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EVALUATING THE INCIDENCE OF MELANOMA AND LUNG CANCER OF CURRENT AND FORMER ACTIVE-DUTY U.S. MILITARY WHO WERE DEPLOYED IN SUPPORT OF OPERATION ENDURING FREEDOM AND OPERATION IRAQI FREEDOM

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DISSERTATION

A dissertation submitted in partial fulfillment of the
Requirements for the degree of Doctor of Philosophy in the
College of Public Health
at the University of Kentucky

By
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Director: Dr. Wayne T. Sanderson, Professor of Biosystems and Agricultural Engineering
Lexington, Kentucky
2021

ABSTRACT OF DISSERTATION

EVALUATING THE INCIDENCE OF MELANOMA AND LUNG CANCER OF CURRENT AND FORMER ACTIVE-DUTY U.S. MILITARY WHO WERE DEPLOYED IN SUPPORT OF OPERATION ENDURING FREEDOM AND OPERATION IRAQI FREEDOM

The incidence of melanoma and lung cancer has been gradually increasing in the United States over the past three decades with the reputed causes due to etiological and environmental exposures, and tobacco usage. There has been concern that melanoma and lung cancer incidence among military personnel may be associated with deployment to environments with intense sun exposure and increased smoking rates due to post-traumatic stress disorder. The aim of this study was to examine associations between deployment in support of Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF), from 2001 through 2015, with subsequent melanoma and lung cancer incidence. We conducted an incidence-density matched case-control study with incident melanoma and lung cancer cases and their respective matched controls. Our cases were individuals in the Armed Forces who were serving in the Army, Navy, Air Force, or Marines during 2001 to 2015, and developed melanoma or lung cancer. For each case, 10 controls were randomly selected from others in the Armed Forces matched on age, sex, branch of service, time in military and year of matching. Conditional logistic regression was used to evaluate associations between deployment, number of deployments, and cumulative time deployed, and melanoma risk. After adjusting for covariates with a biological plausibility to either melanoma or lung cancer, we evaluated individuals who had deployed compared to those who had not deployed were significantly protective to odds of being diagnosed with melanoma or lung cancer. The dissertation further evaluated incidence rates of melanoma and lung cancer between the different branches of service, Army, Air Force, Marines and Navy, between the years 2002 to 2015. The dissertation supports previous research that service members in the Air Force and Navy are at an increased risk for melanoma.

KEYWORDS: U.S. Military, Melanoma, Lung Cancer, Operation Enduring Freedom, Operation Iraqi Freedom

Brian William Kovacic

June 24, 2021

Date

EVALUATING THE INCIDENCE OF MELANOMA AND LUNG CANCER OF CURRENT AND FORMER ACTIVE-DUTY U.S. MILITARY WHO WERE DEPLOYED IN SUPPORT OF OPERATION ENDURING FREEDOM AND OPERATION IRAQI FREEDOM

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CHAPTER 1. MELANOMA

Abstract

Purpose The incidence of melanoma has been gradually increasing in the United States over the past three decades with the reputed cause due to increasing sun exposure and occurrence of sunburns. There has been concern that melanoma incidence among military personnel may be associated with deployment to environments with intense sun exposure. The aim of this study was to examine associations between deployment in support of Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF), from 2001 through 2015, with subsequent melanoma incidence.

Methods We conducted an incidence-density matched case-control study with 1,363 incident melanoma cancer cases and 13,630 matched controls. Our cases were individuals in the Armed Forces who were serving in the Army, Navy, Air Force, or Marines during 2001 to 2015, and developed melanoma. For each case, 10 controls were randomly selected from others in the Armed Forces matched on age, sex, branch of service, time in military and year of matching. Conditional logistic regression was used to evaluate associations between deployment, number of deployments, and cumulative time deployed, and melanoma risk.

Results After adjusting for combat occupation, race, and year entered the service; those individuals who had deployed had a 13% decreased odd of melanoma compared to those who had not deployed (odds ratio [OR] 0.87; 95% confidence interval [95% CI] 0.77-0.99, p-value of 0.043). Active-Duty U.S. military who deployed once or more, compared to those with zero deployments showed no significant association for melanoma cancer

risk. Cumulative days in deployment was stratified into two categories, 1-262 days and 262+ days deployed. Those individuals with cumulative 1+ days in deployment, compared to those with zero cumulative days showed no association for melanoma cancer risk. Lastly, having served in a combat role, whether in deployment status or not, showed an increased melanoma risk across all branches of service.

Conclusion Having been deployed, the number of deployments, and the number of deployment days were not associated with increased odds of having melanoma. In fact, there was reduced melanoma risk associated with all categories of deployment. However, military members serving in a combat role, regardless of deployment history, need to be educated and trained on the hazards of occupational sun exposure. These service members need to be given the proper guidance to protect, identify, and mitigate the caustic effects of melanoma.

Keywords: melanoma; skin cancer; deployment; Army; Navy; Marines; Air Force

Introduction

According to the American Cancer Society, an estimated 96,480 new melanomas cases (about 57,220 in men and 39,260 in women) were diagnosed in 2019 (1-4). Of the 7,230 estimated deaths related to melanoma of the skin in 2019, approximately 4,740 were men and 2,490 were women (5). While melanoma accounts for only 1% - 3% of all types of skin cancer, it has the highest mortality rate amongst all cancers (4). Demographically, melanoma is one of the most frequently diagnosed cancers in adults

ages 20 to 30 years old and is the main cause of cancer death in women 25 to 30 years old (5). Non-Hispanic Whites (NHW) are more than 20 times at risk of developing melanoma compared to African Americans (2-4). Overall, the lifetime risk of melanoma is 2.6% (1 in 38) for NHW, 0.1% (1 in 1,000) for blacks, and 0.6% (1 in 167) for Hispanics (2-4).

Categorically, melanoma has three well documented risks: ultraviolet exposure; genetic predisposition; and immunosuppression (6-7). Ultraviolet exposure risk factors include sun exposure, living in high altitudes, tanning/artificial UV, a history of severe sunburn in childhood or adolescence, or even intermittent intense sun exposure (6-7). Genetic predisposition can include family history, race, and other societal constructs (8-9). Immunosuppression has shown conflicting results as a key component in the development of melanoma (10-12). The etiology connecting melanoma and patients with immunosuppression is demonstrated by the association between dermal invasion of melanoma and its effect on the production of key components for immunity (13-14).

As of December 2015, over 2.8 million U.S. military personnel were deployed outside the continent of the United States (OCONUS) for all services combined - Army, Navy, Marines, and Air Force – totaling approximately ten percent of the entire U.S. military (15). Approximately 6,000 service members have died during deployment in support of OIF and OEF; exposures during deployment may potentially lead to subsequent morbidity and mortality (15-16).

Exposures in the context of day-to-day military operations during OIF and OEF, have been documented and are currently being researched towards integrated care for OEF/OIF veterans (17). According to U.S. Dept of Veteran Affairs (VA), currently there are over twelve environmental, chemical, and endemic disease risk factors affecting

Veterans of OIF and OEF. These include sand, dust, and airborne particles, to occupational hazards and infectious diseases (18-20).

Occupational sun exposure for military members has been documented as a risk factor for melanoma and non-melanoma skin cancers (21). Previous work has shown that early intervention and screening could play a pivotal role in the treatment and prevention melanoma (22). The U.S. military has emphasized treating and screening high-risk populations, to mitigate the risk of skin cancer among service members (23). Examples of these efforts include banning of tanning beds and wide-spread communication campaigns emphasizing the importance of hydration and applying sunscreen while performing work and or reactional activities outdoors (23).

The U.S. military's public health authorities have long-standing mandates for all individuals to apply sunscreen and take other protective measures against harmful UV rays (24). However, according to a survey of Soldiers deployed in these specific combat zones, less than 30% reported regular sunscreen use, and were unprotected from harmful UV rays at least 70% of the time during their normal work duties (25).

There is variation in sun exposure within the deployed Soldier population. Combat arms military personnel do not always have the capability to avoid or limit their sun exposure, and the context of their work prevents them from applying sunscreen. For instance, at times the Soldier is required to actively engage obstacles with an extreme amount of personal protective equipment, and sunscreen could be viewed as a non-essential item (25).

Previous studies have shown that ionizing radiation exposure could be a major hazard for Soldiers who have deployed, in terms of developing melanoma. The VA has

purported that a majority of cancers associated with military service result from radiation exposure (4). While the military has provided ample personal protective equipment, to mitigate this exposure, compliance with properly donning the equipment is still unclear. Those service members who work on nuclear reactors, medical facilities, nuclear weapons, manufacturing and construction, security operations, and air transport operations (in-flight) especially at high altitudes, are all susceptible to high levels of ionizing radiation (26-28). Other studies have shown that the Air Force and Navy, have higher incidence of melanoma compared to the other services with unadjusted incidence rates for melanoma around 2.45 per 10,000 person-years (26-28). One suspected etiological risk factor is the aforementioned cosmic ionizing radiation exposure, which is directly correlated with increasing in altitude. Therefore, Soldiers with aviation-specific occupations may have increased exposure compared to ground forces (29-30).

Materials and Methods

Data Source

A nested case-control study was conducted among Active-Duty personnel who were serving in one of the Armed Forces branches: Army, Navy, Marines, or Air Force, from 2001 through 2015. The data were ascertained from the Armed Forces Health Surveillance Division (AFHSD) who extracted them from the Defense Medical Surveillance System (DMSS), and the Department of Defense (DoD) Automated Central Tumor Registry Database. Deployment data came from AFHSD, United States Army Special Operations Command (USASOC)-Human Resources Command, Marine Corps

Manpower, and Reserve Affairs. Occupational and demographic data for all study subjects was ascertained from DMDC (Defense Manpower Data Center) databases.

Case Ascertainment

Cancer cases were identified using International Classification of Diseases-9 (ICD-9) diagnosis codes for cancer selection (Melanoma / 172.x / Malignant melanoma of the skin) and discharge codes noted in the DoD inpatient and outpatient medical records (DMSS). ICD-03 codes from tumor registry data and pathology reports were also used to identify cases. Diagnostic codes corresponding to notations of cancer in remission, relapse, or metastatic were utilized to confirm cases, but were not used to identify cases – only the initial diagnosis of cancer was included in the case definition. Cases were selected utilizing these criteria:

1) Those identified in the medical record and validated by the tumor registry data
2) Those identified in the medical record and not validated using tumor registry data
3) Those identified in the tumor registry, though not necessarily in the medical record data.

To assign case status using DoD medical records, the AFHSD developed definitions for surveillance purposes. Primary cancers were defined as one hospitalization with any of the defining diagnoses of melanoma in the primary diagnostic position or one hospitalization with a V-code indicating a radiotherapy, chemotherapy, or immunotherapy treatment procedure in the primary diagnostic position. For any individuals who constituted a case, the incidence date was defined as the date of the first

hospitalization or outpatient medical encounter that includes a defining diagnosis for melanoma.

An individual could be considered an incident case only once. Individuals with diagnoses of prior cancers (regardless of type/location) in the medical record were excluded from the study population. Analyses of solid cancers included only invasive tumors; in-situ tumors were excluded.

In our primary analysis, cases were defined using medical records, without any validation from the registry and/or pathology reports. A second set of analyses were restricted to cases identified in the medical record and validated by either cancer registry data or pathology reports. A final set of analyses were restricted to only those cases obtained from the tumor registries. Cases consist of both genders, all races reported, and ages ranging from 18 to 65 years old.

Control Ascertainment

Risk-set sampling was used to select controls. Details on risk-set sampling have been published elsewhere (31-32). In brief, we performed longitudinal sampling of controls through a follow-up period whereby controls were selected from the population at risk of the cancer at the time a case is diagnosed. Ten control subjects were randomly selected from each case's corresponding risk sets as of date of initial cancer diagnoses while matching on age (±5 years), gender, branch of service, and time in service. Risk sets were identified using DoD/DMDC demographic data.

Study Design / Exposure Assessment

Once all cases and controls were identified for each of the three analyses, the DMDC deployment database was queried using a roster of the entire study population (cancer cases and corresponding controls) including personal identifiers, but not a case/control status indicator.

The following deployment-related information was ascertained:

(1) Ever/never deployment status;

(2) Number of deployments;

(3) Number of days deployed based upon the start and end date of each deployment, at any time greater than the minimum empirical latency period.

Exposure status was abstracted for the five assumed latent periods: 0, 1, 4, 8, and 10 years. For example, assuming an eight-year empirical latency period between exposure and cancer diagnosis, the inquiry ascertained data on deployment history between the START of OEF in the Fall of 2001, and January 10, 2004, for a case diagnosed on January 10, 2012, and the corresponding matched controls. All deployments after January 10, 2004, were disregarded. Covariate information to be evaluated as potential confounders, independent risk factors, and effect modifiers included race, smoking status (smoker versus non-smoker), receiving cancer screening (yes versus no), number of immunizations, and year of entry into the service.

Statistical Analysis

Descriptive statistics are presented as frequencies and percentages. Differences in baseline characteristics between cancer cases and controls were assessed using primarily

Chi-square tests of two independent proportions and univariate conditional logistic regression. Student's t test, and univariate logistic regression were used to compare continuous variables between cases and controls. All continuous variables, regardless of distribution, were evaluated with parametric testing due to our robust sample size. Several races and ethnicities were noted for the cases and controls, however due to low number of participants in certain categories only three categories were used to analyze the association between race and melanoma (NHW – ref, Black, and Other).

Our unadjusted conditional logistic regression models were based on predicting the conditional log odds of cancer diagnosis by our three main variables for exposure: 1. deployment (ever versus never); 2. number of deployments; 3. cumulative deployed time (days). Additionally, we evaluated odds ratios by race/ethnicity (White, Black, and Other), smoking history (yes, no), special operations force personnel (yes, no), combat occupation (yes, no), and year entered the Armed Forces Active-Duty status. The three exposure variables were analyzed using conditional logistic regression while adjusting for the following covariates: combat occupation (y vs n), race/ethnicity, and year entered Active-Duty service. Variables with a statistically significant p-value (<0.05), and CI without 1.0, and those covariates that have a biologically plausible association with our outcome of interest were included in the models.

We estimated of the association between deployment (and other potential explanatory variables) and odds of cancer diagnosis by using multivariable conditional logistic regression. Risk comparison between cases and controls was presented as odds ratios (OR) and 95% confidence intervals (95% CI) as well as calculated p-values. The linearity of the exposure-responses between log odds of cancer and continuously

distributed variables were examined by creating indicator variables based on selected categories. The risk variable, 'number of deployments' was categorized into three categories: 0 deployments; 1 deployment; 2-9 deployments and total time deployed was also categorized into three categories: 0 days deployed; 1 – 262 days deployed; and 263+ days deployed. Wald test p-values less than 0.05 were considered evidence of statistical significance.

To assess the association between latency of primary exposure to date of diagnosis, all three of our primary exposure variables and others that are associated with risk for melanoma were evaluated in an unadjusted conditional logistic regression model with corresponding ORs and 95% CI. All categorical variables were No vs Yes, and our two exposure variables for number of deployments and cumulative years deployed were each evaluated as continuous.

Results

The study included 1,363 melanoma cancer cases and 13,630 matched controls. Baseline descriptive statistics (zero latency years) for cases and controls are presented in Table 1.1. Although the cases were age-matched to their controls ($\pm$5 years), the mean age of cases was 35.3 years and the mean age of the controls was 34.6 years, which was a statistically significant difference because of the large size of the study ($p=0.002$). But essentially the ages of the cases and controls were very similar. Almost twice as many of the cases (8.9%) had served in a combat occupation, compared to their controls (4.9%); this was a statistically significant difference ($p <0.0001$). The remaining characteristics

used for matching were not statistically significantly different between cases and controls.

Table 1.2 presents univariate conditional logistic regression results from our three exposures of interest and potential confounders. The odds of developing melanoma among those deployed was 12% less than those who had not deployed (OR=0.88, 95%CI 0.77-0.99, p-value 0.038). Individuals who were deployed once had a 13% decrease in the odds of developing melanoma compared to individuals with zero deployments, (OR 0.87, 95%CI 0.75-0.99, p-value 0.047) and individuals deployed two or more times had an 11% decrease in the odds of developing melanoma. Likewise, service members who deployed for 1-262 days had a decreased odds of melanoma compared to those who did not deploy at all (OR= 0.89, 95%CI 0.77-1.03, p-value 0.610), though this was not statistically significant. Similarly, service members who deployed 263 days or more had a decreased odds of melanoma compared to those who did not deploy at all (OR=0.82, 95%CI 0.72-1.01, p-value 0.211).

The risk of developing melanoma clearly differs by race; compared to NHWs: Blacks had an OR of 0.03 (95%CI 0.01-0.05, p-value <.001) and Other an OR of 0.27 (95%CI 0.22 - 0.33, p-value <.001). Service members who were assigned to a combat arms unit (Combat Occupation) had a 96% increase in the odds of diagnosis for melanoma, compared to those who were not assigned to a combat role (OR 1.96, 95%CI 1.59-2.42, p-value<.001). Those individuals who entered one of the services between the years 1996-2015, respectively had a 25-28% decrease in odds of melanoma, compared to those who entered service between the years of 1964 – 1988, with associated p-values of

<0.001. We found no association with risk of melanoma and those individuals who either smoked or were serving in the Special Forces.

In our multiple conditional logistic regression model (Table 1.3) we evaluated each of the three deployment variables in separate models with the following covariates: combat occupation (yes vs no), race (white, black, other), and year the individual joined the military. These three covariates were statistically significant in our unadjusted model and held their significance in our final model. Service members who deployed versus those who did not deploy demonstrated 13% decreased odds for melanoma (OR 0.87, 95%CI 0.77 - 0.99, p-value 0.043), adjusting for combat occupation, race, and year entry to service. For those individuals who deployed once or more, compared to those who had never deployed presented a non-significant association for the odds of melanoma. When comparing one deployment to zero, (OR 0.87, 95%CI 0.75 - 1.00, p-value 0.054) it dropped its value as being significant, when adjusted for the other covariates. Service members with two or more deployments showed no significant association with odds of melanoma, consistent with our unadjusted modeling (OR 0.85, 95%CI 0.72 - 1.01, p-value 0.069). Cumulative days deployed, when compared to those with zero days for deployment, showed no significant association for either category 1 – 262 days deployed (OR 0.89, 95%CI 0.77-1.03, p-value 0.610) and 263+ days deployed (OR 0.82, 95% CI 0.72-1.01, p-value 0.211) when adjusting for other covariates.

Those service members assigned to a combat occupation had a 46% increase in odds of being diagnosed with melanoma (OR 1.46, 95% CI 1.17 - 1.81, p-value <0.001) after adjusting for all other covariates. The odds ratio for combat status had the greatest change in overall OR from unadjusted to adjusted, 1.96 to 1.46. We further evaluated

combat occupation as a risk factor for melanoma by the number of deployments, number of days of deployment, and branch of service (Tables1.5 and 1.6). Additionally, the odds ratios for the exposure variables were adjusted by race.

With respect to latency periods, we evaluated zero, one, four, eight, and ten years from date of diagnosis. Using an unadjusted conditional logistic regression, we evaluated all exposure variables and several covariates we felt were impactful to the study. With respect to our exposure variables, none showed any association to risk of melanoma, except for the following two: 1. Deployed Years – 1 year latency – showed for every one-year deployed with respect to one year of latency, had 11% decrease in the odds of melanoma (OR 0.89, 95% CI 0.80-0.99). 2. Those individuals who had not deployed vs those who had deployed, with respect to zero years latency, had a 14% increase in odds of melanoma, which was demonstrated in our unadjusted conditional logistic regression model (OR 1.14, 95% CI 1.01-1.30).

Of the covariates of interest, only combat occupation showed any association to risk of melanoma and held its significance across all latency years evaluated. Those individuals serving in a service and support roles, compared to those serving in a combative function, had an approximate 50% decrease in the odds of melanoma regardless of latency year. Neither smoking nor special forces operatives demonstrated any association with odds of melanoma, regardless of latency year.

Discussion

Risk of melanoma has been attributed to the synergistic interaction between genetic factors and sunlight exposure (33-34). Specifically, history of sunburns and

intermittent sun exposure have been postulated as primary risk factors for melanoma (35-36). Sunburns and their severity are influenced by the individual's melanin as it suppresses ultraviolet (UV)-induced damage in human skin (37). NHWs have higher incidence of sunburns compared to African Americans (AA) and Hispanics (38). It is believed that intense periods of exposure to UV radiation increase the risk for developing melanoma to a greater extent than does chronic cumulative UV radiation exposure (39). Geographically, over 70% of melanomas are diagnosed in regions that receive intermittent sun exposure (35). Our study showed that NHWs in the military have an increased odds for diagnosis of melanoma, when compared to AA and members of other racial minority groups. Additionally, our results show a protective association with those who were deployed in regions that have higher cumulative UV radiation exposure, compared to those who were non-deployed and were in regions that have an increase in intermittent sunlight exposure. Of all the unmatched variables race was by far the most associated with melanoma risk. The proportion of the races is differently distributed across the exposure categories; therefore, we feel it necessary to treat race as a confounder in this study.

One explanation for the negative association between deployment in OEF/OIF and melanoma is due to Army regulations mandating limited outdoors activity across the DoD operational bases. Per Army and other DoD regulations (40-41), individuals deployed to areas with heat indexes exceeding established thresholds (40-41), general orders were enacted to restrict all outside movement during these daytime hours and serious consequence for any unit or individual conducting training or physical fitness (42-44). These mandates could have resulted in reduced exposure to harmful UV radiation.

Conversely, those individuals who were not deployed and remained CONUS kept their same training regime and even recreational activities, thereby increasing their overall UV sun exposure (46-48).

Apart from race, combat status showed a strong association with the odds of being diagnosed for melanoma. When we further examined combat status, the odds of melanoma decreased from 1.96 to 1.47 when adjusted for race. We can partially attribute this decrease in odds ratio to the distribution of race in combat status, where 84% of the Soldiers in combat status were white while only 64% in non-combat roles were white. Additionally, these individuals by nature of their role and responsibilities – regardless of deployment status – have a higher exposure to UV rays, and cosmic radiation. Different maneuvers, patrols, convoys, and wartime engagements are all generally performed outdoors, in austere environments, and under intense situations where applying sunscreen or wearing lighter-colored clothing might not be a priority (47).

Our study is not without limitations, we do not know about other major risk factors for melanoma, specifically history of UV exposure or sunburns, which both are established components of developing melanoma later in life. Additionally, we have no information regarding specific job duties and risk of occupational hazards (i.e., chemical, radiation, infantry vs non-infantry) Lastly, we have no data as to where specifically each Soldier was deployed (corresponding longitude and latitude) or for how long (duration of exposure). Lastly, there is always a possibility of misclassification and misdiagnoses.

Conclusion

While matching for age, sex, branch of service, time in military, and year of matching, and adjusting for race and year of entry into the service, our study did not find an increased melanoma risk for SM who were deployed to Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF), from 2001 through 2015. We also did not find increased melanoma risk by deployment status latency periods of 1, 4, 8, or 10 years. We did find that SM in combat roles had increased risk for melanoma across all branches of service. We feel the DoD can allocate resources to research and treatment for other ailments that have been associated with deployment and can affectively rule out melanoma as a cause for concern for deploying Soldiers. However, military members serving in a combat role, regardless of deployment history, need to be educated and trained on the hazards of occupational sun exposure. These service members need to be given the proper guidance to protect, identify, and mitigate the caustic effects of melanoma.

Table 1.1 Army Public Health Center, Edgewood, MD. Melanoma, Matched Case-Control Study 2001-2015

Variable	N (%)	Avg (SD)	Cases (1363)	Controls (13,630)	P-Value
			Matched Variables		
Age (±5yrs)		34.6 (8.5)	35.3 (8.7)	34.6 (8.5)	0.002
Sex					
Female	2244 (15)	204 (15.0)	2040 (15.0)		1.00
Male	12,749 (85)	1159 (85.0)	11590 (85.0)		
Service					
Army	4807 (32.0)	437 (32.1)	4370 (32.1)		1.00
Navy	3707 (24.7)	337 (24.7)	3370 (24.7)		
Air Force	5148 (34.3)	468 (34.3)	4680 (34.3)		
Marines	1331 (8.9)	121 (8.9)	1210 (8.9)		
Time in Military (yrs.)		13.3 (7.9)	13.64 (8.0)	13.21 (7.9)	0.053
Year of Match		2008.7 (3.9)	2008.7 (3.9)	2008.7 (3.9)	1.00
			Covariates		
Race					
White	9741 (65)	1240 (91.0)	8501 (62.4)		<.0001
Asian/PI	557 (3.7)	12 (0.88)	545 (4.0)		
Black	2340 (15.6)	9 (0.66)	2331 (17.1)		
Hispanic	1420 (9.5)	36 (2.6)	1384 (10.2)		

Am. Indian	156 (1.0)	11 (0.81)	145 (1.1)	
Other	365 (2.4)	11 (0.81)	354 (2.6)	
Unknown	414 (2.8)	44 (3.2)	370 (2.7)	
Smoker				
No	12350 (82.37)	1105 (81.1)	11,245 (82.5)	0.176
Yes	2643 (17.63)	258 (18.9)	2385 (17.5)	
Cancer Screen				
No	12313 (82)	981 (72)	11,332 (83)	<0.001
Yes	2680 (18)	382 (28)	2298 (17)	
Immunizations	25.5 (13.2)	24.6 (13.3)	25.6 (13.2)	0.007
Special Forces				
No	13,851 (92.4)	1247 (91.5)	12604 (92.5)	0.186
Yes	1142 (7.6)	116 (8.5)	1026 (7.5)	
Combat Occupation				
No	14,197 (94.7)	1242 (91.1)	12955 (95.1)	<0.001
Yes	796 (5.3)	121 (8.9)	675 (4.9)	
Year of Entry into Service	1995.5 (8.8)	1995.1 (8.95)	1995.6 (8.80)	0.093
Exposure Risk Factors				
Deployed				
No	7618 (50.8)	725 (53.2)	6893 (50.6)	0.038
Yes	7375 (49.2)	638 (46.8)	6737 (49.4)	

Number of Deployments	0.84 (1.12)	0.81 (1.13)	0.85 (1.12)	0.260
0	7618 (50.8)	725 (53.2)	6893 (50.6)	
1	4149 (27.7)	353 (25.9)	3796 (27.9)	0.143
2	1917 (12.8)	177 (13.0)	1740 (12.8)	
>2	1309 (8.7)	108 (7.9)	1201 (8.8)	
Deployed Time (days)	173.5 (265.8)	163.8 (258.4)	174.5 (266.6)	0.155
0	7618 (50.8)	725 (53.2)	6893 (50.6)	
1 – 180	2265 (15.1)	189 (13.9)	2076 (15.2)	0.203
181 – 360	2512 (16.8)	223 (16.7)	2289 (16.8)	
>360	2598 (17.3)	226 (16.6)	2372 (17.4)	

Note. All variables are “0 years - Prior To Incident Encounter/Matching”

Table 1.2 Active-Duty DoD Service Members. Melanoma Incidence-Density Matched Case Control, years 2001-2015. Conditional Logistic Regression Unadjusted Odds Ratios & 95% CI

Variable	Odds Ratios	95 % CI	P-value
	Exposure Variables		
Deployed (Y vs N)	0.88	0.77 - 0.99	0.038
Deployed Number			
0	REF		
1	0.87	0.75 - 0.99	0.047
2 – 9	0.89	0.75 - 1.05	0.169
Deployed Time(days)			
0	REF		
1 – 262	0.89	0.77 - 1.03	0.610
263 – 2439	0.82	0.72 - 1.01	0.211
	Covariates		
Combat Occ (Y vs N)	1.96	1.59 - 2.42	<.001
Race			
White	REF		
Black	0.03	0.01 - 0.05	<.001
Other	0.27	0.22 - 0.33	<.001
Smoker (N vs Y)	0.90	0.78 - 1.05	0.176

Special Forces (N vs Y)	0.87	0.71 - 1.07	0.186
Year of Entry into Service			
1964 – 1988	REF		
1989 – 1995	0.95	0.78 – 1.16	0.636
1996 – 2002	0.75	0.58 – 0.97	0.027
2002 – 2015	0.72	0.54 – 0.98	0.034

Note. All variables are "0 years - Prior To Incident Encounter/Matching"

Table 1.3 Active-Duty DoD Service Members. Melanoma Incidence-Density Matched Case Control, years 2001-2015. Conditional Logistic Regression Adjusted Odds Ratios & 95% CI

Variable	Odds Ratios	95 % CI	P-value
	Exposure Variables		
Deployed (Y vs N)	0.87	0.77 - 0.99	0.043
Deployed Number			
0	REF		
1	0.87	0.75 - 1.00	0.054
2-9	0.85	0.72 - 1.01	0.069
Deployed Time (days)			
0	REF		
1 – 262	0.92	0.79 - 1.07	0.274
263 – 2439	0.82	0.73 – 1.04	0.129
	Covariates		
Combat Occ (Y vs N)	1.46	1.17 - 1.81	<.001
Race/Ethnic			
White	REF		
Black	0.02	0.01 - 0.05	<.001
Other	0.27	0.22 - 0.33	<.001
Year of Entry into Service			

1964 – 1988	REF			
1989 – 1995	0.93	0.76	1.14	0.500
1996 – 2002	0.77	0.59	1.01	0.055
2002 – 2015	0.69	0.50	0.94	0.019

All variables are "0 years - Prior To Incident Encounter/Matching"

All Exposure Variables were entered independent of one another with all covariates for our final model.

Table 1.4 Risk for Diagnosis of Melanoma for Different Latency Periods From: 0, 1, 4, Years. Unadjusted Matched Odds Ratios & 95% Confidence Intervals

	Latency Years		
Variable	0	1	4
Exposure:		OR (95%CI)	
Deployed Number	0.96 (0.91-1.02)	0.98 (0.92-1.05)	0.94 (0.86-1.03)
Deployed Time (yrs.)	0.91 (0.83-1.01)	0.89 (0.80-0.99)	0.88 (0.76-1.02)
Deployed*	1.14 (1.01-1.30)	0.92 (0.81-1.05)	0.92 (0.78-1.07)
Covariates:			
Combat Occ*	0.51 (0.41-0.63)	0.49 (0.40-0.62)	0.51 (0.41-0.65)
Smoker*	0.90 (0.78-1.05)	1.06 (0.9-1.25)	1.04 (0.84-1.29)
Special Forces*	0.87 (0.71-1.07)	0.89 (0.72-1.1)	0.79 (0.62-1.0)

*All categorical variables are No vs Yes

Table 1.5 A Melanoma Incidence-Density Matched Case Control Study - Conditional Logistic Regression - Combat by Times Deployed and Number of Days Deployed

Variable	Odds Ratio	95% CI	p-value
Odds Ratios of Combat Cases by Number of Deployments			
Number Times Deployed			
0	1.47	1.05 – 2.08	0.027
1	1.46	0.91 – 2.35	0.093
2	1.30	0.60 – 2.80	0.680
>2	1.96	0.64 – 5.96	0.460
Odds Ratios of Combat Cases by Number of Days in Deployments			
Time in Deployment (days)			
0	1.47	1.05 – 2.08	0.027
1-180	2.88	0.84 – 9.87	0.093
181-360	1.16	0.58 – 2.32	0.680
>360	1.21	0.72 – 2.02	0.460

*Models adjusted for race and time of entry into the service.

Table 1.6 A Melanoma Incidence-Density Matched Case Control Study - Conditional Logistic Regression - Combat by Branch of Service

	Case	Control	Odds Ratio
		Army	
Combat	61	365	1.30
Non-Combat	376	4005	
		Navy	
Combat	46	228	1.74
Non-Combat	291	3142	
		Marines	
Combat	11	74	1.30
Non-Combat	110	1136	
		Air Force	3.11
Combat	3	6	
Non-Combat	465	4672	

*Models adjusted for race and time of entry into the service.

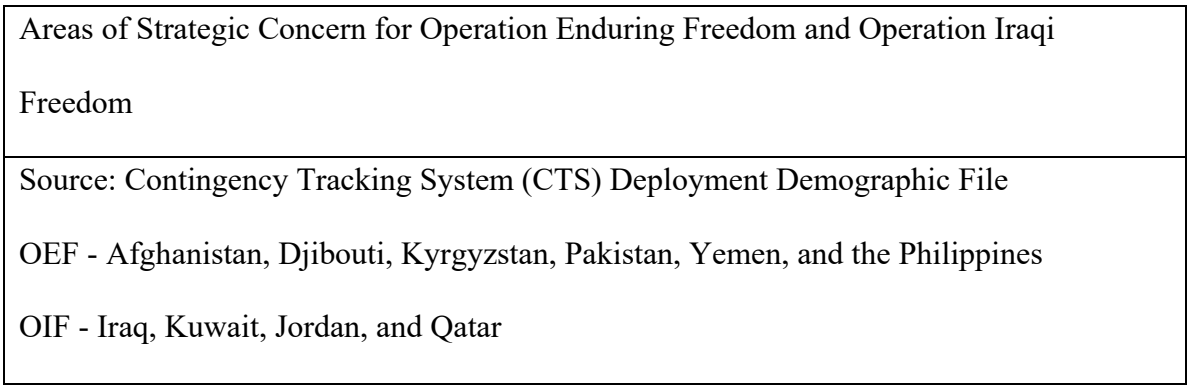

Figure 1.1 Areas of Strategic Concern for Operation Enduring Freedom and Operation Iraqi Freedom

CHAPTER 2. LUNG CANCER

Abstract

Purpose The objective of this study was to examine the associations between a history of deployment in support of Operation Enduring Freedom (OEF) or Operation Iraqi Freedom (OIF), from 2001 through 2015, and the risk of developing lung cancer.

Methods An incidence-density matched case-control study was conducted with 189 incident lung cancer cases and 1,890 matched controls. Individuals in the Armed Forces serving in one of the main branches of service who developed lung cancer between 2001 to 2015 were considered cases. For each case, ten controls were drawn at random from all individuals in the same Branch of Service who were at-risk of lung cancer during the same period as the case but did not develop the outcome. Conditional logistic regression was used to evaluate associations between three different deployment metrics (ever vs never deployed, number of deployments, and cumulative time deployed) and lung cancer risk, adjusted for epidemiologically relevant covariates, in three separate models. Statistical interactions between smoking and the deployment metrics were assessed by comparing conditional logistic regression models with and without a multiplicative interaction term.

Results Analyses of the three-deployment metrics, adjusted for age and smoking status, indicated that being deployed is protective against developing lung cancer (ORs 0.64 to 0.73), but no associations were statistically significant (respective p-values: $\geq$0.05). Having a combat occupation was found to be significantly protective against developing lung cancer (OR=0.43; 95% CI 0.18,0.99; p=0.048). Significant interactions were

observed between smoking status and having ever deployed, while adjusting for combat occupation (P = 0.044). Additionally, we when stratified by smoking status, smokers who had not deployed had a statistically significant increased risk for lung cancer (OR = 2.27, 95%CI 1.39, 3.71). Non-smokers showed no association with lung cancer based on deployment status (OR = 1.16, 95%CI 0.78, 1.73).

Conclusion These findings suggest that environmental exposures while deployed in support of OIF/OEF were not associated with subsequent lung cancer development. We recommend that the Defense Health Agency Campaign Plan emphasize smoking cessation across the Department of Defense, regardless of deployment status.

Introduction

Causes of Cancer

Lung cancer is a disease characterized by genetic, molecular, and biological malformations which develop into a carcinogenesis of lung epithelium (47). Carcinoma of the lung is divided into two separate categories: Non-small-cell lung cancer (NSCLC) which constitutes approximately eighty percent of all lung cancer cases; and small cell carcinoma (SCLC) which is the remaining twenty percent (48). Etiological factors of lung cancer have been attributed to a number of environmental exposures: air pollution, smoke, radon, asbestos and most notably smoking of tobacco products (49).

Lung Cancer in the Military

SCLC and NCLC contribute to over 25% of all cancer deaths in the US (50-52). Similarly, lung cancer in the military is the leading cause of cancer-related deaths, with NSCLC attributing to 87% of these cases (53). Compared to the US population, service members (SM) across all branches were shown to have statistically lower incidence rates (54). Additionally, SM are more likely to have cancer detected earlier, are 25% more likely to receive a diagnosis in general, and higher survival rates than their civilian counterparts (53,55-56). Contrary to the US population, there are no disparities in lung cancer mortality by socioeconomic status nor race/ethnicity among SM (56-57). Previous studies have attributed this to: mandatory periodic health assessments; active and fitness-oriented lifestyle; strict physical fitness and height/weight standards evaluated periodically; and a large push towards smoking cessation from the Surgeon General (56-57).

Exposures for Cancer in the Military

US military personnel with prolonged deployments in the Persian Gulf and Afghanistan, were often exposed to sand, dust, burn-pits, and other air pollutants. Pollutants, such as particle matter (PM) emissions, are a by-product of almost any industrial complex. PM levels are substantially higher in Southwest Asia due to dust storms, lax industry pollution standards, and others, such as: depleted uranium; oil well fires; low-level nerve agents at Iraqi facilities; and radiation from nuclear weapons testing (55,58). Exposure to carcinogenic chemicals for SMs who were deployed at high-risk areas are often increased compared to their non-deployed counterparts. Polychlorinated

biphenyl (PCBs), solvents trichloroethylene (TCE) and perchloroethylene (PCE) have been identified as three such chemicals often in higher concentrations in areas of deployment, compared to in the US (55). Ambient breathing air for SM who work extensively outdoors, such as military police, infantry, and quarter master, have been shown to be carcinogenic (59). Additional exposures for individuals deployed can be attributed to short-term dust storms and motor vehicles disturbance of the desert floor (58).

Other industrial exposures include asbestos which has been used in the construction of older buildings and ships, across the entire Department of Defense (DoD) (60). Service members who worked in shipyards, insulation work, demolition, carpentry, mining and sometimes milling could have been exposed to harmful levels of asbestos. The Department of Human Health Services (DHHS) and World Health Organization (WHO) have documented that consistent occupational exposure to asbestos can cause lung cancer (60).

Smoking is the leading cause of lung cancer across the globe (50). Though, since 2005, smoking in US population has been on a steady decline. Unfortunately, smoking has been reported to be higher among military personnel compared to the US population. Approximately 24% of active-duty personnel are currently identify as current smokers, compared to 19% of the general population (61). The reasons for a greater smoking prevalence in the military are unclear but may be related to work stress. The DoD maintains active smoking cessation programs among all branches of service.

Materials and Methods

Data source

A nested case-control study was conducted among active-duty personnel who were serving in one of the Armed Forces branches: Army, Navy, Marines, or Air Force, from 2001 through 2015. The data were ascertained from the Armed Forces Health Surveillance Branch (AFHSB) who extracted it from the Defense Medical Surveillance System (DMSS), and the DoD Automated Central Tumor Registry Database. Deployment data came from the AFHSB, United States Army Special Operations Command (USASOC)-Human Resources Command, Marine Corps Manpower, and Reserve Affairs. Occupational and demographic data for all study subjects was ascertained from DMDC (Defense Manpower Data Center) databases.

Case Ascertainment

Lung cancer cases were identified using ICD-9 diagnosis codes for cancer selection and discharge codes, noted in the DoD inpatient and outpatient medical records (DMSS). Additionally, ICD-03 codes were used from tumor registry data and pathology reports. Diagnostic codes corresponding to notations of cancer in remission, relapse, or metastatic were utilized to confirm cases, but were not used as the initial diagnosis of cancer.

Cases were those who met one of the following inclusion criteria:

(1) Identified in the medical record and validated by the tumor registry data;

(2) Identified in the medical record and not validated using tumor registry data;

(3) Identified in the tumor registry, but not necessarily in the medical record data.

An individual was considered an incident case only once per lifetime. Individuals with diagnoses of prior cancers (regardless of type/location) in the medical record were excluded from the study population, as were individuals within situ tumors. To assign case status using DoD medical records, the AFHSB developed definitions for surveillance purposes.

Primary cancers were defined as one hospitalization with any of the defining diagnoses of the lung cancer in the primary diagnostic position or one hospitalization with a V-code indicating a radiotherapy, chemotherapy, or immunotherapy treatment procedure in the primary diagnostic position. For any case, the incidence date was defined as the date of '-the first hospitalization-' or outpatient medical encounter that includes a defining diagnosis for lung cancer.

In primary analyses, cases were determined using cases defined using medical records, without any validation from the registry and/or pathology reports. A second set of analyses were restricted to cases identified in the medical record and validated by either cancer registry data or pathology reports. A final set of analyses were restricted to only those cases obtained from the tumor registries.

Control Ascertainment

Risk-set sampling was used to select controls. This involved longitudinal sampling of controls from the population at risk of lung cancer at the time a case was diagnosed. Risk sets were identified using DoD/DMDC demographic files and records. Ten control subjects were randomly selected from each case's corresponding risk sets as of their diagnosis date. The controls in this study must have been at risk of being a case at

the time of being selected. It was possible for a control (no history of cancer at the time matched to a case) to later become a case. It was also possible that controls could be selected as a control more than once at differing times, for other cases. Risk set sampling enables the researcher to accommodate the possibility that the study population is dynamic in that the individual may enter and leave the population during the risk interval. Matching was done on age (±5 years), gender, branch of service, and time in service.

Study Design / Exposure Assessment

Once all cases and controls were identified, the DMDC deployment database was queried using a roster of the entire study population (cancer cases and corresponding controls) including personal identifiers.

The following deployment-related information was ascertained:

(1) Whether a participant ever deployed;

(2) Start and end date of each deployment.

Exposure status was abstracted for the five assumed latent periods: 0, 1, 4, 8, and 10 years. This was done to account for exposures which may not have been contributed to the risk of developing lung cancer because the cancer process has already initiated. Methods for evaluating latency were performed similarly to previous cancer studies (62).

Covariate information evaluated as potential confounders, independent risk factors, and effect modifiers (not including the matched variables) included: race; smoking status (self-reported current smoker versus currently not a smoker); receiving cancer screening (yes versus no); number of immunizations; and year of entry into the service.

The major independent risk factor of concern was deployment. Deployment status could change since this measure of potential exposure assessment applied at the time of sampling for both cases and controls, based on the assumed latency period.

Statistical Analysis

The association between deployment (and other potential explanatory variables) and odds of cancer diagnosis was assessed using multivariable conditional logistic regression. Risk comparison between cases and controls were presented as odds ratios (ORs) and 95% confidence intervals (95% CI) with associated p-values. The linearity of the exposure-responses between log odds of cancer and continuously distributed variables were examined by creating indicator variables based on selected categories. The risk variable, 'number of deployments' was categorized into three categories: 0 deployments; 1 deployment, 2-9 deployments. Total time deployed was also categorized into three categories: 0 days deployed; less than or equal to 365 days deployed, and greater than 365 days deployed. Wald test p-values less than 0.05 were considered evidence of statistical significance.

Descriptive statistics are presented as frequencies and percentages for categorical variables and means with standard deviations for continuous variables. Differences in categorical characteristics between cancer cases and controls were assessed using Chi-square tests of two independent proportions and univariate logistic regression. Student's t test, and univariate logistic regression were used to identify differences in continuous variables between cases and controls. All continuous variables, regardless of distribution, were evaluated using parametric tests due to the robust sample size. The database noted

seven racial and ethnic categories for the cases and controls, however due to low number of participants in certain categories the following three categories were used to analyze the association between race and lung cancer risk: non-Hispanic white (ref), Black, and all other.

Unadjusted conditional logistic regression models were based on predicting the conditional log odds of cancer diagnosis by our three main variables for exposure. Additionally, we evaluated odds ratios by other potential confounding variables such as race, smoking history (No vs Yes), and special forces operations personnel (No vs Yes) combat occupation (No vs Yes) and year entered the Armed Forces active-duty status.

Effect modification and interactions between smoking and the deployment exposures were also evaluated adjusting for risk variables. A Cochran-Mantel-Haenszel stratified analysis was used to evaluate lung cancer risk by deployment by categories of smoking status.

To examine the influence of different latency period assumptions on the estimated effects of deployment on lung cancer odds, we re-ran unadjusted and adjusted conditional logistic regression models for each exposure variable under each assumed latency. All categorical variables were binary, and the two exposure variables for number of deployments and cumulative years deployed were each evaluated as continuous.

Results

Descriptive Statistics

Participant Characteristics

The characteristics of the 189 incident lung cancer cases and 1,890 matched controls are reported in Table 2.1. The average age of cases was 39.2 years which is well below the average age of 70 for lung cancer cases in the US general population (63). Although the controls were age-matched to the cases (±5 years), the cases tended to be older, with 55% of the cases above 40 years old while only 48% of the controls were above age 40. The average ages of the controls were close to the average of the controls with a mean of 38.2 years, but the variance about these means was wide with a standard deviation of 9.6 for the cases and 9.1 for the controls. Cases were mostly men (84%) and non-Hispanic white (64%). The prevalence of current smoking was 44% among the cases and 16% among the controls. It is important to note that 56% of the cases were non-smokers, but this group could have included former smokers. No significant associations were observed between the deployment metrics and lung cancer odds, but controls tended to be somewhat more commonly deployed than cases. However, a significantly greater proportion of controls (8.6%) had served in a combat role than had cases (3.2%) ($p=0.009$).

Unadjusted Conditional Logistic Regression

Deployment Status and Cigarette Smoking on Lung Cancer

The results of unadjusted conditional logistic regression of the deployment variables, and covariates of interest are presented in Table 2.2. The controls were more commonly deployed than the cases. Analysis of the selected exposure metrics indicates that being deployed was slightly protective for developing lung cancer with ORs ranging from 0.71 to 0.75, but none of the comparisons were statistically significant ($p \geq 0.05$). Individuals serving in a combat occupation had a significantly decreased odds of being diagnosed with lung cancer compared to those who did not serve in a combat occupation (OR=0.34, 95%CI 0.15-0.78; p=0.011).

Table 2.3 presents the results of the conditional logistic regression analysis for the deployment, Special Forces, and combat status variables adjusted for age and smoking status. There results yield essentially the same interpretation as the unadjusted results. SMs who were deployed, compared to non-deployed, had a somewhat lower odds of developing lung cancer (ORs ranging from 0.64 to 0.73), but none of the comparisons were statistically significant. No significant association was found between serving in a Special Forces unit and odds for developing lung cancer (OR=0.86; 95%CI 0.49,1.50; p=0.589). Serving in a combat unit however was significantly protective (OR=0.43, p=0.048).

Smoking was the major risk factor for developing lung cancer with 44% of the cases being current smokers while only 16% of the controls were smokers (OR=4.41,

95%CI 3.18-6.13; p<0.001). Smoking was also an important confounding variable with SMs who were deployed being somewhat more commonly smokers than those not deployed (Table 2.4). It is important to note however, that SMs in combat roles were significantly less likely to be smokers than SMs in non-combat units (OR=0.27, p<0.001). Smoking also appeared to be a potential effect modifying variable as the ORs for lung cancer between cases and controls varied markedly between SMs who were deployed or served in a combat role compared to SMs who were not deployed or served in a combat role (Table 2.5). Only 8.5% of the cases and 7.4% of the controls served in Special Forces units, and no statistically significant association was observed between being in Special Forces and the odds of developing lung cancer, or odds of being a smoker.

Statistical interactions between smoking and the exposure metrics were also assessed by comparing conditional logistic regression models with and without a multiplicative interaction term. Significant interactions were observed between current smoking status (No vs Yes) and deployed (ever/never) (P = 0.044) (Table 2.5). Non-smokers, regardless of deployment status, had a decreased odds of being diagnosed with lung cancer compared to smokers. Non-smokers versus smokers who deployed had an OR=0.33 (95%CI:0.21-0.54) and non-smokers versus smokers, who had not deployed had an OR=0.17 (95%CI:0.11-0.27). When analyzing SM who had deployed versus non-deployed, the non-smokers showed no significant association with risk of lung cancer, OR=0.91 (95%CI:0.59-1.41); however, when analyzing those who had deployed vs non-deployed amongst smokers, those smokers who deployed had a decrease in odds of lung cancer OR=0.47 (95%CI: 0.27-0.80). Demonstrating a protective status for individuals

who deployed, consistent with our unadjusted and adjusted ORs for the deployment variable.

When stratified by combinations of deployment (No vs Yes) and smoking status (No vs Yes) the difference in ORs for lung cancer by deployment exposure was significantly greater in smokers than non-smokers, OR=2.27 (95%CI:1.39, 3.71), OR=1.16 (95%CI:0.78, 1.73), p-value for the Breslow-Day test (0.039). The three CMH statistics test the same H_o, all conditional odds ratios are equal to 1, we reject the null with p-values of 0.0083 (Table 2.6).

With respect to latency periods, we evaluated zero, one, four, eight, and ten years from date of diagnosis (Table 2.7). Using an unadjusted conditional logistic regression, we evaluated all exposure variables and the two covariates we felt were impactful to the study. The exposure variables showed no association to risk of lung cancer with latency. Both combat occupation and smoking showed an association with risk of lung cancer. Those individuals serving in a service and support role, compared to those serving in a combat occupation, had an approximate 300% increase in the odds of lung cancer regardless of latency year. Non-smokers compared to smokers, for years 0, 1, and 4, had a 77%, 59%, and 63% decrease in odds of lung cancer, respectively.

Discussion

The primary goal of this study was to evaluate any association with deployment and lung cancer. We found that being deployed, whether adjusted or not for our primary covariates, was protective against lung cancer though not statistically significant. Reasons for this finding may be that SMs who are deployed tend to be healthier in general and

lead to stronger, more active lifestyles than SMs who have never deployed (64). Exercise is associated with a decreased risk of lung cancer (64-66). For SM who were non-deployed, they may become more complacent with their physical fitness compared to those deployed. Deployed SM may also represent a selected-survivor population who are in general healthier and more robust than personnel who are not deployed. We found that deployed personnel had a somewhat higher prevalence of being cigarette smokers.

Smoking is clearly the number one cause of lung cancer across the globe (50). In this study, we found that a history of deployment was associated with smoking. While not statistically significant, SM who had deployed had a greater odds of being current cigarette smokers. Long-term, this could influence the SM's risk of lung cancer (67-68). Studies from the Millennium Cohort identified deployment was associated with smoking initiation and recidivism, especially with prolonged deployments, multiple deployments, or combat exposures (69). We also discovered that deployment status and smoking multiplicative interaction was statistically significant ($p = 0.044$); with the difference in ORs for lung cancer according to deployment much greater in smokers than in non-smokers. This trend was pronounced when we adjusted for combat occupation. We recommend the most important risk reduction strategy towards lung cancer risk would be smoking cessation across the entire DoD. Policies are already in place to help individuals with post-deployment post-traumatic stress disorder (PTSD) which has been linked to increase in tobacco and alcohol usage (70-71). In an effort "Toward A Tobacco-Free Military Population" (72) the idea of establishing a tobacco-free military has been initiated in the past, but has never has any substantial success (72). Through policy changes, the DoD hopes to restrict and deter new tobacco users. Additionally, most US

Military installations are tobacco-free, to include vaping and any form of cannabidiol products. With an emphasis on physical, spiritual, and mental health the Army as well as other branches of service are enacting comprehensive tobacco-control programs (72).

The ages of our cohort were 18 to 65 years old, based upon the standards for all Active-Duty US military members. The average age for our cases was approximately 39 years old, approximately 30 years younger than the average age of lung cancer patients in the general U.S. population (61). We believe we are simply dealing with a subset of people who are diagnosed with lung cancer at a young age, in a very young cohort. One of the limitations of a nested case-control study is you get the cases you get, and they may not reflect all the cases that will eventually become manifest in this cohort. We are not able to yet study all the lung cancer cases that might eventually occur in this cohort as it ages. It is plausible, that someday having been deployed may actually present in the data as a risk factor for developing cancer.

SM working in a combat role had dramatically decreased risk of lung cancer odds compared to SM in other roles, in both unadjusted and adjusted analyses. Based on military standards, combat occupation personnel participate in additional training and exercise programs, necessitated by their job duties and descriptions (73-76). Additionally, sedentary jobs have been associated with an increased risk of lung cancer and could be attribute to our findings (77). Brenner et al, showed higher levels of physical activity are consistently associated with 25% lower risk of developing lung cancer in prospective studies (78). Lastly, a study has shown that SM in a combat unit, had the second lowest rates of current and past smoker compared to those in the service & support, with health

care/medical service corps having the lowest (66). The SM likely also represent an especially healthy, robust selected population.

Socioeconomic status (SES), across the globe, has been associated with lung cancer (79). People living in lower SES tertiles have been shown to have an increased risk in lung cancer compared to their higher SES counterparts (80-81). The increased risk has been attributed to quality of life, race, and access to care (82-84). However, in the military SES has no relation to cancer risk or survival (56-57). We evaluated the association between race and lung cancer in our study, and our results are consistent with other studies that race within the Military Services shows no association with risk of lung cancer. Lung cancer risk associated with SES such as access to care, accessible cessation education, and screening are all but eliminated in Military Services (56-57).

After our analysis for latency (0, 1, 4 years) and its association with odds of diagnosis for lung cancer, we found that deployment and those individuals in a combat occupation were consistently found to be protective. These results are consistent with our previous findings in our adjusted conditional logistic regression models, where latency was not evaluated.

In conclusion, our results show, protective associations between those who had deployed versus non-deployed and odds of lung cancer, though none significant. Smoking, as with a multitude of previous studies, is strongly associated with an increased risk of lung cancer. This study found an interactive association between smoking and deployment. When stratified by smoking, individuals who were smokers and non-deployed, had a drastic increase in risk for lung cancer. Further insight is needed as to the etiology, both physically and mentally with smoking and deployments, as it pertains to

risk of lung cancer. A major limitation in this study was the lack of information on the SM's history of amount and duration of smoking. It is important to know how deployment may have affected the amount of smoking while one was deployed or non-deployed. Although we know the time period and duration of service for the cases and controls, we do not know specifically when or where the SM were deployed. Additional limitations include potential inconsistencies with the diagnoses for lung cancer, and a relatively young cohort who could potentially develop lung cancer later in life.

While the study suffered from these limitations, the analyses consistently showed there was no evidence that being deployed increased SM's risk of developing lung cancer. In fact, being deployed displayed a somewhat protective factor, and serving in a combat role was especially protective. Based upon our findings we would recommend to the DHA Campaign Plan to consider further funding into smoking cessation across the DoD and reallocate research and resources away from lung cancer as a potential threat from overseas deployment.

Table 2.1 Army Public Health Center, Edgewood, MD. Lung Cancer, Matched Case-Control Study 2001-2015

Variable	N (%)	Avg (SD)	Cases (189)	Controls (1,890)	P-Value
Matched Variables					
Age (±5yrs)		38.30 (9.1)	39.20 (9.6)	38.20 (9.1)	0.153
Sex					
Female	341 (16.4)		31 (16.4)	310 (16.4)	1.00
Male	1738 (83.6)		158 (83.6)	1580 (83.6)	
Service					
Army	836 (40.2)		76 (40.2)	760 (40.2)	1.00
Navy	583 (28.0)		53 (28.0)	530 (28.0)	
Air Force	484 (23.3)		44 (23.3)	440 (23.3)	
Marines	176 (8.5)		16 (8.5)	160 (8.45)	
Time in Military (yrs.)		16.02 (8.2)	16.47 (8.6)	15.98 (8.2)	0.433
Year of Match	2008 (4.0)	2008 (4.0)	2008 (4.0)		1.00
Covariates					
Race					
White		1292 (62.2)	120 (63.5)	1172 (62.0)	0.116
Black		399 (19.2)	39 (20.6)	360 (19.1)	
Asian/PI		101 (4.9)	8 (4.2)	93 (4.9)	
Hispanic		162 (7.8)	7 (3.7)	155 (7.5)	

Am. Indian	19 (0.9)	4 (2.1)	15 (0.8)	
Other	48 (2.3)	3 (1.6)	45 (2.4)	
Unknown	58 (2.8)	8 (4.2)	50 (2.7)	
Smoker				
No	1691 (81.3)	106 (56.1)	1585 (83.9)	<.001
Yes	388 (18.7)	83 (43.9)	305 (16.1)	
Cancer Screen				
No	1651 (79.4)	143 (75.7)	1508 (79.8)	0.181
Yes	428 (20.6)	46 (24.3)	382 (20.2)	
Immunizations	25.11 (13.8)	24 (14.4)	25.20 (13.8)	0.378
Special Forces				
No	1923 (92.5)	173 (91.5)	1750 (92.6)	0.599
Yes	156 (7.5)	16 (8.5)	140 (7.4)	
Combat Occupation				
No	1910 (91.9)	183 (96.8)	1727 (91.4)	0.009
Yes	169 (8)	6 (3.2)	163 (8.6)	
Exposure Risk Factors				
Year of Entry into Service	1992 (9.4)	1991.7 (9.7)	1992.2 (9.3)	0.486

Deployed				
No	1084 (52.1)	108 (57.1)	976 (51.6)	0.149
Yes	995 (47.9)	81 (42.9)	914 (48.4)	
Number of Deployments				
0	1084 (52.1)	108 (57.1)	976 (51.6)	0.352
1	556 (26.7)	45 (23.8)	511 (27.0)	
2+	439 (21.1)	36 (19.1)	403 (21.3)	
Deployed Time (days)				
0	1084 (52.1)	108 (57.1)	976 (51.6)	0.352
1 to $\leq$ 365	605 (29.1)	49 (25.9)	556 (29.4)	
>365	390 (14.8)	32 (16.9)	358 (18.9)	

Note: All variables are “0 years - Prior To Incident Encounter/Matching”

Table 2.2 Active-Duty DoD Service Members. Lung Cancer Incidence-Density Matched Case Control, years 2001-2015. Conditional Logistic Regression Unadjusted Odds Ratios & 95% CI

Variable	Odds Ratios	95 % CI	P-value
	Exposure Variables		
Deployed (Y vs N)	0.74	0.52 - 1.05	0.094
Deployed Number			
0	REF		
1	0.75	0.51 - 1.11	0.149
2 – 8	0.72	0.45 - 1.16	0.176
Deployed Time (days)			
0	REF		
1 to ≤ 365	0.75	0.52 – 1.10	0.143
>365	0.71	0.43 - 1.18	0.188
	Covariates		
Combat Occ (Y vs N)	0.34	0.15 – 0.78	0.011
Race			
White	REF		
Black	1.06	0.72 – 1.56	0.767
Other	0.82	0.54 – 1.24	0.348

Smoker (N vs Y)	0.23	0.16 - 0.32	<.001
Special Forces (N vs Y)	0.86	0.49 - 1.50	0.589
Year of Entry into Service			
1963 – 1988	REF		
1989 – 1995	0.95	0.58 – 1.56	0.841
1996 – 2002	0.74	0.37 – 1.45	0.376
2003 – 2015	0.88	0.40 – 1.98	0.755

All variables are “0 years - Prior To Incident Encounter/Matching”

Table 2.3. Active-Duty DoD Service Members. Lung Cancer Incidence-Density Matched Case Control, years 2001-2015. Conditional Logistic Regression Adjusted Odds Ratios & 95% CI

Exposure Variables			
Variables	OR	95% CI	P-value
Deployed (Y vs N)	0.70	(0.48 - 1.00)	0.05
Deployed Number			
0	REF		
1	0.72	(0.48 - 1.07)	0.50
2-8	0.67	(0.41 - 1.07)	0.28
Deployed Time (days)			
0	REF		
1 to ≤365	0.73	(0.49 – 1.08)	0.114
>365	0.64	(0.42 - 1.19)	0.102
Covariates			
Combat Occup (Y vs N)	0.43	(0.18 – 0.99)	0.048
Smoker (N vs Y)	0.23	(0.17 - 0.33)	0.001

All variables are “0 years - Prior To Incident Encounter/Matching”

All Exposure Variables were entered independent of one another with all covariates for our final model.

Table 2.4 Smoking Status by Exposure Metrics - Incidence-Density Matched Case Control Study - Conditional Logistic Regression

Variable	Odds Ratio	95% CI	p-value
Exposure Variables Applied One at a Time while Adjusted for Covariates			
Ever Deployed*			
No	1.00	Ref	---
Yes	1.20	0.91 – 1.57	0.194
Number Times Deployed*			
0	1.00	Ref	---
1	1.17	0.87 – 1.58	0.301
≥2	1.24	0.89 – 1.73	0.211
Time in Deployment (days)*			
0	1.00	Ref	---
≤365	1.16	0.87 – 1.56	0.312
>365	1.27	0.89 – 1.82	0.187
Served in Special Forces*			
No	1.00	Ref	---
Yes	0.89	0.58 – 1.36	0.586
Served in a Combat Role*			
No	1.00	Ref	---
Yes	0.27	0.14 – 0.50	<0.001

*Adjusted by age categories.

Table 2.5 Active-Duty DoD Service Members. Lung Cancer Incidence-Density Matched Case Control, Years 2001-2015. Conditional Logistic Regression Adjusted Odds Ratios & 95% CI, with Interaction Terms

Variable	OR	95%CI	P-value
Combat Occupation	2.27	0.97-5.30	0.058
Deployed (Y) * Smoker (N)			0.044
1. Non-Smoker vs Smoker & Deployed	0.33		0.21-0.54
2. Non-Smoker vs Smoker & Non-Deployed	0.17	0.11-0.27	
3. Deployed vs Non-Deployed & Non-Smoker	0.91	0.59-1.41	
4. Deployed vs Non-Deployed & Smoker	0.47	0.27-0.80	

Table 2.6 Smokers vs Non-Smokers by Deployment for Lung Cancer

Cochran-Mantel-Haenszel Stratified Analysis.

Smokers				Non - Smokers			
	Case	Control	Total		Case	Control	Total
Non-Deployed	46	108	154	Non-Deployed	62	868	930
Deployed	37	197	234	Deployed	44	717	761
Total	83	305	388	Total	106	1585	1691
OR 2.27 (1.39, 3.71)				OR 1.16 (0.78, 1.73)			

Breslow-Day Test for Homogeneity of Odds Ratios	
Chi-Square	4.28
DF	1
Pr > Chisq	0.039

Cochran-Mantel-Haenszel Statistics (Based on Table Scores)

Statistic	Alternative Hypothesis	DF	Value	Prob
1	Nonzero Correlation	1	6.98	0.0083
2	Row Mean Scores Diff	1	6.98	0.0083
3	General Association	1	6.98	0.0083

Table 2.7 Risk for Diagnosis of Lung Cancer for Different Latency Periods From: 0, 1, 4 Years. Matched Odds Ratios & 95% Confidence Intervals

	Latency Years		
Variable	0	1	4
Deployed Number	0.95 (0.81-1.12)	1.02 (0.85-1.21)	0.96 (0.75-1.23)
Deployed Time (yrs.)	0.90 (0.70-1.17)	0.94 (0.71-1.23)	1.04 (0.72-1.51)
Deployed (Y vs N)	0.74 (0.52-1.05)	0.87 (0.60-1.26)	1.00 (0.65-1.56)
Combat Occ*	2.98 (1.29-6.88)	2.81 (1.22-6.50)	2.65 (1.14-6.15)
Smoker*	0.23 (0.16-0.32)	0.41 (0.29-0.59)	0.37 (0.23-0.58)

*Categorical variables are No vs Yes

CHAPTER 3. COMPARING INCIDENCE OF MELANOMA AND LUNG CANCER IN THE US MILITARY, BY BRANCH OF SERVICE FOR YEARS 2001–2015

Abstract

Purpose To examine associations between the different branches of U.S. military service and years of service between 2002 through 2015, for melanoma and lung cancer incidence.

Methods Melanoma and lung cancer incidence rates from 2002 to 2015, among active-duty military personnel were compared using a Poisson Regression Analysis. Data were obtained from the Defense Manpower Data Center, Defense Medical Surveillance System, and the DoD Automated Central Tumor Registry Database.

Results Melanoma crude rates were higher for all other branches of service compared to the Marines; the cancer incidence rates (per 100,000 person-years) were 4.6 for Marines, 9.89 for Air Force, 7.1 for Navy, and 6.05 for the Army. Additionally, the incidence rate ratios (IRR) were significantly higher for all other branches compared to the Marines: 2.16 for Air Force; 1.55 for Navy; and 1.32 for Army. Lung cancer crude incidence rates were lowest for the Marines amongst all branches of service. Additionally, lung cancer IRRs were marginally higher for the Navy (IRR 1.84, CI: 1.01, 3.37, p-value 0.049) compared to the Marines. Melanoma incidence increased 18.6%, from 2002-2008 to 2009-2015 for the entire Department of Defense. Army melanoma incidence rates increased from 2002 to 2015, with a significant test for linear trend (p= 0.0009).

Conclusion These results are consistent with previous studies, showing the Air Force at an increased risk for melanoma due to ionized radiation exposure. Further studies of risk factors for melanoma in the military are needed to explain the rising rates from 2002-

2008 to 2009-2015. While melanoma rates for the Army increased significantly from 2002 – 2014, they dropped off in 2015, and further analysis could show a downward trend.

Keywords:

Introduction

Cancer has been studied extensively in the U.S. military, impart due to the access and availability of medical records and registries. However, few studies have demonstrated a relationship between cancer incidence and the different branches of service. The goal of this study is to examine associations between the different branches of the U.S. military (Army, Navy, Air Force, Marines) with melanoma and lung cancer incidence between the years of 2002 through 2015.

Melanoma

Occupational sun exposure for military members has been documented as a risk factor for melanoma and non-melanoma skin cancers (85). Previous work has shown that early intervention and screening could play a pivotal role in the treatment and prevention melanoma (86). The U.S. military has emphasized treating and screening high-risk populations, to mitigate the risk of skin cancer among service members (87). Examples of these efforts include banning of tanning beds and wide-spread communication campaigns emphasizing the importance of hydration and applying sunscreen while performing work and or recreational activities outdoors (87).

The U.S. military mandates for all individuals to apply sunscreen and take other protective measures against harmful UV rays (88). However, according to a survey of Soldiers deployed in specific combat zones, less than 30% reported regular sunscreen use, and were unprotected from harmful UV rays at least 70% of the time during their normal work duties (89). Lack of adherence could be attributed to service members who actively engage obstacles with an extreme amount of personal protective equipment, and view applying sunscreen as a non-essential (89).

Apart from harmful UV rays, radiation exposure has been attributed to increased risk for melanoma. In fact, the VA states that most cancers associated with military service result from radiation exposure (90). Military personnel that work near nuclear reactors, medical facilities, nuclear weapons, manufacturing and construction, security operations, and air transport operations, are all susceptible to high levels of ionizing radiation (91-93). Previous studies show ionizing radiation as a hazard for all military personnel for developing melanoma cancer. One study reported the Air Force and Navy to have a higher incidence of melanoma compared to the other services, with unadjusted incidence rates for melanoma around 2.45 per 10,000 person-years (91-93). One suspected etiological risk factor for the increased melanoma incidence was cosmic ionizing radiation exposure, which is directly correlated with increasing in altitude. Therefore, Soldiers with aviation-specific occupations may have increased exposure compared to ground forces (94-95).

Lung Cancer in the Military

Small cell lung cancer (SCLC) and Non-small cell lung cancer (NCLC) contribute to over 25% of all cancer deaths in the US (96-98). Similarly, lung cancer in the military is the leading cause of cancer-related deaths, with NSCLC attributing to 87% of these cases (99). However, compared to the US population, service members (SM) across all branches were shown to have statistically lower incidence rates (100). Additionally, SM compared to their civilian counter parts have earlier detection, are 25% more likely to receive a diagnosis, and higher survival rates (99, 101-102). Contrary to the US population, there are no disparities by socioeconomic status nor race/ethnicity groups for survival from lung cancer within the U.S. military (102-103). Previous studies suggest these finding results from a combination of mandatory periodic health assessments, an active and fitness-oriented lifestyle, strict physical fitness and height/weight standards which are evaluated periodically, and access to smoking cessation programs as encouraged by the Surgeon General (102-103).

Exposures for Cancer in the Military

US military personnel with prolonged deployments in the Persian Gulf and Afghanistan, were often exposed to sand, dust, burn-pits, and other air pollutants. Pollutants, such as particle matter (PM) emissions, are a by-product of almost any industrial facility. PM levels are substantially higher in Southwest Asia, from dust storms, lax industry pollution standards, and others, such as: depleted uranium; oil well fires; low-level nerve agents at Iraqi facilities; and radiation from nuclear weapons testing (101,104). Exposure to carcinogenic chemicals for SMs who were deployed at high-risk

areas are often increased compared to their branch counterparts stateside. Polychlorinated biphenyl (PCBs), solvents trichloroethylene (TCE) and perchloroethylene (PCE) have been identified as some of the hazardous chemicals often in higher concentrations in areas of deployment, compared to US (101). PM in the atmosphere and breathing air for SM who work extensively outdoors, such as military police, infantry, and quarter master, have been shown to be carcinogenic (105). Additional exposures to PM for individuals deployed can be attributed to short-term dust storms and motor vehicles disturbance of the desert floor (104).

Other industrial exposures include asbestos which has been used in the construction of older buildings and ships, across the entire Department of Defense (DoD) (106). Service members who worked in shipyards, insulation work, demolition, carpentry, mining and sometimes milling could have been exposed to harmful levels of asbestos. The Department of Human Health Services (DHHS) and World Health Organization (WHO) have documented that this level of exposure to asbestos can cause lung cancer (106).

Though smoking in US population has been on a steady decline, it has been reported to be higher among military personnel with approximately 24% of active-duty personnel are currently smoking every day or regularly, compared to 19% of the general population (107). The reasons for a greater smoking prevalence in the military are unclear but may be related to work stress. The DoD maintains active smoking cessation programs among all branches of service.

Materials and Methods

This study was restricted to active-duty military personnel with a diagnosis of melanoma or lung cancer between 2002 to 2015. Populations estimates for each branch of service were calculated as the average number of individuals enrolled over a calendar year; the data were obtained from the Defense Manpower Data Center.

Cancer cases were identified using ICD-9 diagnosis codes for cancer selection and discharge codes, noted in the DoD inpatient and outpatient medical records (DMSS). Additionally, ICD-03 codes were used from tumor registry data and pathology reports. Diagnostic codes corresponding to notations of cancer in remission, relapse, or metastatic spread were utilized to confirm cases, but were not used as the initial diagnosis of cancer. Cases were those who met one of the following inclusion criteria:

(1) Identified in the medical record and validated by the tumor registry data;

(2) Identified in the medical record and not validated using tumor registry data;

(3) Identified in the tumor registry, but not necessarily in the medical record data.

An individual was considered an incident case only once per lifetime. Individuals with diagnoses of prior cancers (regardless of type/location) in the medical record were excluded from the study population, as were individuals within situ tumors. To assign case status using DoD medical records, the AFHSB developed definitions for surveillance purposes.

Primary cancers were defined as one hospitalization with any of the defining diagnoses of the lung cancer in the primary diagnostic position or one hospitalization with a V-code indicating a radiotherapy, chemotherapy, or immunotherapy treatment procedure in the primary diagnostic position. For any case, the incidence date was

defined as the date of '-the first hospitalization-' or outpatient medical encounter that includes a defining diagnosis for lung cancer. In primary analyses, cases were determined using cases defined using medical records, without any validation from the registry and/or pathology reports.

A second set of analyses were restricted to cases identified in the medical record and validated by either cancer registry data or pathology reports. A final set of analyses were restricted to only those cases obtained from the tumor registries.

Incidence rates (per 100,000 person-years) and 95% confidence intervals (CIs) were calculated, stratified by military branch of service and diagnosis year. Incidence rates were calculated when there were at least 10 cases in each stratum. Incidence rate ratios (IRRs) and 95% CIs were calculated using Poisson Regression, to compare rates over time stratified by military branch of service. To correct for overdispersion when calculating the IRRs and 95& CIs, we used a Negative Binomial for the melanoma analysis and a Pearson Scale for the lung cancer analysis. Goodness-of-fit was estimated by calculating p-values from the degrees of freedom (df) and values following a X_2 distribution. All analyses were conducted using SAS software (version 9.3) and the 2-sided significance level was set at $P < 0.05$.

Results

Melanoma incidence varied by military service branch (Table 3.2). Compared to the Marines, those in the Navy, Army and Air Force had significantly higher rates. Previous studies have shown the Air Force and Navy to have higher rates of melanoma, based upon their exposure to ionizing radiation, and working in higher atmospheric

altitudes (108). Using Marines as our referent group, individuals serving in the Air Force from 2002-2015, had 2.16 times the incident rate, with the Navy and Army demonstrating increased rate ratios of 1.55 and 1.32, respectively.

Compared to the Marines, all other branches of service had higher incidence rates of lung cancer, though only the Navy had a significantly increased rate ratio. Those service members in the Navy had 1.84 times the incident rate compared to the Marines. (Table 3.3)

From 2002-2008 to 2009-2015, melanoma incidence among all branches of service increased significantly (Table 3.4). Though there was no evidence of a linear trend and cancer incidence rates nearly peaking in 2014 and falling drastically in 2015. During this same time period, melanoma cancer crude incidence rates in the U.S. Army have steadily increased (Figure 1), following a linear trend of p-value 0.0009. Figures 1 – 4, show the crude incidence rates and kernel smoothing approach for melanoma for the Army, Air Force and entire DoD. Contrary to the Army, the Air Force and DoD showed no significant increase for melanoma rates.

Lung cancer incidence rates show no significant change from 2002-2008 to 2009-2015 (Table 3.4), additionally rates fluctuated between 2002-2015, showing no significant change in linear trend.

Discussion

Our results showed significant differences in melanoma incidence rates among the different branches of service in the U.S. Military from 2002 – 2015. The overall crude melanoma incidence rates were significantly lower in the Marines than in the other three

branches of service, with the Air Force having the highest. Lung cancer incidence rates were not significantly different by service branch. Melanoma incidence rates increased from 2002-2008 to 2009-2015 for the entire DOD, though lung cancer incidence rates demonstrated no significant increase from the two year-groups studied.

Individuals serving in the Air Force and Navy have an increased risk for melanoma, compared to the Army and Marines (108). Previous studies have found that both military and civilian pilots have a higher risk for melanoma, compared to the general population (109). Zhou and colleagues have attributed this finding to pilots are more likely to be exposed to cosmic ionizing radiation (108). Though increased exposure to cosmic ionizing radiation doesn't tell the whole story, with less than four percent of individuals serving in the Air Force are pilots (110). Other Air Force personnel are exposed to known chemical carcinogens for melanoma (109). These chemicals include fuel, jet engine exhaust, cabin air pollutants, and polychlorinated biphenyls (PCBs) (111). All of these carcinogens have been identified on the surfaces, in component materials, and equipment of older ships and vessels (112). Additionally, SM in the Air Force and Navy have an increased cumulative sun exposure while serving on ships and vessels, compared to Army and Marines.

Melanoma incidence rates significantly increased for the entire DOD from 2002-2008 to 2009-2015, though lung cancer incidence rates showed no significant increase. While the incidence rates of melanoma increased over the course of time, this could be a result from the sun exposure obtained from previous UV encounters. Studies have shown, melanoma related to chronic UV exposure is more likely to be diagnosed later in life (113). When melanoma incidence rates were further evaluated from 2002 to 2016, and

stratified by branch of service, only the Army had statistically significance increase over time (linear trend p-value = 0.0009) (Figure 1). The Gaussian kernel trend shows the DOD and Air Force both had incidence rates increasing up until 2011-2012, then a downward trend towards 2015 (Figures 2-3). Considering the latency with sun exposure and the development of diagnosable melanoma, further research is necessary to understand why the rates for both DOD and Air Force peaked around 2011-2012 and have since declined (Figure 4). We recommend continuing to monitor melanoma incidence rates in the U.S. military in order to determine if this trend continues and incidence rates continue to decrease.

A limitation to this study is we have no demographic data for individuals serving in the U.S. military. We were unable to evaluate age-adjusted rates and accurately compare those to the general population. Additionally, we were unable to evaluate the incidence rates based on sex or race.

Conclusion

From 2005 through 2014, melanoma was the most frequent cancer diagnosis in the Active-Duty population (92). This study supports these findings related to melanoma, though shows a favorable downward trend in incidence rates. Soldiers across the entire DOD still need to be diligent protecting themselves from caustic UV rays, including having adequate sunscreen access, sufficient emphasis on sun protections, and prioritizing preventative care. While smoking rates in the Army have risen compared to the general population, lung cancer incidence was not significantly associated with any branch of service. This could be attributed to policies implemented by Veteran Affairs

and Office of the Surgeon General for smoking cessation and educating on the harmful effects of smokeless tobacco.

Table 3.1 Cancer Incidence Rates & 95% Cis for the US Military by Branch of Service, Years 2002-2015. Ages 18-65, per 100,000 Person-years

Branch	Melanoma	Lung Cancer	Population	Melanoma (95% CI)	Lung Cancer (95% CI)
Army	437	76	7228536	6.05 (5.45, 6.64)	1.05 (0.83, 1.27)
Navy	337	53	474035	7.10 (6.02, 8.08)	1.11 (0.73, 1.51)
Marines	121	16	2633295	4.6 (3.59, 5.60)	0.61 (0.30, 0.92)
Air Force	468	42	4732632	9.89 (8.70, 11.08)	0.89 (0.61, 1.17)
DoD	1363	189	19341495	7.05 (6.45, 7.64)	0.98 (0.83, 1.12)

Table 3.2 Incidence Rate of Melanoma Among U.S. Active-duty Military by Service Branch. 2002-2015, Ages 18-65, per 100,000 Person-years

Branch	Count	Rate	IRR	(95% CI)	P-value
Marines	121	4.6	REF		
Air Force	468	9.89	2.16	(1.73, 2.69)	<.0001
Navy	337	7.1	1.55	(1.23, 1.95)	<.0001
Army	437	6.05	1.32	(1.05, 1.64)	<.0076

Table 3.3 Rates of Lung Cancer Among U.S. Active-duty Military by Service Branch. 2002-2015, Ages 18-65, per 100,000 Person-years

Branch	Count	Rate	IRR	(95% CI)	P-value
Marines	16	.061	REF		
Navy	53	1.11	1.84	(1.00, 3.37)	0.049
Army	76	1.05	1.73	(0.96, 3.11)	0.067
Air Force	42	0.89	1.46	(.078, 2.73)	0.235

Scale pearson value/DF = 1.18

Table 3.4 Incidence Rates of Melanoma and Lung Cancer Among U.S. Active-duty Military by Years Studied. 2002-2015, Ages 18-64, per 100,000 Person-years

Cancer Site	Years	Count	Rate	IRR	(95% CI)
Melanoma	2002-2008	626	6.45	REF	
	2009-2015	737	7.65	1.18	(1.03, 1.36)
Lung	2002-2008	94	0.97	REF	
	2009-2015		0.99	1.02	(0.77, 1.35)

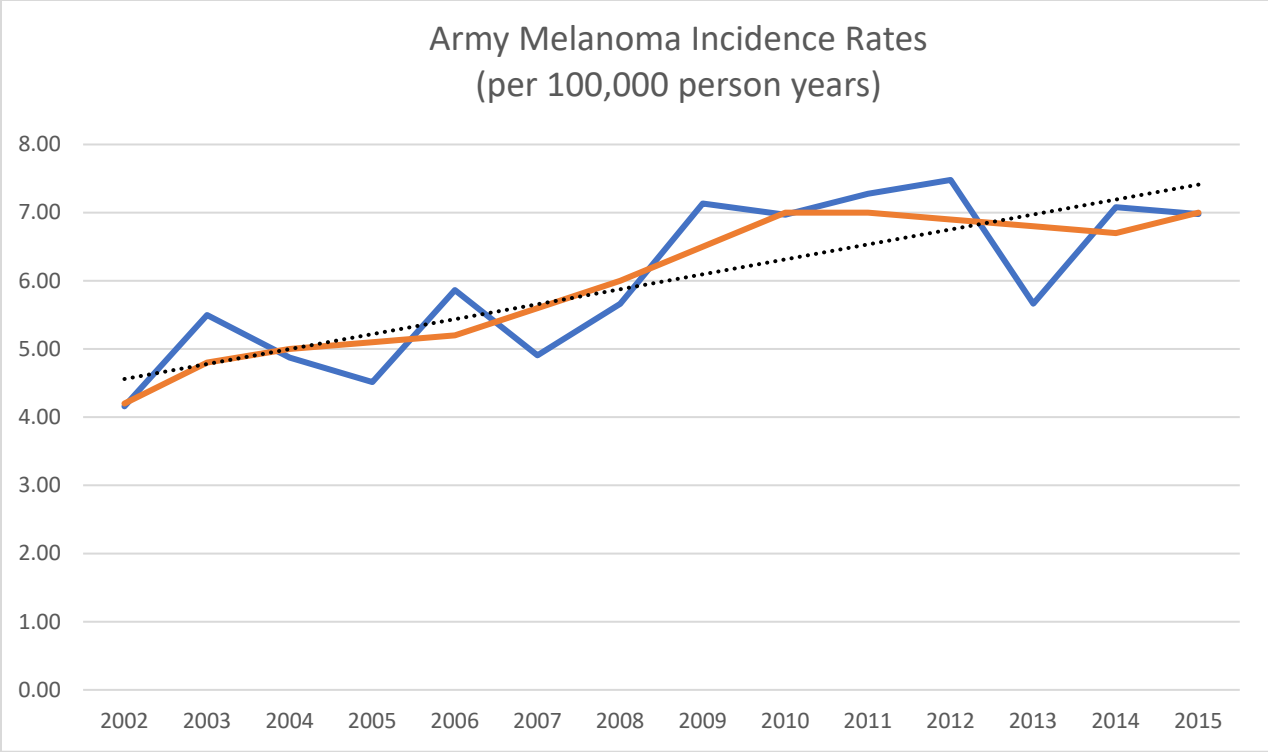

Figure 3.1 Figure Title

Legend: BLUE – Crude Rates; ORANGE – Kernel Smoothing; BLACK – Linear Trend

Linear trend analysis $R^2 = 0.614$; p-value 0.0009; PE: 0.213 (0.106, 0.319)

Shapiro-Wilk p 0.1339 (rates are normally distributed)

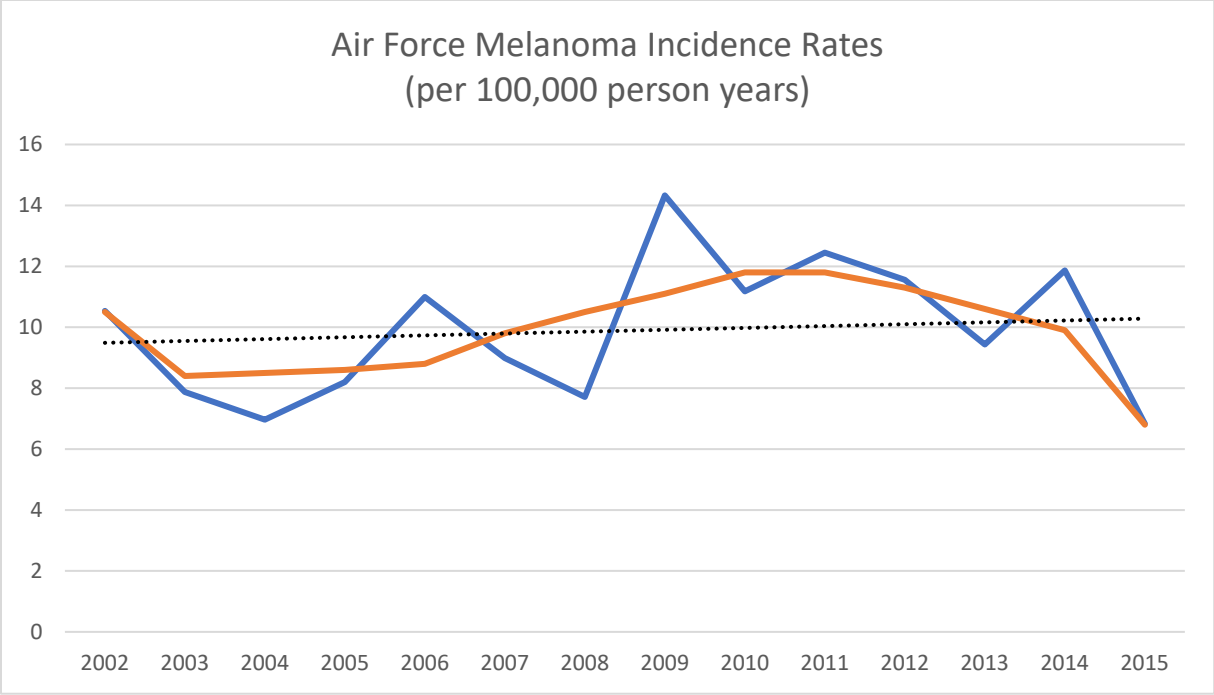

Figure 3.2 Figure Title

Legend: BLUE - Crude Rates; ORANGE - Kernel Smoothing; BLACK – Linear Trend

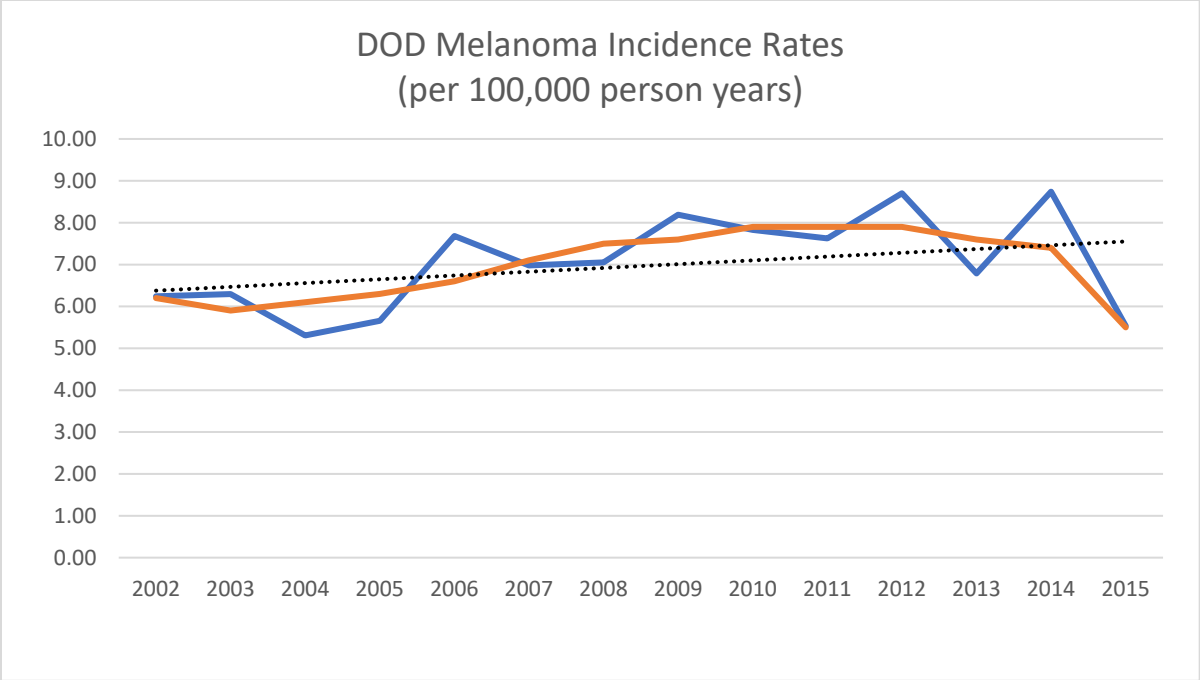

Figure 3.3 Figure Title

Legend: BLUE - Crude Rates; ORANGE - Kernel Smoothing; BLACK - Linear Trend

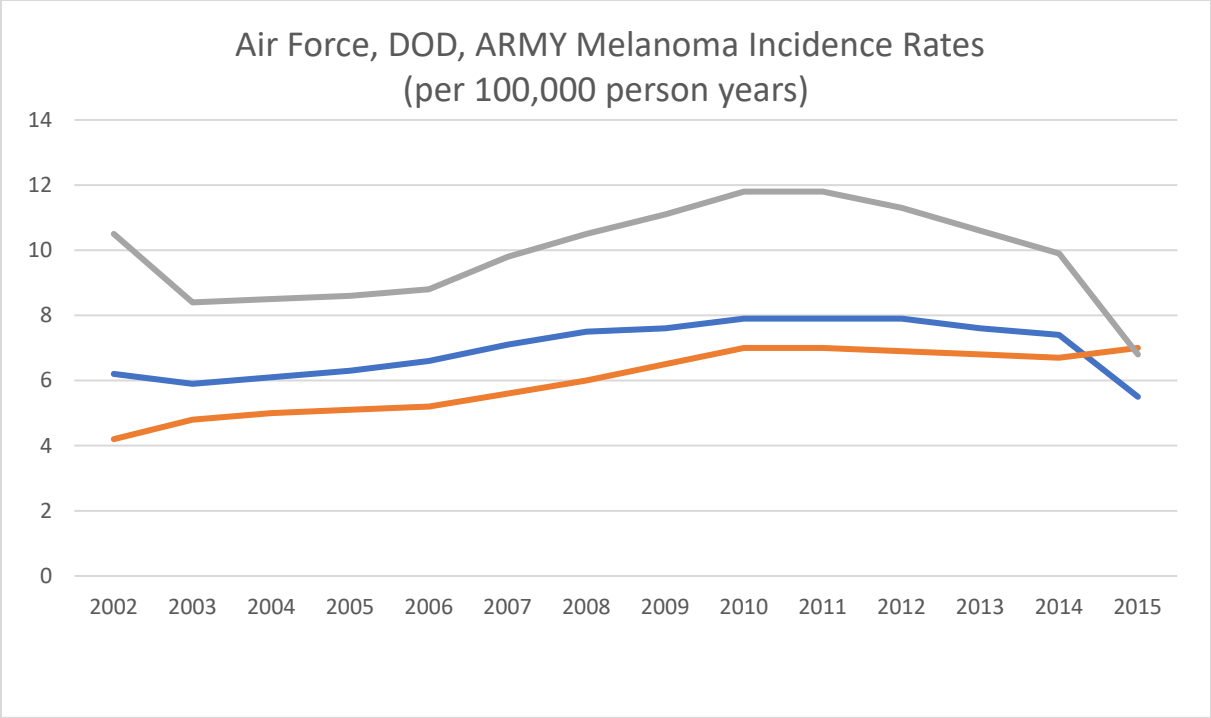

Figure 3.4 Figure Title

Legend: GRAY - AF; BLUE - DOD; ORANGE - ARMY

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