Exhibit 191

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Cancer Incidence among Marines and Navy Personnel and Civilian Workers Exposed to Industrial Solvents in Drinking Water at US Marine Corps Base Camp Lejeune: A Cohort Study

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Background: Drinking water at US Marine Corps Base Camp Lejeune, North Carolina, was contaminated with trichloroethylene and other industrial solvents from 1953 to 1985.

Methods: A cohort cancer incidence study was conducted of Marines/Navy personnel who began service and were stationed at Camp Lejeune ($N = 154{,}821$) or Camp Pendleton, California ($N = 163{,}484$) between 1975 and 1985 and civilian workers employed at Camp Lejeune ($N = 6{,}494$) or Camp Pendleton ($N = 5{,}797$) between October 1972 and December 1985. Camp Pendleton's drinking water was not contaminated with industrial solvents. Individual-level information on primary invasive cancers and *in situ* bladder cancer diagnosed between 1996 and 2017 was obtained from 54 US cancer registries. Proportional hazards regression was used to calculate adjusted hazard ratios (aHRs) comparing cancer incidence between the Camp Lejeune and Camp Pendleton cohorts, adjusted for sex, race, education, and rank (or blue-collar work), with age as the time variable. Precision of aHRs was evaluated using the 95% confidence interval (CI) ratio (CIR).

Results: Cancers among Camp Lejeune Marines/Navy personnel and civilian workers totaled 12,083 and 1,563, respectively. Cancers among Camp Pendleton Marines/Navy personnel and civilian workers totaled 12,144 and 1,416, respectively. Compared with Camp Pendleton, Camp Lejeune Marines/Navy personnel had aHRs ≥1.20 with CIRs ≤3 for all myeloid cancers (HR = 1.24; 95% CI: 1.03, 1.49), acute myeloid leukemia (HR = 1.38; 95% CI: 1.03, 1.85), myelodysplastic and myeloproliferative syndromes (HR = 1.68; 95% CI: 1.07, 2.62), polycythemia vera (HR = 1.41; 95% CI: 0.94, 2.11), and cancers of the esophagus (HR = 1.27; 95% CI: 1.03, 1.56), larynx (HR = 1.21; 95% CI: 0.98, 1.50), soft tissue (HR = 1.21; 95% CI: 0.92, 1.59), and thyroid (HR = 1.22; 95% CI: 1.03, 1.45). Lymphoma subtypes mantle cell and marginal zone B-cell and lung cancer subtypes adenocarcinoma and non-small cell lung cancer also had aHRs ≥1.20 with CIRs ≤3. Compared with Camp Pendleton, Camp Lejeune civilian workers had aHRs ≥1.20 with CIRs ≤3 for all myeloid cancers (HR = 1.40; 95% CI: 0.83, 2.36), squamous cell lung cancer (HR = 1.63; 95% CI: 1.10, 2.41), and female breast (HR = 1.21; 95% CI: 0.97, 1.52) and ductal cancer (HR = 1.32; 95% CI: 1.02, 1.71).

Conclusion: Increased risks of several cancers were observed among Marines/Navy personnel and civilian workers exposed to contaminated drinking water at Camp Lejeune compared with Camp Pendleton. https://doi.org/10.1289/EHP14966

Background

Drinking water at US Marine Corps (USMC) Base Camp Lejeune, North Carolina, is sourced from groundwater supply wells. Eight treatment plants supplied drinking water to different areas of the base. Water from supply wells was mixed at the treatment plant prior to entering distribution as finished water.

Distribution system samples collected between 1980 and 1985 at Camp Lejeune found industrial solvents in the drinking water supplied by two treatment plants [Tarawa Terrace (TT) and Hadnot Point (HP)]. Tetrachloroethylene (PCE) was detected in 2 of the 9 supply wells serving the TT system.[1] Trichloroethylene (TCE) was detected in 6 of the 28 supply wells serving the HP system.[2]

The TT treatment plant began operating in 1952 and served ∼1,850 family housing units. The TT supply wells were contaminated by PCE from an off-base dry-cleaning business, with a maximum measured concentration in the TT distribution system of 215 μg/L.[1]

The HP treatment plant began operation in 1942 and served the base's "mainside," including most workplaces and barracks, field training areas (via mobile "water buffaloes"), family housing, and eating establishments. The HP supply wells were contaminated by on-base sources—leaking underground storage tanks, industrial area spills, and waste disposal sites. The maximum measured concentrations in the HP distribution system were 1,400 μg/L for TCE and 100 μg/L for PCE. Also detected in the distribution system were benzene from fuel tank leaks and vinyl chloride from the degradation of PCE and TCE in groundwater.[2]

Few distribution system samples for volatile organic compounds were taken between 1980 and 1985 at Camp Lejeune, and none prior to 1980. The Agency for Toxic Substances and Disease Registry (ATSDR) conducted historical reconstruction modeling; they determined that contamination of the TT and HP systems began by the mid-1950s and estimated monthly average contaminant concentrations in the TT and HP systems.[1–2] The ATSDR's estimates of monthly average concentrations of PCE in the TT distribution system between January 1975 and February 1985 ranged from 0 to 158 μg/L, with a median of 85 μg/L.[1] Estimated monthly average concentrations of TCE, PCE, and vinyl chloride in the HP distribution system between January 1975 and February 1985 ranged from 0 to 783, 0 to 39, and 0 to 67 μg/L, respectively, with median levels of 366, 15, and 22 μg/L, respectively.[2] Contamination levels in each system varied depending on the supply wells in use, their levels of contamination, and their pumpage rates.[1–2] The highly contaminated

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supply wells serving the TT and HP systems were shut down in February 1985, although benzene concentrations above its maximum contaminant level (MCL) of 5 μg/L were detected in the HP distribution system in late 1985.

The US Environmental Protection Agency (EPA) MCLs are 5 μg/L for TCE, PCE, and benzene, and 2 μg/L for vinyl chloride.[3] A Marine in training is estimated to consume 6 L/d of drinking water three times per week and 3 L/d four times per week.[4] Marines/Navy personnel not in training and civilian workers are estimated to consume 3 L/d.[4] The combined dose from inhalation and dermal routes may be higher than the dose from the ingestion route.[5]

The International Agency for Research on Cancer (IARC) has classified TCE, benzene, and vinyl chloride as known human carcinogens, and PCE as "probably carcinogenic to humans."[6–8] The ATSDR has reviewed occupational and environmental epidemiological studies and evidence from animal and mechanistic studies for TCE, PCE, benzene, and vinyl chloride.[9] Sufficient causal evidence was found for TCE and kidney cancer and non-Hodgkin lymphoma (NHL); PCE and bladder cancer; benzene and NHL and leukemias; and vinyl chloride and liver cancer.[9] Evidence as likely as not or greater but less than sufficient evidence was found for TCE and multiple myeloma, leukemias, and liver cancer; PCE and NHL; and benzene and multiple myeloma.[9]

To our knowledge, three studies have evaluated cancer incidence and drinking water exposures to TCE or PCE. A New Jersey study observed associations between TCE and PCE and NHL, and between TCE and leukemia.[10] A Cape Cod, Massachusetts, study found associations between PCE and cancers of the lung, bladder, rectum, female breast, and leukemia.[11–13] An ATSDR case–control study of male breast cancer incidence found an elevated risk comparing Camp Lejeune Marines with Marines at other bases but was limited to cancers ascertained from the US Veterans Affairs (VA) registry.[14]

The ATSDR has previously conducted cohort mortality studies comparing Marines/Navy personnel and civilian workers stationed or employed at Camp Lejeune from 1975 to 1985 and 1973 to 1985, respectively, with similar cohorts over the same periods at USMC Base Camp Pendleton, California.[15–16] The follow-up period for causes of death was from 1979 to 2008. Both studies found associations for cancers of the kidney, rectum, lung, prostate, leukemias, and multiple myeloma,[15–16] but the findings were limited by the typically long latency periods of these cancers plus the young ages of the cohort members at the end of follow-up and by the limitations inherent in mortality studies. For example, death certificates would miss cancers not considered underlying or contributing causes of death. Moreover, cancers can be miscoded on death certificates because of failure to distinguish primary from metastatic sites or to distinguish between tumor sites that are contiguous.[17]

A cancer incidence study using individual-level data from US population-based cancer registries has a greater capability than a mortality study of evaluating highly survivable cancers. Cancer registry data also include information not available on the death certificate, such as the histology and behavior (i.e., benign, *in situ*, malignant) of the tumor.

The purpose of this cancer incidence cohort study was to determine whether being stationed or employed at Camp Lejeune between 1975 and 1985 (Marines/Navy personnel) or between October 1972 and December 1985 (civilian workers) increased the risk of malignant ("invasive") cancers (and bladder cancer *in situ*) ascertained between 1996 and 2017 compared with being stationed or employed at Camp Pendleton. Sampling of Camp Pendleton's drinking water between 1989 and 2005 did not detect industrial solvents above their MCLs, although lead and copper were detected above their US EPA action levels in some samples taken between 1991 and 2000.[18]

Methods

Study Populations

The ATSDR obtained quarterly personnel data from the Defense Manpower Data Center (DMDC) for Marines/Navy personnel and civilian workers stationed or employed at Camp Lejeune or Camp Pendleton. Civilian workers were included in the study if they were employed during any quarter at either base between October 1972 and December 1985. The DMDC started data collection for civilian workers in October 1972. Marines/Navy personnel were included in the study if they were stationed during any quarter at either base between April 1975 and December 1985. DMDC data did not include military unit codes, necessary to determine base locations, until April 1975. December 1985 was selected as an end point because drinking water distribution system samples taken at Camp Lejeune after 1985 had no contaminant levels above their MCLs.

The civilian worker cohort included 6,494 employed at Camp Lejeune and 5,797 employed at Camp Pendleton who were known to be alive as of 1 January 1996. The DMDC data included base location of employment, social security number, full name (from October 1981 onward), date of birth, occupation code, quarter and year of employment, and self-reported race, sex, and education. Employment start date was not provided in the DMDC data.

The full cohort of Marines/Navy personnel included 208,063 at Camp Lejeune and 225,999 at Camp Pendleton who were known to be alive as of 1 January 1996. DMDC data included full name, social security number, quarter and year of service, date of birth, military unit code, rank, date active duty started, military occupation code, and self-reported race, sex, and education. Deployment and training information was not available in the DMDC data. The USMC provided a list of military unit codes for each base.

Within the full cohort of Marines/Navy personnel, some began active duty prior to 1975, when DMDC data did not include military unit code. Because base locations prior to 1975 were unknown, an individual stationed at Camp Pendleton between 1975 and 1985, and therefore considered unexposed to contaminated drinking water, could have been stationed at Camp Lejeune prior to 1975 and exposed. To minimize this source of exposure misclassification, a subgroup of the full cohort, who began active duty between 1975 and 1985, was the focus of the evaluation of cancer incidence among Marines and Navy personnel. This subgroup consisted of 154,821 at Camp Lejeune and 163,484 at Camp Pendleton who were known to be alive as of 1 January 1996.

Camp Pendleton was selected as the reference population because the base's finished drinking water was not contaminated with industrial solvents.[18] Moreover, Camp Pendleton was similar to Camp Lejeune on demographics, socioeconomic and cultural factors, training activities, and military and civilian employee occupations.

Cancer Ascertainment

A commercial tracing service, the Social Security Administration Data for Epidemiological Researchers, and the National Death Index provided residential addresses, vital status, and date of death. The study obtained individual-level data on all primary, invasive cancer cases and *in situ* bladder cancer cases diagnosed between 1996 and 2017 via linkages with 49 state cancer registries, the District of Columbia registry, Puerto Rico and Pacific Islands registries, and Department of Defense (DOD) and VA registries. *In situ* bladder cancers were included because of the

difficulty distinguishing *in situ* and invasive bladder cancers.[19] For other cancers, only invasive cases were included. Follow-up began on 1 January 1996, because all registries were operating by 1996. Follow-up ended on 31 December 2017 because when linkages occurred some registries did not have complete and verified data after 2017.

Owing to state law restrictions requiring consent of the living patient, the West Virginia Cancer Registry could not provide individual-level data for this study. The Kansas Cancer Registry had a similar state law restriction but obtained consent from and provided individual-level data for most of the matches. All other cancer registries provided individual-level data without requiring patient consent.

All registries except the DOD registry used the same linkage software, Match*Pro (version 1.6.2).[20] Manual review procedures were performed at all registries except the VA and DOD registries. Matching parameters were social security number; date of birth; first, middle, and last name (using a Soundex algorithm); and street address. Blocking parameters (first name, last name, social security number, and date of birth) were used to limit the number of comparisons to those records for which two or more blocking parameters matched.

The linkage software produced three classes of matches: high quality, uncertain, and nonmatches. The thresholds for these three classes were based on pilot tests with three cancer registries and were consistent across all linkages. Excluding the DOD and VA registries, all participating registries manually reviewed uncertain matches to identify any missed cases, and >90% of the registries reviewed all high-quality matches for potential false positives. Based on this review, ∼0.1% of the high-quality matches were identified as false positives. Nonmatches were reviewed for false negatives. Once all the cancer data were received, duplicate records were removed.

Information for each matched tumor record included the primary site of the cancer, histologic type, behavior code, sequence number, age of the patient at diagnosis, and date of diagnosis. Histological subtypes were defined using the Surveillance, Epidemiology, and End Results Program site recode definitions[21–22] and are listed in Table S1.

Data Analyses

Marines/Navy personnel and civilian employees were analyzed separately. The Marines/Navy personnel analyses focused on comparisons between the Camp Lejeune and Camp Pendleton subgroups (i.e., who began active duty between 1975 and 1985). The comparison between the Camp Lejeune and Camp Pendleton full cohort of Marines/Navy personnel (i.e., the cohort unrestricted by the start date of active duty) was conducted as a secondary analysis.

Follow-up began on 1 January 1996 and continued until date of death or 31 December 2017, whichever was earlier. The analyses evaluated individual-level data using Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for each cancer primary site and histological subtype. Age in years (continuous) was the time variable; therefore, all models were adjusted for age. Base location was not lagged because the start of follow-up was >10 y after contamination ended at Camp Lejeune. Schoenfeld residuals were evaluated to check the proportional hazards assumption.[23] The analyses used SAS (version 9.4; SAS Institute, Inc.) and STATA (version 16; StataCorp) software.

Adjusted models for Marines/Navy personnel included sex, race, rank, and education. Adjusted models for civilian workers included sex, race, education, and blue-collar work (yes/no). These factors were included in the adjusted models because disparities in cancer incidence rates are known to occur among different sex, racial, and socioeconomic groups. Rank, education, and blue-collar work were included in the models to adjust for socioeconomic factors. Race is a social construct that was included in the models to account for the impacts of systemic discrimination.

DMDC data for Marines/Navy personnel categorized race as White, Black, Other race, and Unknown. Those coded as Unknown or with a missing code were recoded as Other race. For civilian workers, the DMDC data categorized race/national origin as White Non-Hispanic, Non-Hispanic Black, Hispanic, American Indian or Alaskan Native, Asian or Pacific Islander, Non-Hispanic in Puerto Rico, and invalid. Because of small sample numbers, all race/national origin groups not coded as White Non-Hispanic or Non-Hispanic Black were recoded as Other race, including those with invalid or missing codes.

For education level, the DMDC data included 12 categories for Marines/Navy personnel and 15 categories for civilian workers. Education level was recoded as not a high school graduate, a high school graduate, and a college graduate. Those with missing data were assumed to be high school graduates. For civilian workers, most of the missing data on education occurred in the DMDC data prior to 1982, when name also was not included.

An individual could contribute cancers to more than one primary site but not more than one per site. For example, if a person had recurrent lung cancer records during the follow-up period, only the first diagnosis during the period was included in the lung cancer analysis. However, an individual could contribute to more than one histological subtype of a cancer primary site. For example, an individual diagnosed with lung adenocarcinoma and later with lung squamous cell would be included in the analysis of each of these histological subtypes.

Secondary analyses evaluated categorical variables for the duration of assignment or employment (in quarters of the year) at Camp Lejeune as a proxy for cumulative drinking water exposure. For the Marines/Navy personnel subgroup, duration stationed at Camp Lejeune between April 1975 and December 1985 was categorized as low (1–6 quarters), medium (7–10 quarters), and high (>10 quarters). For the civilian workers, employment duration at Camp Lejeune between October 1972 and December 1985 was categorized as low/medium (1–21 quarters) and high (>21 quarters). Members of the Camp Pendleton cohorts had no duration assigned at Camp Lejeune between April 1975 and December 1985 (Marines and Navy personnel) or employed at Camp Lejeune between October 1972 and December 1985 (civilian workers) and were therefore used as references. The adjusted models included a continuous variable for total annual quarters stationed or employed at either base.

Quantitative bias analyses (QBA) using Excel spreadsheets estimated the possible impacts on the adjusted HRs (aHRs) of confounding from smoking and alcohol consumption and exposure misclassification bias.[24] A QBA involves choosing a bias model (e.g., exposure misclassification), an analytic technique (e.g., a multidimensional analysis), and values for the parameters of the bias model. The values of the bias parameters are applied to the observed data using bias adjustment equations embedded in the spreadsheets to calculate what the aHR would have been if the bias were absent.

The QBA parameters for confounding were the prevalence of the confounding factor in the Camp Lejeune and Camp Pendleton cohorts, and a range of risk ratios (RRs) associating the confounder with the cancer under evaluation. The prevalence of smoking and alcohol consumption among Marines/Navy personnel was based on a 1980 survey of active-duty military personnel that found 53.4% of Marines smoked and about 30% of Marines were heavy drinkers (i.e., consumed ≥5 drinks per typical drinking occasion at least once a week).[25] The QBA assumed that at least two-thirds of

Marines/Navy personnel consumed ≥1 drink/d. For civilian workers, the QBA assumed about half smoked and one-third consumed ≥1 drink/d.

Negative control diseases[26] were used to estimate smoking and alcohol consumption prevalence differences between Camp Lejeune and Camp Pendleton. Negative control diseases for smoking were mortality due to chronic obstructive pulmonary disease (COPD)[27] and cardiovascular disease (CVD). CVD is also associated with metabolic factors such as hypertension, diabetes, non–high-density lipoprotein cholesterol, obesity, and diet.[28] Negative control diseases for alcohol consumption were mortality due to chronic liver disease,[29] alcoholism, and alcoholic liver disease. Smoking-related cancers, such as cancers of the lung, larynx, and bladder,[30] and alcohol-related cancers, such as cancers of the oral cavity/pharynx, larynx, liver, esophagus, colon, and female breast,[31] were not considered negative control diseases because there was evidence in the scientific literature linking these cancers to one or more of the contaminants in the drinking water.[9,11–13,32–37]

To estimate the prevalence difference in smoking or alcohol consumption between the two bases, the QBA used *a*) the observed aHR for the negative control disease comparing Camp Lejeune to Camp Pendleton, and *b*) a range of RR estimates from the literature associating smoking or alcohol consumption with the negative control disease.[27–29] For example, for smoking and the negative control disease COPD, the QBA used a range of RRs from 3.00 to 5.00 based on a systematic review with meta-analysis.[27] (Using higher RRs for smoking and COPD would reduce the prevalence difference between Camp Lejeune and Camp Pendleton, resulting in a lower impact of confounding bias due to smoking.) For alcohol consumption and the negative control disease chronic liver disease mortality, the QBA used RRs ranging from 2.50 to 10.00. This range of RRs was based on a systematic review of alcohol consumption and liver cirrhosis mortality that found RRs of 2.65, 6.83, and 16.38 for drinking 25 g/d (2 drinks/d), 50 g/d (4 drinks/d), and 100 g/d (8 drinks/d) compared with those who never drank alcoholic beverages.[29] To estimate the impact of possible confounding on the observed aHR for a cancer under evaluation, the QBA used *a*) the prevalence difference of the confounder between the two bases, and *b*) a range of RR estimates from the literature associating the confounder with the cancer.[30,31,38–40]

The QBA parameters for exposure misclassification were the sensitivity of the exposure classification, that is, the probability that the truly exposed were correctly classified as exposed (i.e., assigned to Camp Lejeune) and the specificity of the exposure classification, that is, the probability that the truly unexposed were correctly classified as unexposed (i.e., assigned to Camp Pendleton). Exposure misclassification was assumed to be nondifferential and independent[24] because *a*) base assignments derived from the unit codes for Marines/Navy personnel were completed >10 y prior to cancer data collection, and *b*) the base location of employment for civilian workers was recorded in the DMDC database >30 y prior to cancer data collection.

For Camp Lejeune Marines/Navy personnel, the sources of possible exposure misclassification were due to using base assignment as a proxy for exposure to the drinking water. First, errors were possible in the historical research conducted by the DMDC and USMC to determine the base where each unit was located. Second, even if the base assignment of the unit was correct, some individuals may not have been exposed to the contaminated drinking water because they were deployed to a different base (e.g., outside the country) or trained at a different base. Third, some individuals stationed at Camp Lejeune may not have been exposed because all their water consumption (including showering and other water uses) occurred off base (e.g., in off-base housing) or in areas of the base not served by the TT or HP drinking water systems. On the other hand, most of those classified as stationed at Camp Pendleton likely were truly unexposed to the contaminated drinking water.

For Camp Lejeune civilian workers, the main source of exposure misclassification was due to water consumption (including showering and other water uses) occurring mostly or entirely off base (e.g., at their residences). In addition, the workplaces of some of the Camp Lejeune civilian workers may have been located in areas not served by the contaminated drinking water. All civilian workers at Camp Pendleton were assumed to be truly unexposed to contaminated drinking water during the study period. To conduct the QBA of exposure misclassification, sensitivity was set at 1.0, and specificity ranged from 0.81 to 0.91, based on the assumptions that between 75% and 90% of those stationed or employed at Camp Lejeune were truly exposed and that all of those stationed or employed at Camp Pendleton were truly unexposed.

Statistical significance testing was not used.[41–43] Findings were interpreted based on the magnitude of the aHR, its precision using the ratio of the upper to lower limits of the 95% CI (CIR)[44–45] and supporting evidence from the scientific literature on the health effects of TCE, PCE, benzene, and vinyl chloride exposures. Because published meta-analyses evaluating TCE, PCE, and benzene obtained summary RRs ≥1.20,[9] we emphasized aHRs ≥1.20. An appropriate CIR level is not specified in the literature. We considered CIRs ≤3 as indicating reasonable precision of the aHR. This study was approved by the Centers for Disease Control and Prevention (CDC) Institutional Review Board with a waiver of informed consent.

Results

Table 1 provides demographic information for the Marines/Navy personnel subgroup (i.e., who began active duty between 1975 and 1985). Demographic information and results for the full cohort of Marines/Navy personnel are included in Tables S2 and S3.

The Camp Lejeune Marines/Navy personnel subgroup was similar to the Camp Pendleton subgroup on sex, rank, education, age at start and end of follow-up, length of follow-up, quarters in the DMDC data between 1975 and 1985, deaths, and total number diagnosed with cancer. There were higher percentages of personnel who identified as Black at Camp Lejeune and as the Other race category at Camp Pendleton.

Compared with Camp Pendleton, a higher percentage of Camp Lejeune civilian workers were women, Black, and college graduates, and a lower percentage of Camp Lejeune workers were aged >75 y at the end of follow-up, identified as Other race, and died (Table 2). Civilian workers at the two bases were similar on the percentage of blue-collar occupations, length of follow-up, and number of quarters employed between October 1972 and December 1985.

Cox regression analysis of the Marines/Navy personnel subgroup resulted in aHRs ≥1.20 with CIRs ≤3 for all myeloid cancers as a group and separately for acute myeloid leukemia (AML), myelodysplastic and myeloproliferative syndromes, and polycythemia vera; for cancers of the esophagus, larynx, soft tissue, and thyroid; lung cancer histological subtypes, including non-small cell, large cell, and adenocarcinoma; NHL subtypes mantle cell and marginal zone B-cell lymphoma (MZBCL); and squamous cell esophageal cancer (Table 3). In the full cohort, male breast cancer had aHR ≥1.20 with CIR ≤3 (Table S3).

Cox regression analysis of civilian workers obtained aHRs ≥1.20 with CIRs ≤3 for all myeloid cancers as a group, squamous

Table 1. Demographic information for the Marines/Navy personnel subgroup who began active duty between 1975 and 1985, by military base.

Factor	Camp Lejeune [$N = 154{,}821$ (48.6%)]	Camp Pendleton (ref) [$N = 163{,}484$ (51.4%)]	Total ($N = 318{,}305$)
Sex [*n* (%)]			
Male	146,772 (94.8)	157,617 (96.4)	304,389 (95.6)
Female	8,049 (5.2)	5,867 (3.6)	13,916 (4.4)
Race [*n* (%)]			
White	113,525 (73.4)	127,385 (78.1)	240,910 (75.8)
Black	37,138 (24.0)	27,599 (16.9)	64,737 (20.3)
Other race[a]	4,041 (2.6)	8,221 (5.0)	12,262 (3.9)
Missing	117	279	396
Military rank [*n* (%)]			
Rank E1–E4	126,471 (81.7)	132,874 (81.3)	259,345 (81.5)
Rank E5–E9	22,662 (14.6)	23,051 (14.1)	45,713 (14.4)
WO or CO	5,688 (3.7)	7,559 (4.6)	13,247 (4.2)
Education [*n* (%)]			
Not a high school graduate	18,683 (12.1)	25,400 (15.6)	44,083 (13.9)
High school graduate	129,843 (84.1)	129,419 (79.5)	259,262 (81.7)
College graduate	5,943 (3.8)	8,026 (4.9)	13,969 (4.4)
Missing	352	639	991
Age at start of follow-up (1 January 1996) (y)			
Mean ± SD	35.0 ± 3.6	35.2 ± 3.6	35.1 ± 3.6
Median	35	35	35
Age at end of follow-up (31 December 2017 or date of death) (y)			
Mean ± SD	56.3 ± 4.5	56.5 ± 4.5	56.4 ± 4.5
Median	57	57	57
≥60 [*n* (%)]	35,426 (22.9)	39,734 (24.3)	75,160 (23.6)
>69 [*n* (%)]	292 (0.2)	277 (0.2)	569 (0.2)
Died during 2 January 1996–31 December 2017 [*n* (%)]	13,632 (8.8)	14,904 (9.1)	28,536 (9.0)
Length of follow-up (y)[b]			
Mean ± SD	20.3 ± 3.0	20.3 ± 3.0	20.3 ± 3.0
Median	21	21	21
Total person-years of follow-up [*n* (%)]	3,417,738 (48.5)	3,626,570 (51.5)	7,044,308
Quarters in the DMDC data, 1975–1985 (*n*)[c]			
Mean	7.7	7.2	—
Median	7.0	6.0	—
Minimum	1	1	—
Maximum	41	42	—
IQR (25th–75th percentiles)	8 (3–11)	8 (3–11)	—
Cancers			
Total malignancies (including bladder cancer *in situ*) (*n*)	12,083	12,144	24,227
Total individuals with any malignancy or bladder cancer *in situ* [*n* (%)]	11,207 (7.2)	11,329 (6.9)	22,536 (7.1)

Note: —, not applicable; CO, commissioned officer; DMDC, Defense Manpower Data Center; E1–E4, private to corporal; E5–E9: sergeant to sergeant major; IQR, interquartile range; ref, reference; SD, standard deviation; WO, warrant officer.
[a]Other race includes race other than White or Black.
[b]Follow-up was between 1996 and 2017.
[c]Number of quarters at either Camp Lejeune or Camp Pendleton during 1975–1985. The statistics for the Camp Lejeune cohort include quarters at Camp Pendleton during 1975–1985. The Camp Pendleton cohort members were not stationed at Camp Lejeune during 1975–1985.

cell lung cancer, and female breast and ductal cancer (Table 4). NHL had aHR of 1.19 with CIR ≤3. Cancers with aHRs ≥1.20, but with wide CIs (CIRs >3), primarily because of the small numbers of cases, included cancers of the male breast, oral cavity/pharynx and thyroid; AML; myelodysplastic and myeloproliferative syndromes; follicular and diffuse large B-cell (DLBCL) lymphomas; and non-papillary transitional cell bladder carcinoma.

For the Marines/Navy personnel subgroup, monotonic trends[42] for bladder cancer and thyroid cancer were observed, with aHRs ≥1.20 and CIRs ≤3 at the high (>10 quarters) duration of assignment at Camp Lejeune (Table 5). The trend for esophageal cancer was flat with aHR ≥1.20 and CIR ≤3 at the high duration level. Non-monotonic trends with aHRs ≥1.20 and CIRs ≤3 at the high duration level were observed for soft tissue sarcoma, all myeloid cancers as a group, AML, and non-small cell lung cancer.

For the civilian workers, a monotonic trend for lung cancer was observed with aHR ≥1.20 and CIR ≤3 at the high (>21 quarters) duration of employment at Camp Lejeune (Table 6). A non-monotonic trend with aHR ≥1.20 and CIR ≤3 at the high duration level was found for prostate cancer. Several cancers had monotonic trends with aHRs ≥1.20 but with CIRs >3 at the high duration level.

QBA Results

The QBA of the Marines/Navy personnel subgroup analysis obtained aHRs of 0.99 (95% CI: 0.95, 1.03), 1.08 (95% CI: 0.93, 1.27), 0.90 (95% CI: 0.76, 1.07), 0.86 (95% CI: 0.76, 0.99), and 0.93 (95% CI: 0.83, 1.03) for the negative control diseases CVD, COPD, alcoholism, alcoholic liver disease, and chronic liver disease, respectively, as underlying causes of death (Table S4). The CVD result suggested no differences in smoking or metabolic risk factors between the two bases. Using a range of RRs from 3.00 to 5.50 for smoking and COPD[27] to fully explain the aHR of 1.08 for COPD, the prevalence difference between Camp Lejeune and Camp Pendleton would be ≤6% (Table S5). Adjusting for a smoking prevalence difference of 6% and assuming RRs for smoking and lung cancer and laryngeal cancer between 7.00 and 12.00,[30] the aHR of 1.16 for lung cancer would decrease to between 1.05 and 1.06, and the aHR of 1.21 for laryngeal cancer would decrease to between 1.10 and 1.11 (Tables S6 and S7). Assuming RRs for smoking and esophageal cancer ∼2.5,[30,38] the aHR of 1.27 for esophageal cancer would decrease to between 1.18 and 1.25 (Table S8).

The results for the alcohol negative control diseases suggested that Camp Lejeune Marines/Navy personnel consumed less alcohol,

Table 2. Demographic information for civilian workers, by military base of employment.

Factor	Camp Lejeune [$N = 6{,}494$ (52.8%)]	Camp Pendleton (ref) [$N = 5{,}797$ (47.2%)]	Total ($N = 12{,}291$)
Sex [*n* (%)]			
Male	3,026 (46.6)	2,992 (51.6)	6,018 (49.0)
Female	3,468 (53.4)	2,805 (48.4)	6,273 (51.0)
Race [*n* (%)]			
White Non-Hispanic	4,998 (79.7)	4,483 (79.0)	9,481 (79.3)
Non-Hispanic Black	1,178 (18.8)	461 (8.1)	1,639 (13.7)
Other race[a]	98 (1.6)	734 (12.9)	832 (7.0)
Missing	220	119	339
Type of work [*n* (%)]			
Blue collar	2,251 (34.7)	2,260 (39.0)	4,511 (36.7)
White collar	4,243 (65.3)	3,537 (61.0)	7,780 (63.3)
Education [*n* (%)]			
Not a high school graduate	700 (13.0)	483 (10.4)	1,183 (11.8)
High school graduate	3,585 (66.6)	3,678 (79.1)	7,263 (72.4)
College graduate	1,101 (20.4)	487 (10.5)	1,588 (15.8)
Missing	1,108	1,149	2,257
Age at start of follow-up (1 January 1996) (y)			
Mean ± SD	52.9 ± 12.3	55.1 ± 13.2	53.0 ± 12.7
Median	50	53	51
Age at end of follow-up (31 December 2017 or date of death) (y)			
Mean ± SD	72.1 ± 9.9	73.4 ± 10.5	72.7 ± 10.2
Median	71	73	71
>65 [*n* (%)]	4,728 (72.8)	4,288 (74.0)	9,016 (73.4)
>70 [*n* (%)]	3,288 (50.6)	3,270 (56.4)	6,558 (53.4)
>75 [*n* (%)]	2,228 (34.3)	2,415 (41.7)	4,643 (37.8)
Died during 2 January 1996–31 December 2017 [*n* (%)]	2,251 (34.7)	2,433 (42.0)	4,684 (38.1)
Length of follow-up (y)[b]			
Mean ± SD	17.7 ± 6.0	17.0 ± 6.3	17.4 ± 6.1
Median	21	21	21
Total person-years of follow-up [*n* (%)]	120,148 (53.8)	103,234 (46.2)	223,382
Quarters in the DMDC data, October 1972–December 1985 (*n*)[c]			
Mean	19.5	17.6	—
Median	12.0	10.0	—
Minimum	1	1	—
Maximum	53	53	—
IQR (25th–75th percentiles)	32 (3–35)	24 (4–28)	—
Cancers			
Total malignancies (including bladder cancer *in situ*) (*n*)	1,563	1,416	2,979
Total individuals with any malignancy or with bladder cancer *in situ* [*n* (%)]	1,359 (20.9)	1,240 (21.4)	2,599 (21.1)

Note: —, not applicable; DMDC, Defense Manpower Data Center; IQR, interquartile range; ref, reference; SD, standard deviation.
[a]Other race includes DMDC race/national origin categories: Hispanic, American Indian or Alaskan Native, Asian or Pacific Islander, Non-Hispanic in Puerto Rico, and invalid.
[b]Follow-up was between 1996 and 2017.
[c]Number of annual quarters employed at either Camp Lejeune or Camp Pendleton between October 1972 and December 1985.

or had a lower prevalence of drinkers, than Camp Pendleton. Using RRs ranging from 2.50 to 10.00 for alcohol consumption and chronic liver disease[29] to fully explain the aHR for chronic liver disease of 0.93, the alcohol prevalence difference would be between 6% and 10% (Table S9). Adjusting for a 6% alcohol consumption prevalence difference and assuming RRs ranging from 1.25 to 5.25 for alcohol consumption and esophageal cancers,[31,39] the aHR of 1.27 for esophageal cancer would increase to between 1.29 and 1.36 (Table S10), and the aHR of 1.47 for squamous cell esophageal cancer would increase to between 1.49 and 1.57 (Table S11). Assuming RRs for alcohol consumption and laryngeal cancer range from 1.1 to 3.0,[31] adjusting for an alcohol consumption prevalence difference of 6% would increase the aHR of 1.21 for laryngeal cancer to between 1.22 and 1.28 (Table S12). Assuming RRs for alcohol consumption and male breast cancer range from 1.1 (consuming 2 drinks/d) to 6.0 (consuming ≥8 drinks/d),[46] adjusting for an alcohol consumption prevalence difference of 6% would increase the aHR of 1.04 for male breast cancer to between 1.05 and 1.11 (Table S13).

For civilian workers, analysis of the negative control diseases obtained aHRs of 0.91 (95% CI: 0.83, 0.99), 0.91 (95% CI: 0.74, 1.12), 0.62 (95% CI: 0.23, 1.71), 0.54 (95% CI: 0.29, 1.00), and 0.74 (95% CI: 0.48, 1.15) for CVD, COPD, alcoholism, alcoholic liver disease, and chronic liver disease, respectively, as underlying causes of death (Table S14), suggesting Camp Lejeune had lower prevalences of smoking, alcohol consumption, and metabolic risk factors than Camp Pendleton. Conversely, the aHR for COPD as a contributing cause was 1.05 (95% CI: 0.92, 1.20), suggesting smoking was higher at Camp Lejeune. To fully explain this COPD result, the smoking prevalence difference would be 4% (Table S15). Adjusting for a smoking prevalence difference of 4% and assuming RRs for smoking and lung and laryngeal cancers ranging between 7.00 and 12.00,[30] the aHR of 1.15 for lung cancer would decrease to between 1.08 and 1.09, and the aHR of 1.18 for laryngeal cancer would decrease to 1.11 (Tables S16 and S17). Using a range of RRs for smoking and oral cancers between 3.50 and 7.00,[30] the aHR of 1.67 for oral cancers (oral cavity and pharynx) would decrease to between 1.57 and 1.59 (Table S18).

For civilian workers, to fully explain the chronic liver disease aHR of 0.74, the alcohol consumption prevalence difference would be between 15% and 25% (Table S19). Adjusting for a 15% prevalence difference and assuming RRs ranging from 1.10 to 1.60 for alcohol consumption and female breast cancer,[31] the aHR of 1.21 for female breast cancer would increase to between 1.22 and 1.30 (Table S20). Assuming RRs ranging from 1.10 to 3.0 for alcohol consumption and laryngeal cancer,[31] the aHR of 1.19 for laryngeal cancer would increase to between 1.20 and

Table 3. Comparison of cancer outcomes at Camp Lejeune vs. Camp Pendleton, among the Marines/Navy personnel subgroup who began active duty and were stationed at either base between 1975 and 1985 ($N = 318{,}305$).

	Camp Lejeune			Camp Pendleton
Cancer outcome	Cases (*n*)	Unadjusted HR (95% CI)	Adjusted HR (95% CI) CIR	Cases (*n*)
Any malignant cancer (and bladder *in situ*)	11,207	1.07 (1.04, 1.10)	1.05 (1.02, 1.08) 1.1	11,329
Oral cavity and pharynx	709	1.00 (0.90, 1.10)	1.03 (0.93, 1.15) 1.2	766
Oropharynx	423	1.02 (0.90, 1.17)	1.06 (0.93, 1.21) 1.3	446
Hypopharynx	25	0.72 (0.43, 1.19)	0.72 (0.44, 1.20) 2.7	38
Nasopharynx	24	0.99 (0.57, 1.73)	1.10 (0.63, 1.93) 3.1	26
Oral cavity only	132	0.99 (0.78, 1.25)	1.03 (0.81, 1.30) 1.6	144
Overlapping/other	42	1.10 (0.72, 1.69)	1.14 (0.74, 1.75) 2.4	41
Squamous cell oral cancer	640	1.01 (0.90, 1.12)	1.05 (0.94, 1.17) 1.2	686
Esophagus	195	1.23 (1.00, 1.51)	1.27 (1.03, 1.56) 1.5	172
Adenocarcinoma	126	1.11 (0.86, 1.42)	1.19 (0.93, 1.53) 1.6	123
Squamous cell	52	1.57 (1.02, 2.40)	1.47 (0.96, 2.25) 2.3	36
Stomach	169	0.98 (0.80, 1.21)	0.97 (0.78, 1.19) 1.5	186
Liver and bile duct	321	0.85 (0.74, 0.99)	0.91 (0.78, 1.05) 1.3	410
Gallbladder	7	0.76 (0.29, 2.00)	0.62 (0.23, 1.63) 7.1	10
Pancreas	287	1.07 (0.91, 1.27)	1.05 (0.89, 1.24) 1.4	289
Larynx	185	1.20 (0.98, 1.48)	1.21 (0.98, 1.50) 1.5	166
Lung and bronchus	1,295	1.16 (1.07, 1.25)	1.16 (1.08, 1.26) 1.2	1,214
Large cell	36	1.38 (0.84, 2.26)	1.38 (0.84, 2.28) 2.7	28
Small cell	181	1.11 (0.90, 1.37)	1.14 (0.92, 1.40) 1.5	177
Non-small cell	145	1.22 (0.96, 1.55)	1.23 (0.97, 1.56) 1.6	128
Squamous cell	277	1.10 (0.93, 1.30)	1.11 (0.94, 1.32) 1.4	275
Adenocarcinoma	562	1.26 (1.11, 1.42)	1.25 (1.10, 1.41) 1.3	487
Colon and rectum	1,016	1.03 (0.94, 1.12)	1.00 (0.92, 1.09) 1.2	1,066
Adenocarcinoma	864	1.00 (0.91, 1.10)	0.99 (0.90, 1.08) 1.2	929
Colon	601	0.99 (0.89, 1.11)	0.96 (0.86, 1.07) 1.2	655
Rectum	353	1.12 (0.96, 1.30)	1.10 (0.94, 1.28) 1.4	339
Rectosigmoid junction	82	0.97 (0.72, 1.30)	0.98 (0.72, 1.32) 1.8	91
Small intestine	57	0.78 (0.55, 1.09)	0.77 (0.55, 1.08) 2.0	79
Anus	46	0.71 (0.49, 1.04)	0.69 (0.48, 1.01) 2.1	69
Urinary bladder (malignant and *in situ*)	444	1.06 (0.93, 1.20)	1.09 (0.95, 1.24) 1.3	456
Papillary transitional cell carcinoma	320	1.04 (0.89, 1.21)	1.08 (0.93, 1.26) 1.4	333
Non-papillary transitional cell carcinoma	109	1.11 (0.85, 1.44)	1.11 (0.85, 1.46) 1.7	107
Urothelial	429	1.06 (0.93, 1.21)	1.09 (0.95, 1.25) 1.3	440
Kidney and renal pelvis	710	1.06 (0.96, 1.18)	1.06 (0.95, 1.18) 1.2	721
Renal cell and clear cell carcinoma	524	1.01 (0.90, 1.14)	1.03 (0.91, 1.16) 1.3	558
Renal cell carcinoma, NOS	250	1.13 (0.95, 1.35)	1.12 (0.94, 1.34) 1.4	237
Clear cell only	277	0.92 (0.79, 1.08)	0.97 (0.82, 1.14) 1.4	324
Papillary	92	1.34 (0.99, 1.83)	1.18 (0.86, 1.60) 1.9	74
Brain and other CNS	231	1.02 (0.85, 1.22)	1.04 (0.86, 1.24) 1.4	241
Gliomas	203	1.02 (0.84, 1.24)	1.04 (0.86, 1.26) 1.5	212
Soft tissue sarcoma	112	1.21 (0.93, 1.59)	1.21 (0.92, 1.59) 1.7	99
Melanoma	607	0.94 (0.84, 1.05)	1.00 (0.89, 1.11) 1.2	695
Thyroid	284	1.23 (1.04, 1.46)	1.22 (1.03, 1.45) 1.4	247
Mesothelioma	14	1.16 (0.54, 2.47)	1.15 (0.54, 2.46) 4.6	13
Leukemias	314	1.06 (0.91, 1.24)	1.07 (0.91, 1.25) 1.4	319
Lymphoid cancers	979	1.03 (0.95, 1.13)	1.02 (0.94, 1.12) 1.2	1,018
Hodgkin lymphoma	108	1.01 (0.78, 1.31)	1.01 (0.77, 1.31) 1.7	114
Non-Hodgkin lymphoma	550	1.00 (0.89, 1.13)	1.01 (0.90, 1.14) 1.3	588
Mantle Cell	27	1.21 (0.70, 2.09)	1.26 (0.73, 2.19) 3.0	24
Follicular	130	1.03 (0.81, 1.31)	1.07 (0.84, 1.36) 1.6	135
Diffuse large B-cell	160	0.88 (0.72, 1.09)	0.89 (0.72, 1.10) 1.5	194
Burkitt	15	1.33 (0.62, 2.84)	1.53 (0.71, 3.30) 4.6	12
Marginal zone B-cell	43	1.41 (0.89, 2.21)	1.45 (0.92, 2.28) 2.5	33
Multiple myeloma	185	1.22 (0.99, 1.51)	1.13 (0.91, 1.40) 1.5	163
Acute lymphocytic leukemia	23	0.97 (0.55, 1.70)	0.94 (0.53, 1.67) 3.2	25
Chronic lymphocytic leukemia	114	1.01 (0.78, 1.30)	1.02 (0.79, 1.32) 1.7	122
Myeloid cancers (including polycythemia vera, myelodysplastic and myeloproliferative syndromes)	239	1.21 (1.00, 1.45)	1.24 (1.03, 1.49) 1.4	213
Myeloid cancers (including myelodysplastic and myeloproliferative syndromes)	186	1.19 (0.96, 1.46)	1.19 (0.97, 1.47) 1.5	169
Acute myeloid leukemia[a]	104	1.36 (1.02, 1.81)	1.38 (1.03, 1.85) 1.8	82
Chronic myeloid leukemia	39	0.75 (0.50, 1.12)	0.74 (0.49, 1.12) 2.3	56
Myelodysplastic and myeloproliferative syndromes	49	1.66 (1.07, 2.60)	1.68 (1.07, 2.62) 2.4	32
Polycythemia vera	53	1.29 (0.87, 1.93)	1.41 (0.94, 2.11) 2.2	44
Female breast	266	1.00 (0.83, 1.19)	1.00 (0.83, 1.20) 1.4	208
Ductal carcinoma	202	1.04 (0.84, 1.28)	1.03 (0.83, 1.28) 1.5	151
Lobular carcinoma	20	0.72 (0.39, 1.32)	0.82 (0.45, 1.52) 3.4	22
Ductal-lobular carcinoma	14	1.34 (0.56, 3.20)	1.41 (0.58, 3.40) 5.9	8
Male breast	21	1.05 (0.57, 1.90)	1.04 (0.57, 1.90) 3.3	22

Table 3. (*Continued.*)

Cancer outcome	Camp Lejeune			Camp Pendleton
	Cases (*n*)	Unadjusted HR (95% CI)	Adjusted HR (95% CI) CIR	Cases (*n*)
Cervix	24	1.02 (0.55, 1.90)	1.01 (0.54, 1.89) 3.5	17
Uterus	31	0.50 (0.32, 0.78)	0.49 (0.31, 0.78) 2.5	50
Ovary	19	0.84 (0.44, 1.60)	0.85 (0.44, 1.63) 3.7	18
Prostate	2,844	1.18 (1.12, 1.25)	1.08 (1.02, 1.13) 1.1	2,661
Testis	184	0.90 (0.74, 1.10)	0.94 (0.77, 1.14) 1.5	220
Penis	18	1.31 (0.66, 2.59)	1.31 (0.66, 2.61) 4.0	15

Note: Bladder cancer includes *in situ* cases. All other cancers include only malignant cases. Cox regression models for the unadjusted HRs are adjusted for age. (Age as the time variable.). Cox regression models for the adjusted HRs include sex, race, rank and education, with age as the time variable. Total Marines/Navy personnel: Camp Lejeune = 154,821—females = 8,049, males = 146,772; Camp Pendleton = 163,484—females = 5,867, males = 157,617. CI, confidence interval; CIR, confidence interval ratio; CNS, central nervous system; HR, hazard ratio; NOS, not otherwise specified.
[a]Includes acute monocytic leukemia.

1.39 (Table S21). Assuming RRs ranging from 1.25 to 5.25 for alcohol consumption and oral cancers,[31] the aHR of 1.67 would increase to between 1.73 and 2.11 (Table S22).

Because smoking is a very strong risk factor for several cancers, in particular lung and laryngeal cancers, the QBA evaluated the magnitude of the smoking prevalence difference between the two bases necessary to fully explain the observed aHRs for lung and laryngeal cancers in the analyses of Marines/Navy personnel and civilian workers. The QBA found that a difference of ≥10% in smoking prevalence would be necessary (Tables S6, S7, S16, and S17). Given the similarity of the two bases, a percentage difference of this magnitude in the prevalence of smoking was unlikely. Based on the findings for COPD mortality, it is more likely that the difference in smoking prevalence between Camp Lejeune and Camp Pendleton Marines/Navy personnel and civilian workers is between 4% and 6% (Tables S5 and S15). Adjusting for a smoking prevalence difference of 4% or 6% would reduce the aHRs for the smoking-related cancers by <10% (Tables S6–S8 and S16–S18).

For the Marines/Navy personnel subgroup, accounting for nondifferential exposure misclassification would increase aHRs for cancers of the lung, larynx, and esophagus and AML by <9% (Table S23). For civilian workers, accounting for nondifferential exposure misclassification would increase aHRs for cancers of the lung, larynx, oral cavity/pharynx, kidney, and female breast, as well as NHL, by <11% (Table S24).

Discussion

This study evaluated whether Marines/Navy personnel and civilian workers stationed or employed at Camp Lejeune during a portion of the period when the drinking water was contaminated had increased risks of invasive cancers (and bladder cancer *in situ*) ascertained between 1996 and 2017 compared with people who were stationed or employed at Camp Pendleton. The study emphasized aHRs ≥1.20 with CIR ≤3 as strong positive associations. However, aHRs <1.20 or aHRs ≥1.20 with CIRs >3 should not necessarily be considered as lacking importance.

For the Marines/Navy personnel subgroup (i.e., who began active duty between 1975 and 1985), positive associations were found for all myeloid cancers as a group, AML, myelodysplastic and myeloproliferative syndromes, and polycythemia vera. The civilian workers analysis found a positive association for all myeloid cancers as a group. Benzene is a known cause of AML.[8] The ATSDR previously concluded that evidence for a causal association between TCE and AML was at least as likely as not based on TCE's effects on the immune system.[9] Benzene exposure has been associated with myelodysplastic syndrome[47–48] and possibly associated with polycythemia vera.[49]

Analysis of the Marines/Navy personnel subgroup found positive associations for MZBCL and mantle cell lymphoma but not for all NHLs as a group or for the subtypes DLBCL and follicular lymphoma. Among civilian workers, the aHR for all NHLs as a group was 1.19 with CIR ≤3, and DLBCL and follicular lymphoma had aHRs ≥1.20, but with CIRs >3.

There is known etiological heterogeneity among NHL subtypes.[50] A TCE workers study obtained odds ratios (ORs) of 1.4 (95% CI: 0.9, 2.1) and 1.6 (95% CI: 0.7, 3.4) for all NHLs as a group and for the subtype follicular lymphoma in the high-exposure group, respectively, but no association for DLBCL.[51] A study of offshore oil industry workers exposed to benzene obtained aHRs of 1.49 (95% CI: 0.90, 2.48) for all B-cell NHL as a group, 3.64 (95% CI: 0.43, 31.0) for the subtype mantle cell lymphoma, and 1.24 (95% CI: 0.40, 3.85) for the subtype follicular lymphomas, but no association for DLBCL.[52] Meta-analysis of six occupational studies of benzene exposure obtained RRs of 1.33 (95% CI: 1.13, 1.57) for all NHLs as a group, 1.67 (95% CI: 1.01, 2.77) for the subtype DLBCL, and 1.47 (95% CI: 0.95, 2.27) for the subtype follicular lymphoma.[53] Meta-analysis of follicular lymphoma and occupational exposures found RRs of 1.30 (95% CI: 0.86, 1.97) for benzene exposure based on seven studies and 1.35 (95% CI: 1.09, 1.68) for chlorinated solvents based on four studies.[54]

For civilian workers, positive associations were observed for female breast cancer and its subtype, ductal carcinoma. There is known etiological heterogeneity between invasive ductal and lobular carcinoma,[55] but no previous study of solvent exposure has evaluated these subtypes separately. Several studies have evaluated occupational exposures to TCE, PCE, or benzene and female breast cancer. A meta-analysis of occupational studies and breast cancer obtained pooled ORs for benzene and TCE of 1.12 (95% CI: 0.96, 1.31) and 1.19 (95% CI: 0.92, 1.53), respectively.[56] Occupational exposures to PCE and benzene were associated with breast cancer among pre-[57] and postmenopausal[58] women. Environmental exposure to PCE-contaminated drinking water in Cape Cod was associated with increased risk for breast cancer.[13] Mammographic density (i.e., the proportion of radiologically dense breast tissue, a strong risk factor for breast cancer), was found to be higher among PCE-exposed workers receiving mammogram screening, providing support for the associations observed between PCE exposures and female breast cancer.[59]

Analysis of the Marines/Navy personnel full cohort found a positive association for male breast cancer. The full cohort had nearly double the number of cases compared with the subgroup, primarily because the full cohort had a much higher percentage of men ≥60 years of age at the end of follow-up than the subgroup. Approximately 75% of US male breast cancers are diagnosed at ≥60 years of age.[60] For civilian workers, there were seven cases at Camp Lejeune compared with one case at Camp Pendleton. Occupational TCE exposure has been associated with male breast cancer in three studies.[61–63] In a case–control study of male breast cancer, Marines stationed at Camp Lejeune had an elevated risk compared with Marines at all other bases.[14]

Table 4. Comparison of cancer outcomes among Camp Lejeune vs. Camp Pendleton civilian workers employed at either base between October 1972 and December 1985 ($N = 12,291$).

	Camp Lejeune			Camp Pendleton
Cancer outcome	Cases (*n*)	Unadjusted HR (95% CI)	Adjusted HR (95% CI) CIR	Cases (*n*)
Any malignant cancer (and bladder *in situ*)	1,359	1.02 (0.95, 1.10)	1.02 (0.95, 1.11) 1.2	1,240
Oral cavity and pharynx	31	1.49 (0.84, 2.64)	1.67 (0.93, 3.00) 3.2	19
Oropharynx	11	1.21 (0.49, 3.01)	1.32 (0.53, 3.28) 6.2	8
Hypopharynx	3	0.90 (0.18, 4.45)	—	3
Oral cavity only	7	2.09 (0.54, 8.11)	2.05 (0.52, 8.04) 15.5	3
Overlapping/other	8	1.31 (0.45, 3.82)	1.37 (0.47, 4.02) 8.6	6
Squamous cell oral cancer	28	1.85 (0.97, 3.52)	1.99 (1.04, 3.82) 3.7	14
Esophagus	8	0.48 (0.21, 1.12)	0.48 (0.20, 1.16) 5.8	16
Adenocarcinoma	5	0.41 (0.14, 1.19)	0.43 (0.15, 1.27) 8.5	11
Squamous cell	2	0.74 (0.12, 4.46)	—	3
Stomach	17	0.71 (0.38, 1.34)	0.67 (0.35, 1.31) 3.7	23
Liver	9	0.55 (0.24, 1.25)	0.64 (0.27, 1.50) 5.6	16
Liver, bile duct, and gallbladder	18	0.72 (0.39, 1.34)	0.79 (0.42, 1.49) 3.5	24
Pancreas	33	0.65 (0.42, 1.02)	0.68 (0.43, 1.08) 2.5	47
Larynx	13	1.22 (0.53, 2.78)	1.18 (0.49, 2.82) 5.8	10
Lung and bronchus	261	1.13 (0.95, 1.35)	1.15 (0.95, 1.38) 1.5	226
Large cell	7	1.35 (0.43, 4.26)	1.09 (0.33, 3.62) 11.0	5
Small cell	42	1.10 (0.70, 1.72)	1.13 (0.72, 1.79) 2.5	36
Non-small cell	23	0.92 (0.52, 1.64)	0.92 (0.51, 1.65) 3.2	24
Squamous cell	72	1.66 (1.14, 2.42)	1.63 (1.10, 2.41) 2.2	43
Adenocarcinoma	93	1.12 (0.83, 1.51)	1.15 (0.84, 1.56) 1.9	80
Colon and rectum	106	0.91 (0.70, 1.19)	0.93 (0.70, 1.22) 1.7	112
Adenocarcinoma	102	0.96 (0.73, 1.27)	0.99 (0.75, 1.32) 1.8	102
Colon	77	0.98 (0.71, 1.35)	0.97 (0.70, 1.35) 1.9	76
Rectum and rectosigmoid junction	31	0.79 (0.49, 1.28)	0.87 (0.53, 1.44) 2.7	37
Rectum	25	0.94 (0.54, 1.65)	1.02 (0.57, 1.83) 3.2	25
Small intestine	1	0.09 (0.01, 0.70)	—	10
Anus	3	0.41 (0.11, 1.59)	0.41 (0.11, 1.60) 14.5	7
Urinary bladder (malignant and *in situ*)	87	1.02 (0.75, 1.37)	1.10 (0.81, 1.50) 1.9	85
Papillary transitional cell carcinoma	60	0.96 (0.67, 1.37)	1.07 (0.74, 1.56) 2.1	61
Non-papillary transitional cell carcinoma	24	1.28 (0.70, 2.34)	1.30 (0.70, 2.40) 3.4	19
Urothelial	84	1.04 (0.76, 1.41)	1.13 (0.82, 1.55) 1.9	80
Kidney and renal pelvis	58	1.07 (0.73, 1.56)	1.12 (0.76, 1.67) 2.2	49
Renal cell and clear cell carcinoma	43	1.04 (0.67, 1.62)	1.05 (0.67, 1.66) 2.5	37
Renal cell carcinoma, NOS	28	1.24 (0.70, 2.20)	1.18 (0.65, 2.13) 3.3	20
Clear cell only	15	0.81 (0.40, 1.63)	0.89 (0.44, 1.82) 4.1	17
Papillary	3	0.89 (0.18, 4.45)	0.96 (0.18, 5.27) 29.3	3
Brain and other CNS	9	0.49 (0.22, 1.11)	0.49 (0.22, 1.11) 5.0	17
Gliomas	9	0.62 (0.27, 1.46)	0.62 (0.26, 1.47) 5.7	13
Soft tissue sarcoma	7	0.62 (0.24, 1.64)	0.67 (0.25, 1.81) 7.2	10
Melanoma	54	0.93 (0.64, 1.37)	1.03 (0.70, 1.52) 2.2	53
Thyroid	32	1.90 (1.01, 3.56)	1.91 (1.01, 3.63) 3.6	14
Mesothelioma	5	0.98 (0.28, 3.41)	0.96 (0.26, 3.61) 13.9	5
Leukemias	36	0.81 (0.52, 1.26)	0.86 (0.54, 1.36) 2.5	43
Lymphoid cancers	104	1.00 (0.76, 1.32)	1.03 (0.77, 1.38) 1.8	98
Lymphoid excluding Hodgkin	101	1.03 (0.77, 1.36)	1.07 (0.80, 1.43) 1.8	93
Hodgkin lymphoma	3	0.55 (0.13, 2.31)	0.53 (0.12, 2.26) 18.8	5
Non-Hodgkin lymphoma	71	1.13 (0.80, 1.60)	1.19 (0.83, 1.71) 2.1	60
Follicular	15	1.38 (0.62, 3.08)	1.41 (0.63, 3.17) 5.0	10
Diffuse large B cell	27	1.30 (0.73, 2.32)	1.48 (0.81, 2.70) 3.3	20
Burkitt	1	0.22 (0.02, 1.98)	—	4
Marginal zone B cell	2	0.32 (0.06, 1.61)	0.33 (0.06, 1.72) 28.7	6
Multiple myeloma	18	1.02 (0.52, 2.01)	1.04 (0.51, 2.10) 4.1	16
Acute lymphocytic leukemia	1	0.27 (0.03, 2.63)	—	3
Chronic lymphocytic leukemia	11	0.68 (0.31, 1.47)	0.60 (0.27, 1.33) 4.9	16
Myeloid cancers (including polycythemia vera, myelodysplastic and myeloproliferative syndromes)	35	1.20 (0.73, 1.96)	1.40 (0.83, 2.36) 2.8	29
Myeloid cancers (including myelodysplastic and myeloproliferative syndromes)	32	1.10 (0.66, 1.82)	1.27 (0.75, 2.16) 2.9	29
Acute myeloid leukemia[a]	14	1.24 (0.56, 2.73)	1.35 (0.59, 3.09) 5.2	11
Chronic myeloid leukemia	6	0.60 (0.21, 1.70)	0.69 (0.24, 2.01) 8.4	9
Myelodysplastic and myeloproliferative syndromes	14	1.70 (0.73, 3.94)	1.97 (0.79, 4.90) 6.2	9
Female breast	208	1.22 (0.98, 1.51)	1.21 (0.97, 1.52) 1.6	134
Ductal carcinoma	167	1.33 (1.04, 1.72)	1.32 (1.02, 1.71) 1.7	97
Lobular carcinoma	12	0.93 (0.40, 2.16)	0.91 (0.38, 2.20) 5.8	10
Ductal-lobular carcinoma	7	0.42 (0.17, 1.06)	0.36 (0.14, 0.93) 6.6	13
Male breast	7	7.51 (0.92, 61.2)	—	1
Cervix	2	0.50 (0.08, 2.99)	—	3
Uterus	40	0.91 (0.57, 1.44)	0.90 (0.56, 1.44) 2.6	34
Ovary	24	0.74 (0.42, 1.28)	0.71 (0.40, 1.28) 3.2	26
Prostate	303	1.25 (1.06, 1.48)	1.06 (0.89, 1.27) 1.4	247

Note: Bladder cancer includes *in situ* cases. All other cancers include only malignant cases. Cox regression models for the unadjusted HRs are adjusted for age (age as the time variable). Cox regression models for the adjusted HRs include sex, race, rank and education, with age as the time variable. The table does not include mantle cell lymphoma, polycythemia vera and cancers of the nasopharynx, testis and penis because both Camp Lejeune and Camp Pendleton had <3 cases of these cancers. Because of small sample numbers, gallbladder cancer was included with liver and bile duct cancers, and rectosigmoid junction cancer was combined with rectal cancer. Total civilian workers: Camp Lejeune = 6,494—females = 3,468, males = 3,026; Camp Pendleton = 5,797—females = 2,805, males = 2,992. —, Not applicable; CI, confidence interval; CIR, confidence interval ratio; CNS, central nervous system; HR, hazard ratio; NOS, not otherwise specified.

[a]Includes acute monocytic leukemia.

Table 5. Cancer outcomes by duration stationed at Camp Lejeune compared with Camp Pendleton, between 1975 and 1985, Marines/Navy personnel subgroup ($N = 318{,}305$).

	CP	Low duration at CL		Medium duration at CL		High duration at CL	
Cancer outcome	Cases (*n*)	Cases (*n*)	Adjusted HR (95% CI)	Cases (*n*)	Adjusted HR (95% CI)	Cases (*n*)	Adjusted HR (95% CI)
Oral cavity and pharynx	766	413	1.04 (0.92, 1.18)	172	1.12 (0.95, 1.33)	124	0.90 (0.73, 1.11)
Oropharyngeal	446	245	1.09 (0.93, 1.28)	101	1.10 (0.89, 1.37)	77	0.92 (0.71, 1.19)
Hypopharyngeal	38	16	0.79 (0.43, 1.42)	4	0.52 (0.18, 1.48)	5	0.77 (0.28, 2.14)
Nasopharyngeal	26	16	1.13 (0.60, 2.13)	4	1.01 (0.34, 2.97)	4	1.50 (0.46, 4.94)
Oral cavity only	144	78	1.00 (0.76, 1.33)	36	1.31 (0.91, 1.91)	18	0.81 (0.48, 1.38)
Overlapping/other	41	21	1.01 (0.59, 1.73)	13	1.57 (0.84, 2.97)	8	1.09 (0.47, 2.49)
Squamous cell	686	374	1.06 (0.93, 1.21)	157	1.14 (0.96, 1.36)	109	0.89 (0.71, 1.11)
Esophagus	172	108	1.25 (0.98, 1.60)	46	1.28 (0.92, 1.78)	41	1.24 (0.85, 1.80)
Adenocarcinoma	123	69	1.15 (0.85, 1.55)	31	1.27 (0.85, 1.89)	26	1.17 (0.73, 1.86)
Squamous cell	36	29	1.50 (0.91, 2.47)	10	1.17 (0.58, 2.38)	13	1.54 (0.76, 3.15)
Stomach	186	102	0.99 (0.77, 1.27)	34	0.89 (0.61, 1.29)	33	0.99 (0.66, 1.49)
Liver and bile duct	410	205	0.94 (0.79, 1.12)	67	0.89 (0.68, 1.16)	49	0.85 (0.61, 1.17)
Gallbladder	10	3	0.41 (0.11, 1.53)	3	1.60 (0.42, 6.17)	1	0.83 (0.09, 8.02)
Pancreas	289	161	1.06 (0.87, 1.29)	59	0.94 (0.70, 1.24)	67	1.09 (0.82, 1.47)
Larynx	166	114	1.22 (0.96, 1.56)	45	1.42 (1.01, 1.98)	26	1.01 (0.64, 1.59)
Lung and bronchus	1,214	783	1.21 (1.11, 1.33)	280	1.13 (0.99, 1.29)	232	1.01 (0.87, 1.18)
Large cell	28	18	1.31 (0.71, 2.40)	11	1.81 (0.89, 3.65)	7	1.04 (0.42, 2.55)
Small cell	177	116	1.27 (1.00, 1.62)	37	1.03 (0.72, 1.47)	28	0.83 (0.54, 1.27)
Non-small cell	128	89	1.23 (0.93, 1.62)	27	1.10 (0.72, 1.68)	29	1.43 (0.91, 2.26)
Squamous cell	275	166	1.17 (0.96, 1.42)	62	1.09 (0.83, 1.45)	49	0.89 (0.64, 1.24)
Adenocarcinoma	487	339	1.30 (1.13, 1.50)	120	1.19 (0.97, 1.46)	103	1.13 (0.89, 1.43)
Colon and rectum	1,066	593	1.04 (0.94, 1.15)	212	0.91 (0.79, 1.06)	211	0.96 (0.81, 1.12)
Adenocarcinoma	929	514	1.04 (0.94, 1.17)	181	0.90 (0.77, 1.06)	169	0.89 (0.75, 1.07)
Colon	655	351	1.01 (0.88, 1.15)	117	0.80 (0.66, 0.98)	133	0.95 (0.77, 1.16)
Rectum only	339	208	1.12 (0.94, 1.34)	77	1.07 (0.83, 1.37)	68	1.03 (0.78, 1.38)
Rectosigmoid junction	91	49	1.06 (0.74, 1.52)	22	1.14 (0.71, 1.82)	11	0.55 (0.29, 1.07)
Small intestine	79	32	0.72 (0.47, 1.09)	13	0.82 (0.45, 1.49)	12	0.98 (0.50, 1.91)
Anus	69	26	0.65 (0.41, 1.03)	13	0.90 (0.49, 1.65)	7	0.60 (0.26, 1.37)
Soft tissue sarcoma	99	72	1.32 (0.97, 1.80)	17	0.84 (0.50, 1.41)	23	1.35 (0.81, 2.25)
Urinary bladder[a]	456	238	1.02 (0.87, 1.20)	109	1.18 (0.95, 1.46)	97	1.20 (0.94, 1.52)
PTCC	333	168	0.99 (0.82, 1.19)	83	1.25 (0.98, 1.59)	69	1.19 (0.89, 1.58)
NPTCC	107	62	1.13 (0.82, 1.56)	24	1.05 (0.67, 1.65)	23	1.11 (0.67, 1.82)
Urothelial	440	230	1.02 (0.87, 1.20)	107	1.20 (0.97, 1.48)	92	1.17 (0.91, 1.50)
Kidney and renal pelvis	721	431	1.12 (0.99, 1.27)	152	1.01 (0.84, 1.20)	127	0.94 (0.77, 1.16)
RCC and clear cell	558	317	1.07 (0.93, 1.23)	109	0.97 (0.78, 1.19)	98	1.00 (0.79, 1.26)
RCC-NOS	237	147	1.12 (0.91, 1.38)	57	1.16 (0.86, 1.55)	46	1.03 (0.73, 1.46)
Clear cell only	324	171	1.03 (0.85, 1.24)	53	0.83 (0.62, 1.11)	53	0.97 (0.71, 1.34)
Papillary	74	55	1.28 (0.90, 1.83)	21	1.13 (0.69, 1.85)	16	0.84 (0.47, 1.52)
Brain and other CNS	241	141	1.15 (0.93, 1.42)	58	1.13 (0.84, 1.50)	32	0.64 (0.43, 0.94)
Gliomas	212	117	1.08 (0.86, 1.36)	57	1.28 (0.95, 1.72)	29	0.67 (0.44, 1.02)
Melanoma malignant	695	334	0.98 (0.86, 1.12)	149	1.04 (0.87, 1.24)	124	1.01 (0.82, 1.25)
Thyroid	247	157	1.12 (0.91, 1.38)	65	1.30 (0.98, 1.71)	62	1.54 (1.12, 2.11)
Mesothelioma	13	5	0.80 (0.28, 2.27)	4	1.46 (0.47, 4.51)	5	1.78 (0.56, 5.69)
Lymphoid	1,018	583	1.04 (0.94, 1.16)	218	1.03 (0.89, 1.20)	178	0.97 (0.81, 1.15)
Hodgkin lymphoma	114	67	1.03 (0.76, 1.41)	22	0.96 (0.60, 1.52)	19	0.95 (0.56, 1.63)
Non-Hodgkin lymphoma	588	326	1.02 (0.89, 1.17)	121	1.01 (0.83, 1.24)	103	1.00 (0.79, 1.26)
Mantle cell	24	13	1.04 (0.52, 2.08)	9	1.85 (0.85, 4.04)	5	1.20 (0.41, 3.47)
Follicular	135	75	1.03 (0.77, 1.38)	30	1.14 (0.76, 1.70)	25	1.18 (0.73, 1.89)
Diffuse large B cell	194	96	0.91 (0.71, 1.17)	38	0.97 (0.68, 1.39)	26	0.78 (0.50, 1.21)
Burkitt	12	11	2.01 (0.87, 4.66)	0	—	4	1.84 (0.52, 6.46)
Marginal zone B cell	33	26	1.39 (0.82, 2.35)	10	1.64 (0.79, 3.41)	7	1.57 (0.62, 3.95)
Multiple myeloma	163	111	1.21 (0.95, 1.56)	46	1.23 (0.88, 1.72)	28	0.79 (0.51, 1.22)
Myeloid	213	146	1.27 (1.02, 1.58)	45	1.07 (0.77, 1.48)	48	1.36 (0.96, 1.94)
Leukemias	319	189	1.11 (0.92, 1.33)	60	0.91 (0.69, 1.21)	65	1.15 (0.86, 1.55)
ALL	25	14	0.96 (0.49, 1.89)	5	0.93 (0.35, 2.45)	4	0.79 (0.25, 2.49)
CLL	122	68	1.04 (0.77, 1.40)	24	0.98 (0.63, 1.53)	22	1.10 (0.67, 1.82)
AML (myeloid/monocytic)	82	62	1.36 (0.97, 1.90)	18	1.11 (0.66, 1.87)	24	1.90 (1.12, 3.21)
CML	56	22	0.74 (0.44, 1.22)	8	0.68 (0.32, 1.43)	9	0.82 (0.38, 1.78)
Myelodysplastic and myeloproliferative syndromes	32	29	1.65 (0.99, 2.76)	11	1.77 (0.88, 3.58)	9	1.84 (0.79, 4.28)
Polycythemia vera	44	35	1.46 (0.93, 2.30)	9	1.14 (0.55, 2.36)	9	1.42 (0.64, 3.17)
Female breast	208	166	0.96 (0.77, 1.19)	52	1.06 (0.78, 1.44)	48	1.11 (0.78, 1.57)
Ductal carcinoma	151	128	0.97 (0.76, 1.25)	39	1.11 (0.78, 1.59)	35	1.17 (0.78, 1.75)
Lobular carcinoma	22	11	0.81 (0.38, 1.75)	5	0.92 (0.35, 2.44)	4	0.74 (0.24, 2.33)
Ductal-lobular carcinoma	8	10	1.84 (0.68, 4.95)	1	0.50 (0.06, 4.01)	3	1.42 (0.33, 6.06)
Male breast	22	12	1.08 (0.52, 2.21)	4	0.86 (0.29, 2.52)	5	1.15 (0.40, 3.37)
Cervix	17	20	1.19 (0.60, 2.36)	3	0.78 (0.22, 2.69)	1	0.35 (0.04, 2.86)
Uterus	50	20	0.47 (0.27, 0.81)	7	0.64 (0.29, 1.42)	4	0.44 (0.15, 1.30)
Ovary	18	15	0.91 (0.44, 1.90)	1	0.27 (0.04, 2.05)	3	1.22 (0.31, 4.79)

Table 5. (*Continued.*)

	CP	Low duration at CL		Medium duration at CL		High duration at CL	
Cancer outcome	Cases (*n*)	Cases (*n*)	Adjusted HR (95% CI)	Cases (*n*)	Adjusted HR (95% CI)	Cases (*n*)	Adjusted HR (95% CI)
Prostate	2,661	1,495	1.07 (1.01, 1.14)	665	1.04 (0.96, 1.13)	684	1.13 (1.03, 1.24)
Testis	220	121	1.03 (0.82, 1.30)	37	0.87 (0.61, 1.24)	26	0.73 (0.47, 1.13)
Penis	15	9	1.02 (0.44, 2.38)	5	1.82 (0.63, 5.25)	4	2.12 (0.57, 7.84)

Note: HRs adjusted for sex, race, rank, education and total duration in the DMDC data, 1975–1985; age was the time variable. CP (reference group): $N = 163{,}484$. CL: low duration (1–6 quarters), $N = 92{,}826$; medium duration (7–10 quarters), $N = 33{,}075$; and high duration (>10 quarters), $N = 28{,}920$. —, Not applicable; ALL, acute lymphocytic leukemia; AML, acute myeloid leukemia; CI, confidence interval; CL, Camp Lejeune; CLL, chronic lymphocytic leukemia; CML, chronic myeloid leukemia; CNS, central nervous system; CP, Camp Pendleton; DMDC, Defense Manpower Data Center; HR, hazard ratio; NOS, not otherwise specified; NPTCC, non-papillary transitional cell carcinoma; PTCC, papillary transitional cell carcinoma; RCC, renal cell carcinoma.
[a]Includes *in situ* and malignant cases.

A positive association was found for thyroid cancer in the analysis of the Marines/Navy personnel subgroup. Thyroid cancer has been associated with occupational exposure to solvents, including benzene, in the footwear industry among women but not men.[64] A review of studies of occupational solvent exposure and thyroid cancer concluded that findings were "largely null."[65]

The Marines/Navy personnel subgroup analysis found a positive association for soft tissue cancer. The previous Camp Lejeune mortality study also found an elevated risk.[15] Occupational studies of PCE or TCE and soft tissue cancer are often limited by small numbers of cases. Two occupational studies have observed elevated risks for soft tissue cancer and PCE exposure[66] and both PCE and TCE exposure.[67] Conversely, two occupational studies found elevated risks only among females exposed to TCE[61] or working as a dry cleaner.[68]

A positive association was found for laryngeal cancer in the analysis of the Marines/Navy personnel subgroup. Laryngeal cancer has been associated with occupational exposure to PCE in men[35] and exposure to PCE and TCE in women.[34] There was a positive association for esophageal cancer and its subtype, squamous cell, in the analysis of the Marines/Navy personnel subgroup. Three occupational cohort studies have found associations between TCE exposures and esophageal cancer.[9] The previous Camp Lejeune mortality study also observed an elevated risk.[15]

There is known etiological heterogeneity among lung cancer subtypes.[69] The Marines/Navy personnel subgroup analysis found positive associations for large cell, non-small cell, and adenocarcinoma. The civilian workers analysis found a positive association for squamous cell lung cancer. Adenocarcinoma is the most common subtype among nonsmokers.[69] A study of offshore petroleum workers exposed to benzene found a positive trend for exposure duration and adenocarcinoma but not for squamous cell or small cell lung cancer.[70] Pooled analysis of 14 case–control studies of occupational benzene exposure observed cumulative exposure trends for lung cancer and for adenocarcinoma and squamous cell and large cell lung cancer.[71] In studies not evaluating subtypes, lung cancer risk was elevated in 4 dry-cleaning worker studies, with RRs between 1.30 and 1.40,[68,72–74] 2 studies of PCE workers,[32,75] and 1 study of PCE drinking water exposures at Cape Cod.[12]

The Marines/Navy personnel subgroup analysis of duration stationed at Camp Lejeune found a positive association for bladder cancer. Occupational exposure to PCE is associated with bladder cancer.[9,37]

A weakness of this study was the lack of information on smoking, alcohol consumption, and other unmeasured risk factors. However, a strength was the inclusion of a reference population with similar demographic, socioeconomic, and cultural similarities as the exposed population, minimizing the impact of confounding due to unmeasured risk factors. The results for the negative control diseases, COPD, and cardiovascular mortality suggested a minor difference in smoking or metabolic risk factors between the two bases. The results for the negative control diseases for alcohol consumption suggested Camp Lejeune personnel had a lower alcohol consumption than Camp Pendleton personnel.

Smoking and alcohol consumption was encouraged by the military culture, the stress of service, targeted advertising by the tobacco and alcoholic beverage industry, and the lower cost and tax-free availability of these products on base compared with off-base civilian stores.[25] QBA results suggested that confounding due to smoking and alcohol consumption would be minor. Moreover, for cancers both smoking-related and alcohol-related, confounding in this study due to smoking and alcohol consumption may cancel each other.

Using base location as a proxy for drinking water exposure was a possible source of nondifferential exposure misclassification, but QBA results suggested the impact would be minor. Duration stationed or employed at Camp Lejeune as a proxy for cumulative exposure assumed that monthly contamination levels did not fluctuate, but this was incorrect. Therefore, the duration analyses should be interpreted with caution.

The analyses did not account for a latency period, but there was at least a 10-y period between the end of exposure at Camp Lejeune and the start of follow-up. Because of the gap in time between the exposure period and the follow-up period, some cancers with shorter latency periods may have been missed.

Because of the small sample size of civilian workers, some HRs had wide CIs due to the small numbers of cases. For the Marines/Navy personnel subgroup, the small numbers of cases and the wide CIs were likely due to >75% of the cohort being <60 years of age at the end of follow-up. The median age of a cancer diagnosis in the United States is 66 y; the median age for diagnosis of cancers of the bladder, lung, and pancreas, and myelodysplastic syndrome is ≥70 y; and the median age for diagnosis of NHL, AML, multiple myeloma, and cancers of the kidney and liver is ≥64 y.[76]

Many aHRs in this study were <1.50. This is also common in studies of occupational exposures to TCE, PCE, and benzene.[9] Meta-analyses of occupational TCE exposures and kidney cancer, liver cancer, and NHL had summary RRs between 1.3 and 1.4, and a meta-analysis of dry-cleaning work and bladder cancer had a summary RR of 1.47.[9,37,77,78] A meta-analysis of occupational benzene exposure and NHL found a summary RR of 1.27 for studies having quantitative exposure assessments.[79] A pooled analysis of 14 case–control studies of occupational benzene exposure and lung cancer obtained an OR of 1.32 for the highest level of cumulative exposure.[71]

A strength of this study was the collection of cancer incidence data from 54 cancer registries. Participation of these registries was necessary because Marines and Navy personnel resided in every state. Unlike the National Death Index, there is no central cancer registry in the United States that can provide individual-level cancer incidence data linked to personal identifier information of study participants.

Another strength was the evaluation of histological subtypes for several cancers. Findings from occupational studies of the

Table 6. Cancer outcomes by duration employed at Camp Lejeune compared with Camp Pendleton, October 1972–December 1975, among civilian workers ($N = 12{,}291$).

	CP	Low/medium duration at CL		High duration at CL	
Cancer outcome	Cases (n)	Cases (n)	Adjusted HR (95% CI)	Cases (n)	Adjusted HR (95% CI)
Oral cavity and pharynx	19	21	1.86 (0.95, 3.65)	10	1.53 (0.58, 4.00)
Oropharyngeal	8	10	1.90 (0.72, 5.05)	1	0.48 (0.04, 5.23)
Hypopharyngeal[a]	3	2	1.05 (0.17, 6.41)	1	0.69 (0.07, 6.68)
Oral cavity only	3	3	1.58 (0.27, 9.24)	4	2.37 (0.37, 15.23)
Overlapping/other	6	4	1.22 (0.30, 4.92)	4	1.55 (0.34, 7.17)
Squamous cell	14	20	2.54 (1.20, 5.38)	8	1.37 (0.47, 4.01)
Esophagus	16	2	0.26 (0.06, 1.20)	6	0.62 (0.20, 1.96)
Adenocarcinoma	11	1	0.17 (0.02, 1.37)	4	0.63 (0.16, 2.53)
Stomach	23	6	0.39 (0.15, 1.00)	11	1.39 (0.53, 3.60)
Liver	16	5	0.61 (0.21, 1.77)	4	0.83 (0.22, 3.10)
Liver, bile duct, and gallbladder	24	11	0.79 (0.37, 1.69)	7	0.91 (0.33, 2.53)
Pancreas	47	18	0.71 (0.39, 1.29)	15	0.60 (0.30, 1.19)
Larynx	10	9	1.86 (0.65, 5.27)	4	0.59 (0.15, 2.35)
Lung and bronchus	226	134	1.09 (0.87, 1.38)	127	1.26 (0.96, 1.65)
Large cell	5	3	0.78 (0.17, 3.54)	4	1.93 (0.31, 11.95)
Small cell	36	26	1.14 (0.66, 1.95)	16	1.27 (0.61, 2.66)
Non-small cell	24	9	0.64 (0.29, 1.44)	14	1.41 (0.62, 3.20)
Squamous cell	43	36	1.43 (0.89, 2.30)	36	2.28 (1.27, 4.08)
Adenocarcinoma	80	50	1.20 (0.81, 1.78)	43	1.06 (0.68, 1.67)
Colon and rectum	112	61	1.08 (0.76, 1.52)	45	0.75 (0.50, 1.13)
Adenocarcinoma	102	59	1.16 (0.81, 1.67)	43	0.80 (0.52, 1.22)
Colon	76	44	1.08 (0.72, 1.63)	33	0.83 (0.51, 1.37)
Rectum and rectosigmoid junction	37	19	1.15 (0.61, 2.15)	12	0.59 (0.28, 1.25)
Rectum	25	15	1.28 (0.61, 2.68)	10	0.73 (0.31, 1.73)
Anus[a]	7	2	0.50 (0.10, 2.49)	1	0.30 (0.04, 2.45)
Urinary bladder[b]	85	46	1.18 (0.80, 1.75)	41	1.09 (0.69, 1.71)
Papillary transitional cell	61	33	1.16 (0.73, 1.84)	27	1.06 (0.61, 1.83)
Non-papillary transitional cell	19	12	1.51 (0.68, 3.37)	12	1.28 (0.55, 2.96)
Urothelial	80	45	1.23 (0.83, 1.84)	39	1.09 (0.69, 1.73)
Kidney and renal pelvis	49	30	0.91 (0.56, 1.48)	28	1.70 (0.93, 3.13)
Renal cell and clear cell carcinoma	37	21	0.88 (0.49, 1.56)	22	1.36 (0.69, 2.69)
Renal cell carcinoma, NOS	20	14	1.03 (0.49, 2.15)	14	1.48 (0.61, 3.64)
Clear cell only	17	7	0.67 (0.26, 1.72)	8	1.24 (0.44, 3.52)
Papillary[a]	3	1	0.51 (0.05, 4.97)	2	1.41 (0.24, 8.46)
Brain and other CNS	17	5	0.48 (0.16, 1.39)	4	0.48 (0.14, 1.64)
Gliomas	13	5	0.63 (0.20, 1.94)	4	0.53 (0.15, 1.90)
Soft tissue sarcoma	10	6	1.09 (0.35, 3.38)	1	0.18 (0.02, 1.66)
Melanoma	53	31	0.92 (0.57, 1.47)	23	1.28 (0.69, 2.35)
Thyroid	14	23	1.72 (0.86, 3.44)	9	3.00 (0.91, 9.84)
Mesothelioma	5	2	1.08 (0.17, 6.91)	3	0.84 (0.17, 4.18)
Lymphoid	98	59	1.06 (0.74, 1.51)	45	1.00 (0.65, 1.54)
Lymphoid (exc. Hodgkin lymphoma)	93	59	1.12 (0.78, 1.61)	42	1.01 (0.65, 1.58)
Hodgkin lymphoma[a]	5	0	—	3	1.37 (0.32, 5.76)
Non-Hodgkin lymphoma	60	42	1.31 (0.84, 2.03)	29	1.05 (0.62, 1.80)
Follicular	10	12	2.22 (0.86, 5.78)	3	0.60 (0.14, 2.54)
Diffuse large B cell	20	12	1.18 (0.54, 2.61)	15	1.80 (0.78, 4.12)
Marginal zone B cell[a]	6	2	0.61 (0.12, 3.15)	0	—
Burkitt	4	0	—	1	0.76 (0.08, 7.03)
Multiple myeloma	16	11	1.10 (0.47, 2.55)	7	0.99 (0.33, 3.01)
Myeloid cancers[c]	29	17	1.11 (0.58, 2.13)	18	2.04 (0.96, 4.35)
Leukemias	43	17	0.65 (0.36, 1.18)	19	1.43 (0.72, 2.86)
Chronic lymphocytic leukemia	16	5	0.48 (0.17, 1.36)	6	0.93 (0.28, 3.07)
Acute myeloid leukemia[d]	11	6	0.92 (0.32, 2.67)	8	2.53 (0.76, 8.37)
Chronic myeloid leukemia	9	3	0.46 (0.12, 1.78)	3	1.61 (0.29, 8.91)
Myelodysplastic and myeloproliferative syndromes	9	7	2.01 (0.64, 6.33)	7	1.93 (0.56, 6.70)
Female breast	134	161	1.25 (0.98, 1.61)	47	1.01 (0.67, 1.53)
Ductal carcinoma	97	129	1.38 (1.03, 1.84)	38	1.08 (0.67, 1.71)
Lobular carcinoma	10	9	1.06 (0.39, 2.91)	3	0.63 (0.14, 2.82)
Ductal-lobular carcinoma	13	5	0.28 (0.09, 0.83)	2	0.42 (0.07, 2.63)
Male breast[a]	1	2	4.55 (0.41, 51.0)	5	10.01 (1.17, 86.1)
Cervix[a]	3	2	0.68 (0.11, 4.06)	0	—
Uterus	34	30	0.90 (0.53, 1.52)	10	0.91 (0.38, 2.17)
Ovary	26	15	0.63 (0.31, 1.25)	9	0.89 (0.35, 2.24)
Prostate	247	113	0.90 (0.71, 1.15)	190	1.20 (0.94, 1.53)

Note: HRs adjusted for sex, race, blue-collar work (yes/no), education, and total duration in the DMDC data, October 1972–December 1985; age was the time variable. CP (reference group): $N = 5{,}797$. CL: low/medium duration (1–21 quarters), $N = 4{,}231$; and high duration (>21 quarters), $N = 2{,}263$. —, No cases; CI, confidence interval; CL, Camp Lejeune; CNS, central nervous system; CP, Camp Pendleton; DMDC, Defense Manpower Data Center; exc, except; HR, hazard ratio; NOS, not otherwise specified.

[a]Unadjusted results only are presented because of the small numbers of cases.

[b]Includes *in situ* and malignant cases.

[c]Includes myelodysplastic and myeloproliferative syndromes and polycythemia vera.

[d]Includes acute monocytic leukemia.

chemicals in the Camp Lejeune drinking water have differed among the histological subtypes of hematopoietic cancers,[51,52,80] lung cancer,[70–71] and head and neck cancers.[35]

Conclusion

For the Marines/Navy personnel subgroup (i.e., who began active duty between 1975 and 1985), positive associations were observed for all myeloid cancers as a group and separately for AML, myelodysplastic and myeloproliferative syndromes, polycythemia vera; cancers of the esophagus, larynx, thyroid, and soft tissue; MZBCL and mantle cell lymphoma; squamous cell esophageal cancer; and lung cancer subtypes—large cell, non-small cell, and adenocarcinoma. In the full cohort of Marines/Navy personnel, there was a positive association for male breast cancer. For civilian workers, positive associations were observed for all myeloid cancers as a group, squamous cell lung cancer, and female breast and ductal cancer.

Adult cancers have not been evaluated for family members of Camp Lejeune Marines and Navy personnel who resided in base housing served by contaminated drinking water. However, the findings of this study are relevant to all individuals exposed to the contaminated drinking water at Camp Lejeune and add to the literature on the health effects of these contaminants. Continued follow-up of the Marines/Navy personnel subgroup is indicated given that >75% were <60 years of age at the end of follow-up.

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