

# Mortality Among Workers at the Savannah River Site

David B. Richardson, PhD,\* Steve Wing, PhD, and Susanne Wolf, MPH

**Background** Workers employed at the Savannah River Site (SRS) were potentially exposed to a range of chemical and physical hazards, many of which are poorly characterized. We therefore compared the observed deaths among workers to expectations based upon death rates for referent populations.

**Methods** The cohort included 18,883 SRS workers hired between 1950 and 1986. Vital status and cause of death information were ascertained through 2002. Sex-specific standardized mortality ratios (SMR) were computed using U.S. and South Carolina mortality rates. SMRs were tabulated separately for monthly-, weekly-, and hourly-paid men.

**Results** Males had fewer deaths from all causes [SMR = 0.80, 90% confidence interval (CI): 0.78, 0.82], all cancers (SMR = 0.85, 90% CI: 0.81, 0.89), and lung cancer (SMR = 0.88, 90% CI: 0.82, 0.95) than expected based upon US mortality rates. The SMR for cancer of the pleura was 4.25 (90% CI: 1.99, 7.97) for men. The SMR for leukemia was greater than unity for monthly-paid (SMR = 1.33, 90% CI: 0.88, 1.93) and hourly-paid (SMR = 1.36, 90% CI: 1.02, 1.78) men. Female workers had fewer deaths from all causes (SMR = 0.75, 90% CI: 0.69, 0.82) than expected, but more deaths than expected from cancer of the kidney (SMR = 2.58, 90% CI: 1.21, 4.84) and skin (SMR = 3.90, 90% CI: 2.11, 6.61).

**Conclusions** While the observed numbers of deaths in most categories of cause of death were less than expected, there are greater than expected numbers of deaths due to cancer of the pleura and leukemia, particularly among hourly-paid male workers. It is plausible that occupational hazards, including asbestos and ionizing radiation, contribute to these excesses. Am. J. Ind. Med. 50:881–891, 2007. © 2007 Wiley-Liss, Inc.

**KEY WORDS:** cohort studies; mortality study; Savannah River Site; occupational diseases

## INTRODUCTION

In 1950, the E.I. du Pont Nemours and Company (DuPont) contracted with the Atomic Energy Commission to construct

and operate a facility to produce nuclear materials. The facility, located near Aiken, South Carolina, became known as the Savannah River Site (SRS). Over its history, the site has operated five large reactors, two chemical separation areas, a heavy water extraction plant, nuclear fuel, and target fabrication plants, as well as test reactors, power plants, and laboratories. DuPont managed and operated the site through March 1989, when the Westinghouse Corporation took over operations.

Cragle et al. [1998] compared cause-specific mortality in a cohort of 9,860 white male SRS workers who had vital status and cause of death information ascertained through 1986 with mortality of US white men. They found that salaried workers had substantially fewer deaths due to all causes [standardized mortality ratio (SMR) = 0.60, 95% CI: 0.54, 0.67], all cancers (SMR = 0.71, 95% CI: 0.58, 0.87), and lung cancer (SMR = 0.60, 95% CI: 0.41, 0.85) than white

The supplemental table appendices described in this article can be found at <http://www.interscience.wiley.com/jpages/0271-3586/suppmat>.

Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

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\*Correspondence to: David B. Richardson, Department of Epidemiology, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599.  
E-mail: david.richardson@unc.edu

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males in the US population. Non-salaried workers had slightly lower all cause and all cancer mortality rates than the general population (SMRs = 0.85 and 0.86, respectively) but had slightly higher mortality rates for lung cancer (SMR = 1.08, 95% CI: 0.91, 1.28). Leukemia mortality was in excess among salaried (SMR = 1.10, 95% CI: 0.40, 2.40) and non-salaried (SMR = 1.34, 95% CI: 0.80, 2.09) workers when compared to expectations based upon US mortality rates [Cragle et al., 1988, 1998].

Comparison of cause specific mortality of an occupational cohort to an external referent population, usually implemented through indirect adjustment for age and calendar time using SMRs, can help in etiologic research on occupational exposures. This method of analysis is useful in settings in which there is little or no ability to accurately discriminate between workers in a study cohort with respect to exposure level (either because exposure estimates are unreliable or because historical exposures were similar for most workers). Although there are relatively good historical records of SRS workers' exposures to ionizing radiation [Richardson et al., 2006], there is little information about exposures to other chemical and physical hazards at the site, which include acids, solvents, asbestos, and hydrazine [Hickey and Cragle, 1985; Makie et al., 2005].

Interpretation of the SMR as an effect measure that represents the independent effect of occupational exposures requires comparability (or "exchangeability") of the study population and the external referent population. It is widely recognized that this condition is not met for analyses of most common causes of death because of the "healthy worker effect (HWE)," which involves: (1) exclusion of people too sick to work from employment, (2) termination of employment for people who become sick once employed, and (3) socioeconomic and lifestyle differences between people who work and those who don't, particularly in studies of workers employed by corporations that pay their workers relatively well and provide pension and health benefits [McMichael, 1976; Wilcosky and Wing, 1987; Arrighi and Hertz-Picciotto, 1994]. In studies of workers employed in the nuclear industry deficits in all cause and all cancer mortality are often observed when contrasts are drawn to the general population [Vrijheid et al., 2007]. However, for analyses of diseases that are not strongly related to socioeconomic and lifestyle factors, that do not cause symptoms affecting ability to work for long periods prior to death, and that are caused by exposures that occur primarily in the workplace under study and rarely elsewhere, there may be a reasonable degree of exchangeability between the study and referent populations and relatively little bias due to the "HWE." Alternatively, to the extent that SMRs for leading causes of death reflect living conditions, they provide clues about generalized susceptibility of the working population and they may provide useful contrasts with SMRs for specific causes of death that may be related to occupational exposures.

The aim of this article is to report on SMR analyses of an expanded cohort of SRS workers followed through 2002. Analyses contrast mortality rates in the study population to mortality rates for the US and South Carolina.

## MATERIALS AND METHODS

We report on a cohort of 18,883 SRS workers who were hired by DuPont prior to 1987 and who worked at least 90 days. Workers without complete information on name, SSN, date of birth, and date of first hire were excluded. The original study cohort analyzed by Cragle et al. [1988] ( $n = 9,860$ ) was defined as all white male workers who were hired by DuPont prior to 1974 and employed for at least 90 days. We have expanded the cohort to include males and females of all races hired by DuPont prior to 1987; we did not include workers hired in more recent years given the low mortality expected among more recently-hired workers and the changes in record keeping that occurred when Westinghouse Corporation took over as the prime operations contractor from DuPont.

The names and social security numbers of cohort members who had not previously been identified as deceased by Cragle et al. [1998] were submitted to the Social Security Administration (SSA) and the National Death Index (NDI) for determination of vital status through December 31, 2002. We used the NDI-Plus service to obtain underlying and contributing causes of death for deceased workers identified by the NDI. For deaths occurring 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 there was no death indication for a worker and they were confirmed to be alive on January 1, 1979 or later by the SSA or by the site's employment records then they were assumed to be alive as of December 31, 2002. Those lost to follow-up before January 1, 1979 were only considered alive until the date last observed. Decedents for whom the underlying cause of death was unknown contributed to the calculation of the SMR for all causes of death.

The mortality experience of the cohort was analyzed using the NIOSH modified life table analysis system (LTAS) [Steenland et al., 1990; Robinson et al., 2006]. Each cohort member accumulated person-time from their date of entry (completion of 90 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, 2002). Person-time at risk was multiplied by the appropriate U.S. age-, sex-, race- (white or non-white), calendar period-, and cause-specific mortality rates to calculate the expected number of deaths. The ranges of ICD codes associated with each of the categories 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. A 90% confidence interval was computed using exact methods when the number of observed deaths was less than or equal to five (but greater than zero) and an approximation when the number of observed deaths was six or more [Steenland et al., 1990]. 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 South Carolina state mortality rates for the period 1960–2002; person-time and deaths occurring prior to 1960 were excluded from these analyses.

Analyses were conducted with and without stratification by race. Tables of race-specific results are not reported in this paper as SMRs for non-white workers tended to be highly imprecise. Analyses of male workers were conducted stratified by pay code, which was defined as monthly-paid workers, weekly-paid workers, or hourly-paid workers and was based upon the worker's pay code at time of hire. Information on pay code was derived from historical employment history records that were available in hard copy form and were computerized for the purposes of this research project. Monthly-paid workers were primarily engineers, chemists, physicists, and supervisors. Weekly-paid workers were primarily clerical and kindred workers, security personnel, analysts, and technicians. Hourly-paid workers were primarily employed as operators and skilled manual workers. Since over 90% of female decedents were weekly-paid, analyses of female workers were not conducted with stratification by pay code.

Analyses were conducted stratified by duration of employment and calendar period at risk. Duration of employment was treated as a time-varying variable which increased during the interval from the date of first hire in operations at SRS until the date of last employment [Steenland et al., 1990; Cassinelli et al., 1998].

## RESULTS

The cohort included 15,264 men and 3,619 women (Table I). With follow-up through 2002, 27% of the study cohort was deceased (5,098 workers), 72% of the cohort was alive at the end of follow-up (13,590 workers), and 1% was lost to follow-up (195 workers). Information on underlying cause of death was collected for 99% of decedents (5,047 workers).

Table II shows SMRs for male and female SRS workers, using US mortality rates as referents. The number of deaths due to all causes was less than expected based upon national rates for male (SMR = 0.80) and female (SMR = 0.75) SRS workers. The categories of cancer mortality with SMRs above unity among males were cancer of the pleura (SMR = 4.25), breast (SMR = 2.11), eye (SMR = 2.41), connective tissue (SMR = 1.32), and leukemia (SMR = 1.20). None of the non-malignant categories of cause of death were in excess among male SRS workers. Among females, the categories of cancer mortality with SMRs greater than unity were cancer of the tongue, buccal cavity, esophagus, intestine, ovary, kidney, skin, brain, and Hodgkin's disease. The non-malignant categories of cause of death for which SMRs were greater

**TABLE I.** Cohort Description

	Male		Female	
	n	%	n	%
Total	15,264	100	3,619	100
Vital status				
Alive	10,486	68.7	3,106	85.8
Dead	4,709	30.9	389	10.8
Lost to follow-up	69	0.4	124	3.4
Pay code				
Monthly	4,026	26.4	496	13.7
Weekly	3,388	22.2	2,576	71.2
Hourly	7,850	51.4	547	15.1
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>
Year of birth	1935	15	1943	14
Year of hire	1963	13	1970	13
Age at entry (years)	28	7	26	7
Duration of employment (years)	16	13	12	11
Length of follow-up (years)	34	13	30	13

Savannah River Site (SRS) workers who were hired by DuPont prior to 1987 and who worked at least 90 days.

**TABLE II.** Standardized Mortality Ratios by Sex, Based Upon US Mortality Rates (1950–2002)

Cause of death	Sex (number of workers)					
	Male (N = 15,264)			Female (N = 3,619)		
	Obs	SMR	90% CI	Obs	SMR	90% CI
Tuberculosis	3	0.23	0.06, 0.59	0	—	[0.77] <sup>a</sup>
Malignant neoplasms						
Lip	0	—	[0.48]	0	—	[0.01]
Tongue	7	0.83	0.39, 1.56	1	2.16	0.11, 10.23
Other buccal cavity	6	0.63	0.27, 1.25	1	1.75	0.09, 8.29
Pharynx	12	0.63	0.37, 1.03	0	0.00	[0.91]
Esophagus	20	0.42	0.28, 0.62	2	1.25	0.22, 3.95
Stomach	28	0.58	0.41, 0.80	2	0.63	0.11, 1.99
Intestine except rectum	107	0.83	0.70, 0.97	15	1.09	0.67, 1.68
Rectum	18	0.64	0.42, 0.95	0	—	[2.43]
Biliary	29	0.71	0.51, 0.97	2	0.55	0.10, 1.72
Pancreas	75	0.99	0.81, 1.19	5	0.66	0.26, 1.39
Peritoneum	4	0.76	0.26, 1.73	0	—	[0.65]
Larynx	9	0.46	0.24, 0.80	0	—	[0.62]
Trachea, bronchus, lung	497	0.88	0.82, 0.95	27	0.68	0.48, 0.94
Pleura	7	4.25	1.99, 7.97	0	—	[0.06]
Breast	4	2.11	0.72, 4.82	29	0.80	0.58, 1.10
Cervix uteri	—	—	—	2	0.38	0.07, 1.18
Other parts of uterus	—	—	—	3	0.74	0.20, 1.91
Ovary, fallopian tube, and Br	—	—	—	13	1.22	0.72, 1.93
Other female genital organs	—	—	—	0	—	[0.61]
Prostate	114	0.97	0.82, 1.13	—	—	—
Other male genital organs	1	0.19	0.01, 0.89	—	—	—
Kidney	23	0.59	0.40, 0.83	7	2.58	1.21, 4.84
Bladder	30	0.83	0.60, 1.12	1	0.64	0.03, 3.05
Skin	27	0.82	0.58, 1.13	10	3.90	2.11, 6.61
Mesothelioma	2	0.92	0.16, 2.89	0	—	[0.07]
Eye	2	2.41	0.43, 7.61	0	—	[0.09]
Brain and other CNS	42	1.00	0.76, 1.29	5	1.09	0.43, 2.29
Thyroid	0	—	[2.68]	0	—	[0.41]
Bone	1	0.27	0.01, 1.28	0	—	[0.36]
Connective	11	1.32	0.74, 2.19	1	0.81	0.04, 3.84
Other and unspecified	92	0.83	0.69, 0.99	5	0.44	0.17, 0.92
Non-Hodgkin's lymphoma	51	0.88	0.69, 1.11	5	0.85	0.33, 1.78
Hodgkin's disease	5	0.53	0.21, 1.11	1	1.14	0.06, 5.40
Leukemia and aleukemia	68	1.20	0.97, 1.47	5	0.94	0.37, 1.98
Multiple myeloma	19	0.74	0.48, 1.09	1	0.39	0.02, 1.83
Benign and unspecified neoplasms	15	0.81	0.50, 1.25	3	1.24	0.34, 3.21
Diabetes	61	0.50	0.40, 0.62	11	0.71	0.40, 1.18
Diseases of the blood	20	0.98	0.65, 1.42	1	0.40	0.02, 1.91
Mental disease	56	0.89	0.70, 1.11	9	1.61	0.84, 2.81
Diseases of the nervous system	88	0.93	0.77, 1.11	8	0.70	0.35, 1.26
Diseases of the heart	1,598	0.80	0.77, 0.84	74	0.61	0.50, 0.74
Other diseases of the circulatory sys	396	0.90	0.83, 0.98	26	0.56	0.39, 0.78
Respiratory diseases	310	0.69	0.63, 0.76	40	1.01	0.76, 1.32
Diseases of the digestive system	158	0.59	0.52, 0.68	15	0.63	0.39, 0.97
Diseases of the genitourinary system	53	0.64	0.51, 0.81	5	0.55	0.22, 1.15

TABLE II. (Continued)

Cause of death	Sex (number of workers)					
	Male (N = 15,264)			Female (N = 3,619)		
	Obs	SMR	90% CI	Obs	SMR	90% CI
Diseases of the skin	5	0.98	0.39, 2.06	1	1.25	0.06, 5.92
Diseases of the musculoskeletal sys	10	0.76	0.41, 1.29	5	1.35	0.53, 2.84
Symptoms and ill-defined conditions	48	0.75	0.58, 0.95	1	0.17	0.01, 0.82
Accidents	279	0.81	0.73, 0.89	19	0.86	0.57, 1.27
Violence	134	0.68	0.58, 0.78	10	0.78	0.42, 1.33
Other causes	164	0.98	0.86, 1.12	18	0.90	0.58, 1.33
All cancers	1,311	0.85	0.81, 0.89	143	0.83	0.72, 0.96
All deaths	4,709	0.80	0.78, 0.82	389	0.75	0.69, 0.82

SRS workers who were hired by DuPont prior to 1987 and who worked at least 90 days.

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval; CNS, central nervous system.

<sup>a</sup>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.

than unity were benign neoplasms, mental disease, respiratory diseases, diseases of the skin, and diseases of the musculoskeletal system among female workers.

Analyses of SMRs for male and female SRS workers using South Carolina (SC) mortality rates as referents produced similar results to those obtained in analyses using US mortality rates as the referent, although the SMR for cancer of the pleura among males was of smaller magnitude (SMR = 2.82) when based upon SC referent rates (Table A1, available with the electronic version of this article).

Table III shows SMRs for male SRS workers with stratification by pay code, using US mortality rates as the referent. There is substantial variation in the magnitude of the SMR for all cause mortality by pay code. All cause mortality rates were well below national rates (SMR = 0.59) among monthly-paid males. Among weekly-paid male workers all cause mortality rates were 19% below national rates (SMR = 0.81), while among hourly-paid workers all cause mortality rates were closest to national rates (SMR = 0.90). A similar pattern is observed in the SMRs for all cancer mortality when examined by pay code (Table III). Lung cancers constituted the single largest cancer cause of death in this cohort. There is a substantial deficit of lung cancer deaths among salaried male workers (SMR = 0.52), a moderate deficit of lung cancer among weekly-paid males (SMR = 0.75), and an excess of lung cancer mortality among hourly-paid male workers (SMR = 1.12). The SMR for cancer of the pleura was greater than unity for monthly-paid (SMR = 2.28), weekly-paid (SMR = 5.34), and hourly-paid male workers (SMR = 4.79).

Leukemia mortality was in excess among monthly- and hourly-paid men (SMRs = 1.33 and 1.36, respectively) when compared to expectations based upon national referent rates. The majority of cases were myeloid forms of leukemia, with

acute myeloid leukemia constituting the largest number of cases. SMRs were also above unity for mesothelioma, cancer of the pancreas, breast, prostate, eye, and connective tissue in hourly-paid men, non-Hodgkin's lymphoma and cancer of the tongue, intestine, eye, brain, bone, connective tissue, and other and unspecified sites in weekly-paid workers, and cancer of the pancreas, larynx, and Hodgkin's disease among monthly-paid men (Table III).

The pattern of SMRs by pay code was similar for many non-malignant causes of death: SMRs for diseases of the heart, respiratory system, digestive system, and external cause of death were lowest among monthly-paid male SRS workers and highest (near unity) for hourly-paid males. The only non-malignant categories of cause of death for which observed deaths exceeded expectation were diseases of the nervous system and disease of the skin among hourly-paid males, and mental diseases, other diseases of the circulatory system, and diseases of the skin among weekly-paid workers.

Use of SC mortality rates as referents led to relatively modest changes in SMRs from the values derived via analyses using US referent rates (Appendix Table A2, with the electronic version). The lung cancer SMR among hourly-paid male workers was below unity rather than above as in analyses based upon US national referent rates. Notable excesses of leukemia mortality among monthly-paid (SMR = 1.46) and hourly-paid (SMR = 1.50) male workers were observed in analyses using SC referent rates.

Separate SMR analyses, using US mortality rates as the referent, were conducted stratified by race and pay code. The majority of non-white males were hourly-paid workers. The SMR for prostate cancer was greater than unity in analyses of hourly-paid non-white men (SMR = 1.65, 90% CI: 1.13, 2.34) while less than unity in analyses of hourly-paid white males (SMR = 0.86, 90% CI: 0.66, 1.12). The



**TABLE III.** Standardized Mortality Ratios Based Upon US Mortality Rates (1950–2002) by Pay Code

Cause of death	Pay code (number of workers)								
	Monthly-paid (N = 4,026)			Weekly-paid (N = 3,388)			Hourly-paid (N = 7,850)		
	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI
Tuberculosis	0	—	[2.74] <sup>a</sup>	1	0.43	0.02, 2.03	2	0.25	0.04, 0.79
Malignant neoplasms									
Lip	0	—	[0.14]	0	—	[0.11]	0	—	[0.24]
Tongue	1	0.48	0.02, 2.27	3	1.63	0.45, 4.22	3	0.67	0.18, 1.72
Other parts of buccal cavity	2	0.84	0.15, 2.65	2	0.96	0.17, 3.04	2	0.40	0.07, 1.25
Pharynx	2	0.44	0.08, 1.39	4	0.99	0.34, 2.26	6	0.58	0.25, 1.15
Esophagus	6	0.53	0.23, 1.05	7	0.69	0.33, 1.30	7	0.27	0.13, 0.51
Stomach	7	0.58	0.27, 1.09	5	0.50	0.20, 1.04	16	0.61	0.39, 0.93
Intestine except rectum	20	0.58	0.39, 0.85	30	1.05	0.75, 1.42	57	0.86	0.68, 1.07
Rectum	2	0.27	0.05, 0.85	5	0.80	0.32, 1.69	11	0.77	0.43, 1.27
Biliary	4	0.39	0.13, 0.89	6	0.68	0.30, 1.35	19	0.88	0.58, 1.29
Pancreas	20	1.01	0.67, 1.47	11	0.65	0.37, 1.08	44	1.11	0.85, 1.43
Peritoneum	1	0.72	0.04, 3.40	1	0.86	0.04, 4.06	2	0.73	0.13, 2.31
Larynx	5	1.03	0.41, 2.16	1	0.24	0.01, 1.12	3	0.28	0.08, 0.73
Trachea, bronchus, lung	75	0.52	0.43, 0.64	94	0.75	0.63, 0.89	328	1.12	1.02, 1.22
Pleura	1	2.28	0.12, 10.82	2	5.34	0.95, 16.83	4	4.79	1.64, 10.96
Breast	0	—	[0.49]	0	—	[0.42]	4	4.02	1.38, 9.20
Prostate	31	0.98	0.71, 1.32	18	0.76	0.49, 1.13	65	1.04	0.84, 1.28
Other male genital organs	0	—	[1.30]	0	—	[1.30]	1	0.37	0.02, 1.75
Kidney	3	0.29	0.08, 0.75	3	0.33	0.09, 0.86	17	0.85	0.54, 1.28
Bladder	8	0.79	0.39, 1.42	6	0.75	0.33, 1.48	16	0.88	0.55, 1.34
Skin	8	0.91	0.45, 1.64	4	0.51	0.17, 1.17	15	0.93	0.57, 1.43
Mesothelioma (1999–2002)	0	—	[0.60]	0	—	[0.52]	2	1.89	0.34, 5.96
Eye	0	—	[0.23]	1	5.16	0.26, 24.44	1	2.45	0.13, 11.63
Brain	9	0.81	0.42, 1.42	13	1.30	0.77, 2.07	20	0.95	0.63, 1.37
Thyroid	0	—	[0.71]	0	—	[0.61]	0	—	[1.36]
Bone	0	—	[0.96]	1	1.18	0.06, 5.62	0	—	[1.89]
Connective	1	0.46	0.02, 2.19	4	2.09	0.72, 4.79	6	1.42	0.62, 2.80
Other and unspecified	15	0.53	0.33, 0.81	28	1.14	0.81, 1.57	49	0.84	0.66, 1.07
Non-Hodgkin's lymphoma	15	0.97	0.60, 1.49	14	1.05	0.64, 1.64	22	0.76	0.51, 1.08
Hodgkin's disease	3	1.28	0.35, 3.32	0	—	[2.27]	2	0.41	0.07, 1.30
Leukemia and aleukemia	20	1.33	0.88, 1.93	9	0.70	0.37, 1.22	39	1.36	1.02, 1.78
Multiple myeloma	5	0.77	0.30, 1.61	5	0.90	0.36, 1.90	9	0.66	0.34, 1.15
Benign and unspecified neoplasms	3	0.62	0.17, 1.60	4	0.98	0.34, 2.24	8	0.84	0.42, 1.52
Diabetes	12	0.39	0.22, 0.63	14	0.53	0.32, 0.83	35	0.54	0.40, 0.72
Diseases of the blood	5	0.92	0.36, 1.94	4	0.92	0.31, 2.10	11	1.03	0.58, 1.71
Mental diseases	15	0.94	0.58, 1.44	16	1.22	0.77, 1.86	25	0.74	0.51, 1.03
Diseases of the nervous system	20	0.76	0.50, 1.10	18	0.87	0.56, 1.29	50	1.05	0.82, 1.33
Diseases of the heart	328	0.61	0.56, 0.67	371	0.86	0.79, 0.94	899	0.87	0.83, 0.92
Other diseases of the circulatory sys	72	0.62	0.50, 0.75	102	1.13	0.95, 1.33	222	0.96	0.86, 1.08
Respiratory diseases	48	0.39	0.30, 0.50	73	0.77	0.62, 0.93	189	0.83	0.73, 0.94
Diseases of the digestive system	28	0.42	0.30, 0.57	37	0.63	0.47, 0.83	93	0.66	0.55, 0.78
Diseases of the genitourinary system	9	0.42	0.22, 0.74	8	0.48	0.24, 0.87	36	0.81	0.60, 1.07
Diseases of the skin	0	—	[1.24]	2	2.02	0.36, 6.39	3	1.05	0.29, 2.71
Diseases of the musculoskeletal system	2	0.59	0.10, 1.84	2	0.70	0.12, 2.21	6	0.87	0.38, 1.72
Symptoms and ill-defined conditions	13	0.85	0.50, 1.34	5	0.38	0.15, 0.80	30	0.84	0.61, 1.14
Accidents	44	0.52	0.40, 0.67	49	0.61	0.47, 0.77	186	1.03	0.91, 1.16

TABLE III. (Continued)

Cause of death	Pay code (number of workers)								
	Monthly-paid (N = 4,026)			Weekly-paid (N = 3,388)			Hourly-paid (N = 7,850)		
	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI
Violence	18	0.38	0.25, 0.57	24	0.54	0.38, 0.77	92	0.86	0.72, 1.03
Other causes	32	0.75	0.55, 1.01	37	1.06	0.79, 1.39	95	1.07	0.89, 1.27
All cancers	264	0.66	0.59, 0.73	277	0.81	0.73, 0.89	770	0.95	0.90, 1.01
All deaths	913	0.59	0.56, 0.62	1,044	0.81	0.77, 0.86	2,752	0.90	0.87, 0.92

Male SRS workers who were hired by DuPont prior to 1987 and who worked at least 90 days.

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval; CNS, central nervous system.

<sup>a</sup>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.

SMR for lung cancer was greater than unity for hourly-paid white men (SMR = 1.18, 90% CI: 1.07, 1.30) but not for non-white men (SMR = 0.74, 90% CI: 0.54, 0.99). The SMR for leukemia was greater than unity for both non-white (SMR = 1.56, 90% CI: 0.62, 3.28) and white (SMR = 1.34, 90% CI: 0.98, 1.78) hourly-paid males.

Table IV shows SMRs for categories of cancer mortality among male SRS workers by duration of employment. The SMR for leukemia was less than unity for those employed <10 years (SMR = 0.93) and greater than unity for workers employed 10 to <20 years (SMR = 1.57), 20 to <30 years (SMR = 1.06), and 30+ years (SMR = 1.63). SMRs for cancer of the pleura were above unity for workers employed <10 years (SMR = 3.26), 10 to <20 years (SMR = 3.56), 20 to <30 years (SMR = 2.33), and 30+ years (SMR = 9.23). Analyses of all cancers and other specific categories of cancer deaths indicated no notable variation in SMRs with duration of employment.

Table V shows SMRs for leukemia and cancer of the pleura by 5-year calendar periods. The largest excesses of leukemia mortality occur in the periods 1965–1969, 1985–1989, and 2000–2002. Table V also shows SMRs for cancer of the pleura by 5-year calendar periods. There are no deaths due to cancer of the pleura prior to the 5-year period 1985–1989; in that period, and all subsequent periods, the SMR for cancer of the pleura was above unity. The SMR for cancer of the pleura was 30.29 during the period 2000–2002 (based on one death). Analyses of all cancers and lung cancer by calendar period indicated no notable variation in SMRs (not shown).

## DISCUSSION

Workers employed at SRS have fewer deaths due to all causes and all cancers than expected based upon US and SC referent rates. Such observations are typical when the mortality of relatively well-paid workers employed by a large corporation that offers medical and pension benefits is contrasted to the general population [Wilcosky and Wing,

1987], and similar to the results obtained via SMR analyses of a number of other nuclear worker cohorts [Geiger et al., 1992; Vrijheid et al., 2007]. However, the analyses in this article illustrate how evidence of relative deficits in all cause and all cancer mortality among male SRS workers differs by pay code (Tables II and III). There is a substantial HWE for monthly-paid men while there is less evidence of a HWE for hourly-paid men. Such differences in mortality 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 [Sheridan et al., 1993; Shi, 1998]. Historically, hourly-paid workers tended to be drawn from the local and regional labor pool while many monthly-paid (salaried) workers were drawn from universities and employers outside of the region [Reed et al., 2002].

Despite SMRs that were less than unity for many malignant and non-malignant causes, the SMR for leukemia was greater than unity for monthly- and hourly-paid men; this is particularly notable in the analyses using South Carolina referent rates (Table A2). Subsequent analyses may help to understand whether the leukemia excess is associated with the whole body radiation dose estimates that have been quantified for SRS workers. Examination of calendar period at risk suggests that leukemia excesses were not restricted to the late 1960s, as suggested by previous authors [Wartenberg et al., 2001] but rather excess leukemia mortality was still occurring in the period 2000–2002 (Table V). The peak in the leukemia SMR during the calendar period 1965–1969 follows a peak, several years earlier (in 1960), in the annual collective whole body radiation dose; however, consideration of temporal correlations between collective dose and cause-specific SMRs are less informative than dose-response analyses based upon individual records [Richardson et al., 2006].

Deaths due to cancer of the pleura, a disease strongly related to asbestos exposure, were in excess among male SRS workers. The observation is interesting given the findings of the SRS Former Production Worker Health

**TABLE IV.** Standardized Mortality Ratios and Approximate 90% Confidence Intervals for Malignant Categories of Cause of Death Based Upon US Mortality Rates (1950–2002) by Duration of Employment

Cancer cause of death	Duration of employment						20 to <30 years						30 + years					
	<10 years			10 to <20 years														
	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI	Obs	SMR	90% CI
Lip	0	—	[0.20] <sup>a</sup>	0	—	[0.11]	0	—	[0.11]	0	—	[0.11]	0	—	[0.06]	0	—	[0.06]
Tongue	4	1.20	0.41, 2.72	2	1.20	0.21, 3.71	1	0.52	0.03, 2.48	1	0.52	0.03, 2.48	0	—	[1.50]	0	—	[1.50]
Other buccal cavity	5	1.34	0.52, 2.78	0	—	[1.88]	1	0.44	0.02, 2.11	1	0.44	0.02, 2.11	0	—	[1.63]	0	—	[1.63]
Pharynx	5	0.67	0.26, 1.40	3	0.82	0.22, 2.07	1	0.23	0.01, 1.11	1	0.23	0.01, 1.11	3	0.86	0.24, 2.30	3	0.86	0.24, 2.30
Esophagus	8	0.44	0.26, 0.86	4	0.50	0.17, 1.12	3	0.29	0.03, 0.60	3	0.29	0.03, 0.60	5	0.47	0.19, 1.03	5	0.47	0.19, 1.03
Stomach	10	0.53	0.30, 0.85	8	0.84	0.45, 1.46	7	0.62	0.31, 1.09	3	0.62	0.31, 1.09	3	0.35	0.13, 0.91	3	0.35	0.13, 0.91
Intestine except rectum	47	0.95	0.73, 1.21	16	0.70	0.43, 1.04	19	0.60	0.42, 0.92	25	0.60	0.42, 0.92	25	0.97	0.66, 1.35	25	0.97	0.66, 1.35
Rectum	6	0.54	0.23, 1.06	4	0.72	0.24, 1.63	3	0.48	0.13, 1.24	5	0.48	0.13, 1.24	5	0.99	0.40, 2.14	5	0.99	0.40, 2.14
Biliary	9	0.57	0.36, 1.02	3	0.42	0.14, 1.00	9	1.00	0.55, 1.66	8	1.00	0.55, 1.66	8	0.92	0.44, 1.54	8	0.92	0.44, 1.54
Pancreas	31	1.06	0.76, 1.37	13	0.95	0.59, 1.48	20	1.14	0.76, 1.60	11	1.14	0.76, 1.60	11	0.71	0.45, 1.22	11	0.71	0.45, 1.22
Peritoneum	2	0.95	0.46, 3.31	2	1.98	0.10, 4.11	0	—	[1.28]	0	—	[1.28]	0	—	[0.90]	0	—	[0.90]
Larynx	2	0.26	0.06, 0.74	1	0.28	0.03, 1.15	3	0.66	0.22, 1.55	3	0.66	0.22, 1.55	3	0.76	0.27, 1.93	3	0.76	0.27, 1.93
Trachea, bronchus, lung	184	0.85	0.75, 0.95	88	0.93	0.77, 1.10	131	1.01	0.86, 1.16	94	1.01	0.86, 1.16	94	0.77	0.66, 0.94	94	0.77	0.66, 0.94
Pleura	2	3.26	0.58, 10.2	1	3.56	0.18, 16.76	1	2.33	0.12, 10.9	3	2.33	0.12, 10.9	3	9.23	2.58, 24.5	3	9.23	2.58, 24.5
Breast	2	2.69	0.47, 8.36	1	2.76	0.14, 12.87	0	—	[0.43]	1	—	[0.43]	1	2.75	0.15, 13.51	1	2.75	0.15, 13.51
Prostate	38	0.98	0.73, 1.24	20	1.01	0.71, 1.49	35	1.00	0.79, 1.36	21	1.00	0.79, 1.36	21	0.86	0.57, 1.21	21	0.86	0.57, 1.21
Other male genital organs	0	—	[3.29]	1	0.91	0.10, 4.11	0	—	[0.59]	0	—	[0.59]	0	—	[0.34]	0	—	[0.34]
Kidney	10	0.64	0.36, 1.02	3	0.43	0.23, 1.25	6	0.69	0.25, 1.14	4	0.69	0.25, 1.14	4	0.50	0.21, 1.15	4	0.50	0.21, 1.15
Bladder	9	0.68	0.38, 1.14	10	1.54	0.92, 2.61	7	0.75	0.47, 1.52	4	0.75	0.47, 1.52	4	0.55	0.17, 1.14	4	0.55	0.17, 1.14
Skin	13	0.90	0.56, 1.39	3	0.50	0.20, 1.32	6	0.92	0.69, 2.20	5	0.92	0.69, 2.20	5	0.84	0.20, 1.37	5	0.84	0.20, 1.37
Mesothelioma	1	1.12	0.06, 5.24	0	—	[0.26]	0	—	[0.35]	1	—	[0.35]	1	1.47	0.08, 7.25	1	1.47	0.08, 7.25
Eye	1	2.84	0.28, 11.3	0	—	[0.17]	1	5.72	0.58, 23.6	0	—	[0.17]	0	—	[0.13]	0	—	[0.13]
Brain and other CNS	20	1.06	0.66, 1.60	12	1.47	0.84, 2.61	3	0.37	0.12, 1.15	7	0.37	0.12, 1.15	7	1.00	0.51, 2.22	7	1.00	0.51, 2.22
Thyroid	0	—	[1.10]	0	—	[0.49]	0	—	[0.56]	0	—	[0.56]	0	—	[0.52]	0	—	[0.52]
Bone	1	0.56	0.06, 2.27	0	—	[0.78]	0	—	[0.70]	0	—	[0.70]	0	—	[0.44]	0	—	[0.44]
Connective	5	1.38	0.60, 2.68	2	1.31	0.32, 3.78	2	1.20	0.29, 3.41	2	1.20	0.29, 3.41	2	1.32	0.35, 4.02	2	1.32	0.35, 4.02
Other and unspecified	30	0.69	0.51, 0.92	18	0.95	0.64, 1.39	31	1.22	0.85, 1.56	13	1.22	0.85, 1.56	13	0.57	0.38, 0.95	13	0.57	0.38, 0.95
Non-Hodgkin's lymphoma	21	0.89	0.59, 1.22	6	0.58	0.35, 1.24	14	1.12	0.64, 1.60	10	1.12	0.64, 1.60	10	0.88	0.53, 1.53	10	0.88	0.53, 1.53
Hodgkin's disease	2	0.37	0.09, 1.02	1	0.46	0.05, 1.94	2	1.67	0.42, 4.84	0	—	[0.64]	0	—	[0.64]	0	—	[0.64]
Leukemia and aleukemia	22	0.93	0.62, 1.32	16	1.57	0.98, 2.36	13	1.06	0.62, 1.68	17	1.06	0.62, 1.68	17	1.63	1.07, 2.52	17	1.63	1.07, 2.52
Multiple myeloma	5	0.51	0.22, 1.00	5	1.18	0.53, 2.37	4	0.66	0.36, 1.60	5	0.66	0.36, 1.60	5	0.89	0.30, 1.62	5	0.89	0.30, 1.62
All cancers	495	0.82	0.76, 0.88	243	0.89	0.79, 0.98	323	0.90	0.82, 0.99	250	0.90	0.82, 0.99	250	0.79	0.71, 0.88	250	0.79	0.71, 0.88

Male SRS workers who were hired by DuPont prior to 1987 and who worked at least 90 days.

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval; CNS, central nervous system.

<sup>a</sup>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.



**TABLE V.** Standardized Mortality Ratios (and Approximate 90% Confidence Intervals) for Leukemia and Cancer of the Pleura Based Upon US Mortality Rates (1950–2002) by 5-Year Calendar Periods of Observation

	Leukemia			Cancer of the pleura		
	Obs	SMR	90% CI	Obs	SMR	90% CI
1950–1954	0	—	[0.28] <sup>a</sup>	0	—	[0.00]
1955–1959	0	—	[1.35]	0	—	[0.00]
1960–1964	1	0.59	0.03, 2.82	0	—	[0.00]
1965–1969	6	2.69	1.17, 5.31	0	—	[0.03]
1970–1974	3	1.06	0.29, 2.75	0	—	[0.09]
1975–1979	4	1.03	0.35, 2.35	0	—	[0.15]
1980–1984	6	1.09	0.48, 2.16	0	—	[0.22]
1985–1989	11	1.46	0.82, 2.41	4	12.55	4.29, 28.72
1990–1994	11	1.09	0.61, 1.80	1	2.37	0.12, 11.25
1995–1999	12	0.96	0.55, 1.55	1	2.64	0.14, 12.55
2000–2002	14	1.64	0.99, 2.56	1	30.29	1.55, 143.76

Male SRS workers who were hired by DuPont prior to 1987 and who worked at least 90 days.

Obs, observed deaths; SMR, standardized mortality ratio; CI, confidence interval.

<sup>a</sup>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.

Project, which conducted medical evaluations of 1,368 former SRS workers [Makie et al., 2005]. That study found that pleural abnormalities were more common among male SRS workers than in the general population (OR = 2.4), and were associated with occupational asbestos exposure. In our analyses, the largest excess of cancer of the pleura was among workers with 30+ years employment at the site, although elevated SMRs for pleural cancer were also observed among workers with shorter terms of employment. Industrial hygiene reports from the early 1970s indicate that occupational asbestos exposure was a problem at SRS, particularly in the Maintenance Department [Du Pont de Nemours and Co. Savannah River Plant, 1969]. During this period, air samples for asbestos indicated personnel exposures during some sawing operations, for example, exceeded the Threshold Limit Value of 5 fibers/ml (air). Among the seven SRS workers who died of pleural cancer, four were mechanics, one was an engineer, one was a technician, and one was a power plant operator; all were hired prior to 1955 with a median age at hire of 28 years. Excesses of cancer of the pleura have been observed in other nuclear worker cohorts, including studies of workers in Australia [Habib et al., 2005, 2006], the United Kingdom [Muirhead et al., 1999; Omar et al., 1999; McGeoghegan and Binks, 2000, 2001], and France [Telle-Lamberton et al., 2004]. Asbestos exposure is also associated with cancer of the peritoneum. Evidence of excess cancer of the peritoneum in this cohort is less clear: in comparisons to SC death rates SMRs are slightly above unity for each of the pay code groups while SMRs are below unity for each of these

groups when calculations are based upon US referent rates. Previous studies have found that deaths due to malignant mesothelioma often accounted for the majority of deaths classified as pleural cancer [Robinson et al., 2006]. Prior to the tenth 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. Consequently, our SMR analyses for that cause of death are based upon deaths in the period 1999–2002. An excess of deaths due to mesothelioma was observed among hourly-paid workers (based upon two observed deaths) while fewer deaths than expected due to mesothelioma were observed among monthly- and weekly-paid workers. It is interesting to note that prior mortality studies of this cohort did not observe an excess of cancer of the pleura. Examination of the SMR for cancer of the pleura by year of death (i.e., calendar period) reveals that no deaths due to cancer of the pleura were observed prior to the period 1985–1989 and the most notable excesses have been observed in the most recent follow-up period (2000–2002).

More deaths than expected due to breast cancer were observed among hourly-paid males (four deaths observed 0.99 expected). However, given the relatively small number of cases of male breast cancer in this cohort we have little ability to explore associations with duration of employment or other indicators of exposure. Other categories of cancer mortality for which we noted excesses that were based upon small numbers (i.e., less than five deaths) include cancer of the eye among males, and cancer of the tongue, buccal cavity, esophagus, and Hodgkin's disease among females.

In analyses based upon US referent rates, lung cancer mortality was in excess among hourly-paid males and in substantial deficit among monthly-paid males. Differences in cigarette smoking offer a plausible explanation for this gradient in lung cancer SMRs [Sheridan et al., 1993; Shi, 1998], although given the evidence of excess pleural cancer and the potential occupational exposure to a number of lung carcinogens, variation in occupational exposures by pay code could also contribute to the gradient in lung cancer. Cigarette smoking was regulated at SRS; however, regulations were not specific to pay code groups but rather to work areas or locations at the site. Consequently, statistical adjustment for pay code in analyses of exposure-mortality associations may control, in part, for confounding by cigarette smoking; however, residual confounding by cigarette smoking is likely in such analyses.

There are a number of obstacles to the ability to detect adverse effects of occupational exposures via SMR analyses. The strong evidence of a healthy worker effect suggests that SMRs below unity don't necessarily imply the absence of occupational exposure effects; rather, relying on comparisons of observed deaths to expected deaths derived using national or state referent rates may spuriously mask the health effects of occupational exposures. Further, masking of adverse effects of occupational exposures may be exacerbated if a substantial proportion of the study cohort has little or no exposure to the hazards of interest. SMRs that don't discriminate between subgroups based upon exposure level, or simply consider being employed as an indication of exposure, may dilute evidence of any adverse exposure effect by mixing exposed and unexposed members of the study cohort. Despite these obstacles, the findings of this study provide evidence of excess mortality due to leukemia among hourly- and monthly-paid workers, and excess mortality due to pleural cancer among all workers. The evidence of excess cancer of the pleura has not been noted before in this cohort, but is consistent with recent evidence (derived from medical screening) of excesses of pleural abnormalities among former SRS workers. The leukemia excess also is notable in recent years.

The National Academies of Sciences recently reviewed the epidemiological research program on US Department of Energy workers, concluding that this research program should continue, albeit with greater communication, and collaboration between the Departments of Health and Human Services and Energy [National Research Council of the National Academies and Committee to Review the Worker and Public Health Activities Program Administered by the Department of Energy and the Department of Health and Human Services, 2006]. The findings of this study underscore the importance of continued 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 and particularly

to identify occupational diseases that have long induction and latency periods. Such studies may help to inform medical screening programs, occupational health services, compensation programs, and worker protection efforts.

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