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Mortality Patterns Among Paducah Gaseous Diffusion Plant Workers

Caroline Chan, MPH,
Department of Environmental and Occupation Health Sciences, School of Public Health and Information Sciences, University of Louisville, 485 E. Gray Street, Louisville, KY 40202, Phone: 502-852-3290, Fax: 502-852-3304

Therese S Hughes, PhD,
U.S. Department of Health and Human Services, Office of the Secretary/Office of Global Health Affairs, 330 C Street, SW, Switzer Building, Room 2320, Washington DC 20201, Phone: 202-260-0413

Susan Muldoon, PhD, MPH [Assistant Professor],
Department of Epidemiology and Population Health, School of Public Health and Information Sciences, University of Louisville, Louisville Kentucky 40202, Phone: 502-852-8087

Tim Aldrich, PhD, MPH [Associate Professor],
College of Public Health, East Tennessee State University, PO Box 70623, Johnson City TN 37614, Phone: 423-439-4427

Carol Rice, PhD [Professor],
University of Cincinnati, PO Box 670056, Cincinnati OH 45267-0056, Phone: 513-558-1751

Richard Hornung, DrPH [Professor and Director of Biostatistics & Data Management],
Division of General & Community Pediatric Research, Cincinnati Children's Hospital Medical Center, 3333 Burnet Ave, Cincinnati, OH 45229, Phone: (513)636-1948

Gail Brion, PhD, MS [Professor], and
Department of Civil Engineering, College of Engineering, University of Kentucky, 161 Raymond Bldg, Lexington, KY 40506, Phone: 859-257-4467

David J Tollerud, MD, MPH, FACOEM [Professor and Chair]
Department of Environmental and Occupational Health Sciences, School of Public Health and Information Sciences, University of Louisville, 485 E. Gray Street, Louisville, KY 40202, Phone: (502) 852-3290

Caroline Chan: caroline.chan@louisville.edu; Therese S Hughes: therese.hughes@hhs.gov; Susan Muldoon: sbmuld01@gwise.louisville.edu; Tim Aldrich: aldrich@etsu.edu; Carol Rice: ALERDILR@UCMAIL.UC.EDU; Richard Hornung: richard.hornung@cchmc.org; Gail Brion: gbrion@engr.uky.edu; David J Tollerud: djtoll01@gwise.louisville.edu

Abstract

Objective—Determine if PGDP workers had mortality patterns that differed from the general U.S. population, and investigate if mortality patterns were associated with job title or workplace exposures.

Methods—A retrospective occupational cohort mortality study was conducted on 6759 workers. Standardized mortality ratio analyses compared the cohort to the referent U.S. population. Internal comparisons producing standardized rate ratios were conducted by job title, metal exposure, and cumulative internal and external radiation exposures.

Results—Overall mortality and cancer rates were lower than the referent population, reflecting a strong healthy worker effect. Individual non-significant SMRs and SRRs were noted for cancers of the lymphatic and hematopoietic tissue.

Conclusions—Although relatively low exposures to radiation and metals did not produce statistically significant health effects, non-significant elevations for lymphatic and hematopoietic cancers were consistent with previous studies of nuclear workers.

The Paducah Gaseous Diffusion Plant (PGDP) located in Western Kentucky is currently the only operating uranium enrichment facility in the United States (U.S.), and the only one whose worker cohort has not undergone a mortality study. This U.S. Department of Energy (DOE) owned, contractor-operated uranium enrichment facility was commissioned in 1952 as part of a U.S. government program to produce enriched uranium to fuel military reactors and produce nuclear weapons[1,2].

The plant's mission changed in the 1960s from enriching uranium for nuclear weapons to enriching uranium for use in commercial nuclear reactors to generate electricity[1,2,3]. PGDP currently enriches uranium-235 up to 5.5% using the gaseous diffusion process for use in domestic and foreign commercial power reactors[2,3]. In the gaseous diffusion process, the gas is forced through a series of porous membranes with microscopic openings. Because the U-235 is lighter, it moves through the barriers more easily. As the gas moves, the two isotopes are separated, increasing the U-235 concentration and decreasing the concentration of U-238. The enrichment process removes about 85% of the U-238 by separating gaseous uranium hexafluoride (UF6) into two streams: One stream is increased, or enriched, in its percentage of U-235, and the other is reduced, or depleted. The enriched uranium is then transported to nuclear power reactors to generate electricity. The depleted uranium is considered waste and is stored in cylinders on site. Approximately seven thousand individuals have worked at the plant since its inception[1,3].

The 1990s witnessed a growing public awareness and concern about present and historical environmental, safety, and worker health issues from radiation and chemical exposures at the PGDP. Independent studies sponsored by the DOE fueled these concerns[4,5]. Comparisons of findings between uranium enrichment facilities are complicated, because exposure processes and historical periods of operation have differed between facilities, and exposure and dosimetry methods have changed over time[5]. Mortality studies among workers exposed to ionizing radiation at other uranium enrichment facilities had yielded mixed results. For example, studies conducted at the Oak Ridge facility in Tennessee revealed elevated standardized mortality ratios (SMRs) for several outcomes. In the K-25 plant, white males that were hired between 1943 and 1972 had an SMR for leukemia of 1.63 for follow-up until 1984[6]. However, when the follow-up was extended to 1990, the SMR remained elevated, but dropped to 1.35[7]. Another study conducted at the Y-12 plant found elevations in SMRs for lung cancer (1.17), lymphatic cancers (1.32), brain (1.13), and pancreatic cancers (1.36)[8]. And yet another study at the K-25 plant found elevations in the overall SMR (SMR=1.03, CI=1.01- 1.05), together with lung and bone cancer[9]. In contrast, a later study conducted at Portsmouth[10] revealed “all-cause” and “all-cancer” SMRs that were less than expected using U.S. rates, demonstrating a strong healthy worker effect (HWE). The HWE is a phenomenon observed in occupational studies; workers usually exhibit lower overall death rates than the general population, because ill and chronically disabled people are ordinarily not able to meet the demands of labor-intensive work[11,12]. The Portsmouth study did not reveal any statistically significant SMRs for any individual cancers, although excesses of stomach, female genital organs, bone, Hodgkin's, and lymph-reticulosarcoma cancers were noted. The largest occupational retrospective study to date for assessing low doses of ionizing radiation exposure and cancer mortality involved 407,391 nuclear workers in 15 countries. It revealed an excess relative risk for leukemia, excluding chronic lymphocytic leukemia, (1.93 per Sv (CI=< 0§ to 8.47) (§estimate on boundary of parameter space)), but did not show an increased risk for other cancers[13].

In response to concern about past and present radiation and chemical exposures, the National Institute for Occupational Safety and Health (NIOSH) funded a collaborative study by the Universities of Louisville, Kentucky, and Cincinnati to conduct an occupational cohort mortality study titled “Health effects of occupational exposures in PGDP workers”. Of specific concern was exposure to uranium hexafluoride and the presence of transuranic materials including neptunium and plutonium[3,4,5], but the study also attempted to quantify exposure to ionizing radiation, chemicals, and toxic metals at the plant. Mortality patterns associated with job titles that have been grouped according to similarity of tasks and exposures, exposure to arsenic, beryllium, chromium, nickel, and uranium, and cumulative internal and external radiation exposure within the plant are explored.

This report describes the analysis of mortality patterns for 92 causes of death including over 40 cancers for the entire cohort using standardized mortality ratios (SMRs). In addition, mortality patterns for defined groups within the cohort are described using standardized rate ratios (SRRs). While all outcomes were examined, a priori outcomes of interest were based on the literature. For radiation exposure, outcomes of interest include lymphatic and hematopoietic cancers, as well as lung, brain, bone, pancreatic, and stomach cancers. For exposure to metals, the a priori cancer of interest was lung cancer.

Methods

Study Population

This retrospective occupational cohort mortality study consisted of eligible PGDP workers enumerated from employee personnel records. The Institutional Review Boards for the Protection of Human Subjects at the Universities of Louisville, Kentucky, and Cincinnati reviewed and approved the study. Since the study involved the collection of existing data, and the risk to subjects was low, consent was waived.

Demographic, work history and vital status data were collected on 6820 workers. Inclusion criteria required workers to have been employed at the PGDP for at least 30 days from the start of plant operations in September 1952 through December 2003. Expected rates of death from the 1940-2002 U.S. population were compared to actual deaths in the cohort study population for NIOSH's 92 death categories.

Vital Status

Vital status was determined as outlined by Checkoway et al[14] by linking cohort members' personal identifying information from employee records with data from the U.S. Social Security Administration (SSA), the National Death Index (NDI) and individual state departments of health. All known deceased, and any workers with unknown vital status, were submitted to the NDI for cause of death information. Workers of unknown vital status were counted and considered alive with contributed person years of observation up to the date of termination of employment[14]. For known deaths occurring before 1979, prior to the establishment of NDI, death certificates were requested from departments of health in the state each individual worker was believed to have resided at the time of death. All data was subsequently de-identified and is only reported in aggregate form. The characteristics of the cohort are shown in Table 1.

Cause of Death

A total of 1674 deaths were identified out of 6820 workers in the cohort (24.6%). Because of incomplete history and outcome data 61 workers were eliminated resulting in analyses on 6759 workers and 1638 deaths. Deaths were classified and coded to the international classification of diseases (ICD) code that was in effect at the time of death (5^{th} through 10^{th} revision) for the time period 1952-2003 for 92 causes of death including over 40 cancers. A qualified nosologist coded deaths to the ICD-code in effect at the time of death for all deaths that occurred prior to 1979 and for whom death certificates were obtained. Cause of death was obtained on 1638 deaths. Known deaths for which a death certificate could not be retrieved were counted in the other and unspecified causes of death category.

Grouped Job Titles

An original list of job titles consisting of 2,727 unique entries was obtained and edited for duplications and misspellings. Information was provided by company representatives and long-term employees about job duties and work organization. The job titles were subsequently grouped according to similarity of task and exposure, resulting in a total of 44 grouped job titles[15]. The grouped job titles were then ranked in a qualitative and categorical manner based on the relative degree of exposure to various chemicals. Because many employees worked several jobs during their tenure at the plant, an analysis plan was devised that accounted for each grouped job title by developing a binary variable indicating whether the employee ever or never held a particular grouped job title. To ensure maximum power, analyses were limited to grouped job titles that had a minimum of 100 workers and 5% of the person years for the whole cohort. This reduced the number of individual grouped job titles in the analysis from 44 to 11. An initial analysis of job category outcomes based on gender and race revealed that the sample size was very limited for all categories except white males; therefore, all subsequent grouped job analyses included only white males.

Examination of the raw work history records indicated that employees who worked as a Chemical Operator frequently moved to Cascade or Maintenance. Chemical Operator consistently had the highest categorical rankings for five metals and trichloroethylene (TCE) of all the grouped job titles[15,16]. Two additional groups were created in order to better discriminate between workers who had and had not had exposures as a Chemical Operator. The additional groups were defined as: ever worked Cascade not Chemical Operator; and ever worked Maintenance not Chemical Operator. The addition of these groups brings the total job title categories analyzed to 13. The analyzed job titles are shown in Table 2 along with each job title's number of workers and person years at risk.

Analysis of Maintenance Groups

The 44 grouped job titles included 17 job titles that were considered “maintenance” positions. Depending on the category of maintenance, workers may have worked throughout the plant and may have been exposed to a variety of contaminants. While not all 17 maintenance job titles met the criterion for analysis as a separate job title, further grouping of maintenance titles into high, medium, and low levels of exposure was undertaken to better understand mortality patterns for maintenance workers. Relative exposures for each grouped job title were estimated by building on the work of Hahn and Moser[15,16]. Their studies assigned categorical exposure levels for the five metals and TCE that were widely used at the plant. Rankings of 0 to 5 were assigned based on long-term employee interview and plant records. Exposure levels frequently changed over time. To estimate all non-radiation hazards of interest, a qualitative exposure level was calculated by adding the levels of the five metals and TCE (additive exposure level; possible range 0-30). Where levels changed over time for a given exposure, the mean was used.

The additive exposure level was then used to condense the 17 maintenance job title groups into the three categories: high, medium, and low exposure maintenance groups. The high exposure maintenance group consisted of one grouped job title, Maintenance. Subsequently both Maintenance and the category to discriminate from the effects of work as a Chemical Operator, Maintenance not Chemical Operator, were considered separately for the high exposure category. Table 3 displays the maintenance categories and the additive exposure rankings for each grouped maintenance job title.

Neurodegenerative Disease Analysis

In addition to the standard referent dataset of 92 causes of death, NIOSH's Life Table Analysis Software (LTAS) includes a neurodegenerative disease death rate file that analyzes specific causes of death under the category “other motor neuron disease”. This broad category includes the outcomes of Alzheimer's disease, Parkinson's Disease, and amyotrophic lateral sclerosis (ALS). Initial analyses indicated an elevation in “other motor neuron disease”; therefore the neurodegenerative disease rate file was employed to examine specific outcomes in this category.

Metals Analyses

Categorical exposure levels to the metals arsenic, beryllium, chromium, nickel, and uranium were described for each job title in the work of Hahn[15]. Since some ranks were represented by very sparse person-years, this analysis divided the ranks of 0 to 5 into low, medium, and high exposure categories. Ranks 0, and 1 were assigned to the low exposure category, 2 and 3 to medium exposure, and ranks 4 and 5 were assigned to the high exposure category. An individual was considered in the medium or high exposure category beginning at the time that he began working in a job title with a rank corresponding to that category. While an employee could move from a lower rank to a higher rank during their tenure, moving to a lower ranked position did not result in a lower exposure category. For each metal, an internal comparison with the low exposure category as the referent was conducted resulting in an SRR for medium and high exposure to the metal. Due to limited sample sizes for other demographic categories, analyses were conducted for white males only.

Internal and External Radiation Analyses

A surrogate measure, in μg-yrs, of total cumulative internal radiation exposure was derived from urine data to represent the cumulative dose of internally-deposited radionuclides. Total cumulative external radiation exposure was taken from badge data and expressed in mrems. The distribution of total person years assigned to all workers were broken down to 4 equal categories according to how much person-time was spent in each of the 4 ordered cumulative dose categories. The 2^{nd}, 3^{rd}, and 4^{th} quartiles were compared to the 1^{st} quartile of exposure to generate SRRs for white males.

Statistical Analysis

The overall mortality patterns of the PGDP cohort were examined by using LTAS to compare occupational cohort mortality to the U.S. population from 1940 to 2002 for 92 causes of death including over 40 cancers[17]. For data beyond 2002, LTAS estimated rates with data from 2000 to 2002[18]. Data analysis focused on Standardized Mortality Ratios (SMRs) for the entire period of the cohort (1952-2003), producing summary estimates of relative risks over the entire cohort experience. Expected deaths were calculated by multiplying the person-years at risk (PYAR) in the cohort by the rates in the U.S. referent population. LTAS analysis was used to compare the “cause specific” observed number of deaths with the expected number of deaths (SMRs) in each of the 92 causes of death supplied by LTAS. The study also examined the cohort by race, gender, 5-year age category, and 5-year calendar period.

Statistical significance testing was performed by comparing observed with expected numbers of deaths, under the assumption that the observed deaths were Poisson variates (random variables with a Poisson distribution) and the expected deaths were estimated without error. Confidence intervals (95%) were calculated when the number of observed deaths was less than or equal to ten and significant results flagged as $p < 0.05$ or $p < 0.01$. All reported confidence intervals are the 95% confidence interval. For greater numbers of observed deaths, LTAS uses an approximation suggested by Breslow and Day[19].

Standardized rate ratios (SRRs), a direct standardization method in LTAS[19], were used to compare individual grouped job titles to the rest of the cohort, high and medium metal exposures to low metal exposures, and 2nd, 3rd, and 4th quartiles of cumulative internal and external radiation exposure to the 1st quartile of exposure. This internal comparison controls for external factors that may affect outcomes, in particular, the healthy worker effect and regional influences (such as local smoking rates or dietary differences). Job title, metals exposure, and cumulative internal and external radiation were analyzed for white males and, unless otherwise noted, included all ages and calendar periods.

Results

Overall Findings

Table 1 provides the demographic and duration of employment characteristics of the cohort. The majority of the cohort was composed of white males (74%). Among the 6820 workers employed at PGDP between 1952 and 2003, 24.6% (1674) were deceased. Incomplete history or outcome data resulted in the elimination of 61 workers (>1%), and 2.2% (36) of deaths had an unknown underlying cause of death. Of the 1674 deaths, complete person, history, and outcome data were available for 1638. Therefore the cohort analysis was carried out on 6759 workers and 1638 deaths. In looking at duration of employment, the largest group of workers, 33% (2235), was employed at the plant for a period of one to five years.

The all-cause mortality and all-cancer mortality experience of the PGDP cohort was significantly lower than that of the U.S. referent population. The all-cause SMR (SMR=0.73; 95% confidence interval [CI] =0.69-0.76) was based on 1638 observed deaths versus 2253 expected (Table 4). The all-cancer SMR (SMR=0.78; CI=0.71-0.85) was based on 461 observed cases versus 592 expected. Deaths related to “Other Causes,” which include all deaths that do not have a known cause of death, were also significantly reduced indicating higher rates of death classification than the U.S. referent (SMR=0.42; CI=0.27-0.61).

The *a-priori* cancers of interest (hematopoietic, lung, bone, kidney, and stomach cancers) did not show any statistically significant increased mortality rates (Table 4). However, individual non-significant excess mortality rates (SMR>1) were noted for cancers of the lymphatic and hematopoietic tissue (SMR=1.19; CI=0.85-1.61). These included non-Hodgkin's lymphoma (SMR=1.43; CI=0.98-2.01), leukemia (SMR=1.11; CI=0.71-1.65) and multiple myeloma (SMR =1.02; CI=0.49-1.87). Pancreatic cancer was non-significantly elevated (SMR =1.10; 0.75-1.56). Lung cancer had significantly lower mortality rates (SMR=0.72; CI=0.58-0.89).

Outcomes from the analyses of race, gender, 5-year age category, and 5-year calendar period were similar to the overall cohort experience (data not shown). All-cause SMRs were significantly lower than the U.S. referent for all race and gender categories. The 5-year age categories all-cause SMRs were significantly lower than the U.S. referent up to the 70-74 age category. Age categories from 75-89 and above had all-cause mortality rates approximately equal to the U.S. referent. No deaths were observed for several 5-year age category and calendar periods for groups other than white males, limiting the robustness of this analysis for white females and males and females of other races. For white males, all categories had observed deaths, although the youngest age categories (15-19 and 20-24) had few observed deaths (1 and 3, respectively), and the first calendar period, 1950-1954, representing the first two-and-a-half years of plant operations, had only 3 observed deaths. For the remaining 5-year age categories, observed deaths ranged from 11 to 241, and observed deaths for the remaining 5-year calendar periods ranged from 16 to 290.

Non-Cancer Mortality

Most mortality rates for non-cancer causes of death were also lower in the cohort than the general U.S. population (data not shown). For example, the SMR for heart disease was 0.75 (CI=0.67-0.83). Non-significantly elevated SMRs were noted for “other nervous system diseases” (SMR=1.30; CI=0.96-1.72), and “other mental disorders” (SMR=1.11; CI=0.62-1.83). The neurodegenerative disease rate file was used to examine specific outcomes in the category “other nervous system diseases.” The SMR for Alzheimer's disease was significantly elevated (SMR=2.16; CI=1.38-3.21). Further analysis for this outcome by five year age category showed a significant elevation for Alzheimer's deaths for the 70 to 74 years age category (SMR=3.30; CI=1.21-7.18), and near significance for the 75 to 79 and 80 to 84 age categories (SMR=2.35; CI=0.94-4.84 and SMR=2.42; CI=0.97-4.99, respectively). Statistically significant excesses in mortality from suicide deaths were observed when stratified by year and age. An SMR of 2.21 (CI=1.01-4.19) for years 1970-1974 and an SMR of 8.13 (CI=1.69-23.75) for years 1975-1979 in the 40-44 age group was found. Further analysis of suicide deaths in the cohort is explored in a separate analysis (LW Figgs, personal communication, manuscript in preparation).

Analysis by Job Title

Standardized mortality ratios were used for a preliminary look at grouped job titles. Among the a priori cancers of interest, Non-Hodgkin's lymphoma was significantly elevated for the category Security (SMR=3.39; CI=1.10-7.91) and non-significantly elevated for Cascade, Chemical Operator, Maintenance, Maintenance/Converter, Maintenance/Custodial, Maintenance/Roads & Grounds and Office. Non-significant elevations for kidney cancer were found for Chemical Operator (SMR=1.61; CI=0.69-3.17) and Maintenance (SMR=2.13; CI=0.78-4.63). Chemical Operator also had an elevation in brain cancer (SMR=1.52; CI=0.66-3.00). For most grouped job titles, significantly lower rates of death were found for most cancers and for heart disease. A significant elevation was found for colon cancer for the category Office (SMR=2.73; CI=1.18-7.91).

The primary focus of our analyses was internal comparisons using SRRs. Table 5 provides the SRRs for select job titles and causes of death (also see Table, Supplemental Digital Content 1, which provides SRRs for all analyzed job titles and additional causes of death). Job titles with elevated SRRs for all causes include Maintenance/Converter Shop (SRR=1.35; CI=0.83-2.17) and Maintenance/Roads & Grounds (SRR=1.25; CI=0.96-1.63). All-cause mortality was significantly higher for Security compared to all other white males in the cohort (SRR=1.34; CI=1.06-1.71). Non-significant elevations in leukemia were found for the job titles Cascade (SRR=1.16; CI=0.42-3.20), Chemical Operator (SRR=1.49; CI=0.62-3.58), and Security (SRR=1.90; CI=0.56-6.47). In addition, Security had a non-significant elevation in Non-Hodgkin's lymphoma (SRR=2.44; CI=0.91-6.55). Significantly elevated SRRs for specific causes of death included colon cancer for the category Office (SRR=4.91; CI=2.08-11.63), diseases of the heart for Maintenance/Roads & Grounds (SRR=1.70; CI=1.13-2.55) and Security (SRR=1.78; CI=1.17-2.71), lung cancer for Maintenance/Converter Shop (SRR=1.99; CI=1.19-3.35) and Maintenance/Custodial (SRR=2.56; CI=1.09-5.98).

For the maintenance exposure groups, the SMRs for all causes were significantly lower than the U.S. referent for all three levels of exposure reflecting the HWE that characterizes the entire cohort. Mortality from all cancers was also lower than the U.S. referent for all three maintenance groupings, although a statistically significant deficit was only observed in the high exposure category. An SRR analysis was not conducted on the maintenance groupings.

The NIOSH neurodegenerative disease rate file was used to examine specific mortality outcomes in the category “other nervous system diseases” for grouped job titles. An examination using SMRs found a significant elevation in this broad category for Chemical Operator (SMR=1.65; CI=1.01-2.50), and non-significant elevations for the job titles Engineer, Laboratory, and Office (data not shown). The internal comparison found significant elevations in Alzheimer's deaths for the job title Engineer (SRR=2.81; CI=1.01-7.86). Non-significant elevations were found for Maintenance (SRR=1.56; CI=0.68-3.58), Maintenance not Chemical Operator (SRR=2.22; CI=0.76-6.50), and Office (SRR=1.63; CI=0.36-7.39). The job category Laboratory had a near significant elevation for the outcome ALS (SRR=5.30; CI=0.95-29.65).

Analysis of Metal Exposures

Those with medium and high exposures to metals had few differences in outcomes compared to those with low exposures (see Table, Supplemental Digital Content 2, which provides SRRs for medium and high exposures to metals). Those with medium exposure to nickel had a significant elevation in lung cancer (SRR=1.74; CI=1.06-2.85), although those with high exposure had an SRR below 1.00 for that outcome. Medium exposure to uranium resulted in a near significant elevation for all causes (SRR=1.17; CI=0.99-1.38), while high exposure to uranium had an all-cause SRR of 1.00 (CI=0.88-1.14).

Internal and External Radiation Analyses

Table 6 shows an SRR analysis of internal and external radiation exposures for cancers of interest. The 2nd and 3rd quartiles of internal radiation exposures were significantly elevated relative to the 1st quartile for Non-Hodgkin's lymphoma (SRR=9.95; CI=1.22-81.26 and SRR=8.85; CI=1.11-70.88 respectively). The 4th quartile was non-significantly elevated (SRR=5.74; CI=0.72-45.48).

Discussion

This analysis is consistent with the published literature[6,7,12,13]. As expected, a strong healthy worker effect (HWE) was observed in this cohort. PGDP workers experienced lower mortality rates from all deaths (SMR=0.73) and all cancers (SMR=0.77) compared to the U.S. referent population. Previous studies had suggested that long-term follow-up might reduce the HWE[11]. However, another related phenomenon observed more recently in long-term occupational mortality studies is the “healthy worker survivor effect”[20], which tends to diminish exposure-related risk estimates in long term workers because workers who remain employed tend to be healthier than those who terminate.

The analyses by race, gender, 5-year age category, and 5-year calendar period are also consistent with the overall cohort experience. For white males, the results suggest a strong HWE for all calendar periods and ages up to 75.

Despite limitations, SMRs are a critical first step in occupational analyses. It is important to note that results that lack significance do not provide evidence against a true relationship[21]. Despite the overall health of the PGDP cohort, lymphatic and hematopoietic cancers reflected a non-significantly elevated SMR of 1.19 based on 68 observed deaths. Non-Hodgkin's lymphoma, leukemia and multiple myeloma SMRs were elevated. Non-Hodgkin's lymphoma showed the most prominent excess (SMR=1.43; 32 observed deaths).

The internal comparison using SRRs controls for the healthy worker effect and regional influences (such as local smoking rates or dietary differences) and therefore may address some of the SMR limitations. The internal comparison showed that the job titles Maintenance/Converter Shop, Maintenance/Roads & Grounds, Office, and Security had higher, but non-significant, Non-Hodgkin's lymphoma deaths compared to the rest of the cohort. These job titles were not known to have regular radiation exposure. However, prior to 1955, Security did patrol all buildings, and may have had poorly characterized exposures[16]. After 1955, patrols were limited to the periphery. Examination of the work history of the five Security employees who died from Non-Hodgkin's lymphoma showed that all five held the position before 1955 when Security patrolled all buildings.

In examining the SRRs for lymphatic and hematopoietic cancers, Chemical Operators had higher death rates than the cohort for leukemia and multiple myeloma but not Non-Hodgkin's lymphoma, and the job titles Cascade and Security had non-significant elevations in leukemia deaths. However, for the Cascade category, when workers who had also been Chemical Operators were removed, no leukemia deaths were reported, suggesting that the elevation was associated with the job title Chemical Operator.

These findings support trends for hematopoietic cancer risk found in similar cohorts[6,8]. Hematopoietic cancers are of major interest because of the recognized association with radiation exposure. It is well documented that high dose radiation exposure has resulted in immunosuppressive and carcinogenic effects in organs where radionuclides concentrate, specifically for most forms of leukemia[22,23]. Previous DOE studies have also revealed increased SMRs for hematopoietic cancers with low dose radiation exposure, although not always statistically significant. For example, early studies at the Oak Ridge facility and the Mallincrodt Chemical Works revealed statistically higher SMRs for hematopoietic cancers[8], but this trend was not reflected in later studies[24]. The Portsmouth study revealed non-significant excesses of hematopoietic cancers and Hodgkin's Disease[10], and the 15 Country study revealed an elevated relative risk for lymphocytic leukemia[13]. Non-Hodgkin's lymphoma and leukemia showed consistently increased SMRs, an observation supported by the present study. The PGDP cohort had low dose radiation exposures comparable to workers in these studies, with approximately 75% of workers with < 100 mrem cumulative external radiation exposure. The results of this study strengthen the association found in these studies between low dose radiation exposure and hematopoietic cancers.

The internal comparison showed a significant elevation in colon cancer for the grouped job title Office (SRR=4.91; CI=2.08-11.63). This job category also showed non-significant elevations in pancreatic cancer, Non-Hodgkin's lymphoma, Alzheimer's disease, and diabetes. Employees with this job title did clerical jobs, but their offices were located in production buildings, and they may have had transitory exposure to some chemicals[16]. Office workers typically performed more sedentary tasks, and may not exhibit the HWE to the same degree as employees who execute more physical tasks.

Select job titles underwent further analysis with the neurodegenerative disease rate file. Elevations in the “other nervous system diseases” outcome were found to be due to increases in deaths from Alzheimer's disease. As is typical for this disease, deaths from this outcome primarily occurred in individuals over the age of 70, many in their 80s. Reductions in deaths from heart disease and cancers may account for the increase in Alzheimer's deaths.

A limitation of the internal analysis of metals was that few measurements of exposure were found for the early years of work for the cohort. Therefore, categorical values were assigned to each grouped job title, which can introduce misclassification, with bias toward the null hypothesis. In addition, job titles that had higher exposures for one metal tended to have high exposures to all metals, making it difficult to determine an association between a particular metal and an elevated outcome. The a priori outcome of interest with metals exposure was lung cancer. Medium exposure to nickel resulted in a significantly elevated SRR for this outcome, while non-significant elevations were found with medium exposures to uranium and beryllium. With the internal comparison of job titles, significantly elevated SRRs for lung cancer were found for the job titles Maintenance/Converter Shop and Maintenance/Custodial. Maintenance/Converter Shop had slightly elevated exposures to nickel and uranium. Maintenance/Custodial had slightly elevated exposures to beryllium and nickel, and higher exposures to uranium. The job title with the highest exposure to these metals, Chemical Operator, did not have an elevation in lung cancer. Interpretation of these results is limited by overlap in metals exposure and the lack of smoking data.

No patterns from cumulative internal or external radiation exposure were apparent. Exposure to radiation at the plant followed a log-normal distribution, with the majority of employees accumulating little exposure. The categories for radiation exposure were quartiles based on person years at risk. This strategy resulted in very low exposures in the lower quartiles, which may have masked evidence of a dose-response relationship. A further analysis is underway employing modeling techniques to further explore radiation exposure-disease relationships (RW Hornung, personal communication, manuscript in progress).

Limitations to this analysis included lack of smoking data. Based on previous studies similar in scope, it was anticipated that smoking rates would not be significantly different between exposed and unexposed workers and thus would not adversely impact this analysis[25,26]. We did not carry out an analysis of solid cancers not associated with smoking, to minimize potential confounding from smoking, because of low numbers of these outcomes.

In conclusion, this study describes a cohort mortality analysis for a large gaseous diffusion plant. Despite significant reductions in SMRs for all causes and all cancers, elevations in lymphatic and hematopoietic cancers were found for the cohort. The internal comparison showed certain job titles with higher exposures had non-significant elevations of hematopoietic cancers. These findings confirm the relationship found in previous studies between slight elevations in risk of hematopoietic cancers and low levels of radiation exposure[6,7,13].

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1
Paducah Gaseous Diffusion Plant cohort description (1952-2003)

Demographic	No. Workers	Percent
White Males	5016	74%
White Females	1069	16%
Other Races Male	564	8%
Other Races Female	171	3%
Deaths	1638	24%

Table 2

Grouped job titles that meet the analysis criteria of a minimum of 100 workers and 5% of the total cohort person years at risk

JOB TITLE	NO. WORKERS	PYAR
Cascade	1242	37824.87
Cascade NOT Chemical Operator	581	13791.25
Chemical Operator	1242	58178.49
Engineer	832	20731.59
Laboratory	570	16584.66
Maintenance	1301	40437.56
Maintenance NOT Chemical Operator	855	24860.31
Maintenance/Converter Shop	347	11655.23
Maintenance/Custodial	512	12560.33
Maintenance/Electrician	433	12866.33
Maintenance/Roads & Grounds	662	18848.95
Office	1441	41924.91
Security	372	11649.91
TOTAL		215114.77
5% CUTOFF		10755.74

These values are for the full cohort (all race and gender categories). Workers are included in a job title category if they ever held that position; therefore a worker may be included in two or more categories.

Table 3
Maintenance Categories and Additive Exposure Rankings

	No. Workers	Person Years at Risk	Additive Exposure Ranking
High Maintenance			
Maintenance	1301	40437.56	22.5
Maintenance Not Chemical Operator*	855	24860.31	22.5
Medium Maintenance		17412.97	
Maintenance/Fabrication	6	167.40	14.5
Maintenance/Instrument Mech.	321	10507.69	13.5
Maintenance/Lubrication	57	1511.13	17.5
Maintenance/Machining	220	8269.91	16.0
Maintenance/Sheet Metal	32	1088.30	15.0
Maintenance/Welding	13	338.53	17.8
Low Maintenance		38300.58	
Maintenance/Carpenter	32	904.51	10.8
Maintenance/Converter Shop	347	11655.23	8.3
Maintenance/Custodial	512	12560.33	10.0
Maintenance/Electrician	433	12866.33	11.8
Maintenance/Garage	35	1046.08	9.0
Maintenance/Painter	45	1191.35	6.5
Maintenance/Pump & Seal	1	20.23	11.8
Maintenance/Refrigeration	14	385.33	9.0
Maintenance/Roads & Grounds	662	18848.95	10.0
Maintenance/Truck Driver	46	1379.95	8.0

*This is a subset of the Maintenance grouped job title

An overall qualitative exposure level was for each job title by adding the levels of the five metals and TCE (additive exposure level; possible range 0-30). Where levels changed over time for a given exposure, the mean was used. The additive exposure level was then used to condense the 17 maintenance job title categories into the three categories: high, medium, and low exposure maintenance groups. These values are for the full cohort (all race and gender categories). Workers are included in a job title category if they ever held that position; therefore a worker may be included in two or more categories.

Table 4

Standardized Mortality Ratios for select causes of death among 6820 workers at the Paducah Gaseous Diffusion Plant 1952-2003

Category Cause	Observed Deaths	Expected Deaths	SMR	95% Confidence Limits	
				Lower	Upper
All Deaths	1638	2253.50	0.73**	0.69	0.76
All Cancers	461	592.35	0.78**	0.71	0.85
*** Other Causes	27	64.74	0.42**	0.27	0.61
Cancers of the Lymphatic & Hematopoietic Tissue					
ALL	68	57.20	1.19	0.92	1.51
Non-Hodgkin's Lymphoma	32	22.43	1.43	0.98	2.01
Hodgkin's Disease	2	3.32	0.60	0.07	2.18
Leukemia and Aleukemia	24	21.61	1.11	0.71	1.65
Multiple Myeloma	10	9.83	1.02	0.49	1.87
Cancers of the Bone and Connective tissue, Brain, Lung, Pancreatic and Unspecified Sites					
Bone	1	1.40	0.72	0.02	3.99
Connective Tissue	2	3.32	0.60	0.07	2.18
Brain	16	15.94	1.00	0.57	1.63
Kidney	14	14.39	0.97	0.53	1.63
Lung	146	201.55	0.72**	0.58	0.89
Pancreas	32	29.05	1.10	0.75	1.56
Other	37	40.88	0.91	0.64	1.25
Stomach	11	17.47	0.63	0.31	1.13

* Two-Sided $P < 0.05$

** Two-Sided $P < 0.01$

*** Other causes include all deaths that do not have a known cause of death and all deaths related to other causes not included in NIOSH's death categories and corresponding ICD codes.

Table 5

Standardized Rate Ratios for select outcomes and job titles for white males

Category Cause	Job Title	observed deaths	SRR	95%ConfidenceLimits	
				Lower	Upper
All Deaths	Cascade	282	0.97	0.85	1.12
	Chemical Operator	532	1.01	0.88	1.14
	Maintenance	306	0.94	0.83	1.08
	Office	94	1.03	0.82	1.29
	Security	136	1.34	1.06	1.71
All Cancers	Cascade	70	0.83	0.63	1.09
	Chemical Operator	143	0.96	0.74	1.23
	Maintenance	75	0.94	0.61	1.02
	Office	35	1.34	0.92	1.96
	Security	31	1.01	0.67	1.51
Cancers of the Lymphatic & Hematopoietic Tissue					
ALL	Cascade	12	0.92	0.48	1.77
	Chemical Operator	26	1.18	0.69	2.02
	Maintenance	10	0.65	0.33	1.30
	Office	6	1.31	0.52	3.29
	Security	8	1.74	0.82	3.71
Non-Hodgkin's	Cascade	5	0.82	0.30	2.23
	Chemical Operator	9	0.82	0.35	1.92
	Maintenance	5	0.71	0.26	1.90
	Office	3	1.98	0.58	6.69
	Security	5	2.44	0.91	6.55
Leukemia	Cascade	5	1.16	0.42	3.20
	Chemical Operator	11	1.49	0.62	3.58
	Maintenance	3	0.58	0.17	2.00
	Office	2	0.54	0.13	2.33
	Security	3	1.90	0.56	6.47
Cancers of the Brain, Lung, and Pancreas					

Category Cause	Job Title	observed deaths	SRR	95%ConfidenceLimits	
				Lower	Upper
Brain	Cascade	3	0.79	0.22	2.85
	Chemical Operator	8	2.29	0.78	6.71
	Maintenance	3	0.74	0.21	2.66
	Office	1	0.34	0.04	2.62
	Security	2	3.78	0.78	18.29
Lung	Cascade	23	0.72	0.48	1.77
	Chemical Operator	46	0.89	0.54	1.45
	Maintenance	21	0.71	0.44	1.14
	Office	7	0.99	0.45	2.18
	Security	10	0.80	0.41	1.55
Pancreas	Cascade	0	0.94	0.36	2.47
	Chemical Operator	6	0.92	0.39	2.17
	Maintenance	7	1.01	0.43	2.41
	Office	3	1.57	0.42	5.84
	Security	1	0.36	0.05	2.64

Table 6

SRRs for cumulative radiation exposure for white males

Internal Radiation Quartile

	1	2		3		4	
	0-20 ug-yr	21-50 ug-yr		51-125 ug-yr		>125 ug-yr	
Outcome	**(SRR=1) n**	**SRR (95% CI) n**	**n**	**SRR (95% CI)**	**n**	**SRR (95% CI)**	**n**
All Causes	208	1.02 (0.84-1.22)	286	1.06 (0.89-1.26)	411	0.70 (0.57-0.85)	475
All Cancers	73	0.86 (0.62-1.19)	82	0.77 (0.56-1.05)	103	0.61 (0.40-0.94)	129
Lung Cancer	21	0.91 (0.51-1.62)	27	0.95 (0.56-1.63)	41	0.51 (0.30-0.88)	40
Brain Cancer	3	0.66 (0.10-4.16)	2	1.07 (0.24-4.80)	5	0.45 (0.10-2.15)	4
Bone Cancer	0	NR	0	NR	1	NR	0
Kidney Cancer	0	NR	3	NR	3	NR	7
Pancreatic Cancer	5	1.42 (0.43-4.67)	8	0.49 (0.12-1.94)	4	0.97 (0.31- 2.98)	13
Lymphatic & Hematopoietic	6	1.79 (0.66-4.88)	13	1.48 (0.55-4.02)	13	1.35 (0.53-3.41)	25
Non-Hodgkin's	1	9.95 (1.22-81.26)	7	8.85 (1.11-70.83)	8	5.74 (0.72-45.48)	10
Hodgkin's	1	0.67 (0.04-10.73)	1	NR	0	NR	0
Leukemia	4	0.73 (0.18-3.01)	4	0.49 (0.11-2.26)	3	0.77 (0.24-2.50)	10
Multiple Myeloma	0	NR	1	NR	2	NR	5

External Radiation Quartile

	1	2		3		4	
	0-100 mrem	101-500 mrem		501-1000 mrem		>1000 mrem	
Outcome	**(SRR=1) n**	**SRR (95% CI)**	**n**	**SRR (95% CI)**	**n**	**SRR (95% CI)**	**n**
All Causes	236	0.86 (0.62-1.19)	289	0.77 (0.56-1.05)	261	0.61 (0.40-0.94)	594
All Cancers	67	1.08 (0.90-1.29)	82	0.91 (0.76-1.10)	76	0.70 (0.60-0.82)	162
Lung Cancer	24	1.04 (0.60-1.80)	29	0.77 (0.42-1.40)	22	0.61 (0.37-1.00)	54
Brain Cancer	2	2.44 (0.46-12.86)	5	0.59 (0.05-6.58)	1	1.05 (0.21-5.26)	6
Bone Cancer	0	NR	0	NR	1	NR	0
Kidney Cancer	0	NR	3	NR	1	NR	9
Pancreatic Cancer	3	1.66 (0.39-7.02)	6	1.72 (0.42-7.05)	6	1.48 (0.42-5.20)	15
Lymphatic & Hematopoietic	11	1.14 (0.50-2.59)	13	0.67 (0.25-1.75)	7	0.70 (0.34-1.45)	26
Non-Hodgkin's	5	1.20 (0.36-4.01)	6	0.91 (0.24-3.48)	4	0.76 (0.26-2.25)	11

Internal Radiation Quartile

	1	2		3		4	
	0-20 ug-yr	**21-50 ug-yr**		**51-125 ug-yr**		**>125 ug-yr**	
Outcome	**(SRR=1) n**	**SRR (95% CI) n**	**n**	**SRR (95% CI)**	**n**	**SRR (95% CI)**	**n**
Hodgkin's	2	NR	0	NR	0	NR	0
Leukemia	3	2.19 (0.52-9.14)	1	0.36 (0.04-3.55)	1	1.14 (0.31-4.27)	11
Multiple Myeloma	1	0.79 (0.05-12.70)	2	1.70 (0.15-18.76)	2	0.88 (0.10-7.88)	4

NR – statistic not reported because of one comparison group having 0 deaths.

n = observed deaths