UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
READINESS

FEB - 8 2023

The Honorable Mike D. Rogers
Chairman
Committee on Armed Services
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The Department's response to section 750 of the William M. (Mac) Thornberry National Defense Authorization Action Act (NDAA) for Fiscal Year (FY) 2021 (Public Law 116–283), "Study on the Incidence of Cancer Diagnosis and Mortality Among Military Aviators and Aviation Support Personnel," is enclosed. Section 750(a)(2)(B) requests a report on the results of Phase 1 of the study, which determines if there is a higher incidence of cancers occurring for these military aviators and aviation support personnel as compared to similar age groups in the general population through the use of the database of the Surveillance, Epidemiology, and End Results program of the National Cancer Institute.

This study found that compared to the U.S. population after adjusting for age, sex, and race, aircrew had an 87 percent higher rate of melanoma, 39 percent higher rate of thyroid cancer, 16 percent higher rate of prostate cancer, and a 24 percent higher rate of cancer for all sites. Ground crew members had higher incidence of cancers of brain and nervous system (by 19 percent), thyroid (by 15 percent), melanoma (by 9 percent), kidney and renal pelvis (by 9 percent), and of all sites (by 3 percent). However, aircrew and ground crew both had lower or similar cancer mortality rates for all cancer types when compared to the U.S. population. This concludes the Phase 1 epidemiologic study and triggers a Phase 2 study to identify risk factors for the cancer diagnoses identified in the Phase 1 study. Elements to be included in the Phase 2 study are outlined in section 750(a)(3)(c) of the NDAA for FY 2021.

There are known gaps in military cancer case data with no Department of Defense data source containing complete data on cancer diagnoses prior to 1990. This has likely resulted in the Phase 1-a study having underreported the number of military cancer cases since data from the Department of Veterans Affairs (VA) and civilian cancer registries were not included. This lack of cancer data on veterans, Reserve, and National Guard members could bias the results of this Phase 1-a study. To address this limitation, prior to initiating the Phase 2 study, a supplementary Phase 1-b study is being conducted including additional data from the VA and 46 State cancer registries. This Phase 1-b study will supplement the cancer incidence analysis using data from the VA Central Cancer Registry and the Virtual Pooled Registry Cancer Linkage System. Including these two data sources will result in better ascertainment of cancer cases for veterans, Reserve, and National Guard members, and others without access to TRICARE coverage.

Thank you for your continued strong support for the health and well-being of our Service members, veterans, and their families. I am sending similar letters to the appropriate committees of Congress.

Sincerely,

Gilbert R. Cisneros, Jr.

Enclosure:
As stated

cc:
The Honorable Adam Smith
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND
READINESS

FEB - 8 2023

The Honorable Jack Reed
Chairman
Committee on Armed Services
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The Department's response to section 750 of the William M. (Mac) Thornberry National Defense Authorization Action Act (NDAA) for Fiscal Year (FY) 2021 (Public Law 116–283), "Study on the Incidence of Cancer Diagnosis and Mortality Among Military Aviators and Aviation Support Personnel," is enclosed. Section 750(a)(2)(B) requests a report on the results of Phase 1 of the study, which determines if there is a higher incidence of cancers occurring for these military aviators and aviation support personnel as compared to similar age groups in the general population through the use of the database of the Surveillance, Epidemiology, and End Results program of the National Cancer Institute.

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Sincerely,

Gilbert R. Cisneros, Jr.

Enclosure:
As stated

cc:
The Honorable Roger F. Wicker
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

FEB - 8 2023

The Honorable Jon Tester
Chairman
Committee on Veterans' Affairs
United States Senate
Washington, DC 20510

Dear Mr. Chairman:

The Department's response to section 750 of the William M. (Mac) Thornberry National Defense Authorization Action Act (NDAA) for Fiscal Year (FY) 2021 (Public Law 116–283), "Study on the Incidence of Cancer Diagnosis and Mortality Among Military Aviators and Aviation Support Personnel," is enclosed. Section 750(a)(2)(B) requests a report on the results of Phase 1 of the study, which determines if there is a higher incidence of cancers occurring for these military aviators and aviation support personnel as compared to similar age groups in the general population through the use of the database of the Surveillance, Epidemiology, and End Results program of the National Cancer Institute.

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Sincerely,

Gilbert R. Cisneros, Jr.

Enclosure:
As stated

cc:
The Honorable Jerry Moran
Ranking Member

UNDER SECRETARY OF DEFENSE
4000 DEFENSE PENTAGON
WASHINGTON, D.C. 20301-4000

PERSONNEL AND READINESS

FEB - 8 2023

The Honorable Mike Bost
Chairman
Committee on Veterans' Affairs
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

The Department's response to section 750 of the William M. (Mac) Thornberry National Defense Authorization Action Act (NDAA) for Fiscal Year (FY) 2021 (Public Law 116–283), "Study on the Incidence of Cancer Diagnosis and Mortality Among Military Aviators and Aviation Support Personnel," is enclosed. Section 750(a)(2)(B) requests a report on the results of Phase 1 of the study, which determines if there is a higher incidence of cancers occurring for these military aviators and aviation support personnel as compared to similar age groups in the general population through the use of the database of the Surveillance, Epidemiology, and End Results program of the National Cancer Institute.

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Thank you for your continued strong support for the health and well-being of our Service members, veterans, and their families. I am sending similar letters to the appropriate committees of Congress.

Sincerely,

Gilbert R. Cisneros, Jr.

Enclosure:
As stated

cc:
The Honorable Mark Takano
Ranking Member

PHASE 1-a – STUDY ON THE INCIDENCE OF CANCER DIAGNOSIS AND MORTALITY AMONG MILITARY AVIATORS AND AVIATION SUPPORT PERSONNEL

January 2023

The estimated cost of this report or study for the Department of Defense is approximately $304,000 in Fiscal Years 2021 - 2022. This includes $228,000 in expenses and $76,000 in DoD labor.

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TABLE OF CONTENTS

1 EXECUTIVE SUMMARY

Introduction

This report is in response to section 750 of the William M. (Mac) Thornberry National Defense Authorization Act (NDAA) for Fiscal Year 2021 (FY) (Public Law 116–283), "Study on the Incidence of Cancer Diagnosis and Mortality among Military Aviators and Aviation Support Personnel." The Act mandated a study on the incidence of cancer diagnosis and mortality among military fixed wing aviators (aircrew) and aviation support personnel (ground crew). This report presents the findings from the Phase 1-a study, which observed that military aircrew and ground crew were overall more likely to be diagnosed with cancer, but less likely to die from cancer compared to the U.S. population. A Phase 1-b study has been initiated which includes additional data from the Department of Veterans Affairs Central Cancer Registry (VACCR) as well as data from 46 State cancer registries. The findings from the Phase 1-a study and implications for the Phase 2 study are provided below.

Background

- Section 750 of the NDAA for FY 2021 establishes a two-phase study framework.
- Phase 1 requires an epidemiologic study to determine if there is a higher incidence of cancers occurring for military aircrew and ground crew as compared to the U.S. population using the Surveillance, Epidemiology, and End Results (SEER) program database, after adjusting for age, sex, and race.
- If the Phase 1 determination is that there is an increased rate of cancers among military aircrew or ground crew, a second phase is required.
- Most epidemiologic studies have not found a significant difference in rates of cancer diagnosis or death among military aircrew compared to peers in the U.S. population or the U.S. military.
- Few studies have been published on cancer diagnosis or death rates among military ground crew.
- All types of malignant cancer diagnoses were included in this study. However, the following 12 cancers were analyzed separately: colon and rectum, pancreas, melanoma, prostate, testis, urinary bladder, kidney and renal pelvis, brain and other nervous system, thyroid, non-Hodgkin lymphoma, female breast, and lung and bronchus.

Results

- There were 156,050 aircrew and 737,891 ground crew included and followed in the study between 1992 and 2017.
- Military members in both occupational groups were predominantly male and non-Hispanic White, Active Component, and of enlisted rank at entry into the study. Aircrew had a higher proportion of officers compared to ground crew.
- Reserve and National Guard members are more likely to have missing data for cancer diagnoses, therefore, Reserve and National Guard members were excluded from the cancer incidence analysis. Appendix C presents the cancer incidence analysis that includes data from Reserve and National Guard members. In contrast, Reserve and

National Guard member data remained in the cancer mortality analysis.

- The median age at the end of follow-up for the cancer incidence analysis was 41 years for aircrew and 26 years for ground crew. The median age at the end of follow-up for the cancer mortality analysis was 48 years for aircrew and 41 years for ground crew.
- The majority of the aircrew group consisted of members from the Air Force (70.6 percent) and Navy (21.1 percent). The ground crew group also consisted mostly of members from the Air Force (47.8 percent) and Navy (38.3 percent).
- About one-half (50.7 percent, n=79,124) of the aircrew group and less than one-third (31.4 percent, n=231,763) of the ground crew group consisted of individuals who joined military service prior to 1990. A small proportion of aircrew (3.5 percent, n=5,429) and ground crew (3.0 percent, n=21,852) joined military service in the 1960s or earlier.
- Compared to a demographically similar U.S. population in SEER, aircrew had an 87 percent higher rate of melanoma, 39 percent higher rate of thyroid cancer, 16 percent higher rate of prostate cancer, and a 24 percent higher rate of cancer for all sites combined.
- Ground crew members had higher rates of cancers of brain and nervous system (by 19 percent), thyroid (by 15 percent), melanoma (by 9 percent), kidney and renal pelvis (by 9 percent), and of all sites combined (by 3 percent) compared to the demographically similar U.S. population in SEER.
- Aircrew had a 56 percent lower mortality rate for all cancer sites when compared to the demographically similar U.S. population, and ground crew had a 35 percent lower mortality rate.

Discussion

- The finding that aircrew members had higher rates of melanoma and prostate cancer is similar to previous studies. However, the finding of a higher rate of thyroid cancer has not been previously described.
- This is the first time that cancer risk of all sites has been evaluated in a large population of military ground crew personnel. Comparison with previous studies is limited due to the scarce amount of prior research in cancer risk among ground crew populations.
- The finding of lower mortality rates in aircrew and ground crew compared to the U.S. population is similar to the findings of other similar studies.
- It is important to note that the military study population was relatively young compared to the U.S. population. Results may have differed if additional older former Service members had been included in the study, since cancer risk and mortality rates increase with age.
- A 2021 Air Force fighter pilot study included all Air Force personnel with active duty service dating back to 1970. Not all of these Air Force members were included in the present study since standardized personnel data back to 1970 were not available for all service branches.
- Results should be interpreted in the context of the study’s limitations, with the primary limitation being that this study likely underreported the number of military cancer cases since data from the Department of Veterans Affairs (VA) and civilian cancer registries were not included.

- Although not specifically required by section 750 of the NDAA for FY 2021, an augmentation to the phase 1 study is needed prior to initiating a phase 2 study. This "Phase 1-b study" will supplement the cancer incidence analysis using data from the Virtual Pooled Registry Cancer Linkage System (VPR-CLS) and the VACCR. Including these two data sources will result in better ascertainment of cancer cases for veterans, Reserve and National Guard members, and others without access to TRICARE coverage. A Phase 2 study is required to investigate and identify the specific occupational and environmental risk factors associated with the increased risk of the cancers identified in the Phase 1 study.

2 PURPOSE OF REPORT – SECTION 750 OF THE NDAA FOR FY 2021 TASKING

Section 750 of the NDAA for FY 2021 contained the following tasking:

SEC. 750. STUDY ON THE INCIDENCE OF CANCER DIAGNOSIS AND MORTALITY AMONG MILITARY AVIATORS AND AVIATION SUPPORT PERSONNEL.

(a) STUDY.—

(1) IN GENERAL.—The Secretary of Defense, in conjunction with the Directors of the National Institutes of Health and the National Cancer Institute, shall conduct a study on cancer among covered individuals in two phases as provided in this subsection.

(2) PHASE 1.—

(A) IN GENERAL.—Under the initial phase of the study conducted under paragraph (1), the Secretary of Defense shall determine if there is a higher incidence of cancers occurring for covered individuals as compared to similar age groups in the general population through the use of the database of the Surveillance, Epidemiology, and End Results (SEER) program of the National Cancer Institute.

(B) REPORT.—Not later than one year after the date of the enactment of this Act, the Secretary shall submit to the appropriate committees of Congress a report on the findings of the initial phase of the study under subparagraph (A).

(3) PHASE 2.—

(A) IN GENERAL.—If, pursuant to the initial phase of the study under paragraph (2), the Secretary concludes that there is an increased rate of cancers among covered individuals, the Secretary shall conduct a second phase of the study under which the Secretary shall do the following:

(i) Identify the carcinogenic toxins[1] or hazardous materials associated with military flight operations from shipboard or land bases or facilities, such as fuels, fumes, and other liquids.

(ii) Identify the operating environments, including frequencies or electromagnetic fields, where exposure to ionizing radiation (associated with high altitude flight) and nonionizing radiation (associated with airborne, ground, and shipboard radars) occurred in which covered individuals could have received increased radiation amounts.

(iii) Identify, for each covered individual, duty stations, dates of service, aircraft flown, and additional duties (including Landing Safety Officer, Catapult and Arresting Gear Officer, Air Liaison Officer, Tactical Air Control Party, or personnel associated with aircraft maintenance, supply, logistics, fuels, or transportation) that could have increased the risk of cancer for such covered individual.

(iv) Determine locations where a covered individual served or additional duties of a covered individual that are associated with higher incidences of cancers.

(v) Identify potential exposures due to service in the Armed Forces that are not related to aviation, such as exposure to burn pits or toxins[1] in contaminated water, embedded in the soil, or inside bases or housing.

[1] The term "toxin" is written in the FY2021 NDAA Sec. 750, but the presumed meaning is "toxicant."

(vi) Determine the appropriate age to begin screening covered individuals for cancer based on race, gender, flying hours, period of service as aviation support personnel, Armed Force, type of aircraft, and mission.

(B) DATA.—The Secretary shall format all data included in the study conducted under this paragraph in accordance with the Surveillance, Epidemiology, and End Results program of the National Cancer Institute, including by disaggregating such data by race, gender, and age.

(C) REPORT.—Not later than one year after the submittal of the report under paragraph (2)(B), if the Secretary conducts the second phase of the study under this paragraph, the Secretary shall submit to the appropriate committees of Congress a report on the findings of the study conducted under this paragraph.

(4) USE OF DATA FROM PREVIOUS STUDIES.—In conducting the study under this subsection, the Secretary of Defense shall incorporate data from previous studies conducted by the Air Force, the Navy, or the Marine Corps that are relevant to the study under this subsection, including data from the comprehensive study conducted by the Air Force identifying each covered individual and documenting the cancers, dates of diagnoses, and mortality of each covered individual.

(b) DEFINITIONS.—In this section:

(1) The term ‘‘appropriate committees of Congress’’ means—

(A) the Committee on Armed Services and the Committee on Veterans’ Affairs of the Senate; and

(B) the Committee on Armed Services and the Committee on Veterans’ Affairs of the House of Representatives.

(2) The term ‘‘Armed Forces’’—

(A) has the meaning given the term ‘‘armed forces’’ in section 101 of title 10, United States Code; and

(B) includes the reserve components named in section 10101 of such title.

(3) The term ‘‘covered individual’’—

(A) means an aviator or aviation support personnel who— (i) served in the Armed Forces on or after February 28, 1961; and

(ii) receives benefits under chapter 55 of title 10, United States Code; and

(B) includes any aircrew member of fixed-wing aircraft and personnel supporting generation of the aircraft, including pilots, navigators, weapons systems operators, aircraft system operators, personnel associated with aircraft maintenance, supply, logistics, fuels, or transportation, and any other crew member who regularly flies in an aircraft or is required to complete the mission of the aircraft.

2.1 Department of Defense Response

A task force was assembled to conduct the requested study under the oversight of the Defense Health Agency (DHA) and Office of the Deputy Assistant Secretary of Defense for Health Readiness Policy and Oversight within the Office of the Assistant Secretary of Defense for Health Affairs. Representatives from the Service branches, the Armed Forces Health Surveillance Division (AFHSD), National Cancer Institute (NCI), North American Association of Central Cancer Registries (NAACCR), Uniformed Services University of the Health Sciences, and the Murtha Cancer Center participated. The task force established smaller working groups to identify appropriate military data sources, to identify the military study population, and to conduct the analyses for the report.

2.2 Study Strategy

To answer the questions posed by the section 750 of the NDAA for FY 2021 requirement, a two-phase study strategy was mandated:

Phase 1: Conduct an epidemiologic study to determine if there is a higher incidence of cancers occurring among fixed-wing aviators, hereafter referred to as "aircrew", and aviation support personnel, hereafter referred to as "ground crew," compared to the U.S. population using the SEER database after adjusting for age, sex, and race. This phase was led by AFHSD and assisted by NCI, NAACCR, and Service representatives.

Phase 2: Phase 2 is required to be conducted if, under Phase 1, there is determined to be an increased rate of cancers or cancer mortality among military aircrew and ground crew. Phase 2 would consist of identifying the carcinogenic toxicants or hazardous materials associated with military flight operations; identifying operating environments that could be associated with increased amounts of ionizing and nonionizing radiation; identifying specific duties, dates of service, and types of aircraft flown that could have increased the risk for cancer; identifying duty locations associated with higher incidence of cancers; identifying potential exposures due to military service that are not related to aviation; and determining the appropriate age to begin screening military aircrew and ground crew for cancers.

3 BACKGROUND

3.1 Epidemiology of Cancer among Aircrew and Ground Crew

Most epidemiologic studies prior to 2020 have not found a significant difference in rates of cancer or death due to cancer among aircrew compared to peers in the U.S. population or in the U.S. military [1-5]. However, there have been some studies indicating an increased likelihood of select cancers including brain, female breast, prostate, testicular, and melanoma skin cancers [6-16]. Of these, melanoma has been the most consistently found to be higher in incidence among aircrew compared to the general population. A meta-analysis conducted in 2019 indicated that airline pilots and cabin crew had about twice the risk of melanoma compared to the general population, with pilots also being more likely to die from melanoma [10].

The U.S. Air Force School of Aerospace Medicine completed a retrospective cohort study in 2021 comparing cancer incidence and mortality among Air Force fighter aviators who served on active duty between 1970 and 2004 with the U.S. population [17]. In that study, fighter aviators were less likely to be diagnosed with cancer of the colon and rectum, testis, urinary bladder, kidney and renal pelvis, and thyroid and less likely to die from colon and rectum cancer. In contrast, male fighter aviators were both more likely to be diagnosed with and die from melanoma skin cancer, prostate cancer, and non-Hodgkin lymphoma.

Few studies have been published to evaluate rates of cancer or death due to cancer among ground crew personnel. However, the few studies available have generally not indicated any increased risk. A 2019 meta-analysis looked at the association between occupational exposure to radar radiation and all types of cancer among workers, which included military members in airports and on airplanes, and found no significant increase in overall relative risk or mortality of cancer [18]. In addition, a cohort study of over 14,000 aircraft maintenance workers at Hill Air Force Base in Utah between 1952 and 1990 did not find a significant increase in cancer incidence or mortality compared to the Utah general population [19]. Another cohort study that followed over 40,000 Navy veterans of the Korean War with radar exposure found no evidence of increased brain or testicular cancer deaths when followed for over 40 years [20].

4 REPORT OF PHASE 1-A STUDY OF CANCER INCIDENCE AND MORTALITY

4.1 Background

The objective of the Phase 1-a study is to determine whether there is a higher incidence of cancer diagnosis or mortality among aircrew or ground crew, compared to similar age, sex, and race groups in the U.S. population using the NCI's SEER database. The study protocol for Phase 1-a was approved and determined to be "Not Research" by the DHA Office of Human Research Protections on July 27, 2021.

4.2 Methods

4.2.1 Data Sources

Personnel records were obtained from the Defense Manpower Data Center demographic records maintained in the Defense Medical Surveillance System (DMSS) at the AFHSD. DMSS includes occupational records of all members of the Navy, Air Force, and Marine Corps serving in the active, Reserve, and National Guard Components of the U.S. Armed Forces dating back to 1990 and for Army active, Reserve, and National Guard Components dating back to 1985.

SEER is the authoritative source for cancer incidence and mortality statistics for the U.S., and individuals in this database served as the reference group in the study. Mortality data for the U.S. population originated from the National Center for Health Statistics and are released by SEER. The SEER incidence data date back to 1975 and are currently complete through the end of 2018. However, records did not become standardized using Hispanic and non-Hispanic race/ethnicity categories until 1992.

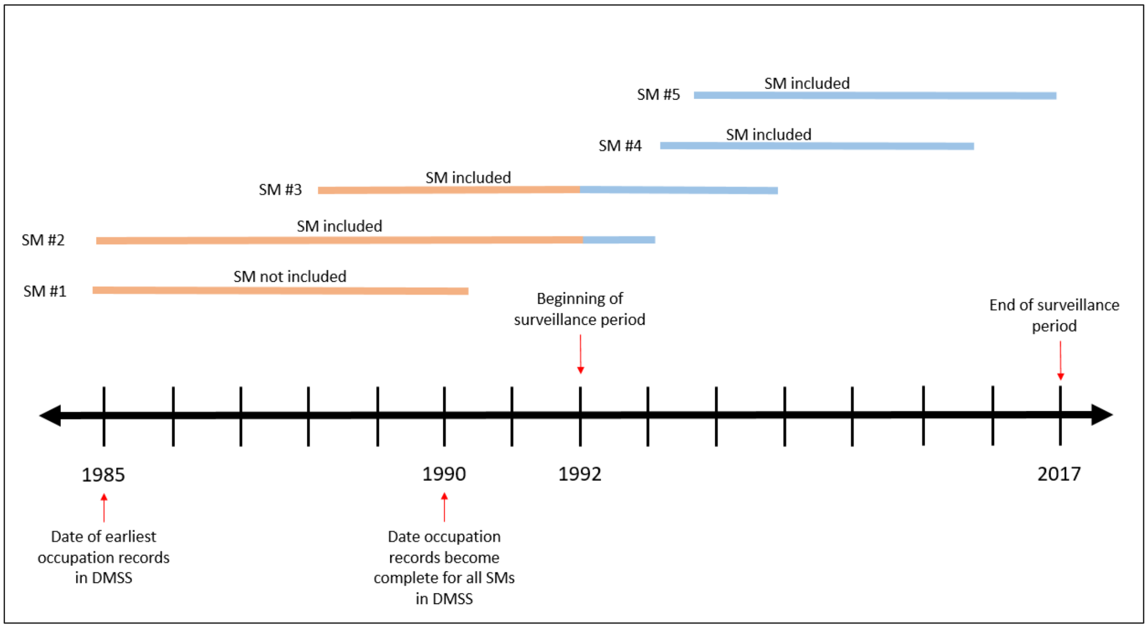
Cancer cases for the military cohort were identified using the Department of Defense's (DoD) cancer registry system Oncolog, formerly known as the Automated Central Tumor Registry, which is overseen by the DHA's Joint Pathology Center. Oncolog includes cancer data reported by military medical treatment facilities on all DoD beneficiaries, including active duty military personnel, retired military personnel, and Reserve and National Guard personnel diagnosed while on active duty. These data date back to the mid-1980s but are not considered complete until 1990. At the time of the report, Oncolog data were complete through the end of 2017. Cancer cases for the military cohort were also identified from the DMSS, which includes inpatient and outpatient administrative (i.e., billing) data for cancer diagnoses that occurred in direct care (i.e., in a military treatment facility) and outsourced care (when reimbursed by TRICARE).

Deaths due to cancer for the military cohort were identified from National Death Index (NDI) Plus data. NDI Plus is the central repository for deaths occurring in the U.S. since January 1979. At the time of request, death records were available through the end of 2018. NDI Plus was accessed through the Joint Department of Veterans Affairs and DoD Suicide Data Repository.

4.2.2 Study Population

Current and former aircrew and ground crew personnel were identified using duty military occupation specialty (DMOS) codes in DMSS. Individuals were included in the study population if: 1) they had an occupation code listed in DMSS, and 2) they were in military service or had an inpatient or outpatient medical encounter at a military treatment facility between 1992 and 2017. Examples of individuals who would be included or not included in the study population are provided in Figure 1. The blue bar in the figure indicates the amount of follow-up time for that individual during the surveillance period.

Figure 1. Examples of Service members (SMs) included and not included in the military study population.



The DMOS codes used to identify aircrew and ground crew were selected by Service representatives and subject matter experts. DMOS records specific to remotely piloted aircraft, helicopters or tiltrotor aircraft were excluded. Because not all Navy DMOS codes distinguished between fixed-wing and helicopter aircrew occupations, Navy DMOS records that occurred in tandem with a Unit Identification Code pertaining to helicopter squadrons were also excluded.

Individuals who spent at least 3 years of military service in an aircrew occupation (not including training time) were classified as aircrew. The remaining individuals were then classified according to the occupation category for which they spent the greatest amount of time in during military service, from the time that personnel data became available in DMSS through the end of the study period. For example, if an individual spent 2 years in aircrew occupations, 1.5 years in ground crew occupations, and 1 year in other occupations, they were classified as aircrew. This categorization was determined by subject matter experts to be the best method for identifying enough aircrew members within reason, after inspection of the data and in the absence of information on flight hours. The methodology also draws from the “usual occupation” approach used by the National Institute for Occupational Safety and Health for occupational epidemiology, which was used in a previous study of malignancy in U.S. Air Force fighter pilots [4].

4.2.3 Outcomes

January 1, 1992 was selected as the start date of follow-up for the study and is the date that the SEER database began using standardized race/ethnicity categories, which was necessary for the analysis. December 31, 2017 was selected as the study period end date because it is the period through which Oncolog tumor registry data were considered complete.

All types of malignant cancer diagnoses were included in this study. However, the following 12 cancers were also analyzed separately: colon and rectum, pancreas, melanoma, prostate, testis, urinary bladder, kidney and renal pelvis, brain and other nervous system, thyroid, non-Hodgkin lymphoma, female breast, and lung and bronchus. These cancers were selected based on concern from veteran advocacy groups and prior cancer studies that demonstrated increased incidence in military populations. DoD cancer cases from Oncolog were categorized according to SEER site recoding instructions available at:
https://seer.cancer.gov/siterecode/icdo3_dwhoheme/index.html.

Oncolog data primarily only includes cases identified in military treatment facilities. DMSS data were included so that cancer cases diagnosed in outsourced care reimbursed by TRICARE would also be identified. Inpatient data are available in DMSS back to 1990 and outpatient data are available back to 1996. Administrative data case-finding algorithms were used to identify incident cancer cases in the DMSS data [21]. The list of qualifying International Classifications of Diseases, 9th and 10th edition (ICD-9 and ICD-10) diagnoses by cancer type can be found in Appendix B. In a previous study, a standardized chart review was conducted to validate the AFHSD DMSS case-finding algorithms and found the algorithms work well for prostate, testis, and thyroid cancers, and for melanoma [23]. However, diagnoses for the gall bladder, small intestine, larynx, miscellaneous, “other” male or female genital organs, and “other” digestive system were excluded from the analysis because the AFHSD algorithm is not good at identifying those types of cancers (positive predictive value ≤50 percent), and those cases would be likely not to be true cancer cases [23]. In addition, DMSS-identified cancers of brain and nervous system, lung and bronchus, bones and joints, and liver cancers were excluded if they occurred after another cancer case of a different site, because these cases were likely to be metastases and not true incident cancers [22].

NDI Plus mortality data were obtained from the Defense Suicide Prevention Office. The underlying cause of death was assigned to a cancer category based on ICD codes consistent with SEER cause of death recode available at https://seer.cancer.gov/codrecode/.

4.2.4 Analysis

For the cancer incidence analysis, two separate analyses were performed: 1) Oncolog and DMSS cancer cases combined, with Reserve and National Guard members excluded from the study population; and 2) Oncolog and DMSS cancer cases combined, with Reserve and National Guard members included. The results of the first analysis are emphasized in this report because Reserve/National Guard members are more likely to seek care outside of the military health system and therefore less likely to be picked up as a case. As a result, including Reserve and National Guard members could bias the results of the study towards seeing no risk for cancer or seeing reduced risk of cancer when that might not be true. Oncolog and DMSS cancer cases were combined because cases in Oncolog may be underreported, particularly for individuals after they leave military service.

For all analyses, cancer cases, cancer deaths, and person-time in the military study population was assigned to unique combinations (called "stratum") for race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, and Other), sex (male, female), and age group category (5-year intervals). Person-time for the cancer incidence analysis was estimated by calculating the time from the earliest date of military service through the latest date of military service or last medical encounter reimbursed by TRICARE. If cancer was diagnosed after the last medical encounter or date in service, then the follow-up period was extended to the date of the cancer diagnosis. Person-time was counted from the beginning of the study period on January 1, 1992, to the end of the study period on December 31, 2017.

NCI investigators calculated the observed number of U.S. population cases and population sizes for each stratum using SEER. SEER uses mid-year population estimates as a proxy for the person-time at risk in the calendar year, and multiple tumors may be counted as cases in the numerator. The number of expected cases is the cases that would be expected to occur in the military cohort had they experienced the same age, sex, and race stratum-specific risks of the U.S. population. The number of expected cases was calculated by AFHSD using the SEER stratum-specific rates, and this expected number of cases was compared to the number of observed cases for the military cohort. This analysis comparing observed to expected number of cases was performed separately for aircrew and ground crew.

Similar calculations were performed for the mortality analysis, which measured the occurrence of death due to malignant cancer of all sites as well as the 12 site-specific cancers. The person-time at risk for death started on January 1, 1992, or at entry into the study population (i.e., first date of military service). It ended at the end of the study period on December 31, 2017, or at the time of death due to any cause. This person-time differed from the incidence analysis because NDI Plus covers all deaths in the United States, and therefore it was expected that deaths occurring in individuals in the military study population could be identified at any point during the surveillance period. All Active, Reserve, and National Guard military Components were included in the mortality analysis since they would all be expected to be included in the NDI Plus data.

Standardized incidence ratios (SIRs) were calculated as the number of observed over the number of expected incident cancer cases (see Appendix D). These ratios were calculated separately for malignant cancer of all sites, for each of the 12 specific cancers, and separately for aircrew and ground crew. Standardized mortality ratios (SMRs) were also calculated for deaths due to malignant cancer of all sites, for each of the 12 listed cancers, and separately for each of the military sub-cohorts. Finally, 95 percent confidence intervals and p-values were generated using a Poisson distribution. All statistical analyses were performed using SAS® software (Version 9.4, SAS Inst, Inc., Cary, NC).

4.3 Results

4.3.1 Introduction

This section describes the military study population, and then presents the results of the two cancer incidence analyses. The results of the first incidence analysis, in which Reserve and National Guard members were excluded, is presented first. The results of the second incidence analysis, in which Reserve and National Guard members were included, is presented second. Finally, the results from the cancer mortality analysis are presented, which includes both active and Reserve/National Guard Component members.

4.3.2 Description of Military Study Population

There were 156,050 aircrew and 737,891 ground crew included in the military cohort, which included both Active and Reserve/National Guard Component members (Table 1). Follow-up time varied depending on the analysis being conducted (see person years in Tables 2-5 and Appendix C tables). Service members in both aircrew and ground crew were predominantly male and non-Hispanic White, Active Component, aged 29 or less at entry into the study, and of enlisted rank at entry. However, aircrew had a higher proportion of officers compared to ground crew, with 49.8 percent enlisted and 48.9 percent officer. The majority of the aircrew group consisted of members from the Air Force (70.6 percent), followed by the Navy (21.1 percent). The ground crew group also consisted mostly of members from the Air Force (47.8 percent) and Navy (38.3 percent). About one-half (50.7 percent, n=79,124) of the aircrew group and less than one-third (31.4 percent, n=231,763) of the ground crew group consisted of individuals who joined military service prior to 1990. A small proportion of aircrew (3.5 percent, n=5,429) and ground crew (3.0 percent, n=21,852) joined military service in the 1960s or earlier.

4.3.3 Age at Follow-up, Diagnosis, and Death

For the cancer incidence analysis (Reserve/National Guard members excluded), the median age at the end of follow-up for malignant cancer of all sites was 41 years for aircrew and 26 years for ground crew. For the cancer mortality analysis, the median age at the end of follow-up for malignant cancer of all sites was 48 years for aircrew and 41 years for ground crew (Reserve/National Guard members included).

The median age at diagnosis for malignant cancer of all sites (Reserve/National Guard members excluded) was 54 years in aircrew and 53 years in ground crew. In contrast, the median age at diagnosis for malignant cancer of all sites was 67 years in the SEER reference population. The median age at death for malignant cancer of all sites was 57 in aircrew and 56 years in ground crew (Reserve/National Guard members included). In the SEER reference population, the median age at death for malignant cancer of all sites was 72 years.

Table 1. Demographics of the military study cohort.

	Aircrew		Ground crew	
	N	%	N	%
Total study population	156,050	100	737,891	100
Age (years)[a]				
29 or less	109,235	70.0	602,835	81.7
30-49	45,778	29.3	128,465	17.4
50+	1,037	0.67	6,591	0.9
Sex				
Male	145,385	93.2	664,782	90.1
Female	10,665	6.8	73,109	9.9
Race/ethnicity				
Non-Hispanic White	134,839	86.4	527,747	71.5
Non-Hispanic Black	6,666	4.3	90,279	12.2
Hispanic	7,953	5.1	69,865	9.5
Non-Hispanic Other	6,592	4.2	50,000	6.8
Service[a]				
Army	4,067	2.6	41,501	5.6
Navy	32,866	21.1	282,701	38.3
Air Force	110,225	70.6	352,307	47.8
Marine Corps	8,892	5.7	61,382	8.3
Component[a]				
Active	128,682	82.5	598,334	81.1
Reserve	14,885	9.5	76,673	10.4
National Guard	12,483	8.0	62,884	8.5
Rank[a]				
Enlisted	77,781	49.8	719,068	97.5
Officer	76,269	48.9	9,738	1.3
Missing/ unknown	2,000	1.3	9,085	1.2
Year at entry into military service				
1940-1949	6	0.0	25	0.0
1950-1959	371	0.2	2,530	0.3
1960-1969	5,052	3.2	19,297	2.6
1970-1979	26,499	17.0	72,729	9.9
1980-1989	47,196	30.2	137,182	18.6
1990-1999	33,059	21.2	193,135	26.2
2000-2009	33,037	21.2	184,979	25.1
2010-2017	10,467	6.7	122,606	16.6
Missing/unknown[b]	363	0.2	5,408	0.7

[a]Age, service branch, Component, and rank were measured at the beginning of follow-up.
[b]Year at entry was defined as missing/unknown for individuals aged <17 years or > 45 years at the date of entry into military service, as these were assumed to be data entry errors.

4.3.4 Cancer Incidence: Military Compared to U.S. Population

Oncolog and DMSS-defined cancer cases: Reserve/National Guard members excluded

There was a total of 4,639,667 malignant cancer cases observed in SEER during the study period. In the military cohort, there were 6,381 malignant cancer cases among aircrew and 12,246 among ground crew.

After adjusting for age, sex, and race/ethnicity, aircrew members had statistically higher incidence of cancers of all sites (by 24 percent), melanoma (by 87 percent), thyroid (by 39 percent), and prostate (by 16 percent), compared to individuals in the U.S. population (Table 2). Incidence of cancers of the colon and rectum, urinary bladder, kidney and renal pelvis, and lung and bronchus were statistically lower compared to individuals in the U.S. population by 44 percent, 35 percent, 17 percent, and 71 percent, respectively. There was not a statistically significant difference between aircrew members and members of the U.S. population for cancers of the pancreas, testis, brain and nervous system, non-Hodgkin lymphoma, and female breast.

Table 2. Observed and expected cancer cases, aircrew compared to U.S. population, 1992-2017.

Cancer site	Person-years	Observed cases	Expected cases	SIR	95% LL	95% UL	p-value
All sites	1,664,080	6,381	5,155	1.24	1.21	1.27	<.0001
Colon and rectum	1,710,570	282	502	0.56	0.50	0.63	<.0001
Pancreas	1,712,278	103	117	0.88	0.72	1.07	0.2079
Melanoma	1,704,826	802	429	1.87	1.74	2.00	<.0001
Prostate	1,625,276	1,542	1,331	1.16	1.10	1.22	<.0001
Testis	1,632,177	196	178	1.10	0.95	1.27	0.1896
Urinary bladder	1,711,338	175	270	0.65	0.56	0.75	<.0001
Kidney and renal pelvis	1,711,281	191	229	0.83	0.72	0.96	0.0107
Brain and nervous system	1,711,872	122	122	1.00	0.83	1.19	1.0000
Thyroid	1,710,520	180	129	1.39	1.20	1.61	<.0001
Non-Hodgkin lymphoma	1,710,287	298	301	0.99	0.88	1.11	0.8752
Female breast	76,832	59	51	1.16	0.88	1.49	0.2949
Lung and bronchus	1,711,977	164	563	0.29	0.25	0.34	<.0001

Ground crew members had statistically higher incidence of cancer of all sites (by 3 percent), brain and nervous system (by 19 percent), thyroid (by 15 percent), melanoma (by 9 percent), and kidney and renal pelvis (by 9 percent), compared to individuals in the U.S. population (Table 3). Ground crew members had statistically lower incidence of cancers of the colon and rectum (by 25 percent), prostate (by 5 percent), urinary bladder (by 10 percent), and lung and bronchus (by 24 percent). There was no statistically significant difference for cancers of the pancreas, testis, female breast, and non-Hodgkin lymphoma.

Table 3. Observed and expected cancer cases, ground crew compared to U.S. population, 1992-2017.

Cancer site	Person-years	Observed cases	Expected cases	SIR	95% LL	95% UL	p-value
All sites	5,023,723	12,246	11,909	1.03	1.01	1.05	0.0022
Colon and rectum	5,100,002	842	1,125	0.75	0.70	0.80	<.0001
Pancreas	5,104,970	240	257	0.93	0.82	1.06	0.3033
Melanoma	5,097,646	937	859	1.09	1.02	1.16	0.0093
Prostate	4,689,565	2,694	2,845	0.95	0.91	0.98	0.0045
Testis	4,700,826	473	467	1.01	0.92	1.11	0.7811
Urinary bladder	5,102,468	463	516	0.90	0.82	0.98	0.0195
Kidney and renal pelvis	5,102,170	559	513	1.09	1.00	1.18	0.0455
Brain and nervous system	5,103,657	340	287	1.19	1.06	1.32	0.0024
Thyroid	5,102,234	369	321	1.15	1.04	1.27	0.0094
Non-Hodgkin lymphoma	5,100,679	667	691	0.97	0.89	1.04	0.3743
Female breast	397,139	239	223	1.07	0.94	1.22	0.3012
Lung and bronchus	5,103,317	800	1,216	0.66	0.61	0.71	<.0001

Oncolog and DMSS-defined cancer cases: Reserve/National Guard members included

When Reserve and National Guard members were included, there were 8,491 malignant cancer cases among aircrew and 17,656 among ground crew. After adjusting for age, sex, and race/ethnicity, aircrew members had statistically higher incidence of melanoma (by 63 percent), thyroid cancer (by 19 percent), and cancer of all sites (by 8 percent), compared to individuals in the U.S. population (Appendix Table C1). Incidence of cancers of the colon and rectum, pancreas, testis, urinary bladder, kidney and renal pelvis, brain and nervous system, non-Hodgkin lymphoma, and lung and bronchus were statistically lower compared to individuals in the U.S. population. There was not a statistically significant difference between aircrew members and members of the U.S. population for cancers of the prostate and female breast. Among ground crew members, incidence of all cancers was statistically lower for ground crew members compared to members of the U.S. population (Appendix Table C2). However, for cancers of the thyroid and brain and nervous system, this difference was not statistically significant.

4.3.5 Cancer Mortality: Military Compared to U.S. Population

During the study period, there were 1,240 deaths due to any malignant cancer among aircrew personnel, 5,784 among ground crew, and 14,471,873 in the U.S. population. After adjusting for age, sex, and race/ethnicity, aircrew members had statistically lower mortality rates due to malignant cancer of all sites (56 percent) when compared to individuals in the general U.S. population (Table 4). Of the 12 cancers that were evaluated separately, aircrew had statistically lower mortality rates due to cancers of the colon and rectum (by 60 percent), pancreas (by 33 percent), prostate (by 34 percent), testis (by 75 percent), urinary bladder (by 52 percent), kidney and renal pelvis (by 40 percent), brain and nervous system (by 24 percent), non-Hodgkin lymphoma (by 58 percent), female breast (by 54 percent), and lung and bronchus (by 74 percent). There was not a statistically significant difference between aircrew and the U.S. population in the mortality rates for melanoma and thyroid cancer.

Table 4. Observed and expected cancer deaths, aircrew compared to U.S. population, 1992-2017.

Cancer site	Person-years	Observed deaths	Expected deaths	SMR	95% Lower CI	95% Upper CI	p-value
All sites	3,188,015	1,240	2,832	0.44	0.41	0.46	<.0001
Colon and rectum	3,188,015	107	269	0.40	0.33	0.48	<.0001
Pancreas	3,188,015	112	168	0.67	0.55	0.80	<.0001
Melanoma	3,188,015	76	85	0.90	0.71	1.13	0.3865
Prostate	3,010,539	63	96	0.66	0.50	0.84	0.0004
Testis	3,010,539	3	12	0.25	0.05	0.74	0.0050
Urinary bladder	3,188,015	26	54	0.48	0.32	0.71	<.0001
Kidney and renal pelvis	3,188,015	53	88	0.60	0.45	0.78	<.0001
Brain and nervous system	3,188,015	103	136	0.76	0.62	0.92	0.0038
Thyroid	3,188,015	8	7	1.16	0.50	2.29	0.7681
Non-Hodgkin lymphoma	3,188,015	49	117	0.42	0.31	0.56	<.0001
Female breast	177,476	8	18	0.46	0.20	0.90	0.0182
Lung and bronchus	3,188,015	224	849	0.26	0.23	0.30	<.0001

Similarly, ground crew personnel had a lower mortality rate (by 35 percent) due to malignant cancer of all sites compared to individuals in the general U.S. population (Table 5). Of the 12 cancers that were evaluated separately, ground crew personnel had lower mortality rates due to cancers of the colon and rectum (by 37 percent), pancreas (by 16 percent), prostate (by 43 percent), urinary bladder (by 25 percent), kidney and renal pelvis (by 21 percent), non-Hodgkin lymphoma (by 34 percent), and lung and bronchus (by 46 percent). There was not a statistically significant difference observed between ground crew personnel and the U.S. population in the mortality rates for melanoma, testicular cancer, brain and nervous system cancer, thyroid, and female breast cancer.

Table 5. Observed and expected cancer deaths, ground crew compared to U.S. population, 1992-2017.

Cancer site	Person-years	Observed deaths	Expected deaths	SMR	95% Lower CI	95% Upper CI	p-value
All sites	13,274,928	5,784	8,927	0.65	0.63	0.66	<.0001
Colon and rectum	13,274,928	535	852	0.63	0.58	0.68	<.0001
Pancreas	13,274,928	426	510	0.84	0.76	0.92	0.0002
Melanoma	13,274,928	215	241	0.89	0.78	1.02	0.1020
Prostate	12,149,032	190	335	0.57	0.49	0.65	<.0001
Testis	12,149,032	38	46	0.83	0.59	1.14	0.2902
Urinary bladder	13,274,928	120	159	0.75	0.63	0.90	0.0015
Kidney and renal pelvis	13,274,928	208	264	0.79	0.69	0.90	0.0004
Brain and nervous system	13,274,928	390	419	0.93	0.84	1.03	0.1683
Thyroid	13,274,928	15	21	0.71	0.40	1.18	0.2197
Non-Hodgkin lymphoma	13,274,928	250	378	0.66	0.58	0.75	<.0001
Female breast	1,125,896	89	97	0.92	0.74	1.13	0.4602
Lung and bronchus	13,274,928	1,377	2,551	0.54	0.51	0.57	<.0001

5 DISCUSSION

5.1 Summary

This study found that compared to the U.S. population after adjusting for age, sex, and race, aircrew had an 87 percent higher rate of melanoma, 39 percent higher rate of thyroid cancer, 16 percent higher rate of prostate cancer, and a 24 percent higher rate of cancer for all sites. Ground crew members had higher incidence of cancers of brain and nervous system (by 19 percent), thyroid (by 15 percent), melanoma (by 9 percent), kidney and renal pelvis (by 9 percent), and of all sites (by 3 percent). However, aircrew and ground crew both had lower or similar cancer mortality rates for all cancer types when compared to the U.S. population. This concludes the Phase 1-a epidemiologic study required by section 750 of the NDAA for FY 2021 and triggers the Phase 2 study to identify risk factors for cancer diagnosis. Prior to initiation of a Phase 2 study, a Phase 1-b study is being conducted which will include additional data from the VACCR as well as data from 46 state cancer registries.

5.1.1 Cancer Incidence

The finding of increased melanoma cancer rates in aircrew is in line with previous studies that have demonstrated higher incidence of melanoma among aircrew compared to non-aircrew populations [7-8, 10, 15, 24]. However, incidence of melanoma was also elevated in ground crew members (by 9 percent). This suggests that air and ground crew could share risk factors associated with increased risk for or detection of malignant melanoma.

The incidence of thyroid cancer was 39 percent higher among aircrew members and 15 percent higher among ground crew compared to the U.S. population. Previous studies have not found significant elevated risk of thyroid cancer incidence or mortality among airline crew relative to the general population [25]. However, a study comparing military thyroid cancer incidence rates to the U.S. population during 1990-2004 found higher military rates among various racial/ethnic groups [26].

Aircrew members were 16 percent more likely to be diagnosed with prostate cancer, which is similar to findings from the 2021 Air Force study which found that male fighter aviators were 19 percent more likely to be diagnosed with prostate cancer compared to the U.S. population [17]. The reasons for this elevated incidence are not well understood. Studies conducted through 2019 have found an average of 41 percent increased risk of prostate cancer in pilots, although this does not include other flight personnel and there is much variation across studies [27].

Ground crew members had higher rates of diagnosis for cancers of the brain and nervous system (by 19 percent), thyroid (by 15 percent), kidney and renal pelvis (by 9 percent), and melanoma (by 9 percent). This is the first time that cancer risk has been evaluated in such a large population of military ground crew, and comparison with previous studies is limited due to the scarce amount of existing information on the topic.

The incidence of cancer of all sites was higher in aircrew (by 24 percent) and slightly higher in ground crew (by 3 percent) compared to the U.S. population. It is currently unclear which type(s) of cancer(s) are driving this association and further analysis is recommended to determine whether this is due to one or multiple cancer types.

5.1.2 Cancer Mortality

This study did not find a higher cancer mortality rate among aircrew or ground crew compared to the U.S. population. In contrast, the mortality rate for malignant cancer of all sites was significantly lower in aircrew (by 56 percent) and ground crew (by 35 percent). A recent study of cause-specific mortality for U.S. veterans of conflicts in Afghanistan and Iraq between 2001 and 2016 found a 44 percent decreased risk for malignant cancer deaths when compared to the U.S. population after adjusting for age, sex, race, and year [28]. This finding of lower mortality rates in military populations compared to the U.S. population is similar to the results of the present study.

A 2021 Air Force study found that fighter aviators had lower rates of death due to colon and rectum cancer but higher rates of death due to melanoma, prostate cancer, and non-Hodgkin lymphoma [17]. One likely explanation for this difference is the age of the study populations. In the fighter pilot study, the average (mean) age at mortality censoring was 64 years and in the current study it was 47 years for aircrew. Thus, it is possible that the present study lacked sufficient follow-up time for progression to mortality in older age groups.

Previous studies have documented the “healthy soldier effect,” which is defined as the proposition that U.S. military members are healthier than the general U.S. population by nature of having to meet military fitness standards [29]. Military members must meet initial physical fitness requirements for accession, maintain and pass periodic fitness tests, and generally have better access to medical care during and after military service. In addition, aircrew members may be required to meet even more stringent physical standards to maintain their flight status. Previous studies have estimated that the healthy soldier effect on cancer mortality is 17-19 percent, meaning that Service members may have a 17-19 percent lower risk of cancer mortality compared to the general population simply by nature of being in the military [29]. However, it has also been suggested that this effect erodes over longer years of follow-up time. In an Australian study of Korea and Vietnam War veterans, cancer mortality rates were similar to those of the general population for the first 20 years of follow-up, but rose between 20 and 30 years post follow-up, and fell back to general population levels after 30 years of follow-up [30]. A study of Royal Norwegian Navy servicemen who served during 1950–2004 reported similar patterns of findings [31].

Another potential partial explanation for why military aircrew or ground crew members could be at higher risk for the diagnosis of certain cancers, but not at higher risk for dying from those cancers, is that Service members have routine medical screenings and physical fitness tests while they are in service. As a result, Service members may be more likely to have some types of cancers detected and diagnosed at earlier stages, thus improving their prognosis. In previous studies, patients diagnosed in the military health system in particular have been shown to have better survival and better screening rates for lung and colon cancer [32-34].

5.2 Study Strengths

This is one of the largest and most comprehensive studies of military aircrew and ground crew cancer risks to-date. Enough women were included in the study that risks for female-specific cancers could be evaluated. The study population includes members who served in different military conflicts over time. By using a standardized data source, the DMSS, the study team was able to quickly identify the study population and adjust for basic demographic factors.

5.3 Study Limitations

5.3.1 Data Availability and Quality

The most significant limitations to this study are related to data availability and quality. Section 750 of the NDAA for FY 2021 defined the military study population as aviators or aviation support personnel who served in the Armed Forces on or after February 28, 1961, and who receive benefits under chapter 55 of title 10, U.S. Code (which includes Active and Reserve/National Guard Component members). The task force was unable to identify an electronic data source containing information on military occupation and dates of service prior to 1990. The 2021 Air Force fighter aviator study included personnel with active duty service dating back to 1970, identified by the Air Force Personnel Center. However, not all of these Air Force members were included in the present study since standardized personnel data back to 1970 were not available for all Service branches.

There are known gaps in the military cancer case data. The task force was unable to identify a data source containing complete data on cancer diagnoses prior to 1990. Veterans, Reserve and National Guard members, and others without access to TRICARE coverage are likely missing cancer data, which could bias the results of the study towards seeing no risk for cancer or seeing reduced risk of cancer when that might not be true. In addition, outpatient data were not available in DMSS until 1996, which likely resulted in missing cancer cases as well as an underestimation of follow-up time for cancer in the military cohort. There are some data sources that should have been included in this study in order to have complete ascertainment of all cancer cases for the military cohort; however, 12 months was not enough time to gather these data. Currently, AFHSD is collaborating with the NAACCR to identify cancer cases for the military study population using the Virtual Pooled Registry Cancer Linkage System (VPR-CLS), which includes U.S. population cancer data from 43 registries across the country between the early 1990s and 2019. AFHSD is also seeking data from the VACCR and together these data sources will provide a more complete count of cancer cases for the military study cohort.

Finally, it should be noted that there were unavoidable differences in the ways that cancer incidence was calculated in the military cohort compared to how incidence was calculated in SEER. SEER uses mid-year population estimates as a proxy for the person-time at risk in the calendar year, and multiple tumors may be counted as cases. However, in the military cohort, rates are calculated by following individuals in the study population over time using person-years, and only the first occurrence of each type of cancer is counted. The effect that this might have had on the final study results is unknown.

5.3.2 Exposure Misclassification

For this Phase 1-a study, DMOS codes were used to identify occupational groups, which has several limitations. Ideally, flight hours and the type of aircraft should be taken into consideration, but these data were not available. In addition, a person's occupation while in military service can change over time. Establishing a causal relationship between a person's military occupation and cancer would require that the exposure (i.e., occupation) or accumulation of exposure to a certain threshold (i.e., years spent in a certain occupation) occurs prior to first cancer diagnosis. The "usual occupation" approach does not take this temporality of exposure and cancer into consideration. Different cancers have different latency periods, which is the time that it takes for cancer to develop following the first exposure to a cancer-causing agent. These latency periods should be taken into consideration but were not for this study. However, the objective of this study was to compare cancer incidence rates in the military population to those in SEER, and latency periods are also not accounted for in the SEER rates.

Finally, DMOS codes are not standardized across branches, which can lead to variability in the types of occupations selected into the aircrew and ground crew groups. The distinction between aircrew and ground crew was not clearly defined for some DMOS codes, and, because data on flight hours were not available, the determination was made by subject matter experts but may have resulted in some occupational misclassification.

5.3.3 Uncontrolled Confounding Factors

There are multiple risk factors associated with cancer that could not be addressed in the Phase 1-a study. Due to the features of cancer registry and medical claims data, data are not available on family history of cancer, smoking, alcohol use, physical activity, overweight/obesity status, recreational environmental exposures, diet, and other lifestyle factors, which may confound the comparison of cancer incidence and mortality between the military study population and the U.S. population. The "healthy soldier" effect may also confound the results of this study. Since military members tend to be healthier than the general population by nature of being in military service, this may obscure any increased risk of cancer or cancer mortality due to occupational exposures.

5.4 Conclusions

The findings of this study suggest that aircrew and ground crew who served in the military relatively recently have higher incidence of cancer compared to individuals in the U.S. population. This finding cannot be generalized to members who served prior to 1990 because it does not include all members who served prior to this date. It also does not imply that military service in aircrew or ground crew occupations causes cancer, because there are multiple potential confounding factors that could not be controlled for in this analysis. The SIRs and SMRs presented in this report should only be used to compare aircrew to the U.S. population and to compare ground crew to the U.S. population. They should not be used to compare cancer risk and mortality rates between aircrew and ground crew since the methods used do not allow for this comparison. Findings further indicate that military aircrew and ground crew have lower risk of death due to cancer compared to the U.S. population. However, it is important to note that study results may have differed had additional older former Service members been included.

The results should be interpreted in the context of the study's limitations, with the primary limitation being that this study likely underreported the number of military cancer cases since data from VA and civilian cancer registries were not included.

5.5 Way Forward

A supplementary Phase 1-b study is being conducted prior to initiating a Phase 2 study in order to augment the cancer incidence analysis using data from the VPR-CLS and the VACCR. This will allow the inclusion of data from veterans, Reserve, and National Guard members. The VPR-CLS is a new system designed to connect state cancer registries across the U.S. It has not yet been used for large military or VA cancer studies, and this study will be the first. An initial query through VPR-CLS identified thousands of cancer cases available for data extraction in 46 state cancer registries. Section 750 of the NDAA for FY 2021 states that Phase 2 shall be conducted if, under Phase 1, there is determined to be an increased rate of cancers among military aircrew and ground crew. Given the findings of higher incidence for some cancers among aircrew and ground crew in the Phase 1 study, the Phase 2 study is required. Phase 2 will consist of identifying the carcinogenic toxicants or hazardous materials associated with military flight operations; identifying operating environments that could be associated with increased amounts of ionizing and nonionizing radiation; identifying specific duties, dates of service, and types of aircraft flown that could have increased the risk for cancer; identifying duty locations associated with higher incidence of cancers; identifying potential exposures due to military service that are not related to aviation; and determining the appropriate age to begin screening military aircrew and ground crew for cancers.

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Appendix A: Acronyms

AFHSD	Armed Forces Health Surveillance Division
CI	Confidence Interval
DHA	Defense Health Agency
DMOS	duty military occupational specialty
DMSS	Defense Medical Surveillance System
DoD	Department of Defense
FY	Fiscal Year
ICD	International Classification of Diseases
NAACCR	North American Association of Central Cancer Registries
NCI	National Cancer Institute
NDI	National Death Index
NDAA	National Defense Authorization Act
SEER	Surveillance, Epidemiology, and End Results
SIR	standardized incidence ratio
SMR	standardized mortality ratio
USAF	U.S. Air Force
VA	Department of Veterans Affairs
VACCR	Veterans Affairs Central Cancer Registry
VPR-CLS	Virtual Pooled Registry Cancer Linkage System

Appendix B: ICD-9 and ICD-10 Diagnosis Codes Used to Identify DMSS Cancer Cases

	ICD-9-CM	ICD-10-CM
Lip	140	C00
Tongue	141	C01, C02
Salivary gland	142	C07, C08
Floor of mouth	144	C04
Gum and other mouth	143, 145	C03, C05, C06
Nasopharynx	147	C11
Tonsil	1460-1462	C09
Oropharynx	1463-1469	C10
Hypopharynx	148	C12, C13
Other Oral Cavity and Pharynx	149	C14
Esophagus	150	C15
Stomach	151	C16
Small intestine	152	C17
Colon and rectum	153, 1540-1541, 1590	C18-C20, C260
Anus, Anal Canal and Anorectum	1542-1543, 1548	C21
Liver	1550, 1552	C220, C222- C229
Intrahepatic Bile Duct	1551	C221
Gallbladder	1560	C23
Other Biliary	1561-1562, 1568-1569	C24
Pancreas	157	C25
Retroperitoneum	1580	C480
Peritoneum, Omentum and Mesentery	1588-1589	C451, C481, C482
Other Digestive Organs	1598-1599	C268-C269, C488
Nose, Nasal Cavity and Middle Ear	160	C30, C31
Larynx	161	C32
Lung and Bronchus	1622-1625, 1628-1629	C34
Pleura	163	C384, C450
Trachea, Mediastinum and Other Respiratory Organs	1620, 1642-1643, 1648-1649, 165	C33, C381-C383, C388, C39
Bones and Joints	170	C40, C41
Soft Tissue including Heart	1641, 171	C47, C49, C380, C452
Melanoma (of the Skin)	172	C43
Non-Melanoma (Skin)	173	C44
Breast	174, 175	C50
Cervix Uteri	180	C53
Corpus Uteri	182	C54
Uterus, NOS	179	C55
Ovary	1830	C56
Vagina	1840	C52

Vulva	1841-1844	C51
Other Female Genital Organs	181, 1832-1835, 1838-1839, 1848-1849	C57, C58
Prostate	185	C61
Testis	1860, 1869	C620, C621, C629
Penis	1871-1874	C60
Other Male Genital Organs	1875-1879	C63
Urinary bladder	188	C67
Kidney and renal pelvis	1890-1891	C64-C65
Ureter	1892	C66
Other Urinary Organs	1893-1894, 1898-1899	C68
Eye and Orbit	190	C69
Brain and other nervous system	191, 192	C70, C71, C72
Thyroid	193	C73
Other Endocrine including Thymus	1640, 194	C37, C74, C75
Hodgkin Lymphoma	201	C81
Non-Hodgkin lymphoma	200, 2020-2022, 2027-2029	C82–C86, C96Z, C969
Myeloma	2030, 2386	C900, C902, C903
Acute Lymphocytic Leukemia	2040	C910
Chronic Lymphocytic Leukemia	2041	C911
Other Lymphocytic Leukemia	2024, 2042, 2048-2049	C912-C914, C916-C919, C91A, C91Z
Acute myeloid	2050, 2070, 2072	C920, C924-C926, C928, C940, C942, C92A
Acute Monocytic Leukemia	2060	C930
Chronic Myeloid Leukemia	2051	C921
Other Myeloid/Monocytic Leukemia	2052-2053, 2058-2059, 2061-2062, 2068-2069	C922-C923, C927, C929, C931-C933, C937, C939, C92Z, C93Z
Other Acute Leukemia	2080	C944, C950
Aleukemic, subleukemic and NOS	2031, 2071, 2078, 2081-2082, 2088-2089	C901, C915, C941, C943, C947, C951, C959, C948
Mesothelioma	N/A	C45
Kaposi Sarcoma	176	C46
Miscellaneous Malignant Cancer	1591, 195-199, 2023, 2025-2026, 2038	C261, C457, C459, C76-C80, C88, C946, C960-C962, C964-C968, C97

Appendix C

Table C1. Observed and expected cancer cases (Oncolog and DMSS data), aircrew compared to U.S. population, 1992-2017. Reserve and National Guard members are included.

Cancer site	Person-years	Observed cases	Expected cases	SIR	95% LL	95% UL	p-value
All sites	2,619,013	8,491	7,834	1.08	1.06	1.11	<.0001
Colon and rectum	2,678,236	386	753	0.51	0.46	0.57	<.0001
Pancreas	2,680,464	136	174	0.78	0.65	0.92	0.0031
Melanoma	2,671,020	1,073	656	1.63	1.54	1.74	<.0001
Prostate	2,531,071	2,030	1,950	1.04	1.00	1.09	0.0716
Testis	2,540,401	247	285	0.87	0.76	0.98	0.0251
Urinary bladder	2,679,172	241	406	0.59	0.52	0.67	<.0001
Kidney and renal pelvis	2,679,321	243	342	0.71	0.62	0.81	<.0001
Brain and nervous system	2,679,999	159	188	0.85	0.72	0.99	0.0356
Thyroid	2,678,310	242	203	1.19	1.05	1.35	0.0080
Non-Hodgkin lymphoma	2,677,955	391	459	0.85	0.77	0.94	0.0012
Female breast	136,027	90	96	0.94	0.76	1.16	0.6083
Lung and bronchus	2,680,098	223	839	0.27	0.23	0.30	<.0001

Table C2. Observed and expected cancer cases (Oncolog and DMSS data), ground crew compared to U.S. population, 1992-2017. Reserve and National Guard members are included.

Cancer site	Person-years	Observed cases	Expected cases	SIR	95% LL	95% UL	p-value
All sites	7,312,190	17,656	20,677	0.85	0.84	0.87	<.0001
Colon and rectum	7,416,703	1,187	1,958	0.61	0.57	0.64	<.0001
Pancreas	7,423,422	352	462	0.76	0.68	0.85	<.0001
Melanoma	7,413,612	1,345	1,437	0.94	0.89	0.99	0.0153
Prostate	6,844,069	4,307	5,342	0.81	0.78	0.83	<.0001
Testis	6,864,627	559	676	0.83	0.76	0.90	<.0001
Urinary bladder	7,419,461	757	1,009	0.75	0.70	0.81	<.0001
Kidney and renal pelvis	7,419,708	784	864	0.91	0.85	0.97	0.0062
Brain and nervous system	7,421,983	415	454	0.91	0.83	1.01	0.0668
Thyroid	7,420,425	448	490	0.91	0.83	1.00	0.0589
Non-Hodgkin lymphoma	7,417,921	918	1,140	0.81	0.75	0.86	<.0001
Female breast	550,761	289	327	0.89	0.79	0.99	0.0373
Lung and bronchus	7,421,054	1,179	2,276	0.52	0.49	0.55	<.0001

Appendix D

Standardized Incidence Ratio (SIR)
The SIR is a ratio of the number of observed cancer cases in the military aircrew and ground crew compared to the number that would be expected to occur in the aircrew and ground crew if they experienced the same cancer rates at the U.S. population. The SIR adjusts for differences in age, sex, and race/ethnicity.

$$\boldsymbol{SIR = \frac{Observed\ Cancer\ Cases\ (O)}{Expected\ Cancer\ Cases\ (E)}}$$

Standardized Mortality Ratio (SMR)
The SMR is a ratio of the number of observed cancer deaths in the military aircrew and ground crew compared to the number that would be expected to occur in the aircrew and ground crew if they experienced the same cancer mortality rates at the U.S. population. The SMR adjusts for differences in age, sex, and race/ethnicity.

$$\boldsymbol{SMR = \frac{Observed\ Cancer\ Deaths\ (O)}{Expected\ Cancer\ Deaths\ (E)}}$$