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

12 September 2024

MEMORANDUM FOR AFGSC/SG

FROM: Epidemiology Consult Service Division
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2510 5th Street, Building 840
Wright Patterson AFB, OH 45433

SUBJECT: Missile Community Cancer Study Epidemiology Investigation Initial (Phase 1B) Results

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EXECUTIVE SUMMARY:

An expanded analysis of cancer incidence in the missile community (Phase 1B) did not identify an elevated incidence of non-Hodgkin Lymphoma nor any of the 13 other individual cancers in the missile community. An initial analysis performed using only Department of Defense Medical Records (Phase 1A) found the potential for elevated incidence of breast and prostate cancer in the missile community compared to the general United States population. The purpose of the Missile Community

Cancer Study is to be extremely diligent in our efforts. The study team knew of the limitations in Phase 1A that precluded optimal capture of cancer cases, so from the original study plan, additional datasets (Department of Defense Medical Records, Department of Veterans Affairs Medical Records, Department of Defense Tumor Registry, and Veterans Affairs Tumor Registry) were included in Phase 1B. Through this effort, researchers identified additional cases of cancer: 1,839 cancers in Phase 1B versus 198 cancers in Phase 1A in the missile community and 53,385 cancers in Phase 1B versus 4,865 cancers in Phase 1A in the non-missile community. Analyzing this additional data did not demonstrate an elevated cancer incidence when comparing the missile community to either the non-missile community or the U.S. population.

In addition to expanding cancer outcome ascertainment, methods for cohort classification and exclusion criteria were refined in Phase 1B. After further discussion with Air Force Global Strike historians, several Air Force Specialty Codes previously identified as “non-missile career fields” were updated to “missile career fields” in Phase 1B. Furthermore, Phase 1A used age at the end of the follow-up period to calculate expected cases of cancer. For Phase 1B, person-time calculations and age at each year of follow-up were used to better estimate incidence rates. In epidemiology studies, person-time is defined as a measurement that estimates the total time that study participants are at risk of developing a disease or dying.

Following our study plan, the next phase of analysis (Phase 1C) examining cancer-specific mortality in the missile community has been started. After analyzing the mortality data, cancer incidence data from civilian tumor registries using the Virtual Pooled Registry (Phase 2) will be added to the four incident cancer datasets (Phase 1B) to optimize the ascertainment of cancer cases among the missile community.

1. INTRODUCTION:

a. *Background:* Military-specific cancer cluster investigations are frequently requested by Department of the Air Force (DAF) leadership and Congress. In a study comparing military population cancer rates to the United States (U.S.) population from 1990-2004, the Department of Defense’s (DoD) Murtha Cancer Center found that incidence rates of breast and prostate cancers were significantly higher in the military among both white and black servicemembers (Zhu et al., 2009).

Prior studies have observed higher cancer rates in certain military career fields. An investigation comparing cancer incidence and mortality in fighter aviators from 2004 -2018 found male fighter aviators had greater adjusted odds of developing cancer of the testis, melanoma of the skin, and prostate cancers when compared to other officers (Webber et al., 2022). Furthermore, when compared with the U.S. population, male fighter aviators were more likely to develop and die from melanoma skin cancer, prostate cancer, and non-Hodgkin lymphoma (Webber et al., 2022), though the underlying cause is currently under investigation (National Defense Authorization Act, 2020).

Missile crew members at Malmstrom Air Force Base (AFB) were previously investigated for occupational and environmental exposures and cancer incidence (Consultative Letter Malmstrom AFB, 2001). In 2001, all identified health hazards were found to be below detectable limits or not exceeding respective occupational exposure limits. Ultimately, this investigation culminated in a report of a safe and healthy work environment for missile personnel (Consultative Letter Malmstrom AFB, 2001). A follow-on study was conducted in 2005 reviewing cancer in missileers at Malmstrom AFB (Garcia, 2005). This case review suffered from two methodological limitations: the researchers were unable to obtain personnel data to evaluate missile group cancer incidence, and the Defense Medical Surveillance System used in the review was not sufficient as a standalone source of cancer incidence data (Garcia, 2005). While this review determined there was no evidence of an increased number of adverse health events that would justify further investigation, it demonstrated there was insufficient evidence from solely using DoD medical data (DMSS) to truly evaluate cancer incidence in missile personnel (Garcia, 2005).

b. *Purpose:* At the request of Air Force Global Strike Command (AFGSC), the United States Air Force School of Aerospace Medicine (USAFSAM)/Defense Centers for Public Health-Dayton (DCPH-D) Epidemiology Consult Service Division assessed the incidence of cancer among Active Duty Department of the Air Force (AD DAF) members with missile community occupations. Concerns of higher-than-expected cancer rates were raised by members of the missile community and initially focused on non-Hodgkin lymphoma (NHL). AFGSC requested a retrospective cohort study—the Missile Community Cancer Study (MCCS)—evaluating the risk of NHL and 13 other common cancers (breast [male and female], colon and rectal, Hodgkin lymphoma, kidney and renal pelvis, leukemia, lung and bronchus, melanoma of the skin, ovarian, pancreatic, prostate, testicular, thyroid, and urinary bladder) compared to the civilian population and to the non-missile AD DAF population. These cancers include the top ten most common cancer types in the U.S., cancers of military significance, and cancers of interest to study stakeholders.

This memorandum provides interim results from Phase 1B of the study using administrative claims data from Tricare Medical Mart (M2) and the Department of Veterans Affairs Corporate Data Warehouse (VA CDW), and tumor registry data from the VA Central Cancer Registry (VACCR) and the DoD Cancer Registry (ONCOLog). The study protocol calls for a phased analysis, with additional data sources being added until incidence and mortality rates are as complete as possible. The next phases incorporate additional data from the National Death Index (Phase 1C) and the Virtual Pooled Registry (VPR) (Phase 2). The VPR is managed by the North American Association of Central Cancer Registries (NAACCR), funded by the National Cancer Institute (NCI), and is designed to efficiently connect researchers with multiple state and local cancer registries.

c. *Study Personnel:*

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(2) Mr. Gregory Wolff, MPH, Senior Epidemiologist, USAFSAM/PHR
(3) Ms. Sarah Fryman, MPH, CPH, Epidemiologist, USAFSAM/PHRR
(4) Mrs. Stefani Ruiz, MHS, Epidemiologist, USAFSAM/PHRR
(5) Mr. James Escobar, MPH, Biostatistician/Data Manager, USAFSAM/PHRR
(6) Ms. Alisa Simon, DrPH, MPH, Biostatistician/Data Manager, USAFSAM/PHRR
(7) Maj Amber F. Britt, DrPH, MPH, CPH, Chief Surveillance & Research Branch, USAFSAM/PHRR

d. *Organizations Contacted*:

(1) Air Force Global Strike Command (AFGSC)
(2) Air Force Global Strike Command Historians
(3) Air Force Surgeon General Tumor Registrar
(4) Armed Forces Health Surveillance Division (AFHSD)
(5) Association of Air Force Missileers
(6) Defense Centers for Public Health-Aberdeen (DCPH-A)
(7) Defense Health Agency Privacy and Civil Liberties Office (DHA PCLO)
(8) Department of Defense Joint Pathology Center's Tumor Registry (DoD ONCOLog)
(9) Department of Veterans Affairs (VA)
(10) Hematology/Oncology Consultant (Uniformed Services University)
(11) Department of Defense Murtha Cancer Center

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(12) National Cancer Institute (NCI)
(13) National Institute for Occupational Safety and Health (NIOSH)
(14) National Institutes of Health (NIH)
(15) Secretary of the Air Force (Sec AF)
(16) Montana Department of Public Health and Human Services—State Epidemiologist
(17) North Dakota Department of Health and Human Services—State Epidemiologist
(18) Surveillance, Epidemiology, and End Results Program (SEER)
(19) Torchlight Initiative
(20) U.S. Congress
(21) Virtual Pooled Registry (VPR)
(22) Wing Leadership (Vandenberg AFB, Malmstrom AFB, F.E. Warren AFB, and Minot AFB)
(23) Wyoming Department of Health-Epidemiologist
(24) Wright State University

2. METHODOLOGY:

a. *Parameters:*

(1) This portion of the multi-phased MCCS was conducted to describe the incidence of cancer in the missile community and compare it to the incidence of cancer in the non-missile community and U.S. general population. A retrospective cohort study was employed to identify AD DAF personnel with accession dates from 1 January 1976 - 31 December 2010. Ascertainment of cancer cases continued through 31 December 2020 allowing for a minimum 10-year follow-up period. Phase 1A of the study utilized DoD M2 administrative claims data (2001-2020) and contained ICD-9 and ICD-10 codes for the 14 cancers of interest. In addition to M2 data, Phase 1B incorporated VA administrative claims data (1991-2020), VACCR cancer registry data (1976-2020), and ONCOLog cancer registry data (1986-2020).

(2) This study was conducted as an occupational assessment of the missile community to identify cancer risks in this population and not to contribute to the generalizable knowledge about cancer or test a research hypothesis; therefore, the 711th Human Performance Wing Institutional Review Board (IRB) determined this effort to be non-human subjects research/public health practice (Protocol #FWR20240053N).

b. *Case Definition and Incidence Rule*s:

(1) The Armed Forces Health Surveillance Division's (AFHSD) *Surveillance Case Definitions* were used to identify the 14 specific cancers based on the World Health Organization's (WHO) International Classification of Diseases, Ninth Revision (ICD-9) and International Classification of Diseases, Tenth Revision (ICD-10) codes (WHO, 2019; WHO 2004; Armed Forces Health Surveillance Division, n.d.). A case was defined as a cancer if any of the following criteria were met:

1. One hospitalization with the cancer-specific ICD-9 or ICD-10 code in the first or second diagnostic position, or

2. One hospitalization with a V or Z code in the first diagnostic position and an ICD-9 or ICD-10 code in the second diagnostic position, or

3. Three or more outpatient medical encounters occurring within 90 days with cancer-specific ICD-9 or ICD-10 codes.

(2) The WHO 2008 ICD for Oncology (ICD-O) case definitions were used for registry data (WHO, 2022). Registry data were prioritized over claims data if patients with the same cancer were in both data sources since registry data are more accurate (histologically confirmed) than claims data.

(3) Cases were counted once per person per cancer type for the entire surveillance period. An individual was counted as many times as they had a different type of cancer (e.g., the same individual diagnosed with colon and breast cancer during the surveillance period would be counted once for each cancer type); however, only one case of cancer was counted per specific cancer type. Only incident records were retained in the final analysis dataset. For cases identified using medical record data, cancer incidence was defined as the date of the case-qualifying medical encounter; incidence was defined as the date of diagnosis for cases identified using registry data. If the same case appeared in both medical encounter and registry data, the registry case was given precedence due to being pathologically confirmed. Overall cancer risk calculations included only the first incident case of diagnosed cancer.

c. *Exclusion Criteria—these individuals were removed from all study analysis:*

(1) Individuals who had a cancer diagnosis preceding military service were excluded from the study cohort.

(2) Individuals with less than one year of military service were excluded from the study cohort. Standard occupational cancer incidence studies generally require a minimum of one year of exposure time (Collatuzzo et al., 2022).

(3) AFPC records younger than 17 (the minimum age for AD service) or older than 62 (the mandatory retirement age) were removed from the cohort, as these were likely transcription errors.

d. *Exposures:*

(1) Exposure Data: The cohort was identified from the Air Force Personnel Center (AFPC) database and included all AD DAF Service Members (SMs) serving from 1 January 1976 - 31 December 2010. Each person was categorized by exposure status as defined by Duty Air Force Specialty Codes (DAFSC) codes. These codes include but are not limited to missile operations officers, missile mechanics, missile systems security specialists (security forces), missile site cooks, and missile facility managers. The missile community members were classified as exposed whereas the non-missile communities comprised the unexposed comparison group.

(2) Exposures in the missile community were further sub-categorized into more specific missile-related exposure groups: Launch Control Center (LCC), Missile Alert Facility (MAF), Launch Facility (LF) Underground or Topside based on the SM ever having a corresponding DAFSC associated with these groups. The LCC is an underground capsule made of thick concrete and steel suspended on giant shock isolators to protect the crew and sensitive electronics from nuclear attack. The MAF is a building above ground with a kitchen and sleeping quarters where missileers not on alert and other support personnel live while performing duties. The LF is the fenced-in secured area that sits on top of the underground missile silo. The LF topside is the area above ground whereas the LF underground is the location where the missile is housed and maintained. The exposure groups were not mutually exclusive, i.e., an individual could have had exposures in two or more exposure groups.

(3) AD DAF SMs who never had any of the DAFSC codes that comprised the four missile exposure groups were categorized into the non-missile comparison group. A SM could be categorized into

more than one missile exposure group but could not be categorized into a missile exposure group and a non-missile exposure group. AF historians from the 20th AF and AFGSC History Office were consulted for proper exposure classification.

(4) Cohort demographics (date of birth, sex, race, and rank) were derived from the AFPC database. Records missing any of these demographics were removed from analysis. Cohort data were merged with outcome data from the administrative claims data and registries. For both cases and non-cases, an individual's demographic information from their last AFPC record was retained for final analysis.

e. *Data sources*:

(1) Tricare M2 DoD administrative claims data: Records with any cancer diagnosis from 1 January 2001 – 31 December 2020 were queried and included inpatient and outpatient care received either through a Military Treatment Facility (MTF) or in the community if the SM used Tricare.

(2) NCI Surveillance, Epidemiology, and End Results (SEER) Program Research Data: Civilian case counts for each of the 14 cancer types and denominators for each of the demographic buckets (age, race, and sex) from 2001-2020 were queried using the SEER*Stat statistical software.

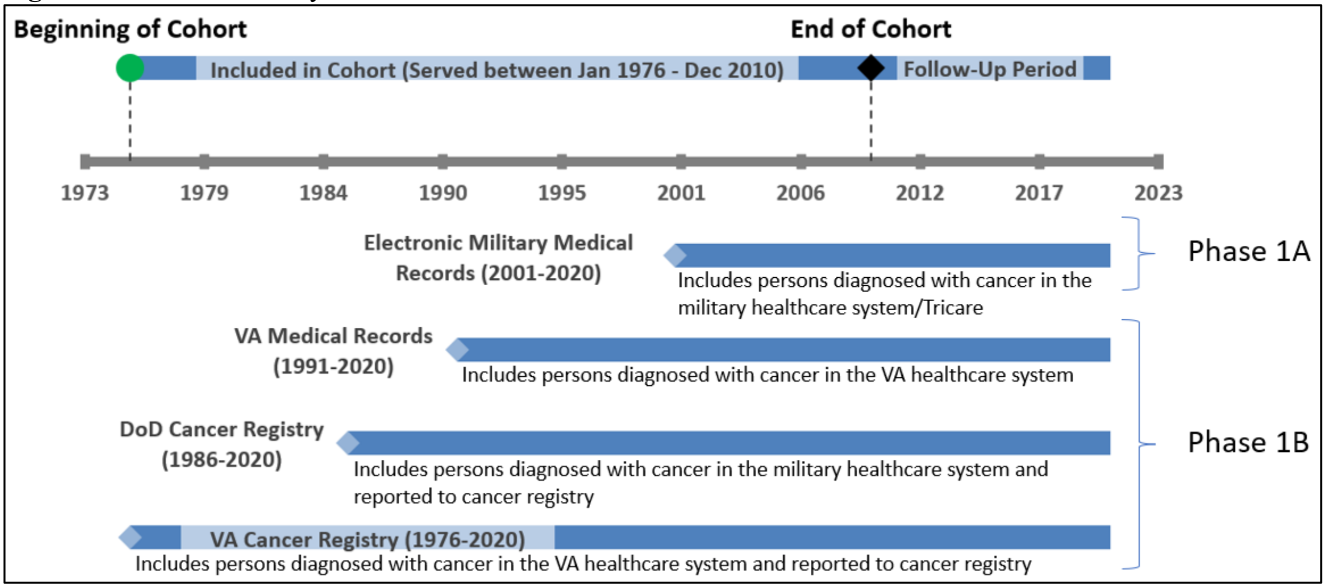
(3) VA CDW administrative claims data: Cohort identifiers were given to the VA CDW to match for any included cancer encounters from 1 January 2001 - 31 December 2020 from VA medical facilities and civilian medical centers being paid for by VA claims.

(4) VA VACCR data: Cancer registry records were acquired for the identified DAF cohort from the VA's central cancer registry. Confirmed cancer cases received were diagnosed from 1 January 1976 - 31 December 2020.

(5) DoD ONCOLog data: Cancer registry records were acquired for the identified DAF cohort from the DoD's Joint Pathology Center's ONCOLog cancer registry. Confirmed cancer cases received were diagnosed from 1 January 1986 - 31 December 2020.

(6) National Death Index (NDI): A date of death variable was added to the cohort dataset from the Defense Suicide Prevention Office. Mortality data were available from 1979-2020. This variable was used as a censoring event as long as the death occurred through 31 December 2020.

Figure 1. Data Availability Timelines of Data Sources for Phases 1A and 1B



f. *Analysis Plan*:

(1) Internal Comparison: Cancer incidence in the missile community was compared to the rest of the AD DAF (non-missile community) using robust Poisson regression (Zou, 2004; Chen et al., 2018; McNutt et al., 2003; Talbot et al., 2023; Egger et al., 2017). Regression analysis was adjusted for sex, age, race, and rank (officer vs. enlisted). Incidence rate ratios and corresponding 95% confidence intervals were estimated using the log link function, with each individual's person-years accounted for using the offset option. P-values of <0.05 were considered statistically significant, meaning that incidence rates were statistically different and unlikely to have occurred by chance.

(2) External Comparison: Cancer incidence in the missile community was compared to the U.S. general population for each of the 14 cancers.

(3) Person-time begins at the first AFPC record date when individuals enter the cohort. Person-time at risk had different cut-off dates for cases and non-cases. For those with cancer, person-time at risk ended on the date of their cancer diagnosis. For those without cancer, person-time at risk ended on either their date of death (if deceased), date of their last medical encounter (if not deceased), or their last AFPC record (if last medical encounter was missing). These respective dates were the basis for an individual's censoring event, i.e., when person-time ended.

(4) All data were managed and analyzed in SAS 9.4 and SAS Enterprise Guide 7.1 (Cary, NC).

3. RESULTS:

a. **Table 1** shows the demographics of the study population. This included 64,930 individuals who served in the missile community (MC) and 1,757,255 individuals who served in the non-missile community (non-MC), making a total of 1,822,184 individuals. Males accounted for 92.92% of the MC, compared to 84.10% of the non-MC. The distribution of age at diagnosis or age at study exit for both missile and non-missile communities was similar.

Officers made up 11.09% of the MC, compared to 12.50% of the non-MC. Most individuals in both groups were white, with 84.41% in the MC and 80.25% in the non-MC. The second largest racial group was black, with 11.68% in the MC and 13.93% in the non-MC. See **Table 1** for additional details.

Table 1. **Characteristics of missile community and non-missile community by demographics (count (column %)) from 1 January 1976 – 31 December 2020**

	Missile Community	**Non-missile Community**	**Total**
Total	64,930*	1,757,255*	1,822,184
Sex			
Male	60,330 (92.92)	1,477,929 (84.10)	1,538,258 (84.42)
Female	4,600 (7.08)	279,326 (15.90)	283,926 (15.58)
Age Ŧ			
17-19	229 (0.35)	15,238 (0.87)	15,467 (0.85)
20-24	10,513 (16.19)	282,124 (16.05)	292,637 (16.06)
25-29	5,328 (8.21)	161,812 (9.21)	167,140 (9.17)
30-34	3,460 (5.33)	135,807 (7.73)	139,267 (7.64)
35-39	4,312 (6.64)	141,705 (8.06)	146,017 (8.01)
40-44	4,264 (6.57)	125,183 (7.12)	129,447 (7.10)
45-49	4,623 (7.12)	116,192 (6.61)	120,815 (6.63)
50-54	5,683 (8.75)	138,355 (7.87)	144,037 (7.90)
55-59	8,085 (12.45)	174,571 (9.93)	182,656 (10.02)
60-64	7,654 (11.79)	169,155 (9.63)	176,809 (9.70)
65-69	5,232 (8.06)	115,817 (6.59)	121,049 (6.64)
70-74	3,047 (4.69)	80,496 (4.58)	83,543 (4.58)
75-79	1,691 (2.60)	55,074 (3.13)	56,765 (3.12)
80-84	657 (1.01)	32,949 (1.88)	33,606 (1.84)
85+	152 (0.23)	12,777 (0.73)	12,929 (0.71)
Rank			
Officer	7,202 (11.09)	219,708 (12.50)	226,910 (12.45)
Enlisted	57,728 (88.91)	1,537,546 (87.50)	1,595,274 (87.55)
Race			
White	54,806 (84.41)	1,410,271 (80.25)	1,465,076 (80.40)
Black	7,582 (11.68)	244,872 (13.93)	252,454 (13.85)
Other	2,542 (3.91)	102,112 (5.81)	104,654 (5.74)
Avg Person-time	23.40	22.99	23.00

*** Individuals were excluded from analysis if they did not have at least 1 year in service. Unique individuals only.**
Ŧ Age is either age at diagnosis for cases or age at the censoring event for non-cases.

b. **Table 2** presents the number of cancer cases among individuals in the MC and non-MC by sex, age, and rank for the period from 1 January 1976 to 31 December 2020. Individuals may have had more than one type of cancer, but not count for more than one case per type of cancer. There were a total of

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1,839 cancer cases in the MC and 53,385 cases in the non-MC, for a total of 55,224 cases. Case demographics were generally similar between the two groups with the exception of sex. Cases peaked in the 45-64 age range for the MC (n=1,215, 66.06%). For the non-MC, the majority of the cases were slightly older in the 50-69 age range (n =33,524, 62.91%). Although age of cases in the MC appears to be younger, the mean (MC=54.69, non-MC=55.67) and median age (MC=56, non-MC= 57) of cases are similar in both cohorts. Most cases were enlisted personnel in both groups (MC n=1,586, 86.24%; non-MC: n=44,728, 83.95%). The majority of incident cases were White in both communities (MC: n=1,453, 79.01%; non-MC: n=39,908, 74.90%). The next largest racial group was Black (MC: n=498, 20.57%; non-MC: n=12,873, 21.82%).

Table 2. **Cancer cases* among missile and non-missile communities by demographics (count (column %)), 1 January 1976 – 31 December 2020**

	Missile Community Cases	**Non-Missile Community Cases**	**Total**
Total	1,839 (2.83)	53,385 (3.04)	55,224
Sex			
Male	1,732 (94.18)	45,686 (85.75)	47,418 (85.86)
Female	107 (5.82)	7,699 (14.43)	7,806 (14.14)
Age at diagnosis			
17-19	0 (0.00)	36 (0.07)	36 (0.07)
20-24	16 (0.87)	738 (1.38)	754 (1.37)
25-29	34 (1.85)	1,369 (2.57)	1,403 (2.54)
30-34	46 (2.50)	1,752 (3.29)	1,798 (3.26)
35-39	96 (5.22)	2,327 (4.37)	2,423 (4.39)
40-44	132 (7.18)	3,199 (6.01)	3,331 (6.03)
45-49	185 (10.06)	4,598 (8.63)	4,783 (8.66)
50-54	293 (15.93)	7,209 (13.53)	7,502 (13.58)
55-59	389 (21.15)	9,932 (18.64)	10,321 (18.69)
60-64	348 (18.92)	10,338 (19.40)	10,686 (19.35)
65-69	175 (9.52)	6,045 (11.34)	6,220 (11.26)
70-74	82 (4.46)	3,353 (6.29)	3,435 (6.22)
75-79	27 (1.47)	1,678 (3.15)	1,705 (3.09)
80-84	11 (0.60)	626 (1.17)	637 (1.15)
85+	5 (0.27)	185 (0.35)	190 (0.34)
Rank			
Officer	253 (13.76)	8,657 (16.24)	8,910 (16.13)
Enlisted	1,586 (86.24)	44,728 (83.95)	46,314 (83.87)
Race			
White	1,453 (79.01)	39,908 (74.90)	41,361 (74.90)
Black	345 (18.76)	11,671 (21.90)	12,016 (21.76)
Other	41 (2.23)	1,806 (3.39)	1,847 (3.34)

*** An individual may have more than 1 type of cancer, but not more than 1 case per type of cancer.**

c. **Table 3** presents the number of cancer cases by cancer type for the missile and non-missile communities from 1 January 1976 to 31 December 2020. Prostate cancer was the most common type among both the MC (n=577, 31.38%) and non-MC (n=16,845, 31.55%). Lung and bronchus cancer was the second most frequently diagnosed for both groups (MC: n=193, 10.49%; non-MC: n=6,338, 11.87%). Colon and rectum cancers (MC: n=191, 10.39%; non-MC: n=4,932, 9.29%) were also relatively common.

NOTE: The counts in Tables 3 and Table 5 are different because Table 3 counts include all cancer cases in the MC from 1976-2020. Table 5 counts include cancer cases in the MC from 2001-2020 in order to allow a more accurate comparison with SEER data. SEER data forms the basis for the civilian comparison group. While SEER data is available back to the 1970's, our data sources for the missile community are most complete starting in 2001.

Table 3. **Cancer cases (count (column %)) by cancer type and exposure status (missile community versus non-missile community) from 1 January 1976 – 31 December 2020**

	Missile Community (N=64,930)	**Non-missile Community (N=1,757,254)**	**Total**
Total Cancer Cases*	**1,839**	**53,385**	**55,224**
Breast (Male and Female)	62 (3.37)	3,744 (7.01)	3,806 (6.89)
Colon and Rectum	191 (10.39)	4,962 (9.29)	5,153 (9.33)
Hodgkin Lymphoma	38 (2.07)	919 (1.72)	957 (1.73)
Kidney and Renal Pelvis	131 (7.12)	2,998 (5.62)	3,129 (5.67)
Leukemia	89 (4.84)	2,288 (4.29)	2,377 (4.30)
Lung and Bronchus	193 (10.49)	6,338 (11.87)	6,531 (11.83)
Melanoma of the Skin	160 (8.70)	3,980 (7.46)	4,140 (7.50)
Non-Hodgkin Lymphoma	126 (6.85)	3,268 (6.12)	3,394 (6.15)
Ovarian	5 (0.27)	309 (0.58)	314 (0.57)
Pancreatic	62 (3.37)	1,377 (2.58)	1,439 (2.61)
Prostate	577 (31.38)	16,845 (31.55)	17,422 (31.55)
Testicular	63 (3.43)	1,566 (2.93)	1,629 (2.95)
Thyroid	73 (3.97)	2,389 (4.48)	2,462 (4.46)
Urinary Bladder	69 (3.75)	2,402 (4.50)	2,471 (4.47)

*** An individual may have more than 1 type of cancer, but not more than 1 case per type of cancer**

d. **Table 4** presents the number of cancer cases (n) and corresponding column percentages (%) among missile community members within different sub-exposure groups for the period from 1 January 1976 - 31 December 2020. Among the MC, prostate cancer again topped the list across all exposure categories (LCC: n=315, 33.40%; MAF: n=443, 31.96%; LF Topside: n=365, 30.49%; LF Underground: n=182, 31.06%). Colon and rectum cancers (ranging from 9.38%-11.77%) and lung and bronchus (ranging from 8.73%-11.60%) were the next most frequent types in each exposure group.

In terms of total cancer cases, there were 943 cases in the LCC group, 1,386 cases in the MAF group, 1,197 cases in the LF Topside group, and 586 cases in the LF Underground group. Individual analyses were performed on each exposure category, comparing the incidence of each cancer in each MC exposure category to both their non-exposed counterparts (LCC vs non-LCC) and to the general U.S.

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population. These analyses did not show any statistically significant increase in cancer in any of the MC exposure groups; however, some of the analyses remain underpowered, meaning that more datapoints are needed. Additional data from Phase 2 will solidify our understanding of cancer risk in the individual exposure groups and the MC overall.

NOTE: Table 4 counts are from individuals who may have been in multiple exposure locations, i.e. the exposures are not mutually exclusive. For example, an individual with cancer could have been included in both the MAF and LCC exposure groups. The sum of cancer cases by row will add up to more than either Table 3 or Table 5.

Table 4. **Cases among missile community (count (column %)) by exposure group, from 1 January 1976 – 31 December 2020**

	Launch Control Center (LCC)* N=30,107	**Missile Alert Facility (MAF)*** N=52,743	**Launch Facility (LF) Topside*** N=47,221	**Launch Facility (LF) Underground*** N=20,680
Total Cancer Cases	**943**	**1,386**	**1,197**	**586**
Breast (Male and Female)	44 (4.67)	51 (3.68)	24 (2.01)	13 (2.22)
Colon and Rectum	101 (10.71)	130 (9.38)	119 (9.94)	69 (11.77)
Hodgkin Lymphoma	16 (1.7)	32 (2.31)	27 (2.26)	8 (1.37)
Kidney and Renal Pelvis	55 (5.83)	102 (7.36)	100 (8.35)	38 (6.48)
Leukemia	39 (4.14)	71 (5.12)	64 (5.35)	31 (5.29)
Lung and Bronchus	91 (9.65)	121 (8.73)	124 (10.36)	68 (11.60)
Melanoma of the Skin	92 (9.76)	128 (9.24)	95 (7.94)	46 (7.85)
Non-Hodgkin Lymphoma	58 (6.15)	100 (7.22)	90 (7.52)	38 (6.48)
Ovarian	1 (0.11)	4 (0.29)	4 (0.33)	1 (0.17)
Pancreatic	34 (3.61)	44 (3.17)	38 (3.17)	20 (3.41)
Prostate	315 (33.40)	443 (31.96)	365 (30.49)	182 (31.06)
Testicular	30 (3.18)	57 (4.11)	51 (4.26)	22 (3.75)
Thyroid	39 (4.14)	61 (4.40)	45 (3.76)	20 (3.41)
Urinary Bladder	28 (2.97)	42 (3.03)	51 (4.26)	30 (5.12)

***Categories are not mutually exclusive**

e. **Table 5** presents the standardized incidence ratios (SIRs) for different types of cancer in the missile community compared to U.S. civilian cases. The SIR is calculated as the ratio of the observed number of cases in the missile community to the expected number based on the U.S. population. This statistical measure is used to determine if the occurrence of cancer in the missile community is high or low, i.e., is it higher or lower than expected given the population, adjusted for differences in age, sex, and race distributions of that community when compared to the general U.S. population? If fewer cases are observed than expected, the SIR is less than 1 whereas if more cases are observed than expected, the SIR is greater than 1.

Almost all of the SIRs were <1.0, suggesting that the missile community had a lower risk of developing these types of cancer than the general U.S. population. Breast cancer had an SIR 1.0, indicating that there was no difference in risk. Moreover, ovarian cancer had an SIR=1.32 but it was not statistically significant (p=0.66) and relied on very low case counts (5 observed cases and 4 expected cases).

NHL was not found to be elevated in the missile community compared to the general U.S. population (SIR=0.57, p≤0.01). The incidence of urinary bladder cancer among the MC was 71% lower compared to the general U.S. population and was the lowest SIR reported (SIR=0.29; p<0.001). For Hodgkin lymphoma, the SIR was not statistically significantly different and close to 1 (0.97).

Table 5. **Standardized Incidence Ratios (SIRs) by cancer type among the missile community, compared to U.S. civilian cases using SEER Research database from 1 January 2001 – 31 December 2020**

Cancer Type	Observed Cases	Expected Cases	SIR	95% CI, lower	95% CI, upper	p-value
All 14 types	1,630	3,198	**0.51**	**0.48**	**0.54**	**≤0.01**
Male and Female Breast	56	56	1.00	0.69	1.40	1.00
Colon and Rectum	171	417	**0.41**	**0.33**	**0.50**	**≤0.01**
Hodgkin Lymphoma	26	27	0.97	0.55	1.58	0.99
Kidney and Renal Pelvis	122	209	**0.58**	**0.46**	**0.73**	**≤0.01**
Leukemia	75	116	**0.65**	**0.47**	**0.87**	**≤0.01**
Lung and Bronchus	180	475	**0.38**	**0.31**	**0.46**	**≤0.01**
Melanoma of the Skin	134	222	**0.60**	**0.48**	**0.75**	**≤0.01**
Non-Hodgkin Lymphoma	111	194	**0.57**	**0.44**	**0.73**	**≤0.01**
Ovarian	5	4	1.32	0.29	3.74	0.66
Pancreatic	56	116	**0.48**	**0.33**	**0.68**	**≤0.01**
Prostate	542	1,023	**0.53**	**0.47**	**0.59**	**≤0.01**
Testicular	34	48	**0.71**	**0.44**	**1.09**	**0.05**
Thyroid	57	82	**0.70**	**0.48**	**0.97**	**≤0.01**
Urinary Bladder	61	211	**0.29**	**0.20**	**0.40**	**≤0.01**

***Bold represents statistically significant findings (p≤0.05)**

f. **Table 6** presents the incidence rate ratios (IRR) for aggregated and specific types of cancers comparing individuals in missile career fields to SM in non-missile career fields, adjusted for age, race, sex, and rank. Cancer incidence occurs at different rates in different age, race, and sex groups so adjusting allows us to standardize the two populations for comparison. The results suggest that there is no statistically significant difference in the incidence of most types of cancer between the two groups, as indicated by the IRR values being close to 1.00 and p-values being above 0.05.

Overall, the MC had a significantly lower IRR (0.94; p≤0.01) of all cancer types in both sexes compared to the non-MC. Specifically, the MC showed statistically lower risks for urinary bladder cancer (IRR=0.70; p≤0.01), lung and bronchus cancer (IRR=0.78; p≤0.01), and prostate cancer (IRR=0.88; p≤0.01). Among the male MC population, overall cancer risk was significantly lower compared to the male non-MC population (IRR=0.94; p=0.02). However, the overall relative difference in cancer incidence among the MC and non-MC females was not statistically significant

(IRR=0.88; p=0.18). There were no statistically significant differences in cancer rates for most other cancer types when comparing MC to non-MC populations.

Table 6. **Cancer cases, by type, of missile career field compared to non-missile career field* from 1 January 1976 - 31 December 2020 (IRR = Incidence Rate Ratio) (SE = Standard Error)**

Cancer Type	**IRR**	**SE**	**95% CI, lower**	**95% CI, upper**	**p-value**
All 14 types (Male and Female)**	**0.94**	**1.02**	**0.89**	**0.99**	**≤0.01**
All 12 types (Female)**	0.88	1.10	0.68	1.07	0.18
All 13 types (Male)**	**0.94**	**1.03**	**0.89**	**0.99**	**0.02**
Breast (Male and Female)	0.99	1.14	0.74	1.24	0.91
Breast (Female)	1.00	1.14	0.73	1.26	0.98
Colon and Rectum	1.01	1.08	0.86	1.15	0.92
Hodgkin Lymphoma	1.23	1.18	0.91	1.55	0.21
Kidney and Renal Pelvis	1.11	1.09	0.93	1.28	0.25
Leukemia	1.00	1.11	0.79	1.21	0.99
Lung and Bronchus	**0.78**	**1.08**	**0.64**	**0.93**	**≤0.01**
Melanoma of the Skin	1.08	1.08	0.92	1.24	0.35
Non-Hodgkin Lymphoma	1.02	1.10	0.84	1.20	0.85
Ovarian (Female)	0.98	1.57	0.10	1.86	0.97
Pancreatic	1.18	1.14	0.92	1.43	0.21
Prostate (Male)	**0.88**	**1.04**	**0.80**	**0.96**	**≤0.01**
Testicular (Male)	1.15	1.14	0.90	1.41	0.27
Thyroid	1.02	1.13	0.79	1.25	0.88
Urinary Bladder	**0.70**	**1.13**	**0.46**	**0.94**	**≤0.01**

***Multiple Poisson regression adjusted for age, race, sex, and rank.**
**** Only the first primary cancer per individual was counted.**

4. DISCUSSION:

Since Phase 1A interim results were released, study methodology was further refined in accordance with guidance from external partners. One significant adjustment required individuals to serve for a minimum of one year in a career field. Standard occupational cancer studies generally require a minimum of one year duration of employment to be included in analysis (Bytnar et al., 2024). This excluded a large number of individuals (N = 205,732) from analysis as they did not contribute one full year of time in the DAF during our cohort timeframe.

Phase 1B used administrative claims data from the DoD and VA as well as cancer registries from the DoD and VA to identify cancer cases, representing the most comprehensive study to date of cancer incidence within the DAF missile community. Prostate cancer was the most commonly diagnosed cancer in both the missile (31.38%) and non-missile communities (31.55%) (**Table 3**). This finding is consistent with results from the U.S. AF Fighter Aviator study (Webber et al., 2022). Prostate cancer is also the most common cancer among males in the U.S. other than skin cancer (American Cancer Society, 2023). Cancers of the lung and bronchus were the second most frequently diagnosed cancers in both the missile (10.49%) and non-missile communities (11.87%). In the U.S. general population, cancers of the lung and bronchus are the third most commonly diagnosed cancer among both men and women, accounting for an estimated 11.7% of all new cancer cases in 2024 (National Cancer Institute, 2022.). The percentage of cancer cases from NHL was similar between the missile community (6.85%) and the non-missile

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community (6.12%). In the U.S. general population, NHL accounts for an estimated 4.0% of all new cancer cases in 2024 (National Cancer Institute, 2022). For both of these comparisons, it should be noted, that this is the percentage of all new cancer cases in the U.S. and not the percentage of cancer cases of the 14 selected cancers in the MCCS.

Across the 14 site-specific cancers that are being studied, the missile community generally had significantly lower SIRs when compared the U.S. civilian population (**Table 4**). Military service members are usually younger, more likely to be male, and generally have better health than the general U.S. population (Webber et al., 2022; Bytnar et al., 2024). Lower incidence could potentially be attributed to the healthy worker effect/healthy soldier effect. On the other hand, all military members have access to no-cost universal health coverage and may be more likely to receive cancer screenings (Bytnar et al., 2024).

Surviving an initial cancer does come with an increased risk of developing a second, unrelated cancer. According to the American Cancer Society, this increased risk is influenced by several factors, including genetic predispositions, lifestyle choices, and the treatments used for the first cancer (American Cancer Society, 2020). The MCCS does include second cancers.

While initial findings from Phase 1A suggested the potential for increased incidence of breast and prostate cancer, this Phase 1B analysis using an expanded (yet still incomplete) dataset did not support this earlier finding. When the Phase 1A memo was published, we urged caution in drawing any conclusions, knowing that the dataset was incomplete. At the time, we estimated that Phase 1A captured <25% of the cancer cases that we would ultimately find. In fact, Phase 1A captured fewer than 10% of the cancer cases that were found in Phase 1B – 5,063 cancer cases were found in Phase 1A compared to 55,224 cancer cases found in Phase 1B. Of the large number of additional cancer cases found in Phase 1B, relatively more cancer cases were found in the non-missile community compared to the missile community. To illustrate this point with the breast cancer numbers – Phase 1A found 13 cases of female breast cancer in the missile community and 570 cases of female breast cancer in the non-missile community. Phase 1B found 62 cases in the MC (nearly 5 times more) and 3,744 in the non-MC (over 6.5 times more). Again, this point is demonstrated with the prostate cancer numbers – Phase 1A found 24 cases of prostate cancer in the missile community and 405 cases of prostate cancer in the non-missile community. Phase 1B found 577 cases of prostate cancer in the MC (24 times more) and 16,845 cases in the non-MC (over 41 times more). In both examples, ascertaining proportionately more cancer cases in the non-missile community accounts for the difference in findings between this analysis and the more limited Phase 1A analysis.

These Phase 1B findings suggest that exposure to occupational hazards associated with the missile career fields has not resulted in a significant increase in the rates of the 14 types of cancers evaluated. However, it is important to note that this analysis only examined the first primary cancers of each listed cancer type and did not account for multiple instances of the same cancer in an individual. This current analysis is also based on an incomplete count of all cancers due to missing substantial numbers of cases from the civilian cancer registries; therefore, the USAFSAM/DCPH-D study team is moving on to Phase 2 as outlined in the study design plan.

The findings of Phase 1B of the MCCS contribute valuable insights into the cancer risk among the missile community; however, this study is not complete. We urge continued restraint in drawing any firm conclusions until Phase 2 datasets are included and analyzed.

5. STRENGTHS & LIMITATIONS:

a. Strengths:

(1) The inclusion of an internal comparison i.e., the non-MC, is a significant strength of this study. This internal comparison uses two military populations that are more similar to each other with regards to fitness standards, overall health, and access to healthcare, and reduces the impact of the healthy soldier effect (Sullivan-Baca et al., 2023).

(2) This study incorporates both administrative claims data and cancer registry data from the DoD and VA creating the most comprehensive dataset for cancer incidence data in this community to date. Adding VPR data in Phase 2 will capture additional incident cases, further completing the cancer incidence data.

(3) The inclusion of all members of the missile community (including maintainers, security forces, food services, etc.) over the large study timeframe created a comprehensive cohort large enough to ensure adequate statistical power to uncover any association with cancer incidence, should one exist. Consultation with historians from the 20th AF and AFGSC, as well as a rigorous review of historical personnel records, provides high confidence that the missile career is accurately represented within the cohort. This comprehensive review of all AFSCs ensured that only missileers who work with intercontinental ballistic missiles (as opposed to surface-to-air missiles and cruise missiles) were included in our analysis. AFSCs included in our final cohort were compared to a comprehensive and chronological listing of missile community strength over the last 50 years with high reliability.

(3) Two study epidemiologists performed independent, parallel analysis of the data—starting with the same datasets and then comparing outcomes after coding the data programs to clean the data. Their analysis yielded similar case counts and results, yielding high internal validity. As such, there is confidence the results are accurate and representative of the true nature of the associations.

(4) USAFSAM/DCPH-D consulted with industry experts including epidemiologists and biostatisticians from NIOSH, DCPH-A, and Wright State University. Their independent evaluation of the interpretation of the methodology, analysis, and study limitations ensures a robust evaluation that is aligned with other occupational study practices.

b. Limitations:

(1) This is a retrospective cohort study; thus, it is limited to the availability of historical data. There is no single source of data that contains all cases of cancer in all populations at all times. Each of the datasets used spans a different timeframe and is limited to a specific affiliation (DoD, VA, or civilian). DoD administrative claims data were not captured electronically before 2001. VA medical records date back as early as 1991. Data from DoD and VA cancer registries go back to 1986 and 1976, respectively, with more complete capture of cancer cases in more recent years. Additionally, the DoD tumor registry only contains patients diagnosed or treated for cancer at an MTF; cases diagnosed off-base are not included if they were not reimbursed by Tricare. Case capture over the entire study timeframe 1976 – 2020 is incomplete, particularly at the beginning. This limitation will be partially addressed through the inclusion of the VPR data—which captures diagnoses outside of the Tricare and VA systems. We estimate that up to 30-50 percent of all cancer cases within our cohort, will be found exclusively in the VPR.

(2) Demographic and medical claims data had internal discrepancies. Though the AFHSD *Surveillance Case Definitions* are a relatively effective algorithm for finding cancers utilizing administrative claims data, coding errors still exist with these types of data (Armed Forces Health Surveillance Division, n.d.). For instance, the AFPC dataset included records where the same individual was listed as having one demographic value in one year and a different demographic value in a subsequent year (i.e., different dates of birth or races). Taking only one record per person (the most recent record for non-cases and the date closest to the diagnosis date for cases) was our standardized approach to handling these incongruencies. It was not practical to record and review all discrepancies, as AFPC is the gold standard for military demographics.

(3) The study design precluded the comparison of sub-exposures (LCC, MAF, LF topside, LF underground) to each other because many individuals were in multiple exposure groups. Most cancers develop over long periods, even decades, after exposure. A latency period, the time between exposure and development of cancer, was not utilized in this study as we wanted to compare our rates to that of the U.S. civilian population using the SEER registry, and SEER does not have a latency period. Additionally, establishing a causal relationship between exposure, such as career field and cancer, was not a realistic goal of this study. This retrospective cohort study was designed to determine if there was a relative difference in cancer incidence between two populations rather than search for causation. Identifying causation for disease conditions with long latency (i.e., conditions that take years to decades to develop after exposure) is next to impossible with descriptive epidemiology. This is due to several factors including the retrospective nature of these studies, unavailable data about numerous individual lifestyle choices (smoking, alcohol usage, body mass index, diet, etc.) that confound the relationships being evaluated, genetic predisposition to cancer, and non-occupational exposures. Furthermore, time in occupation was not investigated but could be a major influence on cancer development, should a causal relationship exist.

(4) It is well known that members of the military have better access to care, are generally healthier than civilians, and require more health screenings to complete their jobs. This is known as the Healthy Soldier Effect (HSE) (Sullivan-Baca et al., 2023). The relationship between the duration of military service and the HSE is complex and varies based on several factors, including the length of service, deployment history, and the individual's overall health status. This analysis does not consider the length of service or attempt to adjust for the HSE. Also, because of increased health screenings, cancer may be detected more often and diagnosed at an earlier stage, potentially biasing results. This could inflate incidence in the military population when compared to the civilian population. Complete data capture will best examine these issues, as well as the upcoming cancer mortality investigation in Phase 1C.

(5) Using administrative claims data in addition to cancer registry data made it impractical to evaluate the stage of cancer at diagnosis. Administrative claims data were included in this study to maximize the capture of incident cancer cases. While studies of AFHSD cancer case definitions have shown good Positive Predictive Value (PPV) in determining incident cases, determining cancer stage at diagnosis from administrative claims data is not reliable. PPV is an indicator of the number of people who were diagnosed with cancer who truly have the disease. It answers the question, “If I have a positive test or diagnosis what is the probability that I actually have the disease?” Future studies should evaluate the capture of incident cancer cases using cancer registries alone; if this is shown to be adequate without including administrative claims data, then cancer stage at diagnosis from cancer registry data should be included in future retrospective observational studies.

(6) The incidence rates of cancer for screen-detectable cancers are impacted by early detection, but this is a complicated relationship. Pap smears (for cervical cancer) and colonoscopy (for colon

cancer) can detect and remove precancerous lesions, effectively preventing cancer and lowering incidence rates. Mammography (for breast cancer) and prostate-specific antigen (PSA) testing (for prostate cancer) can detect early-stage cancers, increasing incidence rates of these cancers. When available, including cancer screening rates in retrospective cohort studies would add additional context to aid in interpretation. While cancer screening data may be available for the military population, this data is not readily available for the comparison U.S. population.

(7) The nature of the data obtained from AFPC gives an annual "snapshot" of an individual's service that is taken in September of each year. Therefore, for a large number of individuals with only a single AFPC record, it was unable to be determined if they had served for <12 months or between 12-23 months. These individuals were excluded from analysis. While the number of persons excluded was large, the effect on study findings is likely to be minimal as these individuals would have the least amount of exposure to the missile community.

(8) Using the date of death to calculate person-time in a retrospective cohort study has several limitations, primarily stemming from the uncertainty of cancer status at the time of death. When person-time ends at the date of death, it assumes that individuals were cancer-free up until that point, which may not always be accurate. Some individuals might have developed cancer before their death, but if they were diagnosed outside the DoD/VA medical systems, these cases would be missed at this phase of analysis. This would mean that individuals who had cancer before death might erroneously be classified as cancer-free for the duration of their person-time (misclassification bias). The likely effect would be an underestimation of cancer rates and risk estimates. In Phase 2, cancer cases diagnosed outside the DoD/VA medical systems will be included using the VPR, leading to the most comprehensive dataset available and more accurate person-time calculations, cancer rates, and risk estimates.

6. CONCLUSION:

During Phase 1B, no statistically significant elevation in cancer rates in the missile community were observed. This underscores the importance of moving on to the next planned phases of the study to evaluate cancer mortality (Phase 1C) and complete the assessment of cancer incidence (Phase 2). USAFSAM/DCPH-D will continue to analyze additional datasets to provide a more comprehensive evaluation of any increased cancer risk associated with service in the missile community. Further investigation into specific subgroups, exposures, and potential confounders may provide deeper insights into the complex relationship between service in the missile community and cancer risk. Additionally, efforts to promote health and wellness initiatives tailored to the unique needs of the missile community remain crucial in mitigating overall health risks, including cancer, within this community.

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