Sleep Characteristics, Mental Health, and Diabetes Risk

A prospective study of U.S. military service members in the Millennium Cohort Study

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OBJECTIVE—Research has suggested that a higher risk of type 2 diabetes associated with sleep characteristics exists. However, studies have not thoroughly assessed the potential confounding effects of mental health conditions associated with alterations in sleep.

RESEARCH DESIGN AND METHODS—We prospectively assessed the association between sleep characteristics and self-reported incident diabetes among Millennium Cohort Study participants prospectively followed over a 6-year time period. Surveys are administered approximately every 3 years and collect self-reported data on demographics, height, weight, lifestyle, features of military service, sleep, clinician-diagnosed diabetes, and mental health conditions assessed by the PRIME-MD Patient Health Questionnaire and the PTSD Checklist–Civilian Version. Statistical methods for longitudinal data were used for data analysis.

RESULTS—We studied 47,093 participants (mean 34.9 years of age; mean BMI 26.0 kg/m^2; 25.6% female). During 6 years of follow-up, 871 incident diabetes cases occurred (annual incidence 3.6/1,000 person-years). In univariate analyses, incident diabetes was significantly more likely among participants with self-reported trouble sleeping, sleep duration <6 h, and sleep apnea. Participants reporting incident diabetes were also significantly older, of nonwhite race, of higher BMI, less likely to have been deployed, and more likely to have reported baseline symptoms of panic, anxiety, posttraumatic stress disorder, and depression. After adjusting for covariates, trouble sleeping (odds ratio 1.21 [95% CI 1.03–1.42]) and sleep apnea (1.78 [1.39–2.28]) were significantly and independently related to incident diabetes.

CONCLUSIONS—Trouble sleeping and sleep apnea predict diabetes risk independent of mental health conditions and other diabetes risk factors.

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The incidence and prevalence of type 2 diabetes have risen dramatically in the U.S. over the past 30 years (1). A decline in sleep duration has been reported over this same time period. For example, full-time workers in the U.S. were more likely to sleep <6 h in 2006 compared with 1975 (2). Further, short sleep duration ≤6 h was reported among 28.3% of U.S. adults in 2004–2007 (3). A recent meta-analysis of 10 studies that comprised a total of 107,756 participants concluded that several sleep characteristics were associated with higher incidence of developing type 2 diabetes, including shorter and longer duration and difficulty initiating and maintaining sleep (4). Multiple pathways have been proposed as potential causal mechanisms for an effect of poor sleep on diabetes risk, including poor sleep as a marker for obstructive sleep apnea, as an activator of the hypothalamic-pituitary axis with greater cortisol secretion, via effects on body weight regulation through hormonal alterations (e.g., leptin, ghrelin, insulin) that may affect appetite regulation, and sleep-mediated inflammatory changes (5–8).

Although it is well known that sleep disorders often accompany mental health conditions such as depression and posttraumatic stress disorder (PTSD), little research has been conducted to examine whether these associated underlying mental health conditions might explain in part the observed associations between sleep characteristics and type 2 diabetes risk. Both depression and PTSD have been reported to predict a higher risk of type 2 diabetes (9,10), and both conditions are also known to adversely affect sleep quality. People with PTSD subjectively reported insomnia and nightmares more frequently and objectively demonstrated a higher rate of sleep-disordered breathing and periodic leg movements (11,12). Depression is associated with multiple characteristics of poor sleep, including insomnia and short and long sleep duration (13).

Several potential mechanisms may explain the associations between sleep disorders, mental health conditions, and diabetes risk. If a sleep disorder is simply a marker for a mental health condition, then statistical adjustment for the mental health condition's presence would remove and thereby explain an observed association between sleep and diabetes risk. If sleep characteristics, on the other hand, predispose to diabetes but mental health disorders do not, then adjustment for sleep characteristics would remove the association between a mental health disorder and diabetes risk.

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Table 1—*Baseline demographic, military, and behavioral characteristics of Millennium Cohort participants by development of diabetes at follow-up*

Baseline characteristics except where indicated	Newly occurring diabetes absent n = 46,710*		Newly occurring diabetes present n = 871		P value
	n	%	n	%	
Trouble sleeping†	18,625	23.4	278	31.9	<0.01
Sleep duration, h					<0.01
<5	2,767	3.5	53	6.1	
5	8,886	11.2	119	13.7	
6	26,084	32.7	289	33.2	
7	23,669	29.7	208	23.9	
8	14,326	18.0	154	17.7	
>8	3,962	5.0	48	5.5	
Sleep apnea present‡	2,094	2.6	90	10.3	<0.01
Female sex	20,175	25.3	214	24.6	0.61
Age, years (mean, SD)	36.6	9.2	42.6	10.0	<0.01
BMI (mean, SD)	26.3	3.5	29.4	4.3	<0.01
Race/ethnicity					<0.01
White, non-Hispanic	57,646	72.3	568	65.2	
Black, non-Hispanic	8,608	10.8	148	17.0	
Other	13,440	16.9	155	17.8	
Educational level					0.01
Some college or less	52,293	65.6	607	69.7	
Bachelor's degree or higher	27,401	34.4	264	30.3	
Combat deployment after baseline§					<0.01
No deployment	58,962	74.0	745	85.5	
Deployed with combat	10,628	13.3	70	8.0	
Deployed without combat	10,104	12.7	56	6.4	
Separated from military after baseline	10,207	12.8	168	19.3	<0.01
Service branch					<0.01
Army	37,631	47.2	431	49.5	
Air Force	23,803	29.9	244	28.0	
Navy and Coast Guard	14,955	18.8	180	20.7	
Marine Corps	3,305	4.2	16	1.8	
Service component					<0.01
Reserve/National Guard	38,534	48.4	477	54.80	
Active duty	41,160	51.7	394	45.2	
Pay grade					<0.01
Enlisted	56,094	70.4	689	79.1	
Officer	23,600	29.6	182	20.9	
Occupation					<0.01
Combat specialists	16,404	20.6	135	15.5	
Health care	9,097	11.4	98	11.3	
Admin/supply‖	23,346	29.3	328	37.7	
Other	30,847	38.7	310	35.6	
Alcohol consumption¶					<0.01
No problems	42,358	53.2	551	63.3	
Problem or binge drinking	37,336	46.9	320	36.7	
Smoking status					0.23
Past/never smoker	67,502	84.7	725	83.2	
Current smoker	12,129	15.3	146	16.8	
Depression	2,103	2.6	44	5.1	<0.01
Panic disorder	937	1.2	30	3.4	<0.01
Other anxiety disorder	1,402	1.8	36	4.1	<0.01
PTSD	2,916	3.7	73	8.4	<0.01

Participants were followed every 3 years for a total of 3 or 6 years, depending on the number of follow-up surveys completed. Baseline characteristic refers to the characteristics present at the start of each 3-year period, at the end of which the occurrence of diabetes was assessed. *Incident diabetes was assessed at each 3-year period separately, with 13,621 participants followed for one 3-year period, and 33,472 participants followed for two 3-year periods. A total of 383 cases occurred during years 0–3 and 488 cases during years 3–6 of follow-up. †Self-report of trouble sleeping over the past 4 weeks. ‡Self-report of previous provider-diagnosed sleep

We assessed the association between sleep characteristics and diabetes risk independent of known diabetes risk factors, mental health conditions, and military service characteristics among Millennium Cohort Study participants. This study is unique in capturing characteristics of several mental health conditions, including depression and PTSD, in a large cohort of people healthy enough to have served in the U.S. military at the outset of the study.

RESEARCH DESIGN AND METHODS

The Millennium Cohort is the largest prospective study using primary data collection ever undertaken by the Department of Defense (DoD). The study began in 2001 with the objective to collect and evaluate data on health, behavioral risk factors, and occupational characteristics related to military service that may be associated with adverse health outcomes (14). Participants are surveyed at enrollment and approximately every 3 years thereafter. This report includes participants from the first enrollment cycle that spanned 2001–2003 and comprised 77,047 participants (36% of those able to be contacted). Approximately 71% of those participants enrolled at baseline responded to follow-up surveys conducted in 2004 and 2007. The surveys were administered via paper and the Internet and included questions on self-reported provider-diagnosed medical conditions, mental health symptoms, physical and functional status, alcohol and tobacco use, occupational status, military exposures, sleep patterns, and demographic information. Details on Millennium Cohort methodology can be found elsewhere (14–16). This study was approved by the Naval Health Research Center institutional review board, and informed consent was obtained from all study participants. This research has been conducted in compliance with all applicable federal regulations governing the protection of human subjects in research (Protocol NHRC.2000.0007).

Study population and data sources

Of the 77,047 participants enrolled at baseline, follow-up surveys were completed by 55,021 participants at year 3 and 54,790 at year 6. Since incident diabetes was the outcome of interest, eligible participants included those who were followed until either the outcome was reported to have occurred at year 3 or 6, or until their last completed follow-up if the outcome was not reported. Exclusions included participants reporting provider-diagnosed diabetes at baseline, missing outcome or exposure data, or if DoD outpatient or inpatient medical encounter data contained codes for type 1 diabetes ($n = 72$) (ICD-9 codes 250.x1 and 250.x3). After application of these exclusions, 47,093 participants remained.

The primary data sources were the self-administered Millennium Cohort surveys and DoD electronic personnel files, managed by the Defense Manpower Data Center (DMDC, Seaside, CA). Survey data included behavioral, demographic, military, and health data. For these analyses, electronic records from DMDC provided information on age, sex, race/ethnicity, education, pay grade, service branch, service component, military occupation, dates of separation, and deployment dates. DMDC information was supplemented with self-reported data to reduce missing values when necessary. All other data for the analyses were from the Millennium Cohort surveys.

Three sleep variables were included in the analyses: *1*) trouble sleeping, *2*) sleep duration, and *3*) sleep apnea. Trouble sleeping was assessed using the sleep items on the PRIME-MD Patient Health Questionnaire (PHQ) and the PTSD Checklist–Civilian Version (PCL-C) (17–20). The PHQ asks, "Over the last 4 weeks, how often have you experienced trouble falling asleep or staying asleep?" The PCL-C asks, "In the past month, have you had trouble falling asleep or staying asleep?" Participants with trouble sleeping were defined as those who responded "moderately" or above on the PCL-C sleep item or "several days" or longer on the PHQ sleep item. Sleep duration was reported as whole number of hours slept in an average 24-h period over the past month. Participants with sleep apnea were identified by self-report as being told by a doctor or other health professional they had sleep apnea.

Several standardized instruments were used to identify people screening positive for mental health disorders. PTSD was assessed using the PCL-C (17), a 17-item self-report screening tool for PTSD symptoms during the past 30 days on a 5-point Likert scale, ranging from 1 (not at all) to 5 (extremely). A positive screen for PTSD at baseline was defined as a report of a moderate or higher level of at least one intrusion symptom, three avoidance symptoms, and two hyperarousal symptoms (criteria established by DSM-IV) (21). Major depressive disorder was assessed using nine items from the PHQ (sensitivity = 0.93; specificity = 0.89) corresponding to the depression diagnosis based on the DSM-IV (19). A positive screen for depression at baseline was defined as *1*) endorsement of depressed mood or anhedonia and *2*) response of "more than half the days" or "nearly every day" to at least five items. Other anxiety (6 items) and panic (15 items) symptoms were also assessed with the PHQ.

An aggregate variable capturing either problem or binge drinking was created as follows. Problem drinking was defined using items from the PHQ on risky behaviors related to alcohol use, such as driving under the influence more than one time over the past year, where endorsement of at least one item indicated problem drinking. Binge drinking was defined as consuming five or more drinks (men) or four or more drinks (women) in 1 day during the past year. Smokers were identified as those ever smoking 100 cigarettes in their lifetime, with those persisting in this habit defined as current smokers and those having quit as past smokers.

In longitudinal models, service branch, service component, pay grade, military occupation, birth year, race/ethnicity, and education were assessed at baseline. Smoking status, alcohol use, BMI, combat deployment, PTSD, depression, anxiety, panic, and all sleep variables were assessed at all available time points.

Outcome

The outcome of interest was incident diagnosed diabetes self-reported on a follow-up survey among people without diabetes at the baseline assessment. At baseline,

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apnea. §Combat exposures were defined as having personally during deployment *1*) witnessed a death due to war, disaster, or tragic event; *2*) witnessed instances of physical abuse; *3*) been exposed to dead or decomposing bodies; *4*) been exposed to maimed soldiers or civilians; or *5*) been exposed to prisoners of war or refugees; and were evaluated at the survey after deployment as having occurred during the same time period as deployment. ‖Includes functional support and administration occupation plus service and supply handlers. ¶Problem drinking was assessed using the PHQ, and binge drinking was defined as consuming five or more drinks for men or four or more drinks for women on at least 1 day in the past year.

Table 2—*Relative odds of incident self-reported diabetes by each baseline characteristic of interest*

Characteristics	OR	95% CI
Main exposures of interest		
Trouble sleeping*		
No	1.00	
Yes	1.45	1.25–1.68
Sleep duration, h		
<5	2.04	1.49–2.81
5	1.46	1.15–1.84
6	1.19	0.99–1.43
7	1.00	
8	1.17	0.95–1.45
>8	1.30	0.93–1.81
Sleep apnea†		
No	1.00	
Yes	2.11	1.66–2.68
Covariates		
Combat deployment‡		
No deployment	1.00	
Deployed with combat	0.77	0.60–0.98
Deployed without combat	0.59	0.44–0.77
Service branch		
Army	1.00	
Air Force	0.94	0.80–1.11
Navy and Coast Guard	1.12	0.93–1.34
Marine Corps	0.73	0.44–1.21
Service component		
Reserve/National Guard	1.00	
Active duty	1.13	0.97–1.31
Pay grade		
Enlisted	1.00	
Officer	0.59	0.47–0.74
Occupation		
Combat specialists	1.00	
Health care	1.15	0.86–1.53
Admin/supply§	1.36	1.10–1.69
Other	1.09	0.88–1.35
Separated		
No	1.00	
Yes	1.55	1.31–1.84
Alcohol consumption¶		
No problems	1.00	
Binge or problem drinking	0.86	0.74–0.99
Smoking status		
Past/never smoker	1.00	
Current smoker	1.37	1.14–1.65
Depression		
No	1.00	
Yes	1.53	1.11–2.12
Panic disorder		
No	1.00	
Yes	2.38	1.62–3.50
Other anxiety disorder		
No	1.00	
Yes	1.98	1.40–2.82
PTSD		
No	1.00	
Yes	1.97	1.53–2.55

participants reported if they had ever been told by a doctor or health professional that they had diabetes or "sugar diabetes." At follow-up assessments, participants responded to the same question in regard to the previous 3 years.

Statistical analyses

Univariate analyses assessed associations of incident diabetes with sleep, military, demographic, behavioral, and mental health characteristics while accounting for multiple periods of observation per subject. Since repeated measurements were available with up to two follow-up assessments per person, generalized estimating equations (GEEs) were used to account for these multiple assessments while adjusting for fixed and time-varying covariates, to estimate adjusted odds of reporting incident diabetes (22). Incident diabetes was determined at each follow-up assessment, and all covariates were evaluated using data from the previous assessment (22).

In all multivariable models, adjustments were performed for known type 2 diabetes risk factors captured in the study: age, sex, education, BMI, and race/ethnicity. The final adjusted models were built using a stepwise backward reduction algorithm that retained all significant variables ($P < 0.10$) (Table 1) while always keeping age, sex, race/ethnicity, education, and BMI in the model. Additionally, mental health variables were added to the final models to determine if this altered the relationship between sleep and diabetes. First-order interaction terms between retained sleep variables and age, sex, and BMI were tested to determine whether the exposure-outcome associations varied by these characteristics. Possible presence of multicollinearity in multivariable models was considered if the variance inflation factor exceeded 4. Best-fitting GEE models were judged using the Quasilikelihood Information Criterion, the measure developed for GEE models analogous to the Akaike Information Criterion. Statistical analyses were performed using SAS statistical software, version 9.3 (SAS Institute, Inc., Cary, NC).

RESULTS—A total of 47,093 participants were included in this analysis and followed for up to 6 years. Incident diabetes was assessed at each 3-year period separately, with 13,621 participants followed for one 3-year period, and 33,472 participants followed for two 3-year periods. A total of 383 cases occurred during years 0–3 and 488 cases occurred during years 3–6 of follow-up. The 488 cases that

did not occur until years 3–6 are also present in the first column of Table 1 as not having diabetes from year 0–3. At baseline, participants overall were on average young (34.9 years of age, SD 9.0 years), slightly overweight (BMI 26.0 kg/m^2, SD 3.3), 25.6% female, and more likely than not to be white, non-Hispanic race, less than college educated, Army service branch, and on active duty (Table 1). Overall, 871 participants newly self-reported diabetes, for a cumulative annual incidence of 3.6/1,000 person-years. Participants who newly self-reported diabetes during follow-up were significantly more likely at baseline to have reported trouble sleeping, sleep duration ≤5 h, and sleep apnea (Table 1). Sleep duration >8 h was reported by similar proportions of participants with and without newly self-reported diabetes. Participants with new-onset diabetes were on average older, had a higher BMI, and were more likely of nonwhite race. Characteristics associated with new-onset diabetes included no deployment, having separated from the military since baseline, Army or Navy/Coast Guard service branch, Reserves/National Guard service component, enlisted pay grade, and administration/supply occupation. Binge or problem drinking was less likely to have been reported in people reporting new-onset diabetes, and current and former smoking frequency was similar in groups with and without new-onset diabetes. All mental health symptoms occurred significantly more frequently among those who newly reported diabetes during follow-up.

Factors associated with a higher odds of incident diabetes in models adjusted for sex and known type 2 diabetes risk factors (age, BMI, education, and race/ethnicity) included trouble sleeping, sleep duration ≤5 h compared with 7 h, and sleep apnea (Table 2). Several military service characteristics remained significantly related to the outcome, including no deployment, enlisted pay grade, administration/supply occupation, and having separated from the military since baseline (Table 2). Binge or problem drinking remained significantly associated, and current smoking emerged as a risk factor for new-onset diabetes after adjustment. Screening positive for

depression, panic, other anxiety disorder, and PTSD were all significantly associated with higher odds of new-onset diabetes in these adjusted models (Table 2).

In the multivariable model (Table 3), sleep characteristics remained significantly and independently associated with higher diabetes odds. The sleep variables that entered the final model included reported trouble sleeping and sleep apnea, which were associated with significant increases in the odds of diabetes of 1.21 to 1.78, respectively. These associations were not only independent of each other but also the other covariates adjusted for in the model (Table 3). Military service characteristics significantly associated with diabetes odds included deployment without combat experience, administration or supply occupations, pay grade, and having separated from the military since baseline. A positive screen for PTSD was significantly associated with higher diabetes odds, independent of sleep characteristics and other covariates in the model, and panic disorder was of borderline significance. Tests for interactions between the sleep variables included in the models in Table 3 and age, sex, and BMI were all nonsignificant ($P >$ 0.10). No variable had a variance inflation factor >4, indicating that collinearity was unlikely. The model in Table 3 was rerun with sleep duration substituted for trouble sleeping but with the other included covariates unchanged. The Quasilikelihood Information Criterion for the model containing trouble sleeping was slightly lower (8,640.9) than when sleep duration was included in the model (8,646.3). The sleep duration variable was insignificant overall in this model ($P = 0.1585$), although two sleep categories were significantly related to diabetes odds (<5-h odds ratio [OR] 1.52 [95% CI 1.09–2.14]; 5-h OR 1.28 [1.01–1.62]). Several additional modifications of the multivariable model shown in Table 3 were conducted. In the first modification, symptoms of depression and anxiety disorder were included in the model to assess whether adjustment for these additional factors altered the association between sleep and diabetes odds. In the second modification, all subjects reporting sleep apnea were removed from the model

shown in Table 3. In each of these modifications, the statistical significance of the associations between the sleep variables and diabetes odds remained unchanged, and the associations were of similar magnitude to those seen in Table 3 (data not shown).

CONCLUSIONS—Our study findings confirm that sleep characteristics are associated with subsequent new-onset self-reported diabetes. These associations persisted after adjustment for multiple mental health conditions known to affect sleep duration and quality, including PTSD and depression (11–13). Therefore, it is unlikely that sleep simply serves as a surrogate marker for associated mental health conditions previously shown to predict higher diabetes risk (9,10). Additionally, participants reporting provider-diagnosed sleep apnea were at higher risk of developing self-reported diabetes during follow-up. Although sleep apnea is associated with higher BMI and both altered sleep quality and quantity, adjustment for these variables did not alter the significance of the higher diabetes risk associated with this condition (23). Overall, these results suggest that the associations between type 2 diabetes risk and mental health conditions and sleep characteristics, if causal, may involve different pathways.

Whereas trouble sleeping and shorter sleep duration were associated with higher risk of diabetes in a model adjusted for known diabetes risk factors, longer sleep duration was not, in contrast to findings that others have reported (4). The reason for this discrepancy is unclear, but it may be due to the relatively younger age of our cohort compared with investigations reporting higher diabetes risk with longer sleep duration (24,25).

The independent role of mental health conditions associated with poor quality and quantity of sleep in predicting risk of diabetes has only been addressed in a limited manner in previous research. The Nurses' Health Study investigators examined sleep as a predictor of incident diabetes in this cohort from 1986–1996 and adjusted for an assessment of depression based on The Short Form 36 Health Survey that was obtained in 1992,

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Table 2 legend (see Table 2, p. 3157): All models adjusted for age, sex, race/ethnicity, education, and BMI in longitudinal multivariable models. *Self-report of trouble sleeping over the past 4 weeks. †Self-report of previous provider-diagnosed sleep apnea. ‡Combat exposures were defined as having personally during deployment *1*) witnessed a death due to war, disaster, or tragic event; *2*) witnessed instances of physical abuse; *3*) been exposed to dead or decomposing bodies; *4*) been exposed to maimed soldiers or civilians; or *5*) been exposed to prisoners of war or refugees; and were evaluated at the survey after deployment as having occurred during the same time period as deployment. §Includes functional support and administration occupation plus service and supply handlers. ¶Problem drinking was assessed using the PHQ, and binge drinking was defined as consuming five or more drinks for men or four or more drinks for women on at least 1 day in the past year.

Table 3—*Longitudinal multivariable regression model of sleep characteristics and mental health symptoms as risk factors for incident self-reported diabetes in the Millennium Cohort*

Characteristics*	OR	95% CI
Trouble sleeping†		
No	1.00	
Yes	1.21	1.03–1.42
Sleep apnea‡		
No	1.00	
Yes	1.78	1.39–2.28
Combat deployment§		
No deployment	1.00	
Deployed with combat	0.86	0.65–1.09
Deployed without combat	0.67	0.50–0.88
Occupation		
Combat specialists	1.00	
Health care	1.14	0.86–1.51
Admin/supply¶	1.27	1.02–1.58
Other	1.01	0.82–1.26
Pay grade		
Enlisted	1.00	
Officer	0.64	0.50–0.80
Separated		
No	1.00	
Yes	1.43	1.20–1.70
Panic disorder		
No	1.00	
Yes	1.46	0.94–2.26
PTSD		
No	1.00	
Yes	1.38	1.02–1.87

*Final model determined using backward stepwise regression that retained all variables with $P < 0.1$ as well as known diabetes risk factors, such that the final model included trouble sleeping, sleep apnea, combat deployment, occupation, pay grade, military separation, sex, race/ethnicity, education, BMI, age, alcohol consumption, smoking status, panic disorder, and PTSD. †Self-report of trouble falling asleep or staying asleep over the past 4 weeks. ‡Self-report of previous provider-diagnosed sleep apnea. §Combat exposures were defined as having personally during deployment *1*) witnessed a death due to war, disaster, or tragic event; *2*) witnessed instances of physical abuse; *3*) been exposed to dead or decomposing bodies; *4*) been exposed to maimed soldiers or civilians; or *5*) been exposed to prisoners of war or refugees; and were evaluated at the survey after deployment as having occurred during the same time period as deployment. ¶Includes functional support and administrative occupation plus service and supply handlers.

approximately midway through the follow-up period (24). Thus, it is unclear whether depression preceded or followed diabetes onset during the first 6 years of follow-up. An analysis using the National Health and Nutrition Examination Survey I Epidemiologic Follow-Up Study adjusted for depression while examining the association between sleep and diabetes incidence, although no association was seen between depression and diabetes incidence in this cohort (25). Lastly, a prospective study of Swedish men assessed the presence of depression with a simple yes/no question, "Do you feel depressed?" and did not provide information on the accuracy of this question in capturing this condition (26). To our knowledge, our study is the first to

consider mental health conditions other than depression as potential confounding factors and to measure their occurrence prior to the onset of diabetes.

Previous prospective research on sleep characteristics and type 2 diabetes risk has not considered whether sleep duration or quality is related to this outcome independent from sleep apnea, a known cause of sleep disturbance. In our fully adjusted analysis, both sleep apnea and trouble sleeping had independent associations with diabetes risk, suggesting that the associations between sleep characteristics and diabetes risk do not merely serve as markers for the presence of sleep-disordered breathing. In addition to the known higher risk of obesity associated with sleep apnea, other factors associated

with sleep-disordered breathing may be involved in higher diabetes risk and include abnormal sympathetic activity and release of proinflammatory mediators such as tumor necrosis factor-α and interleukin-6 (27). In support of the latter, we observed an independent association between sleep apnea and diabetes risk after adjustment for BMI. This suggests that manifestations of sleep apnea other than the impact of greater general adiposity may be associated with diabetes risk, although it is possible that incomplete adjustment due to residual confounding occurred due to the inaccuracy of BMI in characterizing body composition.

The association between trouble sleeping or shorter sleep duration and diabetes risk independent of associated weight gain and sleep apnea is not well understood, but it may be related to both changes in insulin sensitivity, secretion, and glucose effectiveness. One investigation reported significant or borderline-significant reductions in insulin sensitivity, insulin secretion, glucose effectiveness, and the disposition index immediately after a 5-day period of sleep deprivation (4 h of sleep per night) among 11 healthy lean males in a controlled setting (28). All these changes have been associated with higher risk of the development of type 2 diabetes (29). Whether these changes persist with chronic deprivation is unknown.

Several characteristics of military service were significantly associated with lower diabetes risk in multivariable models, including deployment, officer pay grade, and remaining in military service. For most comparisons, military deployment with or without combat exposure was related to a lower risk for diabetes, possibly reflecting selection of people medically fit for deployment who are at lower risk for diabetes. The mental health conditions independently associated with diabetes risk included those characterized by excessive stress, including PTSD and panic disorder. A review of the literature on stress and diabetes risk concluded that both general emotional and job stress were repeatedly associated with a higher risk of developing diabetes in adults (30). Overactivation of the hypothalamic-pituitary axis and abnormal stimulation of the sympathetic nervous system are thought to accompany excessive levels of stress, with accumulation of visceral fat and promotion of an inflammatory state with greater insulin resistance (31). A previous analysis of the members of this cohort recruited in 2001 and followed for 3 years similarly

demonstrated a higher diabetes risk associated with PTSD symptoms.

Several limitations to this study should be noted. First, type 2 diabetes was determined using self-reported data, and it was not confirmed by medical record review. However, because self-reported diabetes compared with physician diagnosis or medical record data have been shown to have a high sensitivity (70–99%; median 81%) and specificity (92–99%), there is less likelihood for misclassification (32). Also, it is possible that individuals self-reporting type 1 diabetes were included in this analysis. However, individuals with a type 1 diabetes diagnosis in their DoD medical records were excluded, although this elimination process would miss those participants no longer receiving care from military treatment facilities after discharge or as Reservists. In addition, positive screens for mental disorders were determined from self-report. Also, we were unable to adjust for diet or family history, which are known risk factors for diabetes. We expect these findings to generalize to younger populations who are sufficiently healthy to enter into the U.S. Armed Forces, but it is unclear whether the results would apply to dissimilar populations.

Self-report of clinician-diagnosed sleep apnea was obtained, and the sensitivity and specificity of this report compared with the medical record are not known. Medical encounter data were not used to confirm diagnoses of diabetes or sleep apnea in this cohort due to the potential for some of its members, particularly those in the Reserves or National Guard, to have received care in non-DoD facilities. Inaccurate classification of sleep apnea and other covariates potentially may have limited our ability to adjust for confounding. Finally, self-reported sleep data were assessed during the prior 4 weeks, and sleep duration was rounded to the nearest whole hour, potentially biasing the estimate of actual sleep time (33–35).

This is the first study, to our knowledge, to examine baseline sleep characteristics in relation to incident diabetes while adjusting for several mental health conditions known to impair sleep and be associated with type 2 diabetes. Furthermore, this research was conducted in a large population-based study of active duty and Reserve/National Guard U.S. military personnel from all service branches. Additional strengths include the large sample size and up to 6-year duration of follow-up. Moreover, no association was found between reporting type 2 diabetes at baseline and nonresponse to the first follow-up questionnaire among the first panel of enrollees, suggesting that the development of diabetes was unlikely to have influenced the probability of responding to the follow-up survey (36). Finally, previous evaluations of possible biases suggest the Cohort is reasonably representative of military personnel in terms of baseline demographic and mental health characteristics, that participants report health and exposure data reliably, and that enrollment in the study is not influenced by health status (14,37–40).

We conclude that trouble sleeping and sleep apnea predict higher diabetes risk, independent of multiple diabetes risk factors and several mental health conditions. Of note, self-reported sleep apnea was also associated with a significantly higher risk for diabetes even after adjustment for other sleep characteristics, BMI, and mental health conditions. Substitution of sleep duration for trouble sleeping in multivariable modeling yielded nearly identical results, with significantly higher risk seen with <6 h of sleep. Confirmation of these findings through further analyses may advance our understanding of diabetes pathophysiology and create new opportunities for prevention.

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