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Occup Environ Med. Author manuscript; available in PMC 2024 June 01.

Published in final edited form as:
Occup Environ Med. 2023 June ; 80(6): 312–318. doi:10.1136/oemed-2022-108628.

Military Occupation and Testicular Germ Cell Tumor Risk among U.S. Air Force Servicemen

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Abstract

Objectives: Testicular germ cell tumors (TGCT) are the most commonly diagnosed malignancy among active duty U.S. military servicemen. Occupational risk factors may play a role in TGCT etiology, although the evidence is inconclusive. The objective of our study was to investigate associations between military occupations and TGCT risk among U.S. Air Force (USAF) servicemen.

Methods: This nested case-control study among active duty USAF servicemen obtained information on military occupations for 530 histologically-confirmed TGCT cases diagnosed during 1990-2018 and 530 individually-matched controls. We determined military occupations using Air Force Specialty Codes ascertained at two time points: at case diagnosis and at a time point on average six years earlier. We computed adjusted odds ratios (ORs) and 95% confidence intervals (CIs) from conditional logistic regression models to evaluate associations between occupations and TGCT risk.

Results: The mean age at TGCT diagnosis was 30 years. Increased TGCT risk was observed for pilots (OR=2.84, 95%CI: 1.20-6.74) and servicemen with aircraft maintenance jobs (OR=1.85, 95%CI: 1.03-3.31) who held those jobs at both time points. Fighter pilots (n=18) and servicemen

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Disclosures
The authors have no disclosures to report.

Declaration of competing interest
The authors report no competing interests.

with firefighting jobs (n=18) at the time of case diagnosis had suggestively elevated TGCT odds (OR=2.73, 95% CI: 0.96-7.72 and OR=1.94, 95%CI: 0.72-5.20, respectively).

Conclusions: In this matched, nested case-control study of young active duty USAF servicemen, we found that pilots and men with aircraft maintenance jobs had elevated TGCT risk. Further research is needed to elucidate specific occupational exposures underlying these associations.

INTRODUCTION

The incidence of testicular germ cell tumors (TGCT), the most common (98%) type of testicular cancer, has increased in the United States and other developed countries over the past several decades.[1] For U.S. men ages 15 to 44 years,[2,3] as well as for all active duty U.S. military servicemen,[4] TGCT is the most commonly diagnosed malignancy. While known to be associated with other male reproductive disorders, such as cryptorchidism, hypospadias and impaired fertility,[5] the etiology of TGCT is not well understood. Established TGCT risk factors include European ancestry, personal or family TGCT history, and taller adult height.[6] Events *in utero* almost certainly influence TGCT risk,[7] however, recent evidence suggests that adolescent and adult risk factors may also play an important role in TGCT etiology.[8] Certain occupations have been associated with increased TGCT risk, including firefighting,[9,10] aircraft maintenance among both military[11,12] and civilian populations,[13] as well as service as a military pilot and aircrew,[14,15] and as a fighter pilot.[16] Despite inconsistencies, these occupational associations led to hypotheses that job-related chemical exposures, such as to per- and polyfluoroalkyl sybstances (PFAS),[17–19] solvents, paints, and hydrocarbons in degreasing/lubricating agents and lubricating oils (e.g., methylcholantene),[11,12] may increase TGCT risk, although confounding from factors related to socioeconomic status (SES) may also play a role.[15,16]

The predominantly young and male U.S. military population, where military personnel may experience different occupational exposures throughout their career/deployments, is valuable for studying occupational risk factors for TGCT. Prior epidemiologic studies reported elevated risk of TGCT in military pilots and aircrew,[15] and fighter pilots,[16] however, to our knowledge, no peer reviewed studies to date have investigated associations of different types of jobs performed during military service with TGCT risk. To address this research gap, the primary aim of our study was to investigate associations between military occupations and TGCT risk among active duty U.S. Air Force (USAF) servicemen. In a secondary aim, we additionally explored these associations by tumor morphology to assess any histology-specific exposures.

METHODS

Study Population and Outcome Ascertainment

The present study is derived from a matched case-control study investigating the association between serum PFAS concentrations and TGCT risk, in which military occupation at different time points was ascertained.[20] Our study population was comprised of active duty USAF male personnel who had serum samples stored at the Department of Defense

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Serum Repository (DoDSR), a central repository maintained by the Armed Forces Health Surveillance Division (AFHSD) of the Defense Health Agency's Public Health Directorate.[21] The DoDSR blood samples are drawn from all military personnel at the time of military accession and, on average, every two years thereafter for mandatory HIV testing.[22] Currently, the DoDSR stores more than 60 million serial serum samples at −30 °C from more than 10 million active duty and reserve personnel in Silver Spring, Maryland. Eligible cases were identified through data linkage between the DoDSR and the Department of Defense (DoD) Automated Cancer Tumor Registry (ACTUR) that records patients diagnosed with and/or treated for cancer at military treatment facilities. Through data linkage, we identified 530 incident TGCT cases during 1990-2018 [Third Edition of the *International Classification of Diseases for Oncology* (ICD-O-3) site code C62 with classic seminoma morphology codes 9060-9062 and 9064 and non-seminoma morphology codes 9065-9102] among active duty USAF personnel with at least one banked DoDSR pre-diagnostic serum sample. TGCT cases with a history of any other malignancies before TGCT diagnosis date, except for non-melanoma skin cancer, were excluded from our study. Using risk set sampling with replacement, 530 controls were individually matched to each case on race/ethnicity, year they entered the military (± 1 year; hereafter referred to as *military accession*), date of birth (± 1 year), and the collection date(s) of the case's serum sample(s) selected for study (± 1 year). Each control was randomly selected from a population of active duty USAF servicemen with samples in the DoDSR who had no history of any malignancies before their matched case's TGCT diagnosis date, except for non-melanoma skin cancer. No control became a case during the study period.

Demographic and military characteristics, including occupational data, for all cases and controls were obtained from the Defense Medical Surveillance System (DMSS), the AFHSD, Defense Health Agency, Silver Spring, Maryland (1986-2018). This study did not include any interviews. All study procedures were reviewed and approved by the Uniformed Services University Institutional Review Board, the AFHSD, the DoD Joint Pathology Center, the Defense Health Agency, and the National Cancer Institute's Division of Cancer Epidemiology and Genetics.

Exposure ascertainment

Air Force occupation was ascertained from Air Force Specialty Codes (AFSCs) obtained from the DMSS for each serviceman in our study. These alphanumeric job codes classify USAF military personnel into specific occupations/career fields, hereafter referred to as *occupations*. Each AFSC corresponds to a job title specific to enlisted personnel or officers. Guided by the Air Force Enlisted Classification Directory (AFECD)[23] and the Air Force Officer Classification Directory (AFOCD),[24] we first classified each airman's occupation based on career group and field specifically indicated by the characters within the AFSC. Because people in the same career field/group may have a range of different jobs and responsibilities, we further grouped participants into occupational groups based on job descriptions (in the AFECD/AFOCD) and professional expertise (P.D.V. and M.A.L.) about similar job exposures. This process resulted in some occupational groups including both enlisted personnel and officers (e.g., administrative/support jobs). Supplemental Table 1 shows a listing of all job titles in each occupation/occupational group.

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We ascertained occupational information at two time points: at the time of serum draw (time 1) and at the case's TGCT diagnosis date (time 2). Because occupational information at time 1 was ascertained shortly after military accession, on average 2.4 years post-accession, a large proportion (45%) of our study population was not occupationally qualified (e.g., basic enlisted airman) at that time. We, therefore, primarily relied on occupational information at time 2, on average 8.2 years post-accession, when approximately only 3% of the population was non-occupationally qualified. For selected occupations of interest based on prior literature (i.e., pilot, fighter pilot, firefighting, and aircraft maintenance),[8,16,25–27] we additionally created occupational groupings that indicated being in a given occupation at both time points (e.g., pilot at time 1 *and* at time 2, aircraft maintenance at time 1 and time 2). We did not have information on occupation timing and duration (e.g., when a serviceman started or ended a job).

Statistical Analyses

We first compared distributions of the demographic and military characteristics between cases and controls. To examine associations between different occupations/occupational groups and TGCT risk, we used conditional logistic regression models conditioned on the individually matched case-control pairs. We estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) comparing risk of TGCT among active duty USAF servicemen in the select occupation to the risk of TGCT among those servicemen in all other occupations. All of the conditional logistic regression models were adjusted for number of deployments before the case diagnosis year (0, 1, 2+). Occupational groups consisting of both enlisted personnel and officers (e.g., administrative/support) were further adjusted for the service member being either an officer or enlisted (i.e., grade) at case diagnosis. With an aim of accounting for grade, for pilot-related occupations of interest (comprised entirely of officers) we also compared TGCT risk between officer pilots and a reference group of officer non-pilots.

To test whether associations between occupation and TGCT risk were specific to either seminomas or non-seminomas, we performed conditional logistic regression analyses stratified by morphology of the cases. We conducted case-only analyses of TGCT subtypes using unconditional logistic regression adjusting for age at diagnosis, race/ethnicity, number of deployments before TGCT diagnosis, and grade, where appropriate, in order to statistically test for differences in associations by morphology.[28] We calculated p-values to test for OR homogeneity across case morphology.

Sensitivity Analyses—With an aim of excluding occupational exposures that occurred too close to the TGCT diagnosis to have etiologic relevance, we performed a sensitivity analysis excluding cases and controls with fewer than three years of service (n=202) at the time of the case diagnosis date. We additionally performed a sensitivity analysis among a subset of participants with information on height (n=689) in order to assess the potential confounding effect of height on the main associations. We compared conditional logistic regression estimates adjusted for number of deployments before case diagnosis and grade, where appropriate, to the estimates additionally adjusted for height (in centimeters) at military accession. To assess the sensitivity of our findings, we also performed the main

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analyses without including the number of deployments as a potential confounding variable, but the results were largely unchanged (data not shown).

For each analysis, we selected occupations/occupational groups for which there were at least five cases and five controls. All of the analyses were performed in SAS version 9.4 (SAS Institute, Inc.; Cary, North Carolina).

RESULTS

Table 1 shows characteristics of cases and controls. Our study population joined the military between 1986 and 2017 (median year 1998). TGCT cases were diagnosed between 1990 and 2018 (median year 2007) at an average age of 29.8 years. Slightly more than half of the cases (55.3%) were diagnosed with seminomas. Cases and matched controls were predominantly of non-Hispanic White background (79.6%), while 10.8% identified as Hispanic, and 2.4% as non-Hispanic Black. At the time of case diagnosis, a higher proportion of cases (22.6%) than controls (17.9%) were officers. Although a large proportion of height and weight information at military accession was missing for both cases and controls (~35%), the median height and weight were similar between the two groups. A higher proportion of cases (72.8%) than controls (67.4%) had not deployed before the case diagnosis year. On average, cases and controls had served in the USAF for 8.2 years at the time of case diagnosis. The average time between the serum sample collection and case diagnosis was 5.8 years.

Findings from analyses of occupation at the time of case diagnosis and odds of TGCT are presented in Table 2. Pilots (including pilot trainees) had elevated TGCT odds (aOR=1.78, 95% CI: 1.06-3.01). The association was stronger, though not statistically significant, for fighter pilots (aOR=2.73, 95% CI: 0.96-7.72). Airmen with aircraft maintenance jobs also had elevated TGCT odds (aOR=1.54, 95% CI: 1.04-2.29). Fire protection occupation (i.e., firefighting) was associated with non-significantly increased TGCT odds (aOR=1.94, 95% CI: 0.72-5.20), while servicemen with occupations in communication/electronics/wire system maintenance, aerospace medical/surgical service, intelligence, and aircraft crew had non-significantly reduced TGCT odds (adjusted ORs range: 0.52-0.67).

In analyses stratified by tumor morphology (Table 3), we generally observed similar occupation findings for each subtype, although associations with the command and control systems operations and aerospace maintenance occupations were significantly stronger for non-seminomas than seminomas (case-only analysis p-values=0.04 for each occupation). The association between aircraft maintenance jobs and non-seminomas was also slightly stronger (aOR=2.00, 95%CI: 1.13-3.52) than for seminomas (aOR=1.28, 95%CI: 0.72-2.27, case-only analysis p-values=0.06).

Table 4 shows associations with TGCT risk for selected occupational groups of interest at the time of serum collection and case diagnosis. The aOR for being a pilot at the time of serum collection was 2.54 (95% CI: 1.11-5.79) and at case diagnosis, it was 1.72 (95% CI: 0.98-3.02). Those who were pilots at both time points had the highest TGCT risk (aOR=2.84, 95% CI: 1.20-6.74). We observed a similar pattern of associations, although

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lower in magnitude, for a combined occupation of pilots and pilot trainees. There were too few fighter pilots and firefighters in the study to conduct the analysis at both time points. Having an aircraft maintenance job at case diagnosis was significantly associated with TGCT (aOR=1.54. 95%CI: 1.04-2.29); the elevated risk was stronger for those in aircraft maintenance at both time points (aOR =1.85, 95% CI: 1.03-3.31).

Because being a pilot or a pilot trainee is a job specific to officers, we could not adjust the main case-control models for grade. However, in addition to comparing the TGCT risk between pilots and all non-pilots (i.e., a reference group consisting of both enlisted personnel and non-pilot officers), we compared pilot officers separately to all enlisted personnel and to all other officers who were not pilots (Supplemental Table 2). For these comparisons, we used pilot and pilot trainee occupation at both time points. Compared to all enlisted personnel, pilot officers (excluding trainees) had a significantly elevated TGCT risk (aOR=2.90, 95% CI: 1.22-6.89). This association slightly attenuated when comparing pilots to the rest of the non-pilot officers (aOR=2.43, 95% CI: 0.96-6.13). We observed a similar pattern when combining pilots and pilot trainees (Supplemental Table 2).

Results from the sensitivity analysis excluding 202 servicemen with less than three years of service at the time of case diagnosis (Supplemental Table 3) were generally similar to those in the main analyses among the full case-control population presented in Table 2. The pilot occupation (excluding or including pilot trainees) remained significantly associated with elevated TGCT risk (aOR_{pilot}=1.80, 95% CI: 1.02-3.18 and $aOR_{pilot/pilot\ trainee}$=1.76, 95% CI: 1.01-3.05), while the association with aircraft maintenance-related jobs slightly attenuated (aOR=1.46, 95% CI: 0.94-2.27). Compared to the main analyses of the full case-control population, the associations between some occupations/occupational groups and TGCT risk strengthened in the sensitivity analysis but were not statistically significant (e.g., aOR=1.83, 95% CI: 0.80-4.15 for command and control systems operations; aOR=2.04, 95% CI: 0.84-4.96 for jobs involving fuels/petroleum). Sensitivity analyses excluding 371 servicemen without information on height are shown in Supplemental Table 4. Further adjustment for height did not significantly alter the associations (i.e., the point estimates changed by <10%).

DISCUSSION

In this nested case-control study of U.S. Air Force servicemen, we found significantly increased risks of TGCT among pilots and aircraft maintenance workers, while non-significantly elevated risks were observed for the sub-category of fighter pilots and for firefighters. We also observed suggestions of reduced TGCT risk among airmen with occupations/occupational groups in communication/electronics/wire system maintenance, aerospace medical/surgical service, intelligence, and aircraft crew.

One of our most consistent findings of elevated TGCT risk for pilots is comparable to the findings of some of the previous studies conducted among USAF servicemen,[14–16] although not all.[29] Previous studies that found elevated risk/odds of TGCT among aviators slightly differed with respect to the exposure metrics. In one study conducted among active duty USAF officers who served for at least a year during 1975-1989, the age-adjusted

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incidence rate of testicular cancer was significantly elevated among those with a professional history of flying compared to those with no flying history (RR=1.84, 99% CI: 1.19-2.86).[14] Similarly, in a study of White active duty USAF officers who were admitted to U.S. military treatment facilities during 1988-1999, those who flew for at least one hour had an elevated risk of testicular cancer (OR=1.74, 95% CI: 1.04-2.92), and there was a suggestion of a dose-response relationship with flight-hours.[15] In a more recent study conducted among active duty USAF officers who entered the military during 1970-2004, fighter aviators (including pilots and backseat aircrew) with at least 100 hours of flying on a fighter airframe had increased age- and race-adjusted incidence of testicular cancer (OR=1.29, 95% CI: 1.15-2.12).[16] However, in a study of active duty USAF officers who entered the military during 1986-2006, Robbins et al. did not find an elevated incidence rate of testicular cancer comparing fighter pilots to all other officers (IRR=0.92, 95% CI: 0.56-1.52).[29] Those investigators relied on “usual occupation” for fighter pilots based on the length of time spent in the occupation and, therefore, approximately 8% of the comparison group also included officers who were fighter pilots at some point in their career.[29] This exposure misclassification, and a shorter study follow-up period, could have contributed to the null finding for testicular cancer risk. It is unclear what exact exposures among military pilots contribute to the elevated TGCT risk, although it has been hypothesized that taller height and higher SES may play a role.[6,15,16] Our sensitivity analysis adjusting for height did not significantly alter the association between pilot occupation and TGCT risk, although the sample size restricted to cases and controls without missing height information was significantly reduced. To further explore the SES hypothesis, we restricted our population to 269 cases and 262 controls with greater than high school education attainment – the association between the pilot occupation (including trainees) and TGCT risk was slightly elevated (OR=2.28, 95% CI: 1.09-4.77) compared to the original (OR=1.78, 95% CI: 1.06-3.01).

Our observed association between aircraft maintenance jobs and elevated TGCT risk is also consistent with findings from previous studies.[11–13] In another smaller U.S. military study conducted among White, active duty U.S. Navy servicemen, a higher testicular cancer incidence was observed among aviation support equipment technicians compared to the total US Navy population of White active duty enlisted servicemen (standardized incidence ratio=6.9, 95% CI: 2.1-14.4), however, estimates were based on only five cases among the aviation support equipment technicians.[11] In a study conducted among the United Kingdom’s Royal Air Force servicemen, age-adjusted incidence for testicular cancer was two-fold higher among personnel working directly with aircraft (e.g., engineers) than those less directly involved.[12] In another study, a greater than expected number of TGCT cases was observed among civilian aircraft maintenance workers; the investigators hypothesized that exposure to an organic solvent mixture containing dimethylformamide could have contributed to the excess TGCT risk.[13] Aircraft maintenance workers are exposed to many different chemicals in lubricants, solvents, paint, and jet propellant, and it has been hypothesized that job-related chemical exposures may contribute to TGCT development, although the biological mechanisms underlying risk are unclear.[11,13,27]

To our knowledge, ours is the first study to investigate the association between the firefighting and TGCT risk in the U.S. military. We found a non-statistically significant

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association with elevated TGCT risk, although the sample size of firefighters was small (12 cases and 6 controls). Several previous studies of cancer risk among civilian firefighters have reported increased incidence of testicular cancer,[9,10] with a recent review of epidemiological studies concluding that the risk of testicular cancer was significantly higher among firefighters than the general population.[10] It is unclear what chemicals may contribute to the association between firefighting and testicular cancer risk, given that firefighters are exposed to a complex mixture of chemicals.[9,10] Recent evidence suggesting that exposure to PFAS chemicals from firefighting foams may be one contributing factor[17–19] should be explored further, especially in the military, given the wide-spread concern of drinking water contamination on the military bases where PFAS-containing firefighting foams were used.[30] We are currently investigating serum PFAS concentrations and TGCT risk in the same nested case-control study from which the occupational data presented here were derived.

We found suggestions of reduced TGCT risk among servicemen in several occupational groups, including communication/electronics/wire system maintenance, aerospace medical/surgical service, intelligence, and aircraft crew. Why personnel with those particular occupations may have lower risk of TGCT is not clear. It is interesting to note that aircraft crew had reduced TGCT risk, while the risk for pilots and aircraft maintainers was elevated. The explanation for this paradox could be that aircraft crew occupational group consisted of officers and enlisted personnel with jobs that have less contact time with aircraft and flightline (Supplemental Table 1) than pilots and aircraft maintainers; therefore, aircrew members are likely less exposed to chemicals such as lubricants, solvents, paint, and jet propellant.

Our study has several strengths. We investigated associations between a wide range of military occupations/occupational groups and TGCT risk in the largest to date TGCT case-control study among active duty USAF servicemen. The matched case-control study design allowed us to reduce potential confounding by age, race/ethnicity, and timing of entering the military. We had sufficient occupational information for some of the main occupations/occupational groups of interest (i.e., pilots and aircraft maintenance) at two different time points. Incident TGCT cases with confirmed pathology were ascertained from a comprehensive and centralized DoD tumor registry that also provided information on tumor morphology. To our knowledge, our study was the first that examined potential differences in the association between occupation and TGCT risk by tumor morphology.

This study also has several limitations. Because we did not have information on occupation timing and length, we made an assumption that servicemen did not change jobs in between the time points we examined and could not investigate dose-response relationships with occupational length. The strong assumption of servicemen not changing jobs between the two time periods could have resulted in exposure misclassification. Although taller adult height is a risk factor for testicular cancer,[6] we were unable to adjust any of the main case-control associations for height due to the large proportion of missing information (~35%), in particular among officers (~70%). However, when we conducted analyses restricted to the subset of participants with information on height, the associations with pilots/pilot trainees, aircraft maintenance workers, and fire protection workers did not change with adjustment for height, arguing against confounding as an explanation for our key findings. Because we did

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not have information on testicular cancer family history or relevant personal medical history (e.g., cryptorchidism), we were not able to account for these risk factor in our analyses. Because we conducted multiple comparisons across many occupations, some of our results may be statistically significant due to chance, although most of our significant findings were confirmed in sensitivity analyses.

In conclusion, our findings from this large, nested case-control study of active duty U.S. Air Force servicemen support the prior evidence that pilots and men with aircraft maintenance jobs have elevated risk of TGCT. We also observed evidence suggestive of an association with TGCT for servicemen with firefighting jobs. Further research in other military populations is warranted to confirm these findings, to further explore the patterns of association across quantitative metrics of occupational history, and to elucidate specific occupational exposures that may contribute to the elevated TGCT risk among USAF servicemen.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This research was supported by the Congressionally Directed Medical Research Program grant #W81XWH1910444 and funding from the Intramural Research Program of the National Cancer Institute and the National Institutes of Health.

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KEY MESSAGES

What is already known on this topic – *summarise the state of scientific knowledge on this subject before you did your study and why this study needed to be done*

- Occupations including firefighting, aircraft maintenance, and being a pilot have been associated with increased risk of testicular germ cell tumors (TGCT), the most common type of testicular cancer, although the evidence is inconclusive, especially among the U.S. military service members.
- No studies to date have comprehensively investigated associations between various types of jobs performed during military service and TGCT risk.

What this study adds – *summarise what we now know as a result of this study that we did not know before*

- Our matched case-control study conducted among young active duty U.S. Air Force servicemen observed that pilot and aircraft maintenance occupations were associated with elevated TGCT risk.
- Fighter pilots and firefighters also had suggestively elevated TGCT risk, while the majority of other occupations and jobs we examined were not associated with increased risk.

How this study might affect research, practice or policy – *summarise the implications of this study*

- Further research, including a comprehensive study of military personnel from all service branches, is needed to elucidate specific occupational exposures underlying the associations we observed.

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Table 1.

Select characteristics of the U.S. Airforce study population

Characteristic	TGCT Cases (N=530)		Controls (N=530)	
	N	(%)	N	(%)
Age at serum sample collection (year)				
<20	141	(26.6)	134	(25.3)
20-24	194	(36.6)	220	(41.5)
25-29	95	(17.9)	76	(14.3)
30-34	64	(12.1)	66	(12.4)
35-39	28	(5.3)	27	(5.1)
40+	8	(1.5)	7	(1.3)
Age at TGCT diagnosis (year)				
<20	10	(1.9)		-
20-24	111	(20.9)		-
25-29	159	(30.0)		-
30-34	113	(21.3)		-
35-39	89	(16.8)		-
40+	48	(9.1)		-
Mean ± SD	29.8 ± 6.6			-
Race/ethnicity at case diagnosis				
Non-Hispanic White	422	(79.6)	422	(79.6)
Non-Hispanic Black	13	(2.4)	13	(2.4)
Hispanic	57	(10.8)	57	(10.8)
Asian/Pacific Islander	6	(1.1)	6	(1.1)
Native American/Alaska Native	5	(0.9)	5	(0.9)
Other	9	(1.7)	9	(1.7)
Unknown	18	(3.4)	18	(3.4)
Education at case diagnosis				
≤High School	261	(49.3)	268	(50.6)
Some College	120	(22.6)	138	(26.0)
Bachelor’s	80	(15.1)	57	(10.8)
Advanced Degree	68	(12.8)	66	(12.4)
Unknown	1	(0.2)	1	(0.2)
Grade at case diagnosis				
Enlisted (E01-E10)	410	(77.4)	435	(82.1)
Officer (O1-O10)	120	(22.6)	95	(17.9)
Height (m) at military accession				
Mean ± SD	1.65 ± 0.24		1.61 ± 0.21	
% Missing	190	(35.8)	181	(34.2)
Weight (kg) at military accession				
Mean ± SD	69.9 ± 2.59		69.5 ± 2.48	
% Missing	190	(35.8)	181	(34.2)

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Characteristic	TGCT Cases (N=530)		Controls (N=530)	
	N	**(%)**	**N**	**(%)**
Number of deployments[1] before case dx year				
0	386	(72.8)	354	(67.4)
1	81	(15.3)	92	(17.4)
2	35	(6.6)	50	(9.4)
≥3	28	(5.3)	32	(5.8)
Years of service at serum sample collection				
Mean ± SD	2.4 ± 3.3		2.4 ± 3.3	
Years of service at case dx				
Mean ± SD	8.2 ± 5.3		8.2 ± 5.2	
Time between serum collection and case dx (years)				
Mean ± SD	5.8 ± 4.4		5.8 ± 4.4	
Calendar year of military accession				
Median (range)	1998 (1986-2017)		1998 (1986-2017)	
Calendar year of serum sample draw				
Median (range)	1999 (1988-2017)		1999 (1989-2017)	
Calendar year at case dx				
Median (range)	2007 (1990-2018)		2007 (1990-2018)	
Tumor morphology				
Seminoma	293	(55.3)		-
Non-seminoma	237	(44.7)		-

Abbreviations: Dx = diagnosis; SD=Standard deviation; TGCT=Testicular germ cell tumors;

[1]Defined as a deployment record with a length of ≥31 days outside of U.S.

NOTE: Controls individually matched to cases on: race/ethnicity, military accession year (± 1 yr), date of birth (± 1 yr), and serum sample collection date (± 1 yr)

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Table 2.

Case-control associations between occupation at case diagnosis and TGCT

	Cases (N=530)	Controls (N=530)	
Occupation (AFSC)	**N**	**N**	**OR (95% CI)**
Aircrew operations (1A)	14	23	0.67 (0.34-1.35)
Command and control systems operations (1C)	17	14	1.22 (0.60-2.49)
Aerospace maintenance (2A)	103	93	1.12 (0.82-1.54)
Fuels (2F)	11	9	1.32 (0.54-3.22)
Material management (2S)	11	11	1.01 (0.43-2.35)
Transportation (2T)	20	23	0.93 (0.50-1.73)
Munitions and weapons (2W)	27	34	0.77 (0.45-1.32)
Communication-Electronics/Wire Systems Maintenance (2E)	12	22	0.56 (0.27-1.13)
Communications/network (3C)	11	10	1.07 (0.43-2.64)
Cyberspace support (3D)	23	18	1.35 (0.70-2.61)
Security forces (3P)	39	38	1.08 (0.67-1.73)
Fire protection (3E7X1)	12	6	1.94 (0.72-5.20)
Aerospace medical/surgical service (4N)	9	17	0.52 (0.23-1.17)
Pilot (11)	36	23	1.72 (0.98-3.02)
Fixed-wing pilot (11A, 11K, 11M, 11R, 11S, 11T)	20	17	1.22 (0.63-2.39)
Fighter pilot (11F)	13	5	2.73 (0.96-7.72)
Pilot Trainee (92T0)	10	5	1.77 (0.53-5.88)
Pilot/pilot trainee (11, 92T0)	46	28	**1.78 (1.06-3.01)**
Space, nuclear, and missile (13)	10	12	0.89 (0.38-2.07)
Civil engineer (3E, 32E)[1]	38	36	1.07 (0.67-1.72)
Intelligence (1N, 14N)[1]	19	30	0.61 (0.34-1.11)
Occupational group based on job description (AFSC)			
Aircraft maintenance (2A, 21A)[1]	69	47	**1.54 (1.04-2.29)**
Aircraft crew (12, 13, 1A, 2A)[1]	24	40	0.60 (0.35-1.04)
Ammunition (3E, 2W)	30	34	0.88 (0.53-1.46)
Fuels/petroleum (2A, 2F, 63)[1]	15	12	1.42 (0.66-3.08)
Electrical/electronics (2A, 2E, 2P, 3D, 3E)	22	32	0.62 (0.34-1.12)
Mechanic/Other maintenance (2A, 2E, 2M, 2T, 3E, 4A)	21	29	0.65 (0.36-1.20)
Law enforcement/Security (3P, 31P, 81)[1]	42	39	1.20 (0.76-1.91)
Radio/Communications/Radar (1C, 2A, 2E, 3C, 3D, 33S)[1]	24	23	1.04 (0.57-1.87)
Medical[1,2]	35	31	1.13 (0.69-1.94)
Administrative/Support[1,3]	139	137	0.99 (0.75-1.33)
Miscellaneous/Other/Unknown[1,4]	44	56	0.78 (0.50-1.20)

All conditional logistic regression models adjusted for number of deployments before case diagnosis (0, 1, 2+)

[1] Models additionally adjusted for grade at case diagnosis

[2]Medical AFSCs: 42, 44, 45, 46, 47, 48, 4C, 4D, 4F, 4N, 4P, 4R, 4Y, 92M1

[3]Administrative/Support AFSCs: 13,16,17,18,20, 21,27, 43,51,60,62,63, 64, 65, 97, 10C, 14N, 1C, 1N, 1W, 21R, 2E, 2G, 2R, 2S, 2T, 32E, 33S, 34M, 36M, 36P, 38F, 38P, 3A, 3C, 3D, 3M, 3N, 3S, 3V, 41A, 4A, 4E, 52R, 5R, 6C, 6F, 7S, 8R, 8M000, 9E

[4]Miscellaneous/Other/Unknown AFSCs: 45, 61, 62, 15W, 1C, 1P, 1S, 1T, 1U, 2A, 2E, 2T, 2W, 3E, 4B, 8F, 9S, 90G0, 9T000

Abbreviations: AFSC =Air Force Specialty Code; OR = Odds Ratio; CI = Confidence Interval; TGCT = Testicular germ cell tumors

Bold indicative of statistical significance

NOTE: Comparison (non-exposed) group is everyone not in selected occupation/occupational group

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Table 3.

Case-control associations between occupation at case diagnosis and TGCT, stratified by tumor morphology

	Seminoma (293 case-control pairs)			Non-seminoma (237 case-control pairs)			
Occupation (AFSC)	**N case**	**N control**	**OR (95% CI)**	**N case**	**N control**	**OR (95% CI)**	***P*** *
Aircrew operations (1A)	8	12	0.66 (0.26-1.72)	6	11	0.75 (0.27-2.13)	0.86
Command and control systems operations (1C)	6	8	0.74 (0.26-2.14)	11	6	1.88 (0.68-5.19)	**0.04**
Aerospace maintenance (2A)	43	49	0.87 (0.56-1.35)	60	44	1.56 (0.97-2.50)	**0.04**
Fuels (2F)	8	3	-	3	6	-	-
Material management (2S)	7	5	1.33 (0.42-4.22)	4	6	-	-
Transportation (2T)	10	12	0.85 (0.35-2.07)	10	11	1.01 (0.42-2.42)	0.74
Munitions and weapons (2W)	13	18	0.74 (0.35-1.55)	14	16	0.79 (0.36-1.74)	0.95
Communication-Electronics/Wire Systems Maintenance (2E)	6	12	0.50 (0.19-1.33)	6	10	0.69 (0.25-1.93)	0.90
Communications/network (3C)	4	2	-	7	8	0.83 (0.28-2.47)	-
Cyberspace support (3D)	12	9	1.40 (0.59-3.35)	11	9	1.21 (0.44-3.34)	0.89
Security forces (3P)	24	18	1.39 (0.72-2.65)	15	20	0.75 (0.37-1.55)	0.08
Fire protection (3E7X1)	3	4	-	9	2	-	-
Aerospace medical/surgical service (4N)	6	8	0.72 (0.25-2.10)	3	9	-	-
Pilot (11)	24	15	1.69 (0.87-3.31)	12	8	2.09 (0.73-6.01)	0.75
Fixed-wing pilot (11A, 11K, 11M, 11R, 11S, 11T)	12	10	1.21 (0.52-2.80)	8	7	1.40 (0.45-4.35)	0.70
Fighter pilot (11F)	9	4	-	4	1	-	-
Pilot Trainee (92T0)	5	4	-	5	1	-	-
Pilot/pilot trainee (11, 92T0)	29	19	1.62 (0.87-3.03)	17	9	2.60 (0.96-7.03)	0.62
Space, nuclear, and missile (13)	6	8	0.78 (0.27-2.27)	4	4	-	-
Civil engineer (3E, 32E)[1]	19	23	0.80 (0.42-1.49)	19	13	1.59 (0.75-3.39)	0.89
Intelligence (1N, 14N)[1]	13	14	0.90 (0.42-1.92)	6	16	0.35 (0.12-0.97)	0.24
Occupational group based on job description (AFSC)							
Aircraft maintenance (2A, 21A)[1]	29	23	1.28 (0.72-2.27)	40	24	**2.00 (1.13-3.52)**	0.06
Aircraft crew (12, 13, 1A, 2A)[1]	13	22	0.57 (0.27-1.19)	11	18	0.57 (0.24-1.34)	0.60
Ammunition (3E, 2W)	13	17	0.78 (0.37-1.67)	17	17	0.96 (0.47-1.95)	0.37

	Seminoma (293 case-control pairs)			Non-seminoma (237 case-control pairs)			
Occupation (AFSC)	**N case**	**N control**	**OR (95% CI)**	**N case**	**N control**	**OR (95% CI)**	***P*** *
Fuels/petroleum (2A, 2F, 63)[1]	12	4	-	3	8	-	-
Electrical/electronics (2A, 2E, 2P, 3D, 3E)	12	20	0.53 (0.23-1.18)	10	12	0.78 (0.32-1.91)	0.67
Mechanic/Other maintenance (2A, 2E, 2M, 2T, 3E, 4A)	9	16	0.49 (0.20-1.21)	12	13	0.79 (0.34-1.86)	0.23
Law enforcement/Security (3P, 31P, 81)[1]	25	19	1.41 (0.74-2.66)	17	20	0.94 (0.47-1.89)	0.12
Radio/Communications/Radar (1C, 2A, 2E, 3C, 3D, 33S)[1]	11	12	0.94 (0.41-2.15)	13	11	1.10 (0.47-2.59)	0.30
Medical[1,2]	25	19	1.32 (0.66-2.64)	12	13	0.90 (0.37-2.18)	0.61
Administrative/Support[1,3]	89	76	1.26 (0.85-1.86)	50	61	0.77 (0.50-1.20)	0.18
Miscellaneous/Other/Unknown[1,4]	20	33	0.58 (0.32-1.07)	24	23	1.02 (0.53-1.95)	0.46

All conditional logistic regression models adjusted for number of deployments before case diagnosis (0, 1, 2+)

[1] Models additionally adjusted for grade at case diagnosis

[2] Medical AFSCs: 42, 44, 45, 46, 47, 48, 4C, 4D, 4F, 4N, 4P, 4R, 4Y, 92M1

[3] Administrative/Support AFSCs: 13,16,17,18,20, 21,27, 43,51,60,62,63, 64, 65, 97, 10C, 14N, 1C, 1N, 1W, 21R, 2E, 2G, 2R, 2S, 2T, 32E, 33S, 34M, 36M, 36P, 38F, 38P, 3A, 3C, 3D, 3M, 3N, 3S, 3V, 41A, 4A, 4E, 52R, 5R, 6C, 6F, 7S, 8R, 8M000, 9E

[4] Miscellaneous/Other/Unknown AFSCs: 45, 61, 62, 15W, 1C, 1P, 1S, 1T, 1U, 2A, 2E, 2T, 2W, 3E, 4B, 8F, 9S, 90G0, 9T000

[*] P-value from tests of OR homogeneity across case morphology from case-only unconditional logistic regression models adjusting for age at diagnosis, race/ethnicity, number of deployments before diagnosis, and grade where appropriate

Abbreviations: AFSC =Air Force Specialty Code; OR = Odds Ratio; CI = Confidence Interval; TGCT = Testicular germ cell tumors

Bold indicative of statistical significance

NOTE: Comparison (non-exposed) group is everyone not in selected occupation/occupational group

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Table 4.

Case-control associations between select occupations at two time points and TGCT risk

	Cases (N=530)	Controls (N=530)	
Occupation/occupational group (AFSC)	**N**	**N**	**OR (95% CI)**
Pilot (11) at serum sample	22	10	**2.54 (1.11-5.79)**
Pilot (11) at case diagnosis	36	23	1.72 (0.98-3.02)
Pilot (11) at serum sample and at case diagnosis	21	8	**2.84 (1.20-6.74)**
Fighter pilot (11F) at serum sample	9	3	-
Fighter pilot (11F) at case diagnosis	13	5	2.73 (0.96-7.72)
Fighter pilot (11F) at serum sample and at case diagnosis	7	2	-
Pilot/pilot trainee (11, 92T0) at serum sample	44	28	**1.79 (1.05-3.08)**
Pilot/pilot trainee (11, 92T0) at case diagnosis	46	28	**1.78 (1.06-3.01)**
Pilot/pilot trainee (11, 92T0) at serum sample and at case diagnosis	41	25	**1.87 (1.06-3.27)**
Aircraft maintenance (2A, 21A) at serum sample [1]	39	28	1.44 (0.86-2.39)
Aircraft maintenance (2A, 21A) at case diagnosis [1]	69	47	**1.54 (1.04-2.29)**
Aircraft maintenance (2A, 21A) at serum sample and at case diagnosis [1]	33	19	**1.85 (1.03-3.31)**

All conditional logistic regression models adjusted for number of deployments before case diagnosis (0, 1, 2+)

[1]Models additionally adjusted for grade at case diagnosis

Abbreviations: AFSC =Air Force Specialty Code; OR = Odds Ratio; CI = Confidence Interval; TGCT = Testicular germ cell tumors

Bold indicative of statistical significance

NOTE: Comparison (non-exposed) group is everyone not in selected occupation/occupational group