Racial Differences in Prostate Cancer Risk Remain Among US Servicemen With Equal Access To Care

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Racial Differences in Prostate Cancer Risk Remain Among US Servicemen With Equal Access to Care

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BACKGROUND. Prostate cancer is the most common cancer among US men, however, the etiology remains unclear. Yet, one consistency is that black non-Hispanic men are at increased risk for prostate cancer compared to white, non-Hispanic men. The goal of this study was to assess relations between demographic and other potential prostate cancer risk factors in the context of the US military healthcare system, which provides equal access to all US servicemen.
METHODS. Military healthcare and demographic data were used to describe risk factors for prostate cancer in the US military from September 1993 to September 2003. Cox's proportional hazards regression was employed to model the time to prostate cancer hospitalization.
RESULTS. Four hundred eight first prostate cancer hospitalizations were identified among 2,761,559 servicemen. The adjusted rate per 100,000 persons rose from 1.41 to 3.62 for white non-Hispanic men and 1.43 to 6.08 for black non-Hispanic men by the end of the study. The increasing incidence over time for combined race/ethnic groups was similar to trends reported in the Surveillance, Epidemiology, and End Results Program for the US civilian population. No association was observed between occupation and prostate cancer hospitalization. However, black non-Hispanic men were at increased risk compared with white non-Hispanic men (hazard ratio = 2.72, 95% confidence interval: 2.12, 3.49).
CONCLUSIONS. No association was observed between occupation and prostate cancer hospitalization. In this relatively young cohort, black non-Hispanic race/ethnicity was found to be predictive of prostate cancer, and this association existed regardless of access to care and socioeconomic status. *Prostate* © 2009 Wiley-Liss, Inc.

KEY WORDS: **epidemiology; military personnel; occupational exposure; prostatic neoplasms**

Abbreviations: ACTUR, Automated Central Tumor Registry; BASD, Basic Active Service Date; CI, confidence interval; DoD, Department of Defense; HCSR, Health Care Service Record; HR, hazard ratio; ICD-9-CM, *International Classification of Diseases*, Ninth Revision, Clinical Modification; PSA, prostate-specific antigen; SEER, Surveillance, Epidemiology, and End Results Program of the National Cancer Institute; SIDR, Standard Inpatient Data Record; US, United States.

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INTRODUCTION

The US military affords an opportunity to study prostate cancer risk in a relatively homogenous and younger population in comparison to the general US population. In the military, there is generally equal access to healthcare, including PSA screening, and therefore more likely to occur than in the general population. Therefore, undiagnosed prostate cancer is less likely to occur in a military control group than might occur in a civilian control group. While trends in the military may be more dramatic than the overall US population due to better access to care and more frequent PSA screening (introduced in 1987–1988) [1], this represents a large, fairly homogeneous cohort, with well-documented occupational codes. The primary objective of this report is to describe the prostate cancer risk in a younger and healthier subset of the US population with equal access to healthcare by investigating military service member data from September 1993 to September 2003 for demographic and other potential risk factors for prostate cancer hospitalization. The secondary objective was to compare yearly prostate cancer hospitalization incidence trends with those of the US population.

MATERIALS AND METHODS

Study Population

The population for this study consisted of all active-duty men, 18 years or older, serving in the US military from September 1, 1993 to September 1, 2003, with at least 6 months of active-duty service. Exclusions included men who were on active duty for <6 months, those who were diagnosed with prostate cancer prior to September 1, 1993, had a prostate cancer diagnosis that could not be validated, had <1 month of follow-up time, or had missing data. Prostate cancer cases were identified using *International Classification of Diseases*, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic coding (ICD-9-CM code 185) in electronically maintained Department of Defense (DoD) hospitalization records. Patients diagnosed with an incident case of prostate cancer between September 1, 1993 and September 1, 2003, with at least 6 months active-duty service prior to diagnosis were defined as cases. Service members diagnosed with prostate cancer prior to the study period (DoD data were first available in 1988) or diagnosed while not on active duty and those with missing data were removed from analyses.

The Defense Manpower Data Center supplied demographic and military data which included date of birth, Basic Active Service Date (BASD), occupation, date of separation from active-duty status, race/ethnicity, pay grade, highest educational grade received, marital status, and service branch. Dynamic variables, such as age and marital status, were specified according to their status at the time of entry into the study period, either September 1, 1993, or BASD, whichever was later.

The primary objective of this study was to identify demographic and occupational risk factors associated with prostate cancer. Hospitalized cases were utilized because they represent the best source to minimize bias associated with the use of electronic medical data. Prostate cancer cases diagnosed in the outpatient setting are difficult to confirm and are dependent upon the patient to seek medical care, therefore healthcare-seeking behavior may bias outpatient diagnoses. Conversely, hospitalized cases were able to be confirmed, and the decision to hospitalize a prostate cancer patient is made by a medical provider, thus has the potential to reduce bias associated with healthcare-seeking behavior of the patient. To identify prostate cancer cases, hospitalization data were obtained from the Standard Inpatient Data Record (SIDR) and the Health Care Service Record (HCSR). SIDR and HCSR are computerized databases of standardized discharge diagnoses for hospitalizations within the Military Health System and for hospitalizations billed to the DoD by private facilities. SIDR contains records with up to eight ICD-9-CM discharge diagnoses and eight procedure codes for each inpatient visit at a DoD medical treatment facility worldwide. HCSR contains records with up to nine ICD-9-CM discharge diagnoses and six procedure codes for each encounter at a civilian provider that was subsidized by the DoD. Information from the patient's first encounter of prostate cancer in either SIDR or HCSR was merged with demographic and military data at the time of entry into the study and at the time of diagnosis.

Validation of Cases

Cases were validated using either procedure codes, pathology reports, or the DoD Automated Central Tumor Registry (ACTUR). A case with an ICD-9-CM code of 185 and an accompanying procedure code of 60.5 (radical prostatectomy) or 57.71 (radical cystectomy), or pathology report indicative of prostate cancer, or registry in the ACTUR for prostate cancer was considered valid.

Statistical Analysis

Descriptive analyses of the population by prostate cancer status included univariate analyses to assess significant associations between prostate cancer status and age, education, marital status, race/ethnicity (white non-Hispanic, black non-Hispanic, and all others, including Hispanics), military pay grade,

service branch, and occupation. Regression diagnostics, including pairwise correlations and the variance inflation factors, were used to examine collinearity among variables. An exploratory regression analysis was completed to identify significant associations and possible confounding, while simultaneously adjusting for all other variables in the model. Regression diagnostics were performed to check modeling assumptions.

Cox's proportional hazards regression was used to model the time to prostate cancer diagnosis. An age-based timescale was used with age 18 as the baseline age and time measured in months elapsed since age 18 [2,3]. Data were left-censored to account for delayed entry into the study period (measured as months elapsed since age 18 until entry into the study), and right-censored to account for attrition from active-duty service or no diagnosis of prostate cancer by the end of the study period. For cases, time until diagnosis was measured as the months elapsed since age 18 until receiving a prostate cancer diagnosis. For non-cases, time was measured as months elapsed from age 18 until the end of the study period or attrition from active-duty status, whichever occurred first.

Annual age- and race-adjusted rates, as well as annual age-adjusted, race-specific rates for newly diagnosed prostate cancer hospitalizations were calculated by the direct method using a weighted average of the annual study population from 1993 to 2003 as the standard population. The annual study populations included all study members whose follow-up time overlapped any part of the year of interest, where years were measured from September 1 through August 31. For example, the 1994 study population included all study members whose follow-up time overlapped any part of September 1, 1993 through August 31, 1994. Age-adjustments were based on ages as of the beginning (September 1) of each year. Observed rates were compared for consistency with rates reported by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute for the same period among men aged 20–54 [4]. The age range of 20–54 years was chosen as the most comparable to that of the US military. Data management and statistical analyses were performed using SAS software version 9.1.3 (SAS Institute, Inc., Cary, NC). This research has been conducted in compliance with all applicable federal regulations governing the protection of human subjects in research (Protocol NHRC.2004.0012).

RESULTS

There were 3,032,125 men on active-duty rosters in the US military from September 1, 1993 to September 1, 2003. Exclusions resulted in a study population of 2,761,559, of which 408 were identified with a prostate cancer hospitalization, with the majority (88.5%) of cases occurring in men <50 years of age. Adjusted rates per 100,000 persons rose from 1.41 to 3.62 during the study period for white non-Hispanic men. For black non-Hispanic men, rates rose from 1.43 in 1993 to 12.04 in 2001, but then decreased to 6.08 by study conclusion (2003). Rates for all US servicemen rose from 1.45 in 1993 to 4.19 in 2002, but then decreased to 3.72 by study conclusion (Table I). Annual age- and race-adjusted

TABLE I. Prostate Cancer Rates Among Active-Duty US Servicemen, September 1993 to September 2003

	White, non-Hispanic			Black, non-Hispanic			Total[b]		
Years[a]	Cases	Rate[c]	95% CI	Cases	Rate[c]	95% CI	Cases	Rate[d]	95% CI
1994	15	1.41	0.69, 2.12	1	1.43	0, 4.22	19	1.45	0.61, 2.29
1995	21	1.98	1.13, 2.82	3	1.55	0, 3.39	26	1.81	0.85, 2.77
1996	21	2.02	1.15, 2.88	4	3.42	0, 6.91	27	2.04	1.00, 3.08
1997	25	2.39	1.45, 3.32	8	4.69	1.09, 8.30	33	2.52	1.34, 3.70
1998	31	2.89	1.87, 3.91	14	8.03	3.85, 12.48	46	3.47	2.06, 4.88
1999	35	3.15	2.10, 4.20	7	4.13	0.89, 7.36	45	3.37	1.96, 4.78
2000	30	2.88	1.84, 3.92	12	6.14	2.63, 9.66	47	3.46	2.01, 4.91
2001	30	2.82	1.80, 3.85	20	12.04	6.48, 17.59	53	3.84	2.29, 5.39
2002	31	3.07	1.98, 4.17	19	9.99	5.35, 14.63	57	4.19	2.56, 5.82
2003	38	3.62	2.46, 4.78	12	6.08	2.54, 9.61	55	3.72	2.09, 5.35

CI, confidence interval.
[a]Years were measured from September 1 through August 31. For example, the 1994 study population included all study members whose follow-up time overlapped any part of September 1, 1993 through August 31, 1994.
[b]Includes White, non-Hispanic, Black non-Hispanic, and Other (Other category not shown separately due to small number of cases).
[c]Adjusted for age at beginning (September 1) of year.
[d]Adjusted for age at beginning (September 1) of year, and race/ethnicity.

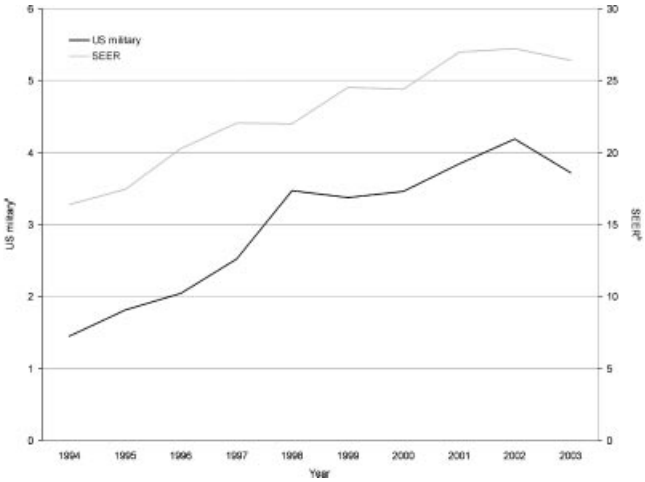

Fig. 1. Comparison of prostate cancer rates, active-duty US servicemen and Surveillance, Epidemiology, and End Results (SEER) Program, 1994–2003. [a]Age- and race/ethnicity-adjusted incidence rates of prostate cancer among US military men (number of cases/100,000). [b]SEER age-adjusted incidence rates of prostate cancer among men ages 20–54, all races (number of cases/100,000).

rates were also compared with SEER age-adjusted rates for all men aged 20–54 years. The military rates were approximately 6–11 times lower than SEER rates, depending upon the year of comparison, but comparable in temporal trend (Fig. 1). The mean ages at diagnosis for white non-Hispanic men, black non-Hispanic men, and Other men were 49.3, 46.5, and 48.6 years, respectively (data not shown). Table II presents the demographic and occupational characteristics of active-duty US military men with a validated prostate cancer hospitalization compared with all active-duty US military men who served during the same period and met study inclusion criteria. US servicemen hospitalized for prostate cancer were proportionately more likely to be older, of black non-Hispanic race/ethnicity, married, more educated, in the Air Force, Army, or Coast Guard, officers, and employed in an electronic equipment repair or healthcare occupation in comparison with US military men from the same time period without a prostate cancer hospitalization. All proportional differences observed were statistically significant (two-sided $P < 0.001$) (Table II).

In multivariable modeling we found that black non-Hispanic men were at increased risk for prostate cancer hospitalization compared with white non-Hispanic men (hazard ratio = 2.72, 95% confidence interval (CI): 2.12, 3.49). No other demographic nor service-related factors were statistically significantly associated with prostate cancer hospitalizations (Table III). The cumulative adjusted hazard of prostate cancer diagnosis as a function of age and race/ethnicity, illustrates that black non-Hispanic men have a significantly greater cumulative hazard of prostate cancer hospitalization compared with men of other race/ethnicities of the same age (Fig. 2).

DISCUSSION

This study used electronically recorded hospitalizations, demographic, and military data to describe demographic and occupational risks for prostate cancer hospitalization among US military men who were serving on active duty between September 1, 1993 and September 1, 2003. Among the goals was to identify demographic and other potential risk factors for prostate cancer hospitalization over a 10-year period in a relatively young and homogenous group. We observed a modest increase in prostate cancer incidence from 1993 to 2003, which is similar in trend to the increases exhibited in the SEER data. Although we observed relatively low incidence rates in this study (1.45–4.19 per 100,000 personnel), which were approximately 6–11 times lower than the SEER rates, depending upon the year, caution must be exercised in comparing these rates to the US general population. Individuals in this study were relatively younger, of better health, and with overall unrestricted access to healthcare services. Additionally, rates computed from DoD hospitalizations alone are not comparable to mortality estimates presented by the National Center for Health Statistics or incidence estimates from the SEER Program of the National Cancer Institute. SEER rates are calculated from data obtained from hospitals, private laboratories, radiotherapy units, nursing homes, and other health service units, for a US population-based sample [5]. These differences in case ascertainment make comparisons between rates observed from hospitalization data to SEER rates difficult. To further illustrate these differences, the Defense Medical Epidemiology Database (DMED) [6] was used to obtain unadjusted rates for prostate cancer outpatient diagnoses for the period 1998–2007. Using DMED, the unadjusted outpatient diagnosis rate for prostate cancer was 15 per 100,000. Although the outpatient prostate cancer diagnosis rates align better with those from the SEER program, hospitalization data were used in this study for the reasons previously described.

In this study, the only statistically significant risk factor for prostate cancer hospitalization was black non-Hispanic race/ethnicity. It has been consistently reported that black non-Hispanic men have the highest incidence and mortality from prostate cancer [7–11], and similar to other studies of this nature, black non-Hispanic men were found to be at higher risk for hospitalization when compared with

TABLE II. Characteristics of Active-Duty US Servicemen and Prostate Cancer Cases, at Entry Into Study, September 1993 to September 2003

Characteristic[a]	US Military[b] (N = 2,761,151)	%	Cases[c] (n = 408)	%
Age at entry into study (years)				
<36	2,464,703	89.3	53	13.0
36–40	183,820	6.7	97	23.8
41–45	81,311	2.9	114	27.9
46–50	25,784	0.9	97	23.8
>50	5,533	0.2	47	11.5
Age at diagnosis (years)				
<36			5	1.2
36–40			18	4.4
41–45			103	25.2
46–50			126	30.9
>50			156	38.2
Race/ethnicity				
White non-Hispanic	1,931,664	70.0	277	67.9
Black non-Hispanic	474,932	17.2	100	24.5
Other	354,555	12.8	31	7.6
Marital status				
Not married	1,705,776	61.8	35	8.6
Married	1,055,375	38.2	373	91.4
Education				
High school graduate or less	2,134,676	77.3	99	24.3
Some college/college graduate	520,919	18.9	121	29.7
Higher education	105,556	3.8	188	46.1
Service branch				
Army	961,756	34.8	154	37.7
Air Force	576,547	20.9	110	27.0
Navy	754,986	27.3	101	24.8
Marines	412,873	15.0	26	6.4
Coast Guard	54,989	2.0	17	4.2
Military pay grade				
Enlisted	2,469,243	89.4	157	38.5
Officer	291,908	10.6	251	61.5
Occupational category				
Combat specialists	780,488	28.3	98	24.0
Electronic equipment repair	218,058	7.9	53	13.0
Healthcare worker	131,444	4.8	69	16.9
Other	1,631,161	59.1	188	46.1

[a]Differences in characteristics between men with and without prostate cancer were tested with the Pearson chi-square test of association. All P values were <0.001.
[b]Active duty for at least 6 months during September 1, 1993 to September 1, 2003.
[c]Cases were identified as having an ICD-9-CM, *International Classification of Diseases*, Ninth Edition, Clinical Modification, code of 185 in their electronic medical record from September 1, 1993 to September 1, 2003. Cases that had an accompanying procedure code of 60.5 (radical prostatectomy) or 57.71 (radical cystectomy), or a pathology report consistent with prostate cancer, or registry in the Automated Central Tumor Registry for prostate cancer, were considered valid.

white non-Hispanic men [8,9,11]. This study is novel in that the majority of cases occurred in US service members <50 years of age and is important in that men serving in the military are of similar health status, have equal access to healthcare, including prostate cancer screening programs, and income, thus minimizing bias that may have been unaccounted for in similar civilian studies. Because free access to healthcare is considered to be one of the most important benefits for all US servicemen, it is also extremely unlikely that biases would exist by differential use of the military healthcare system by race/ethnicity among active-duty servicemen. Although it has been reported that there are differences in use of traditional healthcare

TABLE III. Adjusted Cox Proportional Hazard Model for Prostate Cancer Diagnosis, Active-Duty US Servicemen, September 1993 to September 2003

Characteristic	US Military (N = 2,761,151)	Cases (n = 408)	HR[a]	95% CI	*P*-value
Total	2,761,151	408			
Race/ethnicity					<0.0001
White non-Hispanic	1,931,664	277	1.00		
Black non-Hispanic	474,932	100	2.72	2.12, 3.49	
Other	354,555	31	0.91	0.62, 1.33	
Marital status					0.18
Not married	1,705,776	35	1.00		
Married	1,055,375	373	1.27	0.89, 1.82	
Education					0.93
High school graduate or less	2,134,676	99	1.00		
Some college/college graduate	520,919	121	1.05	0.77, 1.44	
Higher education	105,556	88	1.08	0.72, 1.64	
Service branch					0.82
Army	961,756	154	1.00		
Navy	754,986	101	0.92	0.71, 1.19	
Air Force	576,547	110	0.90	0.69, 1.16	
Marines	412,873	26	0.98	0.64, 1.50	
Coast Guard	54,989	17	1.19	0.71, 1.99	
Military pay grade					0.61
Enlisted	2,469,243	157	1.00		
Officer	291,908	251	1.09	0.78, 1.52	
Occupational category					0.10
Combat specialists	780,488	98	1.00		
Electronic equipment repair	218,058	53	1.34	0.96, 1.88	
Healthcare workers	131,444	69	0.96	0.70, 1.33	
Other	1,631,161	188	0.90	0.70, 1.16	

CI, confidence interval; HR, hazard ratio.
[a]Hazard ratios were adjusted for all characteristics listed in this table.

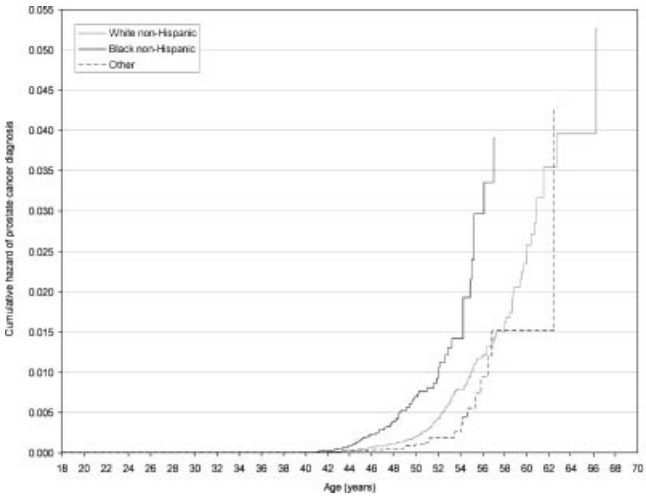

Fig. 2. Cumulative adjusted hazard of prostate cancer hospitalization as a function of age at entry, by race/ethnicity, active-duty US servicemen, 1993–2003.

based upon race/ethnicity [12,13], if this bias were to exist, the effect would most likely underestimate the racial/ethnic differences observed. It is also possible that an increased risk in hospitalization among blacks was due to a medical screening bias, but it is unlikely given that military healthcare providers are required to follow US Preventive Services Task Force recommendations for such screening and all preventive medicine issues [14] during periodic health assessments [15]. However, because general record reviews and periodic health assessments are required annually for all members on active duty, it is possible that prostate cancer cases may be diagnosed earlier in the active military population than in some civilian populations.

Finding differences in prostate cancer risk by race/ethnicity among a relatively young population of men with equal access to healthcare is novel. Exactly why younger black non-Hispanic men are at increased risk for prostate cancer in comparison to younger white non-Hispanic men remains unanswered. However, a

recent study found an association between prostate cancer at an early age in black non-Hispanic men and a specific genetic polymorphism [16]. Additionally, a review of SEER cancer statistics shows that disparity in age-adjusted incidence between white and black men decreases modestly with increasing age [17], indicating perhaps that this increased risk is linked more to intrinsic versus extrinsic factors that occur at younger ages. Although we did not observe a decrease in rates when examining the cumulative hazard, this may be an artifact associated with the relatively young age of this study group.

Few studies have investigated the relationship between occupation and prostate cancer. One case–control study of 416 incident prostate cancer cases and 429 controls aged 65–79 years observed that white non-Hispanic men employed in production, transportation, or material-handling occupations were at significantly increased risk of prostate cancer, while black non-Hispanic men who had served in the military were at significantly decreased risk [18]. Among exposures that may be considered occupational in nature, cadmium has been studied as a possible carcinogen for human prostate cancer [19,20]. Cadmium is commonly used as a component in nickel–cadmium batteries, soldering alloys, pigments, and as a stabilizer for plastic and may be used among those working in the equipment repair specialties—a military occupational category that includes specialists in the maintenance and repair of various types of electronic and allied equipment, including radio, radar, navigation, weapons, and computers. Although men in this study specializing in electronic equipment repair or healthcare were proportionately more likely to have prostate cancer, this association was not statistically significant after adjustment in the Cox proportional hazards modeling.

This study is unique in that it is the first study to report risk factors for hospitalization in a large sample of relatively young men and in a healthcare system that provides uniform access to care. This study is also the first to report the incidence of prostate cancer in a cohort of US servicemen. Although this study used data from a large, diverse population, it is not representative of the US male population, which is typically less physically active and older. Since prostate cancer is predominantly diagnosed in men over the age of 65 and typically after attrition or retirement from the military, the number of cases identified in this active-duty population was relatively low; however, the overall population was sufficiently large to provide robust estimates. Furthermore, using Cox proportional hazards modeling allowed the use of all available information, which included data from individuals who began active-duty service after the start of the study or who withdrew prior to the end of the study.

Although objective data are less biased than self-reported data, there are still a number of limitations to using medical hospitalization data. First, they are based on a professional coder's interpretation of a diagnosis recorded in a patient's medical record. Misreporting or non-reporting in the medical record by a physician will be reflected in the coding and further mistakes can occur during the coding process. To minimize the effect of these and other possible coding errors, early efforts focused on the validation of cases using either procedure codes, pathology reports, or the ACTUR. Second, the electronic medical records used in this study contain historical data only for active-duty service members receiving care within the Military Health System or billed to the DoD by private facilities. Conditions diagnosed prior to military service, although likely rare, would be missed. Similarly, conditions diagnosed in hospitalizations not sponsored by the DoD could not be identified using these records. We expect such events to also be rare, since military medical care is free and was readily available to the men in this cohort. Further, restriction to hospitalization diagnoses allowed for more specificity in prostate cancer diagnosis, though there may have been some cases missed through the outpatient setting. Nevertheless, in an effort to reduce the effect of these limitations, the study population was restricted to active-duty service members with at least 6 months of service, and it is unlikely that an individual with preexisting prostate cancer would be eligible to serve. Finally, it was not possible to rule out bias caused by social, political, or environmental factors, such as smoking, diet, and exercise due to the limited nature of the data used for this study.

CONCLUSIONS

In summary, this study has examined risk factors and incidence estimates for prostate cancer hospitalization in a military population. Similar to other research studies, we found black non-Hispanic race/ethnicity to be a predictor of prostate cancer. Our findings, however, illustrate that this association exists at a relatively young age, and regardless of access to care and/or socioeconomic status. This supports other findings that, in comparison with men of other races and ethnicities, black non-Hispanic men may share yet-to-be explored differences that are important in prostate cancer etiology.

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Prostate cancer is the most common cancer among US men, yet the etiology of this disease remains unclear. This study used military health care and demographic data to describe the incidence of prostate cancer in the US military from September 1993 to September 2003, and to identify demographic and occupational risk factors for prostate cancer hospitalization. Annual rates of first-encounter prostate cancer were adjusted for age and race. Cox's proportional hazards regression was employed to model the time to prostate cancer diagnosis. This study supports previous observations of an increased prostate cancer risk among black non-Hispanic men. Further, this study illustrated that this association exists regardless of access to care or socioeconomic status, which has not previously been reported in the literature. This finding suggests that black, non-Hispanic men may share yet-to-be-explored differences that may be important in prostate cancer etiology.

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