DEPARTMENT OF THE AIR FORCE
711TH HUMAN PERFORMANCE WING (AFRL)
WRIGHT-PATTERSON AFB OHIO

24 May 2021

MEMORANDUM FOR 157 ARW/CC

FROM: USAFSAM/PHR
Epidemiology Consult Service Division
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2510 5th Street, Building 840
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SUBJECT: Pease Military Cancer Mortality Study

References: (a) Surveillance, Epidemiology, and End Results Program (www.seer.cancer.gov) DevCan database: "SEER 21 Incidence and Mortality, 2000–2017, with Kaposi Sarcoma and Mesothelioma." National Cancer Institute, DCCPS, Surveillance Research Program, Surveillance Systems Branch, released April 2019, based on the November 2018 submission.
(b) Michael Fay et al., "Age-conditional Probabilities of Developing Cancer," *Statistics in Medicine* 22, no. 11 (June 2003): 1837–1848.
(c) Melanie Wall et al., "Factors Associated with Reporting Multiple Causes of Death," *BMC Medical Research Methodology* 5, no. 4 (January 2005): 1–13.
(d) Steven Samuels et al., "Power and Detectable Risk of Seven Tests for Standardized Mortality Ratios," *American Journal of Epidemiology* 133, no. 11 (June 1991): 1191–1197.
(e) Timothy Lash et al., "A Comparison of the National Death Index and Social Security Administration Databases to Ascertain Vital Status," *Epidemiology* 12, no. 2 (March 2001): 259–261.
(f) *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General* (Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, 2014), 139–351.
(g) *Toxicological Profile for Perfluoroalkyls*, Chapter 2: Health Effects (Atlanta, GA: U.S. Department of Health and Human Services, Agency for Toxic Substances and Disease Registry, 2018), 418–433.
(h) Wilm Tambeur et al., "Standardized Mortality Ratios as a User-friendly Performance Metric and Trigger for Quality Improvement in a Flemish Hospital Network: Multicentre Retrospective Study," *British Medical Journal Open* 9, no. 9 (September 2019): e029857.

1. INTRODUCTION:

a. *Purpose:* This memorandum summarizes the Pease Military Cancer Mortality Study, an investigation of cancer deaths among U.S. Air Force service members stationed at Pease Air Force Base / Air National Guard Base (hereafter "Pease") between 1970 and 2018. The study was requested by 157 ARW/CC on 4 March 2019 via memorandum to NGB/SG. The request was later redirected to the Epidemiology Consult Service Division (USAFSAM/PHR). In partnership with public health experts from Pease, the Air National Guard, and the State of New Hampshire, USAFSAM/PHR finalized the study design on 18 December 2019 and obtained Air Force Research Laboratory IRB approval on 5 March 2020 (protocol #FWR20200052N).

b. *Background:* Human exposure to per- and polyfluoroalkyl substances (PFAS) has increased as a public health concern over the past decade. The City of Portsmouth closed a drinking water well on the Pease International Tradeport on May 2014 after a water sample tested positive for perfluorooctanoic acid, a type of PFAS, at a concentration exceeding the Provisional Health Advisory level. This prompted health concerns among individuals who had been associated with Pease, including service members who were currently or formerly stationed on the installation. Public meetings held in 2015 and 2016 revealed several health concerns, including malignancies (https://www.dhhs.nh.gov/dphs/investigation-pease.htm).

The Centers for Disease Control and Prevention's (CDC) National Center for Environmental Health (NCEH) and the Agency for Toxic Substances and Disease Registry (ATSDR), in response to the National Defense Authorization Acts of 2018 and 2019, began a multi-site health study to study how drinking water that contains PFAS may harm health (https://www.atsdr.cdc.gov/pfas/activities/pease.html). ATSDR's "Pease Study" is the first site of this national, multi-site study, which will assess the human health effects of PFAS exposure.

This present study is distinct from ATSDR's Pease Study as well as the Pease Blood Testing Program completed in 2016 by the New Hampshire Department of Health and Human Services (https://www.dhhs.nh.gov/dphs/documents/pease-pfc-blood-testing.pdf). Since state and national studies are already addressing PFAS exposure in the population and the human health effects thereof, this study was commissioned to analyze only cancer mortality among service members stationed at Pease, with a comparison to the general U.S. population.

c. *Study Personnel:*

(1) Lt Col Bryant Webber, MD, MPH, Preventive Medicine, USAFSAM/PHR
(2) Ms. Kimberly Giacalone, MPH, Epidemiologist, USAFSAM/PHRR
(3) Mr. Robert Coleman Jr., MPH, Epidemiologist, USAFSAM/PHRR
(4) Mr. James Escobar, MPH, Data Manager, USAFSAM/PHRR
(5) Dr. Alisa Simon, PhD, Biostatistician, USAFSAM/PHRR
(6) Mr. Greg Wolff, MPH, Senior Epidemiologist, USAFSAM/PHR
(7) Lt Col David Stuever, MPH, Branch Chief, USAFSAM/PHRR

2. METHODOLOGY:

a. *Study Design and Population:* This was a retrospective cohort study of all active, guard, and reserve U.S. Air Force service members assigned to Pease at any time between 1 January 1970 and 31 December 2018. The outcome of interest was cancer mortality—both overall and stratified by site (e.g., kidney or melanoma of the skin). Although latency periods exist between a carcinogenic exposure and carcinogenesis, and between carcinogenesis and cancer death, a simultaneous endpoint was established for the exposure and outcome surveillance periods to maximize capture of outcomes. Had the existence, extent, and timing of potential carcinogens been known, it may have been desirable to antedate the exposure endpoint by the minimum known duration between carcinogenic exposure and death.

b. *Comparison Group:* The mortality experience of Pease members was compared to that of the general U.S. population, accounting for differences in sex, age, and race. It was determined that a national comparison group would be most fitting for a cohort of people who were born, raised, and stationed in states across the nation. Depending on the exposure(s) of concern, a nearby metropolitan or statewide comparison group may be preferable for studies exclusively of guardsmen who have been lifelong state residents.

c. *Outcomes:* The primary outcome of interest for this study was death caused by cancer, expressed as a standardized mortality ratio (SMR), or the ratio of cancer deaths observed in Pease members to cancer deaths expected in Pease members based on national data for similar people in the United States. An SMR is calculated by dividing the observed number of deaths by the expected number of deaths. An SMR value of 1.0 indicates an equal number of observed and expected deaths, a value greater than 1.0 indicates more deaths than expected, and a value less than 1.0 indicates fewer. For example, if 25 Pease members died from leukemia, but only 20 such deaths would be expected, the SMR for leukemia would equal 1.25 (or 25/20). Conversely, if 10 died from stomach cancer and 20 such deaths would be expected, the SMR for stomach cancer would equal 0.5 (or 10/20). Since an SMR value of greater than or less than 1.0 may be due to statistical chance alone—rather than a true difference between the observed and expected counts—the value should always be interpreted in light of statistical significance testing; this is detailed in paragraph 2c(7).

d. *Data Sources and Analysis:*

(1) A roster of Pease members was established from personnel files from three sources: the Air Force Personnel Center (active and reserve from 1970–2018 and Air National Guard from 1995–2018), the Defense Manpower Data Center (Air National Guard from 1979–1994), and the Pease Personnel Office (Air National Guard from 1970–1978). In addition to name and social security numbers, which were required for merging with death certificates, personnel records included date of birth, sex, race, component, rank, dates of arrival and separation from Pease, and primary Air Force Specialty Code (AFSC). Some records were incomplete.

(2) Component was classified as active, guard, or reserve. Rank was classified as airmen (E1–4), non-commissioned officers/senior enlisted (E5–9), junior officers (O1–3), or senior officers (O4–10). Primary AFSC was used to assign members into one of five occupational categories: operations; maintenance and logistics; support; medical and professional; or other. These categories correspond to current Department of Defense career groups of 1, 2, 3, 4–6, and 7–9. Since military occupation nomenclature has changed over time, retired codes were manually assigned to one of the five occupational categories using prior versions of the Air Force Enlisted Classification Directory, the Air Force Officer Classification Directory, and the Occupational Conversion Index (DoD Index 1312.1-1). Time on station was calculated as (date of separation – date of arrival) / (365 days), and stratified as <1, 1–4, 5–9, and ≥10 years. Time-sensitive variables, such as component and rank, were defined according to the last record in the file.

(3) The cohort roster was merged with death certificate data archived in the National Death Index Plus (NDI-Plus), the centralized repository for deaths occurring in the United States since 1 January 1979. At the time of request, death records were available through 31 December 2018. NDI-Plus was accessed through the Joint Department of Veterans Affairs and Department of Defense Suicide Data Repository. The data request was approved by the Board of Governors, Defense Suicide Prevention Office, on 1 April 2020. Consistent with methodology employed by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program, the primary analysis utilized the underlying cause of death from the death certificate. To maximize capture, the Air Force Mortality Registry (AFMR) was also queried for deaths in the Pease population. The AFMR includes death certificate information for most Airmen who died while on active duty or on retired status, and some separated Airmen, beginning in 1970.

(4) Conditions listed on death certificates are coded in NDI-Plus according to the Ninth and Tenth Revisions of the *International Classification of Diseases* (ICD-9 and ICD-10). NDI transitioned from ICD-9 to ICD-10 on 1 January 1999. Cancer deaths were captured using ICD-9 codes 140–209 and ICD-10 codes C00–C96. Since they are not reportable to cancer registries, basal and squamous cell skin cancers were excluded. Cancer site stratification followed SEER taxonomy (https://training.seer.cancer.gov/icd10cm/appendix-b/).

(5) Expected cancer deaths (for all cancers and each cancer site) were based on the experience of the general U.S. population, after indirect adjustment for sex, age, and race. Expected death counts were calculated in the Cancer Query System (CanQueS), the online portal to DevCan (https://surveillance.cancer.gov/devcan/canques.html). This system provides cancer mortality risk statistics from the SEER 21 Registries Incidence and Mortality database, which encompasses the years 2000 through 2017. Since deaths of Pease members occurred throughout this 18-year period, all data were used and weighted equally by time period. Per SEER methodology, ages were categorized in 5-year increments based on age at observation endpoint—either the date of death or 31 December 2018, the last day of the observation period (e.g., the 70–74 age group would include someone who turned 70 on 31 December 2018 and someone who turned 75 on 1 January 2019). Race was stratified as white, black, and other, with expected deaths in the lattermost category calculated using all races. Each person in the cohort was assigned to one of 102 unique combinations of sex, age category, and race (e.g., black

females aged 70–74 years). Expected deaths were calculated for each sex-age-race category, with mortality probability based on five decimal places (e.g., 0.00217 or 0.217%). The starting age was established at 15 years, rather than birth, because service members by definition would be at least 15 years-old when stationed at Pease. (While 18 years-old may have been a preferable cutoff, DevCan utilizes 5-year increments.) The ending age was established at both the beginning and end of each 5-year period, with the expected deaths calculated as the average of the two (e.g., for black females aged 70–74 years, the number of expected deaths was defined as the average of the expected deaths with ending ages of 70 and 75).

(6) Personnel files were incomplete for some service members. Those missing race (n=77) were assigned to the other category. Those missing date of birth (n=39) were excluded from SMR analyses. Missing sex (n=3) was manually imputed based on first names.

(7) SMRs with 95% confidence intervals (CI) and two-sided p values were calculated using exact Poisson regression. The alpha level was not adjusted, despite the presence of 28 null hypotheses (i.e., SMR for all cancers and for 27 site-specific cancers). This reflected an *a priori* decision to minimize false-negative findings, at the risk of false-positive findings. A Bonferroni correction for multiple comparisons would have reduced the alpha level from 0.05 to 0.002.

(8) Since carcinogenetic exposures can be related to the environment or occupation, SMRs were also calculated after stratifying the population according to component, rank, military occupation, and years on station. These secondary analyses were performed for all cancers and for sites with statistically elevated SMRs in the primary analysis.

(9) The record axis conditions enumerated on the death certificates were also explored. Record axis conditions—of which up to 20 can be listed per certificate—comprise comorbidities that may or may not have been related to the underlying cause of death. A condition listed in the record axis, but not as the underlying cause of death, often denotes an ailment the decedent died *with*, not *from*. It is invalid to include these record axis conditions as observed cancer deaths because the expected cancer deaths from SEER are based solely on underlying causes of death. Record axis conditions are hereafter described as "mentioned causes of death."

(10) SAS Enterprise Guide v7.1 was used to merge databases, DevCan v6.7.8 (via CanQueS) to determine expected cancer deaths, and SAS/STAT v14.2 to calculate SMRs.

3. RESULTS:

a. *Subjects:* During the 49-year surveillance period, 34,987 Air Force service members were stationed at Pease for at least one day. Most were male (90.6%), white (90.2%), and served in the active component (81.9%). The mean age at last observation was 62.5 years (**Table 1**).

Table 1. Demographic and Military Characteristics of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018 (N=34,987)

Characteristic	Number	Percent
Sex		
Male	31,703	90.61
Female	3,281	9.38
Missing†	3	0.01
Age at Last Observation, years		
<20	64	0.18
20–24	282	0.81
25–29	417	1.19
30–34	490	1.40
35–39	479	1.37
40–44	561	1.60
45–49	1,085	3.10
50–54	3,367	9.62
55–59	5,525	15.79
60–64	6,709	19.18
65–69	7,112	20.33
70–74	4,522	12.92
75–79	2,191	6.26
80–84	1,473	4.21
85–89	546	1.56
90–94	97	0.28
≥95	28	0.08
Missing‡	39	0.11
Race		
White	31,554	90.19
Black	2,921	8.35
Other	435	1.24
Missing§	77	0.22
Component		
Active	28,639	81.86
Guard	5,944	16.99
Reserve	342	0.98
Missing^	62	0.18

Rank		
E1–4	19,117	54.64
E5–9	11,807	33.75
O1–3[#]	2,644	7.56
O4–10	1,419	4.06
Military Occupation		
Operations	4,065	11.62
Maintenance and Logistics	13,677	39.09
Support	9,774	27.94
Medical and Professional	5,562	15.90
Other	1,462	4.18
Missing[§]	447	1.28
Time on Station, years		
<1	31,918	91.23
1–4	1,309	3.74
5–9	1,211	3.46
≥10	548	1.57
Missing[^]	1	0.01

[†]Those with missing sex were manually assigned based on first name

[‡]Those with missing age were excluded from analyses

[§]Those with missing race or military occupation were combined with the *Other* category for analyses

[^]Those with missing component or time on station were analyzed as a unique group

[#]Includes one Air Force warrant officer

b. *Total Mortality and Cancer Mortality:* NDI-Plus identified 6,183 deaths among Pease members, of which 1,956 (31.6%) listed cancer as the underlying cause. Three deaths were found in the Air Force Mortality Registry, all of which were in NDI-Plus. Deaths occurred in males (n=1,854) and females (n=102), with 82.6% in those aged 50–79 years (n=1,616). In keeping with the distribution of the Pease cohort, 90.9% occurred in white service members (n=1,778); 14 deaths occurred in members who identified as a race other than white or black (**Table 2**). No deaths were identified among service members without an available date of birth (n=39).

Table 2. Total Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, by Sex, Age, and Race (N=34,987)

Age, years	Female		Male		
	Black	White	Black	White	Other[‡]
20–24	--	--	--	2	--
25–29	--	--	2	3	--
30–34	--	1	--	10	--
35–39	1	3	2	16	--
40–44	--	5	5	37	--
45–49	2	11	9	90	1
50–54	1	16	14	168	--
55–59	1	21	28	218	3
60–64	--	20	36	309	4
65–69	1	7	29	334	4
70–74	--	3	15	210	2
75–79	1	5	11	155	--
80–84	--	3	5	97	--
85–89	--	--	1	31	--
90–94	--	--	--	3	--

[†]Based on the underlying cause of death

[‡]All deaths were in those with a race other than white or black; none had a missing race variable

c. *Observed and Expected Cancer Mortality with Standardized Mortality Ratios:* The most common cancer death was lung and bronchus (n=586 [30.0% of all cancer deaths]), followed by colon and rectum (n=184 [9.4%]), pancreas (n=120 [6.1%]), and prostate (n=118 [6.0%]). Based on the demographically-matched general U.S. population, 1,979 cancer deaths were expected in the Pease service member population—nearly identical to the observed value of 1,956 cancer deaths (SMR=0.99; 95% CI: 0.94–1.03; p=0.607). Lung and bronchus, prostate, and breast cancer deaths were 15%, 22%, and 51% higher than expected, respectively. By contrast, colon and rectum cancer death was 22% lower than expected, and other and unspecified cancer death was 42% lower than expected. The SMRs for the remaining 22 cancer sites were not statistically significant at the pre-defined alpha level of 0.05 (**Table 3**).

Table 3. Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, Overall and by Site, with Standardized Mortality Ratios (N=34,948)

	Observed	Expected	SMR (95% CI)[‡]	p value[‡]
All Cancers	1,956	1,979.49	0.99 (0.94–1.03)	0.607
Lung and Bronchus	586	510.77	1.15 (1.06–1.24)	0.001
Colon and Rectum	184	236.76	0.78 (0.67–0.90)	<0.001
Pancreas	120	118.64	1.01 (0.84–1.21)	0.925
Prostate	118	97.02	1.22 (1.01–1.46)	0.043
Leukemia	90	74.12	1.21 (0.98–1.49)	0.080
Esophagus	81	75.53	1.07 (0.85–1.33)	0.559
Non-Hodgkin Lymphoma	81	68.28	1.19 (0.94–1.47)	0.145
Liver and Intrahepatic Bile Duct	76	94.04	0.81 (0.64–1.01)	0.064
Brain and Other Nervous System	72	69.58	1.03 (0.81–1.30)	0.803
Kidney and Renal Pelvis	60	54.02	1.11 (0.85–1.43)	0.450
Urinary Bladder	51	44.38	1.15 (0.86–1.51)	0.356
Melanoma of the Skin	44	41.16	1.07 (0.78–1.44)	0.699
Myeloma	39	33.88	1.15 (0.82–1.57)	0.421
Oral Cavity and Pharynx	39	42.89	0.91 (0.65–1.24)	0.618
Stomach	38	47.45	0.80 (0.57–1.10)	0.187
Breast	33	21.80	1.51 (1.04–2.13)	0.030
Soft Tissue including Heart	21	17.52	1.20 (0.74–1.83)	0.464
Larynx	20	19.66	1.02 (0.62–1.57)	0.999
Female Genital System[§]	15	12.18	1.23 (0.69–2.03)	0.489
Gallbladder and Other Biliary	8	4.06	1.97 (0.85–3.88)	0.110
Small Intestine	7	4.44	1.58 (0.63–3.25)	0.323
Mesothelioma	6	10.61	0.57 (0.21–1.23)	0.193
Hodgkin Lymphoma	5	6.34	0.79 (0.26–1.84)	0.785
Bone and Joint	4	7.25	0.55 (0.15–1.41)	0.303
Thyroid	4	4.96	0.81 (0.22–2.06)	0.895
Anus	3	2.89	1.04 (0.21–3.03)	1.000
Other and Unspecified[^]	151	259.26	0.58 (0.49–0.68)	<0.001

CI: confidence interval; SMR, standardized mortality ratio

[†]Based on the underlying cause of death

[‡]Exact Poisson used to compare Pease service members with the general U.S. population after indirect adjustment for sex, age (in 5-year increments), and race (white, black, and other/missing)

[§]Includes ovary (n=7), uterus corpus (n=4), cervix uteri (n=2), and other (n=2)

[^]Includes malignancy without site specification (n=89), secondary malignancy (n=34), malignancy of independent multiple sites (n=11), malignancy of other and ill-defined sites (n=6), other respiratory (n=4), other digestive (n=2), other endocrine (n=2), Waldenstrom macroglobulinemia (n=1), eye (n=1), and other male genital (n=1)

d. *Secondary Analyses*: Active component service members had higher-than-expected mortality from lung and prostate cancer, but equivalent mortality from all cancers and breast cancer. Death due to all cancers was 24% lower than expected for Guard members (**Table 4**). By rank, death due to all cancer was 21% lower than expected for junior enlisted members and 35% lower for junior officers. Conversely, all cancer and lung cancer deaths were 25% and 52% higher than expected, respectively, for non-commissioned officers/senior enlisted members, and breast cancer death was 2.68 times higher for senior officers (**Table 5**). By occupation, lung cancer death was 32% higher than expected in the maintenance and logistics career field, and all cancer death was 11% lower than expected in the medical and professional career field (**Table 6**). By time on station, death due to all cancers was 51% lower than expected for members stationed at Pease for 5–9 years, while being non-significantly higher for those with <1 year on station and non-significantly lower for those with 1–4 years or ≥10 years on station (**Table 7**).

Table 4. Select Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, by Component, with Standardized Mortality Ratios (N=34,886[‡])

	Observed	Expected	SMR (95% CI)[§]	p value[§]
Active Duty				
All Cancers	1,740	1,697.73	1.02 (0.98–1.07)	0.311
Lung and Bronchus	525	436.70	1.20 (1.10–1.31)	<0.001
Prostate	105	83.31	1.26 (1.03–1.53)	0.024
Breast	26	17.16	1.52 (0.99–2.22)	0.056
Guard				
All Cancers	190	248.52	0.76 (0.66–0.88)	<0.001
Lung and Bronchus	55	64.61	0.85 (0.64–1.11)	0.254
Prostate	12	11.92	1.01 (0.52–1.76)	1.000
Breast	5	3.26	1.40 (0.45–3.26)	0.581
Reserve				
All Cancers	23	27.92	0.82 (0.52–1.24)	0.408
Lung and Bronchus	4	7.90	0.51 (0.14–1.30)	0.211
Prostate	1	1.47	0.68 (0.02–3.79)	1.000
Breast	2	0.91	2.13 (0.26–7.69)	0.484

CI: confidence interval; SMR, standardized mortality ratio

[†]Based on the underlying cause of death

[‡]Members missing the service component variable (n=62) were excluded; three cancer deaths occurred in members missing the service component variable (SMR=0.55; 95% CI: 0.11–1.62)

[§]Exact Poisson used to compare Pease service members with the general U.S. population after indirect adjustment for sex, age (in 5-year increments), and race (white, black, and other/missing)

Table 5. Select Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, by Rank, with Standardized Mortality Ratios (N=34,948)

	Observed	Expected	SMR (95% CI)[‡]	p value[‡]
E1–4				
All Cancers	617	785.87	0.79 (0.72–0.85)	<0.001
Lung and Bronchus	162	172.64	0.94 (0.80–1.09)	0.443
Prostate	26	23.44	1.11 (0.72–1.63)	0.650
Breast	17	12.17	1.40 (0.81–2.24)	0.222
E5–9				
All Cancers	1,086	871.23	1.25 (1.17–1.32)	<0.001
Lung and Bronchus	374	246.05	1.52 (1.37–1.68)	<0.001
Prostate	65	54.65	1.19 (0.92–1.52)	0.188
Breast	7	4.83	1.45 (0.58–2.99)	0.425
O1–3[§]				
All Cancers	110	169.95	0.65 (0.53–0.78)	<0.001
Lung and Bronchus	20	47.78	0.42 (0.26–0.65)	<0.001
Prostate	9	8.01	1.12 (0.51–2.13)	0.818
Breast	3	3.18	0.94 (0.19–2.76)	1.000
O4–10				
All Cancers	143	152.56	0.94 (0.79–1.10)	0.467
Lung and Bronchus	30	44.29	0.68 (0.46–0.97)	0.030
Prostate	18	10.92	1.65 (0.98–2.60)	0.061
Breast	6	1.63	3.68 (1.35–8.01)	0.013

CI: confidence interval; SMR, standardized mortality ratio

[†]Based on the underlying cause of death

[‡]Exact Poisson used to compare Pease service members with the general U.S. population after indirect adjustment for sex, age (in 5-year increments), and race (white, black, and other/missing)

[§]Includes one Air Force warrant officer

Table 6. Select Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, by Occupation, with Standardized Mortality Ratios (N=34,501[‡])

	Observed	Expected	SMR (95% CI)[§]	p value[§]
Operations				
All Cancers	265	287.81	0.92 (0.81–1.05)	0.186
Lung and Bronchus	65	80.46	0.81 (0.62–1.03)	0.088
Prostate	24	17.20	1.40 (0.89–2.08)	0.140
Breast	1	1.59	0.63 (0.02–3.50)	1.000
Maintenance and Logistics				
All Cancers	779	755.27	1.03 (0.96–1.11)	0.397
Lung and Bronchus	261	197.66	1.32 (1.17–1.49)	<0.001
Prostate	46	37.44	1.23 (0.90–1.64)	0.194
Breast	7	4.97	1.41 (0.57–2.90)	0.467
Support				
All Cancers	483	482.31	1.00 (0.91–1.09)	0.987
Lung and Bronchus	140	117.91	1.19 (1.00–1.40)	0.052
Prostate	21	21.53	0.98 (0.60–1.49)	1.000
Breast	9	4.27	2.11 (0.96–4.00)	0.061
Medical and Professional				
All Cancers	307	343.90	0.89 (0.80–1.00)	0.047
Lung and Bronchus	86	85.22	1.01 (0.81–1.25)	0.961
Prostate	22	14.96	1.47 (0.92–2.23)	0.104
Breast	15	9.74	1.54 (0.86–2.54)	0.142
Other				
All Cancers	92	83.67	1.10 (0.89–1.35)	0.389
Lung and Bronchus	27	22.17	1.22 (0.80–1.77)	0.355
Prostate	4	4.40	0.91 (0.25–2.33)	1.000
Breast	1	0.97	1.03 (0.03–5.73)	1.000

CI: confidence interval; SMR, standardized mortality ratio

[†]Based on the underlying cause of death

[‡]Members missing the occupation variable (n=447) were excluded; 30 cancer deaths occurred in members missing the occupation variable (SMR=1.13; 95% CI: 0.76–1.61)

[§]Exact Poisson used to compare Pease service members with the general U.S. population after indirect adjustment for sex, age (in 5-year increments), and race (white, black, and other/missing)

Table 7. Select Cancer Deaths[†] of U.S. Air Force Service Members Assigned to Pease, January 1970 – December 2018, by Time on Station, with Standardized Mortality Ratios (N=34,947[‡])

	Observed	Expected	SMR (95% CI)[§]	p value[§]
<1 Year				
All Cancers	1,892	1,871.12	1.01 (0.97–1.06)	0.635
Lung and Bronchus	561	482.73	1.16 (1.07–1.26)	0.001
Prostate	115	91.57	1.26 (1.05–1.51)	0.020
Breast	32	20.82	1.54 (1.05–2.17)	0.027
1–4 Years				
All Cancers	33	45.29	0.73 (0.50–1.02)	0.070
Lung and Bronchus	13	10.98	1.18 (0.63–2.02)	0.619
Prostate	2	1.99	1.01 (0.12–3.64)	1.000
Breast	0	0.53	0.00 (0.00–6.97)	1.000
5–9 Years				
All Cancers	25	50.74	0.49 (0.32–0.73)	<0.001
Lung and Bronchus	8	13.97	0.57 (0.25–1.13)	0.126
Prostate	1	2.66	0.38 (0.01–2.10)	0.512
Breast	1	0.31	3.25 (0.08–18.1)	0.530
≥10 Years				
All Cancers	6	12.37	0.49 (0.18–1.06)	0.074
Lung and Bronchus	4	3.06	1.31 (0.36–3.34)	0.734
Prostate	0	0.80	0.00 (0.00–4.63)	0.900
Breast	0	0.13	0.00 (0.00–25.6)	1.000

CI: confidence interval; SMR, standardized mortality ratio

[†]Based on the underlying cause of death

[‡]A member missing the time on station variable was excluded; this member had not died from cancer

[§]Exact Poisson used to compare Pease service members with the general U.S. population after indirect adjustment for sex, age (in 5-year increments), and race (white, black, and other/missing)

e. *Mentioned Causes of Death:* An additional 4,227 service members died from a non-cancer cause. Of these, 151 (3.7%) had at least one cancer mentioned on their death certificates, with a total of 179 mentioned cancers. The most frequently mentioned cancers were prostate (n=41), other and unspecified (n=30), lung and bronchus (n=25), leukemia (n=16), non-Hodgkin lymphoma (n=15), and colon and rectum (n=13). The most common underlying causes of death for these decedents included diseases of the circulatory system (n=66), diseases of the respiratory system (n=31), diseases of the digestive system (n=19), and external causes (n=13).

4. LIMITATIONS: Several limitations should be considered when interpreting these results.

a. *Under-capture of Cases:* Pease service members who died from or with cancer may have been missed. Deaths that occurred before 1979 or outside the United States would not be found in NDI-Plus. Such deaths would likely appear in AFMR if the decedent was then on active duty or retired status, and could possibly appear in AFMR if the decedent was separated. Since no deaths were found exclusively in AFMR, and since NDI-Plus is a comprehensive registry that is superior even to the Social Security Administration Death Master File, it is reasonable to conclude that case under-capture did not dramatically alter the findings of this study.

b. *Assumptions:* This study presupposes that death certificates accurately capture the cause of death. If someone dies from an unrecognized malignancy and the death is attributed to another cause, such as dementia or cardiovascular disease, the underlying cause of death would be incorrect. Any misclassification, however, would be non-differential between Pease members and the rest of the population, and mortality studies in the United States routinely utilize the underlying cause of death from death certificates. The study also presupposes that Airmen not in NDI-Plus (or AFMR) were still alive on 31 December 2018, the final day of the surveillance period. If members died but were not captured by the mortality registries, their exposure time would be artificially inflated and the expected cancer counts would be overestimated. This would generate lower SMRs, biasing results toward the null hypothesis of no difference. Finally, in order to maximize outcome capture, this study employed a single surveillance period endpoint, despite the fact that some time must lapse between carcinogenic exposure and cancer death. The assumption of equal susceptibility to cancer death, regardless of surveillance entry date, is an inherent limitation of the study. Assessing the long-term cancer mortality experience of the recently stationed cohort will not be possible for several decades.

c. *Missing Data:* Although personnel rosters were largely complete, demographic and military variables were absent for some service members. Since sex, age, and race are required for SMR calculations, missing values for these variables had to be imputed or excluded. Sex (missing n=3) was manually assigned by name. Race (missing n=77) was grouped with “other” and evaluated according to the “all race” category in SEER. Age (missing n=39) was dropped, meaning that these members did not contribute to the expected number of deaths, even though none had died according to the mortality registries. This approach amplified statistical power—i.e., maximized the ability to find a difference in mortality among Pease members—even if it meant slightly exaggerating the SMR. Those who were missing values in secondary analysis variables (e.g., rank) were analyzed independently rather than being imputed or excluded.

d. *Residual Confounding by Age:* In any investigation of this nature, the ideal comparison group is identical to the study group in everything except the exposure. In this study, differences between the exposed (Pease) and unexposed (U.S. population) were mitigated by accounting for three variables strongly associated with cancer mortality: sex, age, and race. By virtue of the study design, adjustment for these confounding variables was performed indirectly. In other words, the sex-age-race-specific cancer mortality rates from the general U.S. population were applied to the demographic composition of the Pease cohort. Ideally, the exact probability of

cancer mortality for each Pease service member would be known. Cancer mortality data for the U.S. population, however, are arranged in 5-year increments. Therefore, members were bucketed in 5-year windows and the mean probability of death was determined for the beginning and end of each window. Since a 70 year-old black female would be assigned the same probability of dying from cancer as a 74 year-old black female—despite the latter's higher probability in fact—there is residual confounding by age. This could modestly bias the results in either direction.

e. *Residual Confounding by Year:* Likewise, cancer mortality risk in the general U.S. population, and presumably in the Pease population, has varied over time. The probability of dying from many cancers (e.g., lung or breast cancer) has decreased, presumably due to earlier detection and better therapeutics, while the probability of dying from other cancers (e.g., liver or pancreatic cancer) has increased. Because of these fluctuations, an average of U.S. mortality data from 2000–2017 was used; this time period corresponds to 76% of the cancer deaths in the Pease population (18% occurred before 2000 and 6% occurred in 2018). This methodology accounts for some but not all of the period effect associated with cancer mortality, leaving residual confounding by year.

f. *Imprecise Estimates for Rarer Cancer Sites:* The precision of an SMR is directly related to the number of observed outcomes. This relationship is apparent in Table 3: As the site-specific death count decreases, the ratio of the SMR upper confidence limit to the lower confidence limit increases. In other words, the SMR estimates become increasingly imprecise. Exact Poisson regression was used to stabilize these confidence estimates. Nonetheless, some researchers would exclude outcomes with fewer than ten observations—in our case, gallbladder and other biliary cancer, small intestine cancer, mesothelioma, Hodgkin lymphoma, bone and joint cancer, thyroid cancer, and anus cancer.

g. *Generalizability:* This study was limited to Air Force service members stationed at Pease between 1970 and 2018. Its findings may not be applicable to contractor or civilian personnel or to service members stationed at Pease before this time period.

5. DISCUSSION: Cancer mortality among Airmen who were stationed at Pease at any time between January 1970 and December 2018 (N=34,987) was similar to that in the general U.S. population, accounting for sex, age, and race. Compared to the 1,956 cancer deaths that occurred, 1,979 were expected (SMR=0.99; 95% CI: 0.94–1.03).

It is not obvious why deaths from lung, prostate, and breast cancer were higher than expected, or why deaths from colorectal and other and unspecified cancers were lower than expected. One potential explanation is a difference in carcinogenic exposures between the Pease cohort and the U.S. population. Smoking is the leading risk factor for lung cancer and one of many risk factors for breast cancer, but it is not causally associated with prostate cancer (which was also higher in the Pease population), while it is causally associated with colorectal cancer (which was lower in the Pease population). PFAS have been linked to an elevated risk of kidney cancer, but not to lung, prostate, or breast cancer. Another potential explanation is a difference in healthcare access or delivery. However, since lung, prostate, breast, and colorectal cancers are screen-detectable

and treatable, healthcare disparities would be expected to shift these four cancers in the same direction. The incongruity in SMRs between colorectal cancer and the other three cancers contradicts this expectation. A third explanation is that death certificates for Pease decedents, compared with those of their civilian peers, more often listed the precise cancer site as the underlying cause of death. This might explain why the greater-than-expected deaths from lung, prostate, and breast cancers (n=107) were offset by the fewer-than-expected deaths from other and unspecified cancers (n=108). If this is true, the SMR for all cancers may be a more reliable endpoint than the SMR for any particular cancer site. A final explanation relates to probability theory: Using the customary significance level of 0.05, a "statistically significant" result is expected based on chance alone for 5% of independent hypotheses. Since this study analyzed 27 unique cancer sites, at least one site would be expected to have a significant SMR based simply on statistical chance.

Four additional findings should be highlighted. First, no clear association was found between time on station and cancer mortality. The SMR for all cancer deaths was below 1.0 for members stationed at Pease for at least one year—significantly so for those on station for 5–9 years (SMR=0.49; 95% CI: 0.32–0.73). This finding would be unlikely if a carcinogen was widely circulating on the installation during the surveillance period. Second, no career field was disproportionately affected, suggesting against an occupational carcinogenic exposure. Third, only 3.7% of decedents who died from a non-cancer etiology had a cancer recorded on their death certificates, which disputes the idea of widespread cancer mortality. It also supports use of the underlying cause of death, which is conventional methodology for mortality studies in the United States. Fourth, although breast cancer mortality was 2.68 times higher than expected among senior officers, the absolute count of six observed deaths (compared to 1.63 expected deaths) is not as large as many other cancer deaths in this group.

6. CONCLUSION: The number of cancer deaths among U.S. Air Force service members who were stationed at Pease Air Force Base / Air National Guard Base over the past 50 years is nearly identical to the number of cancer deaths expected based on demographically-matched U.S. population data. Deaths from certain cancers (i.e., lung, prostate, and breast) were higher than expected, whereas deaths from other cancers (i.e., colorectal and other and unspecified) were lower than expected. Although the study was not designed to evaluate specific workplace or environmental exposures, nor to determine a precise cancer risk associated with service at Pease, the findings would be unlikely had community-wide carcinogenic exposure occurred. The results of this study do not obviate the need for other investigations, such as the Pease Study currently underway by ATSDR.

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