 2006; Schubauer-Berigan et al., 2011]. Each cohort member accumulated person-time from their date of entry (completion of 30 days of employment) until the earliest of the following: the date of death for deceased cohort members, the date last observed for persons lost to follow-up, or the ending date of the study (December 31, 2008). Person-time at risk was multiplied by quinquennial age-, calendar period-, sex-, race (white or non-white)-, and cause-specific U.S. mortality rates to calculate the expected number of deaths. The ranges of ICD codes associated with each category of cause of death used in these analyses are described by Robinson et al. [2006]. The ratio of observed to expected number of deaths was expressed as the SMR. Decedents for whom the underlying cause of death was unknown contributed to the calculation of the SMR for all cause mortality. A 95% confidence interval was computed using exact methods when the number of observed deaths was ≤ 10 (but >0) and an approximation when the number of observed deaths was 11 or more [Schubauer-Berigan et al., 2011]. If the number of observed deaths was zero, neither an SMR nor a confidence interval was calculated; rather, we report the observed and expected numbers of deaths. The mortality analysis was repeated using Tennessee state mortality rates for the period 1960–2008; person-time and deaths occurring prior to 1960 were excluded from these analyses.

SMRs were calculated separately for males and females. Analyses of male workers were conducted stratified by worker's pay code at time of hire (monthly-, weekly-, or hourly-paid workers), which was derived from employment history records. Monthly-paid male workers were primarily engineers, chemists, physicists, and other research staff. Weekly-paid male workers were primarily clerks and kindred workers, technicians, and security personnel. Hourly-paid male workers were primarily employed as laborers, machinists, pipefitters, operators and other skilled manual workers, although some trades changed over time. Since most female workers were weekly-paid, analyses of female workers were not conducted with stratification by pay code. Race-specific results are not reported in this paper as mortality ratios for non-white workers tended to be highly imprecise.

In addition to exposures in the workplace being studied, exposures from other employment (and non-occupational exposures) also influence SMRs. Although complete non-ORNL employment histories are not available, information is available on employment at other DOE facilities including the Tennessee Eastman Corporation (TEC), Y-12 uranium enrichment facility, and K-25 gaseous diffusion plant, other nuclear weapons facilities in Oak Ridge, TN [Frome et al., 1997]. Therefore, we report SMRs for select causes of death separately for those employed only at ORNL and for those with known employment at other DOE facilities.

RESULTS

The cohort included 16,912 men and 5,919 women (Table I). With follow-up through 2008, 45% of the men and 27% of the women were deceased, 57% were alive at the end of follow-up, and 2% were lost to follow-up. Information on underlying cause of death was collected for 99% of decedents. The distribution of workers with respect to pay code was notably different for males and females: 83% of females were weekly-paid, while 43% of males were monthly-paid, 35% weekly-paid, and 21% hourly-paid. Among the 7,587 workers who had ever worked at another DOE facility, 3659 were first hired at ORNL, while the remainder came from another facility to ORNL.

Table II shows SMRs for men. Lung cancer SMRs were somewhat below unity among hourly-paid (SMR = 0.93, 95% CI: 0.80, 1.08), lower for weekly-paid (SMR = 0.79, 95% CI: 0.69, 0.90), and very low for monthly-paid men (SMR = 0.34, 95% CI: 0.29, 0.40), while the SMR for cancers of other respiratory sites was elevated for hourly-paid men (SMR = 1.82, 95% CI: 0.22, 6.58). Mortality from cancer of the pleura was substantially elevated for hourly-paid (SMR = 12.09, 95% CI: 4.44, 26.32) men. Bladder cancer SMRs were elevated for hourly-paid (SMR = 1.89, 95% CI: 1.26, 2.71) and weekly-paid (SMR = 1.52, 95% CI: 1.07, 2.11) men. Skin cancer mortality was elevated among hourly-paid (SMR = 1.29, 95% CI: 0.70, 2.16) and weekly-paid (SMR = 1.03, 95% CI: 0.60, 1.65) men. Mortality from mesothelioma was elevated for weekly-paid men (SMR = 2.24, 95% CI: 0.61, 5.73) and monthly-paid men (SMR = 1.37, 95% CI: 0.44, 3.20).

TABLE I. Cohort Description

	Male		Female	
	n	%	n	%
Total	16,912	100	5,919	100
Paycode				
Hourly	3,624	21.4	342	5.8
Weekly	5,953	35.2	4,912	83.0
Monthly	7,335	43.4	665	11.2
Missing	0		0	
Race				
White	15,569	92.1	5,281	89.2
Non-white	1,343	7.9	638	10.8
DOE facilities				
ORNL only	11,067	65.4	4,177	70.6
ORNL and others	5,845	34.6	1,742	29.4
Vital status				
Alive	8,973	53.1	4,118	69.6
Dead	7,636	45.1	1,591	26.9
Lost to follow-up	303	1.8	210	3.6
	Mean	**(SD)**	**Mean**	**(SD)**
Year of birth	1930	(16)	1937	(15)
Year of hire	1960	(12)	1964	(13)
Age at entry, years	30	(8)	26	(8)
Length of follow-up, years	39	(13)	39	(14)

Oak Ridge National Laboratory workers who were hired prior to 1985 and who worked at least 30 days.

Table II also shows that among hematopoietic malignancies, SMRs for non-Hodgkin's lymphoma (NHL) were above unity in all pay groups (SMR = 1.10, 95% CI: 0.69, 1.67; SMR = 1.02, 95% CI: 0.69, 1.46; and, SMR = 1.26, 95% CI: 0.97, 1.62 for hourly-, weekly-, and monthly-paid workers, respectively). Hodgkin's disease was elevated among weekly-paid men (SMR = 1.58, 95% CI: 0.64, 3.26). Leukemia SMRs were above unity in hourly- (SMR = 1.33, 95% CI: 0.87, 1.93) and weekly-paid (SMR = 1.03, 95% CI: 0.71, 1.46) men. The SMR for multiple myeloma was 1.28 for hourly-paid men (95% CI: 0.66, 2.24).

All-cause mortality was 10%, 15%, and 45% below national rates among hourly-, weekly-, and monthly-paid men, respectively. The non-malignant categories of cause of death for which observed deaths exceeded expectation included diseases of the blood and blood forming organs among hourly-paid (SMR = 1.08, 95% CI: 0.50, 2.06) and weekly-paid (SMR = 1.04, 95% CI: 0.55, 1.78) men,

TABLE II. Standardized Mortality Ratios Based Upon US Mortality Rates by Pay Code

Pay code Cause	Hourly				Weekly				Monthly			
	Obs	SMR	95% CI		Obs	SMR	95% CI		Obs	SMR	95% CI	
Tuberculosis	1	0.17	0.00	0.94	5	0.33	0.11	0.77	0	—	[9.51]	
Malignant neoplasms												
MN lip	1	5.42	0.14	30.21	0	—	[0.33]		0	—	[0.41]	
MN tongue	2	0.71	0.09	2.57	3	0.70	0.14	2.04	2	0.33	0.04	1.20
MN other buccal	2	0.63	0.08	2.27	7	1.45	0.58	2.99	3	0.43	0.09	1.26
MN pharynx	2	0.33	0.04	1.18	8	0.88	0.38	1.74	2	0.15	0.02	0.56
MN esophagus	7	0.43	0.17	0.89	21	0.88	0.54	1.34	26	0.71	0.46	1.04
MN stomach	12	0.69	0.35	1.20	22	0.76	0.48	1.16	18	0.49	0.29	0.77
MN intestine	42	0.90	0.65	1.22	65	0.93	0.71	1.18	90	0.82	0.66	1.01
MN rectum	8	0.77	0.33	1.52	11	0.66	0.33	1.18	15	0.65	0.36	1.06
MN biliary, liver, gall bladder	15	1.00	0.56	1.65	12	0.53	0.28	0.93	16	0.46	0.26	0.75
MN pancreas	28	1.01	0.67	1.46	33	0.80	0.55	1.12	60	0.93	0.71	1.20
MN peritoneum, oth and unspec site di	0	—	[1.90]		1	0.33	0.01	1.86	2	0.46	0.06	1.67
MN larynx	6	0.91	0.33	1.97	7	0.71	0.29	1.46	2	0.14	0.02	0.50
MN trachea, bronchus, lung	176	0.93	0.80	1.08	214	0.79	0.69	0.90	148	0.34	0.29	0.40
MN pleura	6	12.09	4.44	26.32	1	1.44	0.04	8.00	1	0.87	0.02	4.85
MN other respiratory sites	2	1.82	0.22	6.58	1	0.60	0.02	3.36	1	0.42	0.01	2.33
MN breast	1	1.46	0.04	8.12	3	2.85	0.59	8.34	0	—	[1.58]	
MN prostate	48	0.95	0.70	1.25	74	0.97	0.76	1.21	104	0.83	0.68	1.00
MN other male genital	1	0.71	0.02	3.96	2	0.77	0.09	2.77	1	0.32	0.01	1.78
MN kidney	4	0.29	0.08	0.75	5	0.25	0.08	0.58	12	0.37	0.19	0.65
MN bladder and other urinary	29	1.89	1.26	2.71	36	1.52	1.07	2.11	36	0.94	0.66	1.30
MN skin	14	1.29	0.70	2.16	17	1.03	0.60	1.65	26	0.96	0.63	1.40
Mesothelioma (1999–2008)	1	0.78	0.02	4.37	4	2.24	0.61	5.73	5	1.37	0.44	3.20
MN eye	0	—	[0.29]		0	—	[0.46]		0	—	[0.67]	
MN brain and other nervous	14	1.07	0.58	1.79	21	1.05	0.65	1.61	26	0.86	0.56	1.26
MN thyroid	0	—	[0.97]		1	0.68	0.02	3.78	2	0.87	0.11	3.16
MN bone	2	1.59	0.19	5.76	0	—	[2.10]		3	1.12	0.23	3.28
MN connective	2	0.75	0.09	2.7	3	0.75	0.15	2.18	7	1.09	0.44	2.25
MN other and unspec. site (min)	35	0.93	0.65	1.29	51	0.89	0.66	1.17	49	0.55	0.41	0.73
Non-Hodgkin's lymphoma	22	1.10	0.69	1.67	30	1.02	0.69	1.46	62	1.26	0.97	1.62
Hodgkin's disease	1	0.38	0.01	2.12	7	1.58	0.64	3.26	5	0.90	0.29	2.10
Leukemia	27	1.33	0.87	1.93	32	1.03	0.71	1.46	41	0.83	0.60	1.13
Multiple myeloma	12	1.28	0.66	2.24	9	0.66	0.30	1.26	20	0.91	0.55	1.40
Benign and unspec neoplasms	6	0.88	0.32	1.91	6	0.57	0.21	1.23	11	0.67	0.34	1.20
Diabetes mellitus	41	0.89	0.64	1.21	42	0.61	0.44	0.82	39	0.35	0.25	0.48
Dis. blood and blood-forming organs	9	1.08	0.50	2.06	13	1.04	0.55	1.78	15	0.71	0.40	1.18
Mental and psych. disorders	19	0.70	0.42	1.09	40	0.99	0.70	1.34	50	0.68	0.50	0.90
Nervous system disorders	43	0.95	0.69	1.28	73	1.10	0.86	1.38	121	0.95	0.79	1.14
Diseases of the heart	621	0.82	0.76	0.89	938	0.78	0.73	0.84	857	0.49	0.46	0.52
Other dis. circulatory system	156	0.86	0.73	1.01	279	0.94	0.83	1.05	252	0.60	0.53	0.68
Dis. respiratory system	191	1.03	0.89	1.19	243	0.86	0.76	0.98	206	0.44	0.38	0.51
Diseases digestive system	63	0.71	0.54	0.90	99	0.71	0.58	0.87	80	0.40	0.32	0.50
Diseases genito-urinary syst.	35	0.95	0.66	1.32	40	0.67	0.48	0.92	47	0.51	0.38	0.68
Dis. skin and subcutaneous	1	0.48	0.01	2.68	2	0.61	0.07	2.22	4	0.85	0.23	2.18
Dis. musculoskeletal and connective	10	1.94	0.93	3.57	8	1.03	0.44	2.02	14	1.10	0.60	1.85
Sympt. and ill-def. conditions	57	2.61	1.98	3.38	88	2.48	1.99	3.05	36	0.78	0.54	1.07
Accidents	90	0.92	0.74	1.13	131	0.75	0.63	0.89	104	0.49	0.40	0.60
Violence	48	0.94	0.69	1.25	77	0.89	0.70	1.11	65	0.64	0.49	0.82
Other and unspec. causes	42	0.81	0.58	1.09	93	1.13	0.91	1.38	117	0.95	0.79	1.14
All cancers	522	0.96	0.88	1.04	701	0.86	0.80	0.93	785	0.61	0.57	0.66
All deaths	1,955	0.90	0.86	0.94	2,878	0.85	0.82	0.88	2,803	0.55	0.53	0.57

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval.
Male Oak Ridge National Laboratory workers who were hired prior to 1985 and who worked at least 30 days.

respiratory system diseases among hourly-paid men (SMR = 1.03, 95% CI: 0.89, 1.19), nervous system disorders among weekly-paid men (SMR = 1.10, 95% CI: 0.86, 1.38), and musculoskeletal system diseases among hourly-, weekly-, and monthly-paid men (SMR = 1.94, 95% CI: 0.93, 3.57; SMR = 1.03, 95% CI: 0.44, 2.02; and, SMR = 1.10, 95% CI: 0.60, 1.85, respectively). Deaths certified to symptoms, signs and ill-defined conditions were elevated among hourly-paid (SMR = 2.61, 95% CI: 1.98, 3.38) and weekly-paid (SMR = 2.48, 95% CI: 1.99, 3.05) men. Analyses of SMRs for males based on Tennessee state mortality rates as the referent produced similar results to those obtained in analyses using US mortality rates as the referent, although the SMRs for bladder cancer were of larger magnitude when based upon Tennessee referent rates and the deficits of lung cancer were greater (Supplementary Table A1, available with the electronic version of this article).

Table III shows SMRs for women. Categories of cancer mortality with SMRs greater than unity were cancer of the pharynx (SMR = 1.15, 95% CI: 0.24, 3.37), esophagus (SMR = 1.70, 95% CI: 0.78, 3.23), rectum (SMR = 1.08, 95% CI: 0.49, 2.05), peritoneum (SMR = 1.71, 95% CI: 0.47, 4.38), bladder (SMR = 2.20, 95% CI: 1.20, 3.69), skin (SMR = 1.06, 95% CI: 0.46, 2.09), connective tissue (SMR = 1.18, 95% CI: 0.32, 3.03), and leukemia (SMR = 1.64, 95% CI: 1.09, 2.36). The number of deaths due to all causes was less than expected based upon national rates (SMR = 0.85, 95% CI: 0.81, 0.90). Non-malignant categories of cause of death for which SMRs were greater than unity include tuberculosis (SMR = 1.01, 95% CI: 0.28, 2.60), death due to benign and unspecified neoplasms (SMR = 1.07, 95% CI: 0.49, 2.03), nervous system disorders (SMR = 1.21, 95% CI: 0.95, 1.52), and deaths due to symptoms and ill-defined conditions (SMR = 2.07, 95% CI: 1.47, 2.83), accidents (SMR = 1.06, 95% CI: 0.82, 1.36), and violence (SMR = 1.41, 95% CI: 0.99, 1.96). Analyses of SMRs for females based on Tennessee state mortality rates as the referent produced similar results to those obtained in analyses using US mortality rates as the referent (Supplementary Table A2, available with the electronic version of this article).

The relative excess of deaths due to pleural cancer and mesothelioma was greater among men who had worked at other DOE facilities as well as ORNL (SMR = 4.25, 95% CI: 1.16, 10.89 and SMR = 2.72, 95% CI: 1.09, 5.60) for deaths due to pleural cancer and mesothelioma, respectively) compared to those who had only worked at ORNL (SMR = 2.85, 95% CI 0.78, 7.30 and SMR = 0.73, 95% CI 0.15, 2.12) for deaths due to pleural cancer and mesothelioma, respectively). SMRs for cancer of the bladder and other urinary organs also were higher among men who had also worked at other DOE facilities (SMR = 1.49, 95% CI: 1.09, 1.99), particularly those who ever worked at K-25 (SMR = 1.88, 95% CI: 1.18, 2.85) and those who ever worked at TEC (SMR = 1.95; 95% CI: 1.07, 3.28), than men who had only worked at ORNL (SMR = 1.19; 95% CI: 0.90, 1.54). Excess leukemia mortality occurred among men who only worked at ORNL (SMR = 1.13; 95% CI: 0.88, 1.43), while there was not an excess of leukemia among men who had worked at other DOE facilities (SMR = 0.77; 95% CI: 0.52, 1.11).

There were no deaths due to cancer of the pleura prior to 1980; in 1980–1984, and in all subsequent periods through 1999, the SMR for cancer of the pleura among men was above unity (Table IV). Specific reference rates for death due to mesothelioma only began to be tabulated in 1999; for the period 1995–1999, and all subsequent 5-year periods, the SMR for mesothelioma among men was above unity (Table IV). Lagging entry by 5 years had no effect on the SMRs for time periods from 1990 onwards, since workers entered follow-up through 1985. No deaths due to pleural cancer or mesothelioma were observed among women (Table III). The largest relative excess of leukemia mortality among men occurred in the period 1965–1969; the largest relative excesses of deaths due to NHL among men occurred in the periods 2000–2004 and 2005–2008 (Table IV).

DISCUSSION

Prior mortality studies of ORNL workers were limited by the fact that most workers were alive at the end of follow-up and therefore not informative for analyses regarding cause-specific mortality [Checkoway et al., 1985; Wing et al., 1991; Frome et al., 1997]. A major motivation for updating vital status follow-up information through 2008 for this cohort was to more completely study the mortality experience of workers employed at ORNL. Similar to past studies of ORNL workers, this updated cohort of ORNL experienced lower death rates than the US population. Low death rates relative to the nation are to be expected because people who are too sick to work are excluded from employment and because employment itself promotes health through economic, social, and psychological mechanisms, especially for workers employed by large companies that provide steady employment, relatively good wages, health and safety protections, medical insurance, and pension benefits. SMRs for the two leading causes of death in the USA, heart disease and cancer, are less than unity for men (Table II) and women (Table III).

Despite evidence that this is a relatively healthy population, some groups of ORNL workers had higher mortality rates than the US population for diseases that are plausibly related to occupational exposures. SMRs for

TABLE III. Standardized Mortality Ratios Among Female Oak Ridge National Laboratory Workers Who Were Hired Prior to 1985 and Who Worked at Least 30 Days.

Cause	Obs	SMR	95% CI	
Tuberculosis	4	1.01	0.28	2.60
Malignant neoplasms				
MN lip	0	—	[0.03]	
MN tongue	1	0.70	0.02	3.88
MN other buccal	1	0.54	0.01	3.01
MN pharynx	3	1.15	0.24	3.37
MN esophagus	9	1.70	0.78	3.23
MN stomach	7	0.68	0.27	1.40
MN intestine	37	0.79	0.56	1.09
MN rectum	9	1.08	0.49	2.05
MN biliary, liver, gall bladder	7	0.55	0.22	1.13
MN pancreas	23	0.84	0.54	1.27
MN peritoneum, oth and unspec site di	4	1.71	0.47	4.38
MN larynx	1	0.56	0.01	3.12
MN trachea, bronchus, lung	110	0.89	0.73	1.07
MN pleura	0	—	[0.16]	
MN other respiratory sites	0	—	[0.84]	
MN breast	89	0.89	0.71	1.09
MN cervix	5	0.37	0.12	0.87
MN other parts of uterus	14	0.98	0.54	1.65
MN ovary	28	0.85	0.56	1.22
MN other female genital	1	0.45	0.01	2.50
MN prostate	0	—		
MN other male genital	0	—		
MN kidney	6	0.67	0.25	1.47
MN bladder and other urinary	14	2.20	1.20	3.69
MN skin	8	1.06	0.46	2.09
Mesothelioma (1999–2008)	0	—	[0.39]	
MN eye	0	—	[0.28]	
MN brain and other nervous	6	0.46	0.17	1.00
MN thyroid	0	—	[1.45]	
MN bone	0	—	[1.06]	
MN connective	4	1.18	0.32	3.03
MN other and unspec. site	31	0.84	0.57	1.19
Non-Hodgkin's lymphoma	15	0.77	0.43	1.27
Hodgkin's disease	0	—	[2.19]	
Leukemia	28	1.64	1.09	2.36
Multiple myeloma	6	0.67	0.25	1.47
Benign and unspec neoplasms	9	1.07	0.49	2.03
Diabetes mellitus	34	0.62	0.43	0.86
Dis. blood and blood-forming organs	4	0.46	0.12	1.17
Mental and psych. disorders	34	0.97	0.67	1.36
Nervous system disorders	75	1.21	0.95	1.52
Diseases of the heart	350	0.70	0.63	0.78
Other dis. circulatory system	178	0.93	0.80	1.08
Dis. respiratory system	157	0.97	0.82	1.13
Diseases digestive system	42	0.55	0.39	0.74
Diseases genito-urinary syst.	25	0.63	0.41	0.92
Dis. skin and subcutaneous	2	0.68	0.08	2.47
Dis. musculoskeletal and connective	10	0.81	0.39	1.49
Sympt. and ill-def. conditions	39	2.07	1.47	2.83
Accidents	65	1.06	0.82	1.36
Violence	36	1.41	0.99	1.96
Other and unspec. causes	60	0.97	0.74	1.25
All cancers	467	0.87	0.79	0.95
All causes	1,591	0.85	0.81	0.90

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval.
The bracketed value is the expected number of deaths. SMRs and associated confidence intervals were not calculated if the observed number of events was zero.

cancer of the pleura, a disease strongly related to asbestos exposure, were elevated among hourly- and weekly-paid men (Table II), during 1980–1999 (Table IV), and among men who were employed at other US DOE facilities in addition to ORNL. Excess mortality due to pleural cancer has also been observed among workers at the Savannah River Site, another nuclear weapons plant in the southeastern USA; and, an excess of deaths due to pleural cancer has been reported among nuclear workers at a national laboratory in Australia [Habib et al., 2005, 2006], nuclear facilities in the United Kingdom [Muirhead et al., 1999; Omar et al., 1999; McGeoghegan and Binks, 2000, 2001], and France [Telle-Lamberton et al., 2004]. Previous studies have found that deaths due to malignant mesothelioma often accounted for the majority of deaths classified as pleural cancer [Steenland et al., 1990; Robinson et al., 2006]. Prior to the 10th revision of the ICD there was not a separate code for malignant mesothelioma; mesothelioma deaths were coded to the site specified on the death certificate. In our SMR analyses an excess of deaths due to mesothelioma was coincident with a change from ICD-9 to ICD-10 coding for causes of death in 1999. The observed excess of deaths due to pleural cancer and mesothelioma differ from prior reports on mortality among ORNL workers, perhaps reflecting updated follow-up of the cohort and inclusion of workers with employment at other DOE facilities in the current study (the excess of pleural cancer and mesothelioma was greater among men who had worked at other DOE facilities).

An excess of deaths due to bladder cancer is another finding that differs from previous reports [Checkoway et al. 1985; Wing et al., 1991]. In the current analysis we observed excess bladder cancer among hourly- and weekly-paid men, women, and among workers who had worked at other DOE facilities. Smoking is a strong risk factor for

TABLE IV. Standardized Mortality Ratios (and Approximate 95% Confidence Intervals) for Leukemia and Non-Hodgkin's Lymphoma (NHL) Based Upon US Mortality Rates by 5-Year Calendar Periods of Observation

	Leukemia			NHL			Pleura cancer			Mesothelioma		
Period	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI	Obs	SMR	95% CI
1943–1964	2	0.32	0.04, 1.17	5	1.32	0.43, 3.07	0	—	[0.01]	—	—	—
1965–1969	11	2.96	1.47, 5.29	1	0.32	0.01, 1.77	0	—	[0.05]	—	—	—
1970–1974	6	1.27	0.47, 2.78	5	1.20	0.39, 2.80	0	—	[0.16]	—	—	—
1975–1979	9	1.43	0.66, 2.72	4	0.74	0.20, 1.89	0	—	[0.33]	—	—	—
1980–1984	9	1.08	0.49, 2.05	4	0.53	0.14, 1.35	1	3.04	0.08, 16.94	—	—	—
1985–1989	8	0.77	0.33, 1.52	5	0.47	0.15, 1.10	1	2.32	0.06, 12.94	—	—	—
1990–1994	11	0.84	0.42, 1.50	17	1.21	0.70, 1.94	4	7.55	2.06, 19.34	—	—	—
1995–1999	12	0.76	0.39, 1.34	19	1.08	0.65, 1.69	2	4.33	0.52, 15.63	1	1.61	0.04, 8.96
2000–2004	15	0.85	0.48, 1.41	29	1.61	1.08, 2.31	0	—	[0.08]	4	1.18	0.32, 3.03
2005–2008	17	1.16	0.67, 1.85	25	1.79	1.16, 2.65	0	—	[0.05]	5	1.85	0.60, 4.31

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval.
Male ORNL workers who were hired prior to 1985 and who worked at least 30 days.
The bracketed value is the expected number of deaths. SMRs and associated confidence intervals were not calculated if the observed number of events was zero.

bladder cancer; however, the relative risk of lung cancer due to smoking is roughly an order of magnitude higher than for bladder cancer, and the SMR for lung cancer is below unity even for hourly-paid men. These findings suggest that the reported SMRs for bladder cancer may be negatively confounded by smoking, since smoking may have been less common among ORNL workers than among the general population. We found that the bladder cancer excess was somewhat larger among ORNL workers who had also worked at other DOE facilities, such as the K-25 gaseous diffusion facility. A previous study suggested excess bladder cancer among K-25 workers, a facility where workers had potential for exposure to uranium dust and chemicals including epoxy resin, solvents, powdered nickel, and nickel oxides [Cragle et al., 1992]. More hourly-paid workers than monthly-paid workers were employed at other DOE facilities located in Oak Ridge, TN, and therefore the physical and chemical hazards to which hourly- and weekly-paid employees were exposed at other Oak Ridge, TN facilities may have been less common for monthly-paid workers. Further efforts are needed to assess specific exposures that may be related to the elevated SMR for bladder cancer observed among ORNL workers.

An excess of leukemia was observed among females and hourly-paid male workers. The leukemia excess was among workers who were not known to have worked at a DOE facility other than ORNL, and is consistent with prior findings of excess leukemia mortality at ORNL compared to other Oak Ridge facilities [Frome et al., 1997]. Ionizing radiation is an established cause of leukemia, and a prior follow-up of a subgroup of this cohort showed that excess leukemia mortality was higher among men who were monitored for internal radionuclide contamination than among other men. Additionally, prior studies have shown positive associations between external ionizing radiation dose and leukemia mortality in this cohort [Checkoway et al., 1985; Wing et al., 1991]; and, a pooled analysis of non-CLL leukemia risk among US nuclear workers found that risk estimates for ORNL workers were intermediate in magnitude when compared to Hanford, Los Alamos National Laboratory, Savannah River Site, and Portsmouth Naval Shipyard workers [Schubauer-Berigan et al., 2007]. The SMR for leukemia has diminished in more recent calendar periods, as has the annual collective dose for workers at the site. Future work will investigate associations between individual radiation dose estimates and leukemia mortality in this cohort with updated follow-up.

Differences in mortality by pay code may reflect differences between pay code groups in occupational and environmental exposures and living conditions, including regional differences in factors such as diet and tobacco use. For example, lung cancer SMRs were nearest to unity among hourly-paid males and substantially less than unity among monthly-paid males. Differences in cigarette smoking offer a plausible explanation for this gradient in lung cancer SMRs, although given the evidence of excess pleural cancer and the potential occupational exposure to a number of lung carcinogens, including ionizing radiation, variation in occupational exposures by pay code could also contribute to the gradient in lung cancer.

Despite the deficit in mortality for many major nonmalignant categories of cause of death, the excess from diseases of the musculoskeletal system among men is notable and has not been reported previously. The excess of deaths due to symptoms and ill-defined conditions is consistent with observations of previous investigators, who have attributed this to local and regional practices in assignment of causes of death [Cragle and Fetcher, 1992]. Excess mortality attributed to symptoms and ill-defined conditions may result in downward bias in SMRs for specific causes. This would tend to have small impact on common causes of death but could make a larger impact on more uncommon causes such as site-specific cancers.

This study provides evidence of excess mortality due to bladder cancer, leukemia, mesothelioma, and pleural cancer among hourly paid males, excess bladder cancer and leukemia among females, and evidence of excess NHL among males in the most recent years of follow-up. The evidence of excess mortality due to bladder cancer, mesothelioma, cancer of the pleura, and NHL has not been noted before in this cohort. The leukemia excess among males has been reported previously though evidence of excess leukemia mortality among females has not. The findings of this study underscore the importance of long-term follow-up of former nuclear workers in order to understand the range of potential occupational health effects associated with production activities in the nuclear weapons complex—particularly to identify occupational diseases with long latency periods and occupational exposures with enduring effects.

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