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Research Article

Sleep Disturbance, Diabetes, and Cardiovascular Disease in Postmenopausal Veteran Women

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Abstract

Purpose of the Study: To compare the prevalence and cardiometabolic health impact of sleep disturbance among postmenopausal Veteran and non-Veteran participants in the Women's Health Initiative (WHI).

Design and Methods: The prevalence of five categories of sleep disturbance—medication/alcohol use for sleep; risk for insomnia; risk for sleep disordered breathing [SDB]; risk for comorbid insomnia and SDB (insomnia + SDB); and aberrant sleep duration [SLD]—was compared in 3,707 Veterans and 141,354 non-Veterans using logistic or multinomial regression. Cox proportional hazards models were used to evaluate the association of sleep disturbance and incident cardiovascular disease (CVD) and Type 2 diabetes in Veterans and non-Veterans.

Results: Women Veterans were more likely to have high risk for insomnia + SDB relative to non-Veteran participants. However, prevalence of other forms of sleep disturbance was similar across groups. Baseline sleep disturbance was not differentially associated with cardiometabolic health outcomes in Veteran versus non-Veteran women. Risks for SDB and insomnia + SDB were both linked to heightened risk of CVD and diabetes; SLD was consistently linked with greater risk of CVD and diabetes in non-Veterans but less strongly and consistently in Veterans.

Implications: Efforts to identify and treat sleep disturbances in postmenopausal women are needed and may positively contribute to the attenuation of cardiometabolic morbidity risk. Increased awareness of women Veterans' vulnerability to postmenopausal insomnia + SDB may be particularly important for health care providers who treat this population.

Key Words: Women, Veterans, Sleep, Postmenopausal Health

Cardiometabolic morbidity and mortality are salient health concerns among postmenopausal women, including Veterans, whose risk may be further impacted by their high prevalence of smoking (Hoerster et al., 2012), posttraumatic stress disorder (PTSD; Hughes, Jouldjian, Washington, Alessi, & Martin, 2013), and sleep disturbances (Hoerster et al., 2012). Given the fact that there are nearly 1 million women Veterans (WVs) aged 50 or older currently living in the United States (U.S. Department of Veterans Affairs, 2014), it is surprising that no extant research has examined the association of sleep and postmenopausal cardiometabolic morbidity in this population. The present work is a first step toward addressing this literature gap.

Cardiometabolic Risk and Morbidity Among Military Populations

Several prior studies document a higher prevalence of cardiometabolic risk factors, including tobacco use, obesity, and metabolic abnormalities in both military and Veteran populations relative to non-Veterans (Hoerster et al., 2012; McKinney, McIntire, Carmody, & Joseph, 1997; Weitlauf et al., 2015). Moreover, gender-specific research on this topic suggests a 42% prevalence of hypertension, a 39% prevalence of hyperlipidemia, and an 18% prevalence of diabetes among postmenopausal WVs aged 55–64 years (c.f., Vimalananda et al., 2013). Military occupational hazards, including war zone deployment, combat, or military sexual trauma, may also impact cardiometabolic morbidity via sleep disruption (Frayne et al., 1999; Frayne, Skinner, Sullivan, & Freund, 2003). Specifically, PTSD symptoms, including hyperarousal and the experience of nightmares, may increase nocturnal awakenings or arousals from sleep, resulting in sleep fragmentation. This may both generally decrease sleep quality and ultimately compound risk for chronic illness. Specifically, PTSD may contribute to increased risk of metabolic syndrome in Veterans, including women, via neuro-endocrine-immune abnormalities (Heppner et al., 2009). Sleep fragmentation may also increase upper airway collapsibility and contribute to the increased risk of SDB in individuals with PTSD (Krakow, Ulibarri, Moore, & McIver, 2015). These potential mechanisms underscore the importance of research that addresses modifiable risk factors that may improve cardiometabolic health in individuals exposed to military occupational hazards (c.f., Rosenbaum et al., 2015).

Figure 1 presents a conceptual model of three pathways from military service to cardiometabolic risk, morbidity and mortality based, in part, on Seeman and Crimmins' biopsychosocial model of aging (2001).

Military Service and Sleep Disturbance Risk

Military personnel and Veterans have four times greater risk for sleep disturbance than the general population (Armed Forces Health Surveillance Center, 2010a, 2010b; Faestel, Littell, Vitiello, Forsberg, & Littman, 2013). Although most prior research has focused on men, early work describes an alarming prevalence of insomnia complaints among military (Armed Forces, 2010a) and Veteran women (Fung et al., 2013; Hughes et al., 2013). High rates of aberrant sleep duration (SLD) have also been documented in Veterans (Swinkels, Ulmer, Beckham, Buse, & Registry, 2013). This is cause for concern as aberrant SLD, particularly very short sleep, is strongly associated with increased cardiometabolic risk and has been linked with smoking, obesity, hypertension, diabetes, and mental health conditions (e.g., PTSD and depression), all of which are prevalent among Veterans, including women (Stranges et al., 2008). The prevalence of use of sleep aids (e.g., medication or alcohol for sleep) among Veterans has not been fully investigated; however, a sharp uptick in use of sleep aids among postmenopausal women in general is well documented (Kaneita et al., 2007; Quera-Salva, Orluc, Goldenberg, & Guilleminault, 1991).

Military occupational risks, such as prolonged deployment or duty assignments that severely restrict sleep, are a primary precursor to circadian rhythm dysfunction, sleep fragmentation, sleep dissatisfaction, insomnia, or aberrant SLD in military and Veteran populations (Figure 1; Dijk & Czeisler, 1994; Faestel et al., 2013). High rates of sleep-interfering health risk behaviors, for example, tobacco, alcohol (Hoerster et al., 2012; Swinkels et al., 2013), and military-related traumatic exposures and resultant PTSD may also interfere with sleep (Jordan et al., 1991; Lavie, 2001). As mentioned previously, sleep fragmentation is a candidate mechanism for the higher prevalence of sleep disordered breathing (SDB) in individuals with PTSD (Figure 1; Krakow et al., 2015). Taken together, the number of sleep-interfering exposures of Veteran women may increase risk for insomnia, SDB, and their combination: comorbid insomnia + SDB.

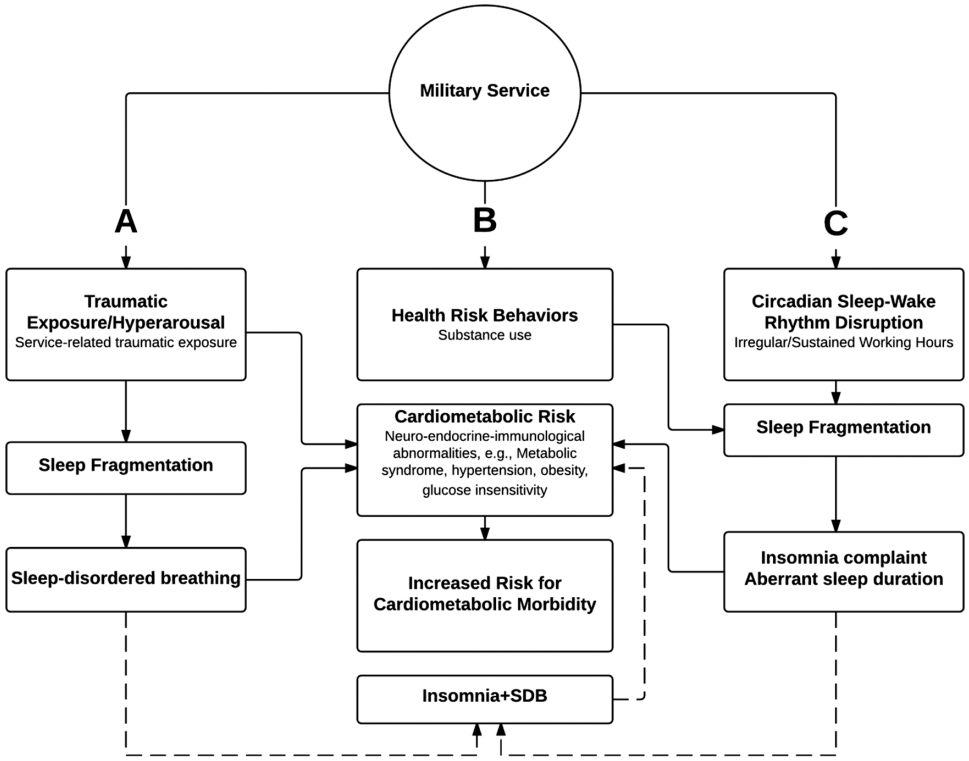

Figure 1. Conceptual framework adapted from biopsychosocial model of healthy aging (Seeman & Crimmins, 2001). We propose three pathways from military service to cardiometabolic morbidity via sleep disturbance in postmenopausal women veterans: (**A**) traumatic exposure/hyperarousal and associated sleep-disordered breathing (SDB); (**B**) health risk behaviors; and (**C**) circadian sleep–wake rhythm disruption and associated insomnia complaint or aberrant sleep duration. The dashed line represents the hypothesized association of comorbid insomnia and SDB on cardiometabolic morbidity.

Sleep Disturbance and Cardiometabolic Risk

Poor sleep associated with insomnia or SDB has been empirically linked to many cardiometabolic consequences including obesity, hypertension, and impaired glucose metabolism (Grandner, Sands-Lincoln, Pak, & Garland, 2013; Knutson, 2012) as well as accelerated morbidity (Figure 1; Cappuccio, Cooper, D'Elia, Strazzullo, & Miller, 2011; Knutson, 2012; Loke, Brown, Kwok, Niruban, & Myint, 2012; Sands et al., 2013; Sands-Lincoln et al., 2013). When SDB and insomnia co-occur—insomnia + SDB—these health risks may be intensified (Fung et al., 2013; Luyster et al., 2014; Ong & Crawford, 2013). Given the heightened prevalence of insomnia, SDB, and health risk behaviors that compound sleep and cardiometabolic health problems, comorbid insomnia + SDB may be a particularly important health risk among postmenopausal WVs.

To address this possibility, the present study will utilize data drawn from the Women's Health Initiative (WHI) to comparatively examine the prevalence and consequences of five categories of sleep disturbance, including use of medication/alcohol for sleep, aberrant SLD, risk for insomnia, risk for SDB, and comorbid insomnia + SDB risk, on the postmenopausal cardiometabolic health among nearly 4,000 postmenopausal WV participants and more than 140,000 non-Veteran participants in the WHI. We hypothesize that WVs will have greater likelihood of all five sleep disturbance categories at baseline relative to their non-Veteran counterparts. We will also examine whether the association of sleep disturbance on incident cardiovascular disease (CVD) and Type 2 diabetes during the 20-year follow-up vary as a function of Veteran status.

Design and Methods

Study Population

The study population was a subset of the 161,808 Veteran and non-Veteran participants from the Clinical Trial (CT) and Observational Study of the WHI, a longitudinal study of postmenopausal health and mortality risks in women aged 50–79 years at enrollment (Anderson et al., 2003; Hays et al., 2003; The Women's Health Initiative Study Group, 1998). The study population of the WHI was recruited nationally between 1993 and 1998 through 40 clinical centers and is representative of the racial/ethnic and geographic diversity of the U.S. women population (Anderson et al., 2003; Hays et al., 2003; The Women's Health Initiative Study Group, 1998). If eligible, participants in the CT could enroll in one or more of the

three trial components, including the Hormone Therapy Trials (estrogen or estrogen + progesterone), the Dietary Modification Trial, or the Calcium/Vitamin D Trial, and were randomized to the intervention or control groups of each (Hays et al., 2003). Institutional Review Boards from all sites approved the study, and all participants provided written informed consent.

Data were collected using self-administered forms, in-person or by phone interviews, and clinical measurements. The WHI follow-up efforts are ongoing; the present work includes data through 2013.

Study Variables

Veteran Status

Participants were self-identified as Veterans if they responded affirmatively to the baseline question, "Have you served in the U.S. armed forces on active duty for a period of 180 days or more." This standard measure of Veteran status has been used in several national surveys, including those conducted by the Centers for Disease Control and Prevention (Hoerster et al., 2012; Koepsell, Reiber, & Simmons, 2002; Lehavot et al., 2014). Those who responded negatively were classified as non-Veterans, whereas those with missing information were excluded.

Self-Reported Sleep Disturbances Encompassed Five Different Baseline Variables

Medication(s) or Alcohol for Sleep (No/Yes)

This was affirmatively defined as baseline self-reported use of medication or alcohol for sleep or verified use of a sedative/hypnotic medication. Use of sedative/hypnotic medications was identified by matching the participant's prescription medications brought in during in-person visits to the Master Drug Data Base (Medi-Span, Indianapolis, IN) which includes a therapeutic hypnotic class code (600000–610000) provided by the American Hospital Formulary Service. Endorsement of medication or alcohol as a sleep aid may suggest a measure of sleep dissatisfaction or complaint not captured by the remaining sleep disturbance measures.

Risk of Insomnia

This was defined based on the Women's Health Initiative Insomnia Rating Scale (WHIIRS) score (Levine, Kaplan, et al., 2003; Levine, Lewis, et al., 2003), a 5-item scale assessing self-reported sleep initiation insomnia (or sleep latency), sleep maintenance insomnia, early morning awakening, and sleep quality. Each item was coded 0 to 4 for frequency or quality resulting in a total score range of 0–20, with higher scores indicating poorer sleep. We defined scores ≥9 as indicating high risk for insomnia and <9 as low risk (Levine, Kaplan, et al., 2003).

High Risk for SDB

This addressed risk factors for sleep apnea adapted from the Berlin Questionnaire (Netzer, Stoohs, Netzer, Clark, & Strohl, 1999), including snoring history, tiredness, and history of high blood pressure or obesity (Mustafa, Erokwu, Ebose, & Strohl, 2005). One point was awarded for each of the following items: (1) self-reported snoring ≥3 times a week; (2) self-reported falling asleep during quiet activities ≥3 times a week; and (3) either hypertension (self-reported physician diagnosis or measured systolic blood pressure [BP] ≥ 140 mm Hg or diastolic BP ≥ 90 mm Hg) or measured obesity (body mass index [BMI] > 30 kg/m^2). Scores ranged from 0 to 3 points, with scores ≥2 defined as high risk for SDB and <2 as low risk.

Comorbid Insomnia and SDB Risk

High risk for insomnia + SDB was assigned to participants who were designated as high risk for both conditions, as defined earlier. Conversely, low risk of insomnia + SDB was assigned to participants with either low risk for both or high risk for only one.

Sleep Duration

SLD was based on self-report and defined as very short (≤5 hours), short (6 hours), average (7–8 hours), and long (≥9 hours; Swinkels et al., 2013). By definition, all categories of SLD outside of average were considered aberrant for this study.

Adjudicated Cardiometabolic Health Outcomes

Cardiovascular Disease

CVD was defined as physician-adjudicated report of one of the following: clinical myocardial infarction (MI), definite silent MI (definite evolving Q wave MI), possible silent MI (possible evolving Q wave MI), definite or possible coronary heart disease (CHD) death, angina, coronary artery bypass graft (CABG), percutaneous transluminal coronary angioplasty, carotid artery disease (CAD), congestive heart failure (CHF), stroke, or peripheral vascular disease (PVD). CVD events were initially identified through annually mailed follow-up contacts and regularly scheduled study-related follow-up medical examinations and were confirmed through local and central adjudication. CVD-related deaths were confirmed via the National Death Index Plus (Curb et al., 2003).

Diabetes

Diabetes was defined as self-reported treatment (pills or insulin injections) for diabetes. A validity study conducted in a subset of the WHI participants suggested that self-report was a reasonably good indicator of diagnosed diabetes when compared with medication inventories and fasting glucose (Margolis et al., 2008), as well as medical records (Jackson et al., 2014).

Additional Variables

Baseline Prevalent Disease

Either diabetes or CVD (i.e., self-reported physician diagnosis of stroke, MI, CHF, angina, CABG, percutaneous transluminal coronary angioplasty, CAD, or PVD) was used to identify participants to be excluded from each of the respective cardiometabolic outcome analyses.

Covariates

Covariates included demographic characteristics such as age, self-reported race/ethnicity, education, and whether living with a partner (married or in a marriage-like relationship); health status indices, including body mass index (BMI); presence of vasomotor symptoms (i.e., hot flashes or night sweats); and health risk behaviors, including smoking status (current, former, or never), and physical activity (MET-hours per week; Ainsworth et al., 1993). Self-reporting napping is a symptom associated with several of our key exposure variables, including insomnia, aberrant SLD and daytime sleepiness due to SDB. To address this confound, self-reported napping was included as a covariate. Assignment to the WHI study arms was also included as a covariate, as was baseline prevalence of depression, based on the Burnam Scale (Burnam, Wells, Leake, & Landsverk, 1988). Consistent with prior WHI work, we used a cutoff of ≥0.06 to identify women with symptoms consistent with depressive disorders (Bertone-Johnson et al., 2011; Spangler et al., 2008).

Data Analysis

We first examined the baseline demographic and health behavior characteristics of the study sample, stratified by Veteran status.

We next examined baseline prevalence of medication or alcohol use for sleep, high risk for insomnia, high risk for SDB, high risk for insomnia + SDB, and aberrant SLD in WV and non-Veteran participants. We further examined whether WVs and non-Veterans differed in sleep disturbance at baseline for all dichotomous variables using generalized linear models with a log link (Poisson distribution) to obtain estimates of the prevalence ratio (PR) and 95% confidence intervals (CIs) using robust standard errors (Zou, 2004). For SLD, which had more than two categories, we employed multinomial logistic regression with average SLD as the reference group. In order to aid in interpretation, we calculated the difference in the probability of being within each category between Veterans and non-Veterans (the marginal effect) along with 95% CIs. Refer to Tables 2–4 for sequential adjustment of covariates in each analysis.

Finally, to estimate the association between each of the sleep disturbance exposures and incident CVD and diabetes, we employed Cox proportional hazards models to obtain estimates of the hazard ratio (HR) and 95% CIs. We included an interaction term between Veteran status and sleep disturbance in order to determine whether associations differed between WVs and non-Veterans. Disease occurrence time was defined as days from enrollment to each of CVD and diabetes, and censoring time for non-events as days from enrollment to the earlier of the date of last follow-up contact or September 20, 2010 for diabetes and September 20, 2013 for CVD. We excluded participants with CVD or diabetes at baseline from their respective models and adjusted for all variables in Adjustment 3 as earlier, excluding depression.

All analyses were conducted in Stata 13.0 (StataCorp, 2013).

Results

A total of 145,061 women had baseline data on Veteran status and at least one measure of sleep disturbance, 3,707 of whom identified as Veterans (2.6%, Table 1, Figure 2). WVs were older (49.8% Veterans 70–79 years old vs 21.7% non-Veterans), more educated (46.9% Veterans at least college graduates vs 39.5% non-Veterans), and more likely to be former or current smokers (54.1% vs 48.2% non-Veterans). WVs were less likely to have vasomotor symptoms (26.0% vs 32.7%).

Prevalence of Sleep Disturbance

At baseline, the unadjusted prevalence of the various sleep disturbances among the 145,061 included women was comparable between WVs and non-Veterans (Tables 2 and 3); medication or alcohol for sleep was 24.7% and 24.6% for WVs and non-Veterans, respectively. Similarly, insomnia risk was 30.5% and 30.8%, SDB risk was 25.1% and 24.9%, and insomnia + SDB risk was 10.3% and 9.5% for WVs and non-Veterans, respectively. SLD was also similar between WVs and non-Veterans; very short SLD was 8.5% and 8.3%, short SLD was 26.2% and 27.5%, and average SLD was and 60.2% and 59.9% for non-Veterans and WVs, respectively. WVs reported significantly higher unadjusted prevalence of long sleep (5.1%) compared with non-Veterans (4.3%).

In fully adjusted analyses, there were no differences between the 3,462 WVs and 132,812 non-Veterans in baseline use of medication or alcohol for sleep (Table 2; PR = 1.00, 95% CI = 0.94, 1.06), high risk for insomnia (PR = 1.00, 95% CI = 0.95, 1.05), or high risk for SDB (PR = 1.02, 95% CI = 0.97, 1.08). Prevalence of high risk for insomnia + SDB in WVs was 1.13 times that of non-Veterans (95% CI = 1.02, 1.24). There were no differences between WVs and non-Veterans in the probabilities for very short or long SLD (Table 3).

Sleep Disturbance and CVD

Among participants who did not have prevalent CVD but did report at least one sleep disturbance at the WHI

Table 1. Characteristics of non-Veteran and Veteran Women in the Women's Health Initiative With At Least One Measure of Sleep Disturbance at Baseline

Total	Non-Veteran		Veteran	
	N[a]	%[a]	*N*[a]	%[a]
	141,354	100.0	3,707	100.0
Age (years)				
<50–59	46,222	32.7	783	21.1
60–69	64,455	45.6	1,077	29.1
70–79	30,677	21.7	1,847	49.8
Race/ethnicity				
American Indian/Alaskan Native	601	0.4	25	0.7
Asian/Pacific Islander	3,978	2.8	45	1.2
Black/African American	12,790	9.0	261	7.0
Hispanic/Latino	5,573	3.9	85	2.3
White	116,373	82.3	3,231	87.2
Other	1,669	1.2	47	1.3
Education				
Less than high school	7,412	5.2	62	1.7
High school diploma/GED	24,148	17.1	376	10.1
Some college or vocational/training school	53,046	37.5	1,516	40.9
College graduate or greater	55,839	39.5	1,739	46.9
Living with a partner				
No	116,640	82.5	2,865	77.3
Yes	24,238	17.1	832	22.4
Smoking status				
Never	71,416	50.5	1,624	43.8
Former	58,731	41.5	1,693	45.7
Current	9,537	6.7	317	8.6
Physical activity				
Inactive (0–1.7 METS/week)	31,212	22.1	778	21.0
Low (>1.7 to <8.4 METS/week)	39,765	28.1	995	26.8
Medium (8.4 to <20 METS/week)	39,254	27.8	1,062	28.6
High (≥20 METS/week)	30,871	21.8	866	23.4
BMI				
Underweight	1,244	0.9	44	1.2
Normal	48,528	34.3	1,243	33.5
Overweight	48,336	34.2	1,319	35.6
Obese	41,948	29.7	1,062	28.6
Vasomotor symptoms[b]				
No	94,329	66.7	2,719	73.3
Yes	46,180	32.7	964	26.0
Depression				
No	122,923	87.0	3,288	88.7
Yes	15,333	10.8	341	9.2
Napping ≥3 times per week				
No	122,237	86.5	3,096	83.5
Yes	18,498	13.1	597	16.1
Cardiovascular disease at baseline				
No	125,241	88.6	3,157	85.2
Yes	13,601	9.6	461	12.4
Diabetes history at baseline				
No	132,807	94.0	3,487	94.1
Yes	8,449	6.0	216	5.8

Table 1. *Continued*

Total	Non-Veteran		Veteran	
	N[a]	%[a]	*N*[a]	%[a]
	141,354	100.0	3,707	100.0
Study assignment				
Observational study	85,319	60.4	2,297	62.0
Clinical Trials[c]				
Estrogen intervention	4,435	3.1	111	3.0
Estrogen control	4,428	3.1	136	3.7
Estrogen + progestin intervention	6,925	4.9	204	5.5
Estrogen + progestin control	6,923	4.9	192	5.2
Dietary modification intervention	13,348	9.4	333	9.0
Dietary modification control	19,976	14.1	434	11.7

Notes: BMI = body mass index; GED = General Educational Development; METS = Metabolic Equivalents.
[a]Numbers may not add to totals and percents to 100 due to missing information.
[b]Defined as hot flashes and night sweats
[c]Women could also be randomized to the calcium and vitamin D intervention or control arms, which overlapped with the other clinical trials and occurred 12–24 months after initial randomization.

baseline, the incidence of CVD was 9.4 per 1,000 person-years of follow-up among 124,716 non-Veterans and 13.1 per 1,000 person-years among the 3,150 WVs. In fully adjusted analyses, there were no differences in the association between sleep disturbance and CVD by Veteran status among the 3,008 Veterans and 119,915 non-Veterans with all covariates (*p* values for interaction: .14 to .94; Table 4). Almost all markers of poor sleep health were associated with incident CVD during the 20-year follow-up among non-Veterans, with mostly positive effects of similar magnitude observed in WVs (Table 4). WVs who reported using medication or alcohol for sleep at baseline were 26% more likely to develop CVD than nonusers (95% CI = 1.03, 1.54) and non-Veterans were 17% more likely (95% CI = 1.13, 1.21). We observed an almost 30% increased risk of CVD for women at high risk for SDB among both WVs (HR = 1.28, 95% CI = 1.05, 1.56) and non-Veterans (HR = 1.29, 95% CI = 1.24, 1.34), as well as for high risk for insomnia + SDB among both WVs (HR = 1.24, 95% CI = 0.94, 1.64) and non-Veterans (HR = 1.27, 95% CI = 1.21, 1.34). Among non-Veterans, there were weak associations between high risk for insomnia and CVD (HR = 1.08, 95% CI = 1.05, 1.12) as well as very short SLD and CVD (HR = 1.15, 95% CI = 1.09, 1.23), whereas no significant associations were detected in WVs.

Sleep Disturbance and Diabetes

Incident diabetes development during follow-up occurred at a rate of 8.7 per 1,000 person-years follow-up for both the 132,077 WVs and 3,475 non-Veterans without prevalent diabetes and with at least one sleep disturbance measure at baseline.

Associations between sleep disturbance and incident diabetes did not vary by Veteran status (*p* values for interaction: .36 to .82; Table 4). Among the 3,312 WVs and 126,721 non-Veterans with all covariates, there were no statistically significant associations between incident diabetes and use of medication or alcohol for sleep or high risk for insomnia (Table 4). There was, however, a 26% and 37% increase in risk of diabetes associated with high risk for SDB in WVs (95% CI = 0.99, 1.59) and non-Veterans (95% CI = 1.32, 1.43). Even larger increases were associated with high risk for insomnia + SDB, with a 49% increase in WVs (95% CI = 1.11, 2.00) and 30% increase in non-Veterans (95% CI = 1.23, 1.37; Table 4). Very short SLD, relative to average SLD, was associated with increased risk of diabetes in non-Veterans (HR = 1.12, 95% CI = 1.05, 1.19), with a nonsignificant trend for an effect in WVs (HR = 1.22, 95% CI = 0.85, 1.75). Among non-Veterans, long SLD relative to average was also positively associated with diabetes (HR = 1.12, 95% CI = 1.03, 1.22).

Discussion

Our study characterized the prevalence of sleep disturbance in 3,707 postmenopausal women Veteran and non-Veteran participants from the WHI, specifically prospectively examining the association of sleep disturbances with incident CVD and diabetes. Results revealed a significantly heightened risk for comorbid insomnia + SDB among Veterans, relative to non-Veterans. However, risk of other forms of sleep disturbance (i.e., medication/alcohol use for sleep, risk for insomnia, risk for SDB, or aberrant SLD) was similar across groups. Moreover, sleep disturbances were not associated with greater risk of cardiometabolic morbidity among WVs compared with non-Veterans; rather, poor sleep health at baseline was associated with increased risk of cardiometabolic morbidity in both groups.

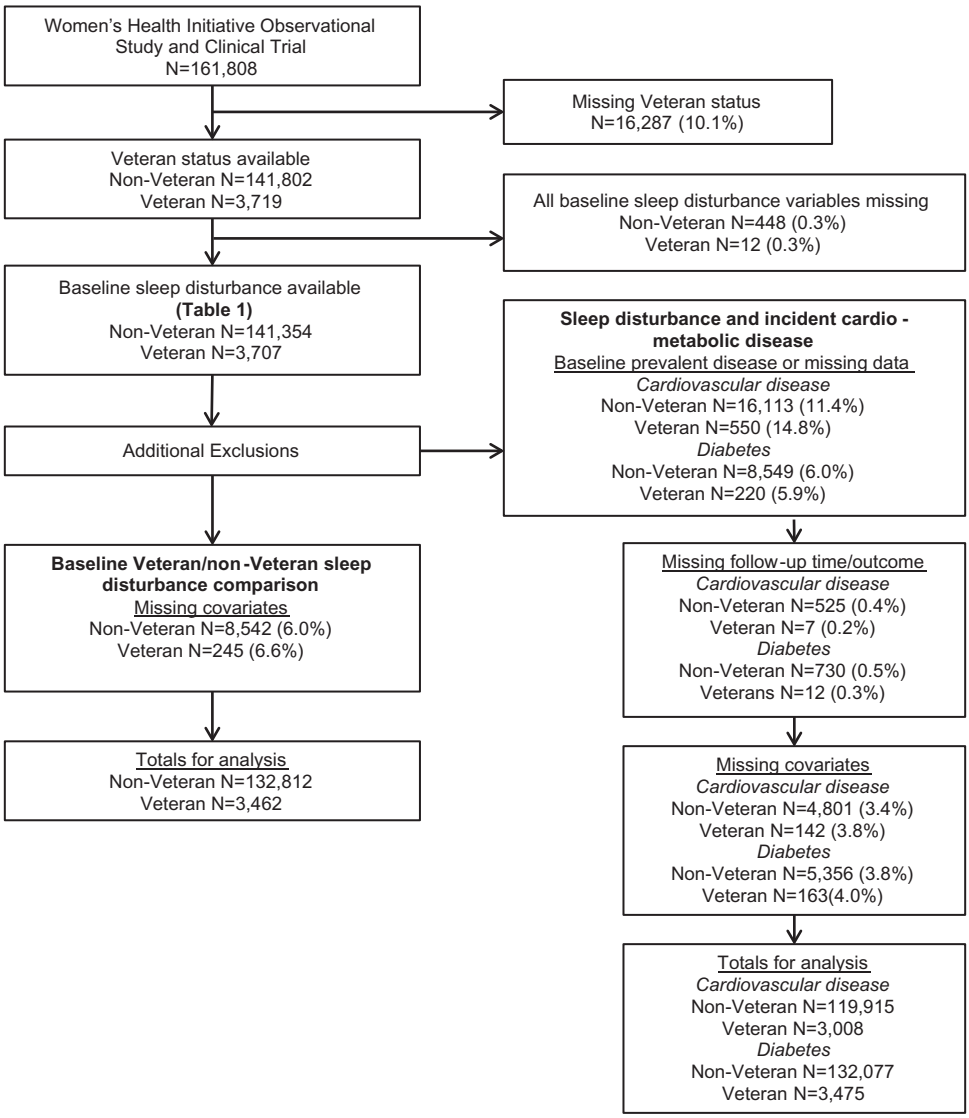

Figure 2. Flow diagram for study inclusion and exclusion. A total of 141,354 non-Veterans and 3,707 Veterans had baseline data on sleep disturbance, which reflects the study population described in Table 1. Additional exclusions were made for each study question.

Findings related to the greater prevalence of comorbid insomnia and sleep-disordered breathing (insomnia + SDB) risk among WVs are noteworthy as it may signal heightened risk for inflammation and its associated negative physical health consequences (Gupta & Arnedt, 2012) as well diminished cognitive functioning (Zimmerman & Aloia, 2012). Thus, further research that examines the association of insomnia + SDB and depression, cancer, and risk for mild cognitive impairment, and dementia, among older postmenopausal WVs may be fruitful.

Though the reasons underlying their greater vulnerability to comorbid insomnia + SDB remain unknown, the heightened prevalence of key health risk behaviors (e.g., smoking) among WV participants is likely a salient contributing factor. Lifetime prevalence of PTSD was not measured in the WHI; however, the significant prevalence of this disorder among WVs is well documented (Dobie et al., 2004; Turner, Turse, & Dohrenwend, 2007) and may contribute to the observed heightened rates of high risk for insomnia + SDB (Krakow et al., 2015). That we did not find a differential relationship between sleep disturbance and cardiometabolic morbidity by Veteran status is perhaps surprising in this light. Nevertheless, this may reflect the fact that fully adjusted models accounted for many salient demographic and health risk behaviors that varied by Veteran status. It may also reflect the higher prevalence (and thus greater risk of exclusion from analyses) of cardiometabolic disease among WVs at the WHI baseline.

Findings depart from the prior literature in several important ways. In contrast to several prior studies, we did not find an overall heightened prevalence of sleep disturbances in Veterans relative to non-Veterans (Fung et al., 2013; Hughes et al., 2013). However, important differences in our study methodology and population may explain

Table 2. Association Between Veteran Status and Sleep Disturbance At Baseline

	Non-Veterans[a]		Veterans[a]		Veterans compared with non-Veterans					
					Unadjusted		Adjustment 1[b]		Adjustment 2[c]	
	N	%	*N*	%	PR (95% CI)	*p* Value	PR (95% CI)	*p* Value	PR (95% CI)	*p* Value
Medication or alcohol for sleep	32,303	24.6	845	24.7	1.02 (0.96, 1.08)	.51	1.00 (0.94, 1.06)	.98	1.00 (0.94, 1.06)	.88
High risk for insomnia	40,717	30.8	1,049	30.5	1.00 (0.96, 1.05)	.90	1.00 (0.95, 1.05)	.99	1.00 (0.95, 1.05)	.91
High risk for SDB	32,990	24.9	864	25.1	1.00 (0.95, 1.06)	.92	1.02 (0.97, 1.08)	.41	1.02 (0.97, 1.08)	.46
High risk for insomnia and SDB	12,540	9.5	355	10.3	1.09 (0.99, 1.19)	.10	1.13 (1.02, 1.24)	.02	1.13 (1.02, 1.24)	.02

Notes: CI = confidence interval; BMI = body mass index; PR = prevalence ratio; SDB = sleep disordered breathing.

[a]Numbers and percents reflect those from the fully adjusted model (Adjustment 2), thus sample sizes from unadjusted and Adjustment 1 models are at least as large as those reported in the table.

[b]Adjusted for age (continuous), race (White/non-White), education (nominal), BMI (continuous), and current smoker (no/yes).

[c]Adjusted for age (continuous), race (White/non-White), education (nominal), BMI (continuous), current smoker (no/yes), living with a partner (no/yes), physical activity (MET-hours per week, continuous), vasomotor symptoms (no/yes), depression (no/yes), napping at baseline (<3 times per week or 3+ times per week), and study arm (nominal).

Table 3. Association Between Veteran Status and Sleep duration At Baseline

	Non-Veteran[a]		Veteran[a]		Veterans compared with non-Veterans					
					Unadjusted		Adjustment 1[b]		Adjustment 2[c]	
	N[a]	%	*N*[a]	%	Diff (95% CI)	*p* Value	Diff (95% CI)	*p* Value	Diff (95% CI)	*p* Value
Very short	10,956	8.3	293	8.5	0.59 (−0.35, 1.52)	.22	1.12 (0.12, 2.11)	.03	0.98 (−0.01, 1.97)	.05
Short	36,558	27.5	907	26.2	−1.11 (−2.55, 0.33)	.13	−0.83 (−2.31, 0.66)	.28	−0.93 (−2.43, 0.57)	.22
Average	79,440	59.9	2,084	60.2	−0.22 (−1.82, 1.39)	.79	−0.81 (−2.44, 0.81)	.33	−0.51 (−2.14, 1.11)	.54
Long	5,746	4.3	175	5.1	0.74 (0.02, 1.45)	.04	0.52 (−0.18, 1.23)	.14	0.47 (−0.24, 1.17)	.20

Notes: BMI = body mass index; CI = confidence interval; Diff = difference in percent (percentage points).

[a]Numbers and percents reflect those from the fully adjusted model (Adjustment 2), thus sample sizes from unadjusted and Adjustment 1 models are at least as large as those reported in the table.

[b]Adjusted for age (continuous), race (White/non-White), education (nominal), BMI (continuous), and current smoker (no/yes).

[c]Adjusted for age (continuous), race (White/non-White), education (nominal), BMI (continuous), current smoker (no/yes), living with a partner (no/yes), physical activity (MET-hours per week, continuous), vasomotor symptoms (no/yes), depression (no/yes), napping at baseline (<3 times per week/3+ times per week), and study arm (nominal).

Table 4. Adjusted Association Between Sleep Disturbance At Baseline and Incident Health Outcomes, by Veteran Status

	Non-Veterans		Veterans		*p* Value for interaction
	HR[a] (95% CI)	*p* Value	HR[a] (95% CI)	*p* Value	
Cardiovascular disease[b] (Incident cases: non-Veterans = 14,166; Veterans = 474)					
Medication or alcohol for sleep	1.17 (1.13, 1.21)	<.001	1.26 (1.03, 1.54)	.02	.47
High risk for insomnia	1.08 (1.04, 1.12)	<.001	1.04 (0.85, 1.26)	.73	.66
High risk for SDB	1.29 (1.24, 1.34)	<.001	1.28 (1.05, 1.56)	.02	.95
High risk for insomnia and SDB	1.27 (1.20, 1.34)	<.001	1.24 (0.94, 1.63)	.13	.87
Sleep duration					
Very short	1.15 (1.08, 1.22)	<.001	1.12 (0.81, 1.55)	.50	.88
Short	1.07 (1.03, 1.11)	.001	0.90 (0.73, 1.12)	.36	.14
Average	1.00 (Ref)	—	1.00 (Ref)	—	—
Long	1.07 (0.99, 1.16)	.08	0.87 (0.56, 1.36)	.55	.37
Diabetes[c] (Incident cases: non-Veterans = 12,003; Veterans = 309)					
Medication or alcohol for sleep	1.04 (0.99, 1.08)	.10	1.12 (0.86, 1.44)	0.40	.58
High risk for insomnia	1.04 (0.99, 1.08)	.06	1.16 (0.92, 1.47)	0.21	.36
High risk for SDB	1.37 (1.32, 1.43)	<.001	1.26 (0.99, 1.59)	0.06	.47
High risk for insomnia and SDB	1.30 (1.23, 1.37)	<.001	1.49 (1.11, 2.00)	.01	.35
Sleep duration					
Very short	1.11 (1.05, 1.19)	<.001	1.22 (0.85, 1.75)	.28	.63
Short	1.03 (0.99, 1.07)	.20	1.08 (0.84, 1.40)	.54	.68
Average	1.00 (Ref)	—	1.00 (Ref)	—	—
Long	1.12 (1.03, 1.22)	.01	1.05 (0.62, 1.79)	.84	.82

Notes: CI = confidence interval; HR = hazard ratio; SDB = sleep disordered breathing.

[a]Adjusted for baseline age (continuous), race (White/non-White), education (nominal), BMI (continuous), living with partner (no/yes), physical activity (continuous, MET-hours per week), vasomotor symptoms (no/yes), napping (<3 times per week/3+ times per week), current smoker (no/yes), and study arm (nominal).

[b]Defined as adjudicated clinical myocardial infarction (MI), evolving Q wave MI (definite silent MI), possible evolving Q wave MI (possible silent MI), definite or possible coronary heart disease death, angina, coronary artery bypass graft, percutaneous transluminal coronary angioplasty, carotid artery disease, congestive heart failure, stroke, and peripheral artery disease.

[c]Defined as first time receiving treatment for diabetes.

this difference. In addition, Sands-Lincoln and colleagues (2013) reported that postmenopausal women in the WHI Observational Study with a combined high risk for insomnia and long SLD (≥10 hours) had higher incident CHD than postmenopausal women without these problems. In contrast, our findings suggest that high risk for insomnia, short SLD, and very short SLD are associated with higher risk of CVD in the non-Veteran group. Failure to replicate Sands-Lincoln's (2013) work may be due to slightly different methodology, that is, a more liberal definition of long SLD (≥9 vs ≥10 hours) or broader inclusion of the WHI participants.

Limitations include use of an observational design, which means our findings represent associations, not causal linkages, among our core variables of Veteran status, sleep disturbance, CVD, and diabetes. Second, Veteran status and all measures of sleep disturbance (with the exception of some components of SDB risk) were self-reported symptoms. Measures of insomnia and SDB were not diagnostic, and all self-reported sleep disturbances may be subject to reporting bias—increasing the risk of misclassification (e.g., assigned a sleep disturbance when none existed). However, it is unlikely that any misclassification differed between Veterans and non-Veterans, and this type of nondifferential measurement error would be expected to bias associations toward null values rather than a true effect. Third, there were, undoubtedly, important but unmeasured confounding factors that were not accounted for in our findings. Specifically, the lack of contextual details about Veterans' prior military service and military-related exposures (e.g., trauma) that might confound results is a notable limitation. Finally, generalizability of our findings may be limited as the study population was voluntarily recruited, not derived from a population-based sample, and reflects a unique cadre of WVs who are age consistent with military service during and before the Vietnam War. Given the tremendous evolution in roles and opportunities for military women since that time, findings may not generalize to more contemporary Veteran cohorts. Methodological strengths of our study include the use of a large, nationally

recruited group of postmenopausal women in WHI (The Women's Health Initiative Study Group, 1998), a strong rate of participant retention, and the inclusion of rigorously adjudicated health outcomes (cardiometabolic morbidity variables).

Conclusion

This work represents the first large-scale effort to delineate the prevalence of sleep disturbance in postmenopausal WVs and examines the potential synergistic effects of Veteran status and sleep disturbance on postmenopausal cardiometabolic outcomes. Findings of WVs' heightened prevalence of risk for comorbid insomnia and SDB offer important implications for clinical practice and policy—illuminating the value of routine screening for sleep disturbances, particularly insomnia, sleep disordered breathing, and their co-occurrence in postmenopausal WVs. Treatment of insomnia + SDB may require a multidisciplinary team (i.e., combination cognitive behavioral therapy for insomnia and positive airway pressure therapy) underscoring the importance of WVs' access to both medical and behavioral health care providers. Further research that replicates and confirms our findings is needed, as is research that investigates the etiologic factors associated with Veterans' heightened prevalence of postmenopausal sleep disturbances, and addresses optimal treatment strategies, is also needed.

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