ORIGINAL RESEARCH

Chronic Kidney Disease and Military Service in US Adults, 1999-2018

Scott Reule, MD, MS[a,b]; Kristine Ensrud, MD, MPH[a]; Jaeden Danko[a]; Donal Sexton, MB[c]; Laura Siegle, RN[a]; Areef Ishani, MD, MS[a]; Craig Solid, PhD[d]; Robert Foley, MB[a]

Background: Although the management of chronic kidney disease (CKD) has changed considerably in US adults, it is uncertain whether the burden, risk factors, and temporal trends of CKD are similar regarding prior military service.
Methods: This observational study used National Health and Nutrition Examination Survey data to quantify the association between CKD and military service in a generalizable sample of US adults between 1999 and 2018.
Results: The respective frequencies (standard error [SE]) of CKD and military service were 15.2% (0.3) and 11.5% (0.3). The proportion (SE) with CKD was significantly higher among those with prior MS vs the overall population (22.7% [0.7] vs 15.2% [0.3]; $P < .001$). Within the military service population, the proportion (SE) with CKD differed by era: 1999 to 2002, 18.9% (1.1); 2003 to 2006, 24.9% (1.5); 2007 to 2010, 22.3% (1.5); 2011 to 2014, 24.3% (1.7); and 2015 to 2018, 24.0% (1.8) ($P = .02$). Following adjustment for age, sex, and race and ethnicity, prior military service was associated ($P < .05$) with a higher likelihood of CKD (adjusted odds ratio, 1.17; 95% CI 1.06-1.28). Adjusted associations of CKD differed in groups with and without military service for the 40 to 64 years age group, ≥ 65 years age group, female sex, and family poverty ($P < .05$ vs variable-specific reference category).
Conclusions: Military service is associated with a higher likelihood of CKD in US adults. Risk factors for CKD differed among many subgroups both with and without military service history. Future research is needed to better determine whether military service constitutes a unique risk factor for CKD.

Author affiliations can be found at the end of this article.
Correspondence: Scott Reule (reul0011@gmail.com)

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Chronic kidney disease (CKD) affects nearly 37 million people (11%) in the US and is a leading cause of death and morbidity. Due to their older age and higher prevalence of comorbid conditions, the prevalence of CKD among veterans is approximately 34% higher than in the general population and the fourth most common chronic disease diagnosed among US veterans.[1,2] US veterans and those with prior military service (MS) may be at a particularly high risk for CKD and associated health care outcomes including increased hospitalization and death. The observed excess burden of CKD is not mirrored in the general population, and it is unclear whether prior MS confers a unique risk profile for CKD.

Current estimates of CKD burden among veterans or those with prior MS are widely variable and have been limited by unique regions, specific exposure profiles, or to single health care systems. As such, there remains a paucity of data examining CKD burden more broadly. We performed a study in the adult population of the US to quantify associations with the extent of CKD, enumerate temporal trends of CKD among those with prior MS, describe risk within subgroups, and compare heterogeneity of risk factors for CKD by MS.

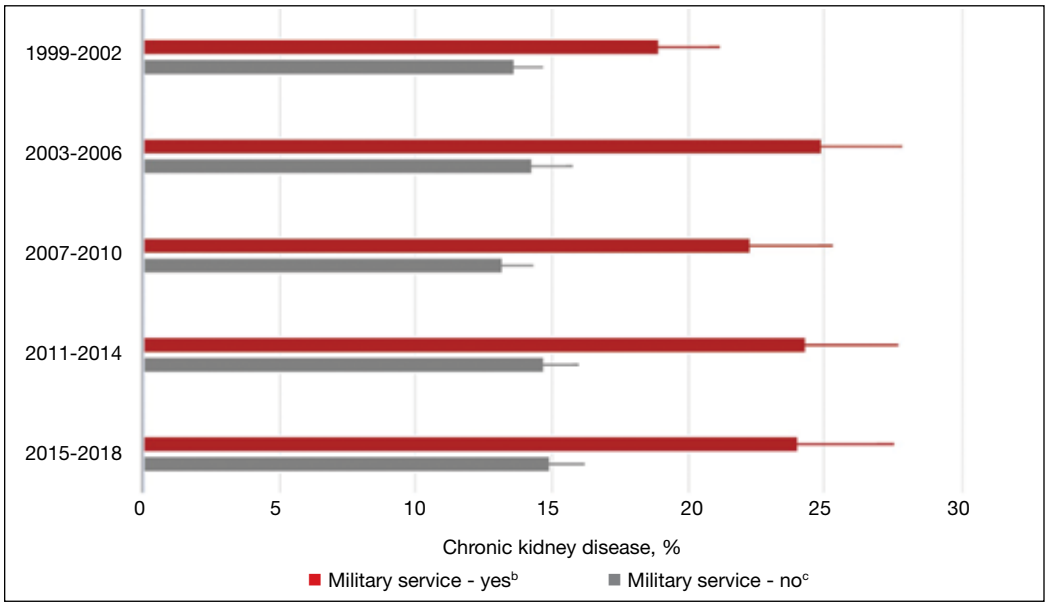
METHODS

The National Health and Nutrition Examination Survey (NHANES) is a suite of nationally representative, cross-sectional surveys of the noninstitutionalized US population. It is conducted by the National Center for Health Statistics and uses a stratified, clustered probability design, with surveys carried out without interruption, collated, and made accessible to the public at 2-year intervals.[3] The survey consists of a questionnaire, physical examination, and laboratory data.

The inclusion criteria for our study were age ≥ 20 years along with serum creatinine and urinary albumin-creatinine measurements. The following definitions were used for the study:

- CKD: Estimated glomerular filtration rate < 60 mL/min/1.73 m^2 calibrated to isotope dilution mass spectrometry (IDMS).
- Traceable: Creatinine-based CKD Epidemiology Collaboration formula or urinary albumin-creatine ratio ≥ 30 mg/g.
- MS: Positive response to the questions "Did you ever serve in the Armed Forces of the United States?" (1999 to 2010) or "Have you ever served on active duty in the US Armed Forces, military Reserves, or National Guard?" (2011 to 2018).

FIGURE 1 Chronic Kidney Disease by Military Service Era[a]



[a]Error bars are 95% CIs; χ^2 test used to compare proportions.
[b]$P = .02$.
[c]$P = .10$.

- Diabetes: Self-reported history, medication for diabetes, or glycated hemoglobin ≥ 7%.
- Hypertension: Blood pressure ≥ 140/90 or ≥ 130/40 mm Hg in the presence of diabetes, medication for hypertension, cardiovascular disease, or CKD, myocardial infarction, cardiac failure, or cerebrovascular disease by self-report.[2,3]

Analysis

Primary sampling unit, stratum, and weight variables were employed throughout to generate parameter estimates that are generalizable to the US population.[4,5] The χ^2 test and logistic regression, respectively, were employed for comparison of proportions and estimation of odds ratios. R Version 4.1.2 was employed for data analysis.

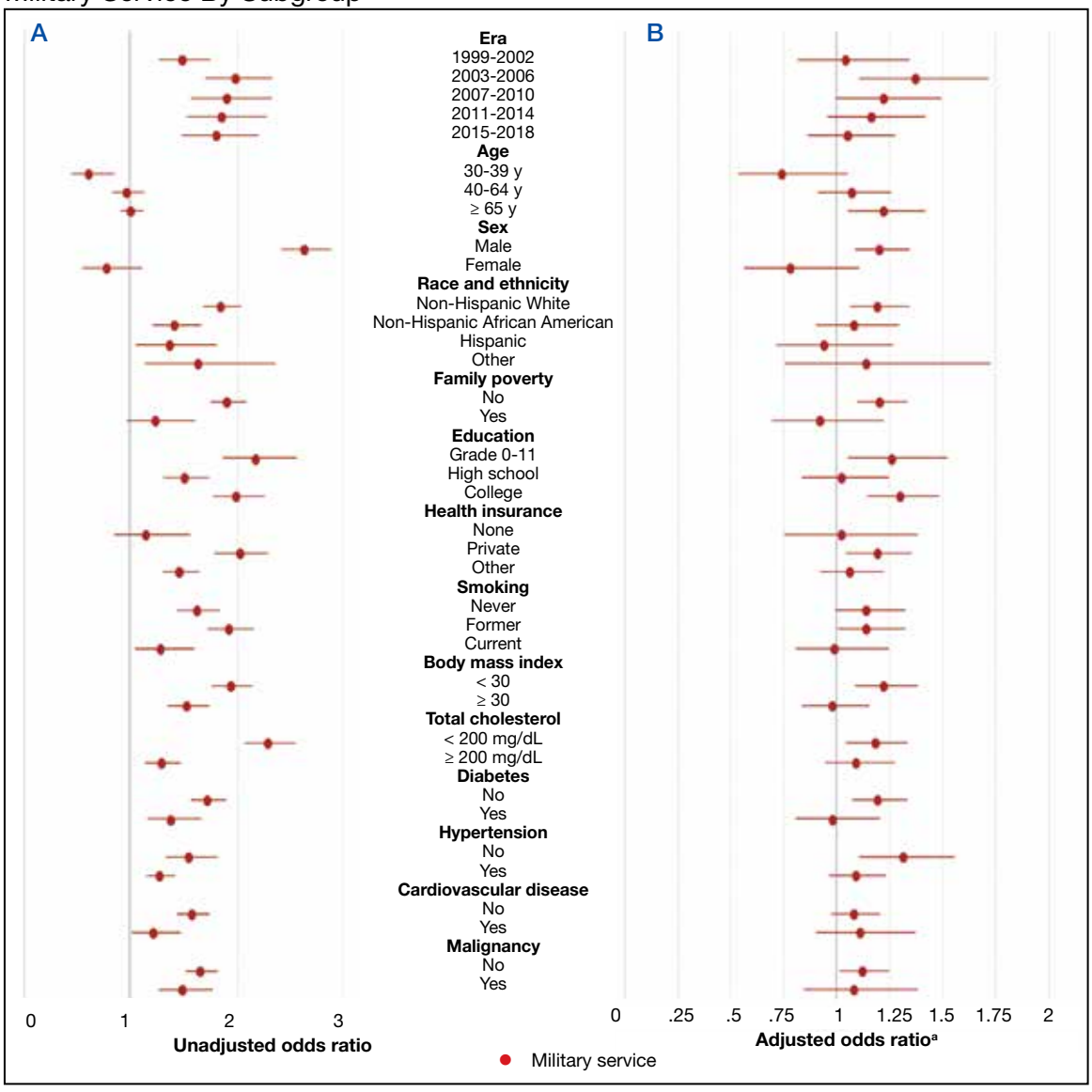
RESULTS

In the overall sample, the frequencies (95% standard error [SE]) of CKD and prior MS were 15.2% (0.3) and 11.5% (0.3) (Table 1). The proportion (SE) with CKD was significantly higher among those with prior MS vs the overall population: 22.7% (0.7) vs 15.2% (0.3) ($P < .001$). Significant associations with CKD were observed ($P < .05$) by age, sex, race and ethnicity, family poverty, school education, health insurance, smoking, body mass index, diabetes, hypertension, cardiovascular disease, and malignancy. Within those reporting prior MS, the proportion (SE) with CKD differed by era: 1999 to 2002, 18.9% (1.1); 2003 to 2006, 24.9% (1.5); 2007 to 2010, 22.3% (1.5); 2011 to 2014, 24.3% (1.7); and 2015 to 2018, 24.0% (1.8) ($P = .02$) (Figure 1).

Without covariate adjustment, prior MS was significantly associated with an increased risk of CKD (unadjusted odds ratio [OR], 1.78; 95% CI, 1.64-1.93; $P < .05$) (Table 2). Prior MS was significantly associated with CKD in the following subgroups: 2003 to 2006, 2011 to 2014, 2015 to 2018, age groups of 40 to 64 years and ≥ 65 years, male sex, non-Hispanic White and Hispanic ethnicity, school education of grade 0 to 11, and private or other health insurance. Additional comorbidities strongly associated with CKD included hypertension (OR, 6.37; 95% CI, 5.37-7.55), diabetes (OR, 4.16; 95% CI, 3.45-5.03), and cardiovascular disease (OR, 4.20; 95% CI, 3.57-4.95).

In the population reporting prior MS, the unadjusted OR of CKD vs 1999 to 2002 was greater for all other examined eras; with the greatest likelihood observed

FIGURE 2 Binary Logistic Regression Odds Ratios for Chronic Kidney Disease and Military Service By Subgroup



[a]Adjusted for age, sex, and race and ethnicity.

for the 2003 to 2006 era. Unadjusted ORs of CKD differed in groups with and without prior MS (*P* value for interaction < .05) for 2003 to 2006, those aged 40 to 64 years and ≥ 65 years, female sex, non-Hispanic African American and Hispanic race and ethnicity, family poverty, high school education, private health insurance, any smoking history, diabetes, hypertension, and cardiovascular disease (Figure 2A).

Following adjustment for age, sex, and race and ethnicity, MS was associated with a 17% higher likelihood of CKD (adjusted odds ratio [AOR], 1.17; 95% CI, 1.06-1.28; *P* < .01) (Table 3). Prior MS was significantly associated (*P* < .05) with CKD in the subgroups: age groups 40 to 64 years and ≥ 65 years, non-Hispanic African American, and body mass index ≥ 30. Among those with prior MS, comorbidities strongly associated with CKD in adjusted models included hypertension (AOR, 3.86; 95% CI, 3.18-4.69), diabetes (AOR, 3.05; 95% CI, 2.44-3.82), and cardiovascular disease

TABLE 1 US Adults With CKD and MS in the National Health and Nutrition Examination Survey[a]

Characteristics	US adults no MS, % (SE)	MS, % (SE)	CKD, % (SE)	MS + CKD, % (SE)
All		11.5 (0.3)	15.2 (0.3)	22.7 (0.7)
Era				
1999-2002	18.0 (0.6)	14.7 (0.6)	14.4 (0.5)[b]	18.9 (1.1)[c]
2003-2006	19.1 (0.8)	13.5 (0.6)	15.7 (0.7)	24.9 (1.5)
2007-2010	19.9 (0.7)	11.2 (0.6)	14.2 (0.4)	22.3 (1.5)
2011-2014	21.1 (0.8)	9.8 (0.5)	15.7 (0.6)	24.3 (1.7)
2015-2018	21.9 (0.7)	9.2 (0.6)	15.8 (0.6)	24.0 (1.8)
Age group				
20-39 y	37.5 (0.5)	4.7 (0.2)	6.3 (0.2)	3.9 (0.7)
40-64 y	44.7 (0.4)	11.6 (0.4)	11.6 (0.3)	11.3 (0.7)
≥ 65 y	17.8 (0.3)	25.9 (0.5)	42.9 (0.6)	42.9 (1.2)
Sex				
Male	48.2 (0.2)	22.2 (0.5)	13.3 (0.3)	23.5 (0.7)
Female	51.8 (0.2)	1.6 (0.1)	16.9 (0.4)	13.6 (2.1)
Race and ethnicity				
Non-Hispanic White	68.5 (1.0)	13.6 (0.3)	15.4 (0.3)	23.3 (0.7)[c]
Non-Hispanic African American	10.8 (0.6)	10.9 (0.4)	17.6 (0.4)	22.4 (1.4)
Hispanic	13.9 (0.8)	4.3 (0.3)	12.8 (0.4)	16.5 (1.9)
Other	6.9 (0.3)	6.8 (0.6)	14.1 (0.7)	20.5 (2.8)
Family poverty				
No	85.8 (0.4)	12.6 (0.3)	14.5 (0.3)	22.6 (0.7)[b]
Yes	14.2 (0.4)	5.6 (0.3)	18.0 (0.6)	21.1 (2.1)
Education				
Grade 0-11	17.3 (0.4)	7.7 (0.4)	21.8 (0.5)	36.0 (1.8)
High school	23.9 (0.4)	12.2 (0.5)	16.6 (0.5)	22.1 (1.1)
College	58.8 (0.7)	12.4 (0.3)	12.6 (0.3)	20.6 (0.9)
Health insurance				
None	17.9 (0.4)	5.8 (0.3)	10.0 (0.4)	11.2 (1.5)
Private	49.1 (0.7)	10.8 (0.3)	15.0 (0.4)	24.4 (1.0)
Other	33.0 (0.6)	15.7 (0.5)	18.3 (0.4)	23.3 (1.0)
Smoking				
Never	53.8 (0.5)	7.5 (0.2)	14.2 (0.3)	20.4 (0.9)
Former	28.5 (0.3)	18.8 (0.5)	18.5 (0.5)	27.4 (1.0)
Current	17.7 (0.4)	12.1 (0.5)	12.9 (0.4)	15.5 (1.3)
Body mass index				
< 30	64.5 (0.4)	11.1 (0.3)[d]	13.2 (0.3)	21.2 (0.8)[c]
≥ 30	35.5 (0.4)	12.2 (0.4)	18.0 (0.4)	23.9 (1.1)
Total cholesterol				
< 200, mg/dL	56.4 (0.4)	12.0 (0.3)[d]	14.6 (0.3)[b]	25.6 (0.9)
≥ 200, mg/dL	43.6 (0.4)	11.0 (0.3)	14.8 (0.4)	17.8 (0.9)
Diabetes				
No	89.8 (0.2)	10.8 (0.3)	11.9 (0.3)	17.8 (0.7)
Yes	10.2 (0.2)	18.0 (0.6)	40.9 (0.8)	47.3 (2.1)
Hypertension				
No	65.7 (0.4)	8.9 (0.3)	5.8 (0.2)	8.4 (0.6)
Yes	34.3 (0.4)	17.0 (0.4)	32.3 (0.5)	36.7 (1.2)
Cardiovascular disease				
No	93.3 (0.2)	10.5 (0.3)	13.1 (0.2)	18.3 (0.6)
Yes	6.7 (0.2)	25.7 (0.9)	44.9 (1.0)	48.4 (2.0)
Malignancy				
No	90.7 (0.2)	10.4 (0.3)	13.7 (0.3)	19.8 (0.7)
Yes	9.3 (0.2)	22.4 (0.7)	29.3 (0.8)	35.9 (1.6)

Abbreviations: CKD; chronic kidney disease; MS, military service.
[a]χ^2 test used to compare proportions; $P < .001$ unless otherwise indicated.
[b]Not significant; Missing values, weighted percent (SE): race and ethnicity, 7.2 (0.3); family poverty, 0.1 (0.0); smoking, 1.2 (0.1); body mass index, 0.7 (0.0); total cholesterol, 0.4 (0.0); and diabetes, 3.1 (0.1).
[c]$P < .05$.
[d]$P < .01$.

(AOR, 2.51; 95% CI, 2.09-3.01). In the population with prior MS, the adjusted likelihood of CKD vs 1999 to 2002 was similar across all eras. Adjusted associations of CKD differed in groups with and without prior MS for age groups 40 to 64 years and ≥ 65 years, female sex, and family poverty ($P < .05$) (Figure 2B).

DISCUSSION

We observed that prior MS was associated with CKD, all eras were associated with CKD in the subgroup with MS, and risk factors for CKD differed among many subgroups both with and without MS history, a finding that remained present in adjusted models. In addition, the finding of CKD was relatively common among those with prior MS (approximately 15%) and was most strongly associated with increasing age and comorbidities frequently associated with CKD.

Although many studies have demonstrated associations of US veteran status with various comorbidities, including hypertension, obesity, and diabetes, these studies often are limited to those both qualifying and receiving care within the US Department of Veterans Affairs (VA) health care system.[6-9] The crude proportion of individuals reporting multiple chronic conditions, which included hypertension, diabetes, and weak or failing kidneys, was 49.7% for US veterans compared with 24.1% for nonveterans.[2] Large-scale, nationally representative cohorts for use in this context have been limited by the heterogeneity of definitions of CKD applied with limited timeframes yielding variable estimates.[1,10] Moreover, few studies have examined the clinical epidemiology of CKD more broadly in the US among those with prior MS. For example, a PubMed search on March 3, 2022, with the terms "epidemiology", "military service", and "chronic kidney disease" produced only 9 citations, one of which examined trends among a non-US cohort and quantifying disease burden another among adolescents.

Whether or not prior MS confers a unique risk profile for CKD is unknown. While our findings of an increased CKD burden among those reporting MS may partially reflect observed increases in baseline comorbidities, the observed excess CKD among those with MS remained across multiple categories even after adjustment for baseline demography. As several studies have demonstrated, enlistment into MS may select for a more diverse population; however those enlisted personnel may be of lower socioeconomic status and possibly at higher risk of CKD.[11,12] Our findings of important differences in baseline determinants of health mirror this. The proportion of MS respondents with CKD vs CKD alone reporting a high school education or lower was higher (36.0% vs 21.8%) as well as among those with a history of family poverty (21.1% vs 18.0%).

Limitations

Our study has several limitations, including its cross-sectional study design, a lack of longitudinal data within individuals, and exclusion of institutionalized individuals. Limitations notwithstanding this study has several important aspects. As prior MS is highly variable, we were limited in our inability to stratify by service type or length of service. For example, veteran status is conferred to a "Reservist or member of the National Guard called to federal active duty or disabled from a disease or injury incurred or aggravated in line of duty or while in training status also qualify as a veteran" (13 CFR § 125.11). For the purposes of our study, prior MS would include all active-duty service (veterans) as well as reservists and National Guard members who have not been activated. This may be more representative of the overall effect of MS, as limitation to those receiving care within the VA may select for an older, more multimorbid population of patients, limiting generalizability.

In addition, more detailed information regarding service-related exposures and other service-connected conditions would allow for a more granular risk assessment by service type, era, and military conflict. Our finding of excess CKD burden among those with prior MS compared with the overall population is timely given the recent passage of the Promise to Address Comprehensive Toxics (PACT) Act. Exposure to and injury from Agent Orange—a known

TABLE 2 Unadjusted Odds Ratios for Chronic Kidney Disease in US Adults[a]

Criteria	Adult US population	Military service subgroup
Military service		
No	1 (reference)	—
Yes	1.78 (1.64-1.93)	—
Era		
1999-2002	1 (reference)	1 (reference)
2003-2006	1.11 (0.97-1.27)[b]	1.42 (1.14-1.77)[c,d]
2007-2010	0.98 (0.89-1.09)[b]	1.23 (0.98-1.54)[b]
2011-2014	1.10 (0.99-1.23)[b]	1.38 (1.09-1.73)[d]
2015-2018	1.11 (0.99-1.25)[b]	1.35 (1.06-1.72)[e]
Age group		
20-39 y	1 (reference)	1 (reference)
40-64 y	1.96 (1.78-2.16)	3.09 (2.17-4.39)[c]
≥ 65 y	11.17 (10.19-12.24)	18.32 (12.95-25.91)[c]
Sex		
Male	1 (reference)	1 (reference)
Female	1.32 (1.24-1.41)	0.51 (0.36-0.73)[c]
Race and ethnicity		
Non-Hispanic White	1 (reference)	1 (reference)
Non-Hispanic African American	1.17 (1.10-1.25)	0.95 (0.80-1.13)[b,c]
Hispanic	0.81 (0.74-0.87)	0.65 (0.50-0.85)[c,d]
Other	0.90 (0.79-1.02)[b]	0.85 (0.60-1.19)[b]
Family poverty		
No	1 (reference)	1 (reference)
Yes	1.30 (1.19-1.42)	0.92 (0.70-1.19)[b,c]
School education		
Grade 0-11	1 (reference)	1 (reference)
High school	0.71 (0.66-0.77)	0.50 (0.40-0.63)[c]
College	0.52 (0.48-0.56)	0.46 (0.39-0.55)
Health insurance		
None	1 (reference)	1 (reference)
Private	1.58 (1.43-1.75)	2.57 (1.90-3.47)[c]
Other	2.01 (1.83-2.21)	2.42 (1.77-3.30)
Smoking		
Never	1 (reference)	1 (reference)
Former	1.38 (1.29-1.47)	1.47 (1.28-1.69)[c]
Current	0.90 (0.82-0.98)[e]	0.71 (0.57-0.89)[c,d]
Body mass index		
< 30	1 (reference)	1 (reference)
≥ 30	1.44 (1.35-1.53)	1.17 (1.01-1.34)[c,e]
Total cholesterol		
< 200 mg/dL	1 (reference)	1 (reference)
≥ 200 mg/dL	1.01 (0.95-1.09)[b]	0.63 (0.54-0.73)[c]
Diabetes		
No	1 (reference)	1 (reference)
Yes	5.11 (4.74-5.51)	4.16 (3.45-5.03)[c]
Hypertension		
No	1 (reference)	1 (reference)
Yes	7.71 (7.15-8.31)	6.37 (5.37-7.55)[c]
Cardiovascular disease		
No	1 (reference)	1 (reference)
Yes	5.43 (4.98-5.92)	4.20 (3.57-4.95)[c]
Malignancy		
No	1 (reference)	1 (reference)
Yes	2.61 (2.39-2.84)	2.27 (1.93-2.65)

[a]Binary logistic regression used to estimate odds ratios, without adjustment; $P < .001$ unless otherwise indicated.
[b]Not significant.
[c]$P < .05$ for interaction with military service.
[d]$P < .01$.
[e]$P < .05$.

TABLE 3 Adjusted Odds Ratios for Chronic Kidney Disease in US Adults[a]

Criteria	Adult US population	Military service subgroup
Military service		
No	1 (reference)	—
Yes	1.17 (1.06-1.28)[b]	—
Era		
1999-2002	1 (reference)	1 (reference)
2003-2006	1.05 (0.92-1.18)[c]	1.22 (0.94-1.57)[c]
2007-2010	0.90 (0.81-1.00)[d]	0.99 (0.78-1.25)[c]
2011-2014	0.99 (0.89-1.11)[c]	0.99 (0.76-1.28)[c]
2015-2018	0.93 (0.82-1.06)[c]	0.91 (0.69-1.19)[c]
Age group		
20-39 y	1 (reference)	1 (reference)
40-64 y	2.02 (1.83-2.22)	3.11 (2.19-4.42)[e]
≥ 65 y	11.85 (10.80-13.00)	19.42 (13.67-27.59)[e]
Sex		
Male	1 (reference)	1 (reference)
Female	1.26 (1.18-1.35)	0.93 (0.65-1.33)[c,e]
Race and ethnicity		
Non-Hispanic White	1 (reference)	1 (reference)
Non-Hispanic African American	1.59 (1.49-1.70)	1.67 (1.36-2.05)
Hispanic	1.25 (1.15-1.36)	1.05 (0.76-1.46)[c]
Other	1.20 (1.04-1.39)[d]	1.27 (0.83-1.92)[c]
Family poverty		
No	1 (reference)	1 (reference)
Yes	1.60 (1.46-1.76)	1.24 (0.91-1.68)[c,e]
School education		
Grade 0-11	1 (reference)	1 (reference)
High school	0.80 (0.74-0.87)	0.66 (0.52-0.82)
College	0.64 (0.59-0.70)	0.65 (0.54-0.78)
Health insurance		
None	1 (reference)	1 (reference)
Private	0.84 (0.76-0.94)[b]	0.92 (0.67-1.25)[c]
Other	1.01 (0.91-1.12)[c]	0.97 (0.70-1.33)[C]
Smoking		
Never	1 (reference)	1 (reference)
Former	1.11 (1.03-1.20)[b]	1.08 (0.93-1.27)[c]
Current	1.22 (1.11-1.35)	1.01 (0.78-1.30)[c]
Body mass index		
< 30	1 (reference)	1 (reference)
≥ 30	1.47 (1.37-1.58)	1.36 (1.15-1.60)
Total cholesterol		
< 200 mg/dL	1 (reference)	1 (reference)
≥ 200 mg/dL	0.90 (0.84-0.97)[b]	0.79 (0.67-0.94)[b]
Diabetes		
No	1 (reference)	1 (reference)
Yes	3.46 (3.16-3.79)	3.05 (2.44-3.82)
Hypertension		
No	1 (reference)	1 (reference)
Yes	4.78 (4.39-5.21)	3.86 (3.18-4.69)
Cardiovascular disease		
No	1 (reference)	1 (reference)
Yes	2.69 (2.45-2.95)	2.51 (2.09-3.01)
Malignancy		
No	1 (reference)	1 (reference)
Yes	1.26 (1.14-1.39)	1.18 (0.98-1.43)[c]

[a]Binary logistic regression used to estimate odds ratios for with adjustment for age, sex, and race and ethnicity; $P < .001$ unless otherwise indicated.
[b]$P < .01$.
[c]Not significant.
[d]$P < .05$.
[e]$P < .05$ for interaction with military service.

service-connected exposure associated with incident hypertension and diabetes—may be a significant contributor to CKD that may have a significant era effect. In addition, water contamination among those stationed in Camp Lejeune in North Carolina has notable genitourinary associations. Finally, burn pit exposures in more recent military conflicts may also have important associations with chronic disease, possibly including CKD. While similar attempts at the creation of large-scale US veteran cohorts have been limited by incomplete capture of creatinine, the large proportion of missing race data, and limited inclusion of additional markers of kidney disease, our use of a well-described, nationally representative survey along with standardized capture of clinical and laboratory elements mitigate the use of various societal or other codified definitions.[1]

CONCLUSIONS

Prior MS is associated with an increased risk of CKD overall and across several important subgroups. This finding was observed in various unadjusted and adjusted models and may constitute a unique risk profile of risk.

Author affiliations

[a]Minneapolis Veterans Affairs Medical Center, Minnesota
[b]University of Minnesota Medical School, Minneapolis
[c]Trinity College Dublin School of Medicine, Ireland
[d]Solid Research Group, LLC, St. Paul, Minnesota

Author disclosures

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Ethics and consent

This research was conducted using publicly available, deidentified National Health and Nutrition Examination Survey data.

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