ORIGINAL ARTICLE

Associations of Sleep-disordered Breathing and Insomnia with Incident Hypertension and Diabetes

The Hispanic Community Health Study/Study of Latinos

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Abstract

Rationale: Sleep disorders are associated with hypertension and diabetes, which are primary risk factors for cardiovascular diseases and mortality. It is important to understand these associations in Hispanic/Latino individuals, in whom cardiovascular death is the leading cause of mortality.

Objectives: To investigate the prospective associations of sleep-disordered breathing (SDB) and insomnia with incident hypertension and diabetes among U.S. Hispanic/Latino people over 6 years of follow-up and to assess potential sex differences in these associations.

Methods: Data from 11,623 Hispanic/Latino participants in the Hispanic Community Health Study/Study of Latinos (visit 1, 2008–2011; visit 2, 2014–2017) were analyzed using survey logistic regression models, adjusting for potential confounders.

Measurements and Main Results: SDB (apnea–hypopnea index of 5 or more) and insomnia (Women's Health Initiative Insomnia Rating Scale of 9 or more) were measured at baseline. Incident hypertension (stage 2 or greater) and diabetes were defined according to national guidelines. In the target population, 52.6% were women, with a mean age of 41.1 ± 14.9 years at baseline. SDB was associated with 1.54 higher adjusted odds of incident hypertension (95% confidence interval [CI], 1.18–2.00) and 1.33 higher odds of incident diabetes (95% CI, 1.05–1.67) compared with no SDB. Insomnia was associated with incident hypertension (odds ratio, 1.37; 95% CI, 1.11–1.69) but not with diabetes. The association between insomnia and incident hypertension was stronger among men than among women.

Conclusions: SDB was associated with incident hypertension and diabetes. Insomnia was associated with incident hypertension. These findings support the importance of sleep disorders as modifiable targets for disease prevention and reduction.

Keywords: sleep-disordered breathing; insomnia; hypertension; diabetes; Hispanic/Latino

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At a Glance Commentary

Scientific Knowledge on the Subject: Sleep disorders are highly prevalent in the general population and are associated with hypertension and diabetes, which are primary risk factors for cardiovascular diseases and mortality. Although the majority of literature on sleep disorders and cardiometabolic diseases has focused on non-Hispanic white individuals, it is important to understand the associations in Hispanic/Latino populations who have not only high rates of hypertension and diabetes but also higher rates of sleep disturbances compared with non-Hispanic white populations. To our knowledge, no prior empirical studies have examined the prospective relationships between sleep disorders and incident hypertension and diabetes among U.S. Hispanic/Latino adults of diverse backgrounds.

What This Study Adds to the Field: This study presents the first empirical evidence on the prospective associations between the two most common sleep disorders (sleep-disordered breathing and insomnia) with two of the most important cardiovascular risk factors (hypertension and diabetes) among a large cohort ($n = 11{,}623$) of U.S. Hispanic/Latino adults. Results show that sleep-disordered breathing was significantly associated with incident hypertension and diabetes. Insomnia was significantly associated with incident hypertension, with a stronger association in men than in women. These findings suggest that sleep disorders represent underrecognized, undertreated, and modifiable targets for cardiometabolic disease prevention and reduction among U.S. Hispanic/Latino adults.

Hypertension and diabetes are among the leading global risk factors for cardiovascular diseases and premature mortality (1–3). It is estimated that approximately one of three adults in the United States has hypertension and one of nine has diabetes (1, 2). Detection, treatment, and control of hypertension and diabetes are adopted by the World Health Assembly in 2013 as global noncommunicable disease targets (4). Efforts are warranted to identify modifiable risk factors for hypertension and diabetes.

Sleep disorders (e.g., sleep-disordered breathing [SDB] and insomnia) are highly prevalent in the general population and are associated with an increased prevalence of hypertension and diabetes (5–21). Mechanisms include altered endocrine, metabolic, and immune system responses to sleep disturbances and curtailed sleep that result in increased blood pressure, decreased insulin sensitivity, and impaired glucose tolerance (22, 23). Research has also indicated sex differences in the relationships between suboptimal sleep and cardiometabolic diseases, but the evidence is inconclusive (24, 25).

Although the majority of literature on sleep disorders and cardiometabolic diseases focused on non-Hispanic white subjects, it is important to understand the associations in Hispanic/Latino subjects. The Hispanic/Latino population currently accounts for 17.8% (57.5 million) of the U.S. population and is expected to double within the next four decades (26). Compared with their non-Hispanic white counterparts of similar age, Hispanic/Latino individuals have higher risks of sleep disturbances (e.g., SDB), a similar risk of hypertension but a higher proportion of cases of uncontrolled blood pressure, and a higher risk of diabetes (27–31). The few prior studies on the roles of sleep disorders in the cardiometabolic health of Hispanic/Latino populations, though suggestive, are limited by cross-sectional designs, relatively small samples, and underrepresentation of various Hispanic/Latino heritage groups (7, 32–34). To our knowledge, no prior empirical studies have examined the prospective relationships between sleep disorders and incident hypertension and diabetes among U.S. Hispanic/Latino adults of diverse backgrounds.

This study investigated the prospective associations of the two most common sleep disorders (SDB and insomnia) (35, 36) with incident hypertension and diabetes and potential sex differences in the associations among a cohort of U.S. Hispanic/Latino subjects. Data for this study came from the HCHS/SOL (Hispanic Community Health Study/Study of Latinos), the largest study of cardiovascular risk factors and sleep traits in U.S. Hispanic/Latino individuals. Some of the results of these studies have been previously reported in the form of an abstract (37).

Methods

Study Design and Study Participants

The HCHS/SOL is a community-based cohort study of 16,415 self-identified Hispanic/Latino persons aged 18–74 years recruited from randomly selected households in four U.S. field centers (Bronx, New York; Chicago, Illinois; Miami, Florida; and San Diego, California). Details of the sampling methods and design have been published (38, 39). Briefly, the baseline study recruited participants between 2008 and 2011 from defined geographic areas to provide a representative sample of these target areas, including participants of Cuban, Dominican, Mexican, Puerto Rican, Central American, and South American backgrounds. Of all individuals who were screened and invited and who met eligibility criteria, 41.7% ($n = 16{,}415$) were enrolled. Visit 2 took

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place between 2014 and 2017 and reexamined 11,623 participants from the baseline sample, with an average follow-up time of 6.1 years (SD, 0.8 yr). The study was approved by the institutional review boards at each participating institution, and written informed consent was obtained from all participants.

Exposures of Interest

At baseline, sleep health was assessed by standardized questions and a validated type 3 home sleep apnea test that provided objective recordings of airflow (via nasal pressure), oximetry, position, and snoring (ARES Unicorder 5.2; B-Alert). Sleep records were scored at a central sleep reading center by trained scorers blinded to all other data (7). Apnea–hypopnea index (AHI3) was calculated based on the average number of all apneas plus hypopneas associated with a 3% desaturation per hour of sleep. SDB was defined as an AHI3 of $\geqslant$5. Interscorer and intrascorer reliability of the AHI3 using this device was excellent; compared with full polysomnography, the sensitivity and specificity for detecting an AHI3 $\geqslant$5 were shown to be 80% and 88%, respectively (7, 40).

Insomnia was evaluated using the Women's Health Initiative Insomnia Rating Scale (WHIIRS), a standardized instrument of perceived insomnia symptoms that was developed and validated in a racially/ethnically diverse sample (41). Insomnia was defined as a score of 9 or greater, which corresponds with a high risk of insomnia.

We also explored subtypes of the sleep disorders because prior studies have indicated that SDB with sleepiness and insomnia with objective short sleep duration might represent subtypes associated with more detrimental effects on health (42, 43).

Outcomes of Interest

Prevalent (stage 2 or greater) hypertension was defined as a systolic blood pressure $\geqslant$140 mm Hg, a diastolic blood pressure $\geqslant$90 mm Hg, or the receipt of antihypertensive medication within 4 weeks before the visit (44). Incident hypertension was defined as not having hypertension at baseline and having hypertension at visit 2.

Diabetes was defined based on the American Diabetes Association definition as a fasting plasma glucose $\geqslant$126 mg/dl, 2-hour postload plasma glucose $\geqslant$200 mg/dl, or HbA1c $\geqslant$6.5% (45), with an additional criterion of self-reported use of antidiabetic medication within 4 weeks before the visit. We used the universal term "diabetes" because the analyses did not discriminate between type 1 and type 2 diabetes. Incident diabetes was defined as not having diabetes at baseline and having diabetes at visit 2.

Covariates

In line with prior work, we controlled for potential confounders measured at baseline, including sociodemographic factors, health behaviors, and adiposity, which are considered to be important risk factors for both sleep disorders and incident metabolic diseases (7, 46, 47). The adjusted sociodemographic factors included age, sex, Hispanic/Latino background, marital status (married/living with a partner, single, separated/divorced/widower), and education (no high school diploma or General Educational Development credential [GED], at most a high school diploma or GED, and greater than high school diploma or GED). Health behaviors included alcohol use (never, former, and current) and smoking (never, former, and current) status. Adiposity was measured by body mass index (BMI) derived from weight and height (underweight/normal, overweight, and obese) and waist circumference, which was measured using standardized protocols (39). We also controlled for time between visits and indicators for field centers to account for potential systematic differences across sites.

Statistical Analyses

Descriptive statistics are presented for the overall sample and for the two analytic samples (one for incident hypertension and the other for incident diabetes), accounting for the complex survey design and sampling weights. For the main analyses, survey logistic regression models were used to estimate the odds of 6-year incident hypertension and diabetes associated with SDB and insomnia, controlling for covariates. A sequential modeling approach was used, with model 1 including only the sleep disorders (entering simultaneously into the model); model 2 also adjusting for sociodemographics, health behaviors, time between visits, and indicators for field centers; and model 3 also adjusting for BMI and waist circumference. Interaction terms between the sleep disorders and sex were introduced to evaluate potential effect modification. We performed sex-stratified analyses when the interaction term was statistically significant ($P < 0.05$).

Prespecified sensitivity analyses explored alternative ways to model SDB and insomnia by introducing both variables as continuous (instead of as binary) variables, by introducing SDB as a categorical variable defined according to clinical cutoffs (with an AHI $\geqslant$5, $\geqslant$15, and $\geqslant$30 indicating mild, moderate, and severe SDB, respectively), and by introducing insomnia according to a different cutoff (WHIIRS of 10 or more instead of 9 or more). Sleep subphenotypes were explored by evaluating SDB with comorbid sleepiness (Epworth Sleepiness Scale of 11 or more) (48) by looking at those with neither SDB nor sleepiness, those with SDB only, those with sleepiness only, and those with both SDB and sleepiness. For insomnia, we evaluated insomnia with comorbid self-reported short sleep duration (6 h or less) by looking at those with neither insomnia nor short sleep duration, those with insomnia only, those with short sleep duration only, and those with both insomnia and short sleep duration. We evaluated the combination of SDB and insomnia both by testing for statistical interaction between these terms and by modeling each term alone and in combination. We reran the analyses by adjusting additional covariates, including years lived in the United States, household income, physical activity, depressive symptoms, prevalent diabetes at baseline (when modeling incident hypertension), and prevalent hypertension at baseline (when modeling incident diabetes). In *post hoc* exploratory analyses, we explored the mechanisms between the sleep disorders and the cardiometabolic outcomes by including the following potential mediators in the analyses: change in BMI between visit 1 and visit 2, average heart rate during sleep at baseline (a marker of sympathetic nervous system activity [SNA]) (49), and baseline levels of high sensitivity CRP (C-reactive protein).

All analyses were conducted in R version 3.5.3 (https://www.r-project.org/) using survey packages. All tests were two sided, with a significance level of 5%.

Results

Descriptive Results

Of the 11,623 participants, 1,424 (12.3%) did not undergo a sleep study or had insufficient sleep data for analyses. An additional 93

(0.8%) participants were excluded for missing data on covariates. For incident hypertension analyses, participants who had prevalent hypertension at visit 1 ($n = 3,139$) or had missing data on hypertension ($n = 2$) were excluded, yielding an analytic sample of 6,965. For incident diabetes analyses, participants who had prevalent diabetes at visit 1 ($n = 2,062$) or had missing data on diabetes ($n = 21$) were excluded, yielding an analytic sample of 8,023 (*see* Figure E1 in the online supplement).

Table 1 presents overall descriptive statistics by incident hypertension (excluding those with hypertension at baseline or those with missing data on hypertension) and by incident diabetes (excluding those with diabetes at baseline or those with missing data on diabetes). Overall, approximately half of the participants were women, and the mean age at baseline was 41.1 years (SD, 14.9 yr). Six main Hispanic/Latino heritage groups were represented. SDB was more common in men, whereas insomnia was more common in women. Hypertension incidence was similar in women and men, whereas diabetes incidence was slightly higher in men than in women.

Sleep Disorders and Incident Hypertension

Table 2 presents the adjusted odd ratios (ORs) of the associations between sleep disorders and incident hypertension. In fully adjusted models, SDB was significantly associated with increased odds of incident hypertension (OR, 1.54; 95% confidence interval [CI], 1.18–2.00). Insomnia was also significantly associated with higher odds of incident hypertension (OR, 1.37; 95% CI, 1.11–1.69). There was no evidence that a sex difference existed in the association between SDB and incident hypertension ($P = 0.70$ for the interaction term; Figure 1). A significant interaction between insomnia and sex was found for incident hypertension ($P = 0.03$ for the interaction term; Figure 1). In sex-stratified analyses, insomnia was associated with incident hypertension among men (OR, 1.87; 95% CI, 1.31–2.68). In contrast, no association was observed between insomnia and incident hypertension among women.

Sleep Disorders and Incident Diabetes

Table 2 presents the regression results of the associations between each sleep disorder and incident diabetes. When only the sleep disorders were included in model 1, both SDB and insomnia were significantly associated with incident diabetes. After adjusting for covariates, the association between SDB and incident diabetes remained (OR, 1.33; 95% CI, 1.05–1.67) whereas the association between insomnia and incident diabetes did not (OR, 1.13; 95% CI, 0.89–1.45). We observed no evidence that sex modified the associations between either sleep disorder with incident diabetes (Figure 1).

Sensitivity Analyses

We reran the analyses using alternative ways to model SDB and insomnia, including an assessment of their joint effects. For hypertension, there was no evidence that increasing severity of SDB category beyond an AHI $\geqslant$5 was associated with increasing odds of incident disease in fully adjusted models (Table E1). In contrast, odds of incident diabetes were highest for individuals with the most severe SDB category (AHI $\geqslant$30). When we examined subtypes of SDB and insomnia, we found no evidence that comorbid SDB and sleepiness (vs. SDB only) or comorbid insomnia and short sleep duration (vs. insomnia only) differed regarding associations with incident hypertension or diabetes compared with the simpler phenotypes (Table E2). The interaction term between SDB and insomnia had a P value of 0.94 in the model estimating incident hypertension and a P value of 0.24 in the model estimating incident diabetes. However, the comorbid SDB and insomnia phenotype was associated with both incident hypertension and diabetes. Compared with insomnia alone, a stronger OR was observed for this combined phenotype for incident hypertension but not for incident diabetes (Table E3). Similar results to the primary analyses were found when the analyses were adjusted for additional covariates (e.g., physical activity).

Results of the *post hoc* exploratory analyses show that including the change in BMI from visit 1 to visit 2 in the final model did not change the significance of the observed associations between the sleep disorders and the cardiometabolic outcomes, although the magnitude of the associations decreased modestly (e.g., by 6.5% for the OR relating SDB to hypertension; Table E4). Including average heart rate during sleep in the final model also did not materially alter the main effects model (e.g., effect estimate was reduced by 3.9% for the OR relating SDB to hypertension; Table E4). No changes in the results were observed for models including CRP (data not shown). There is thus limited evidence that change in BMI, average heart rate during sleep, or CRP level mediated the associations between the sleep disorders and the cardiometabolic diseases.

Discussion

To the best of our knowledge, this study presents the first empirical evidence on the prospective associations between SDB and insomnia with 6-year incident hypertension and diabetes among U.S. Hispanic/Latino subjects. Results show that SDB was associated with both incident hypertension and diabetes, whereas insomnia was associated with incident hypertension. The association between insomnia and incident hypertension was stronger among men compared with women, despite women reporting more insomnia symptoms.

Prior studies documenting the role of SDB and insomnia on cardiometabolic disorders have focused predominantly on non-Hispanic white populations (5, 6, 8, 9, 50); for instance, data from the Sleep Heart Health Study demonstrated that SDB was cross-sectionally associated with hypertension (9), and a prospective association was shown with data from the Wisconsin Sleep Cohort Study (6). A few recent studies focused on Hispanic/Latino populations (7, 32). Using visit 1 data from HCHS/SOL, Redline and colleagues reported that SDB was associated with prevalent hypertension and diabetes, whereas Ramos and colleagues reported that insomnia was not associated with prevalent hypertension (7, 32). These findings used cross-sectional designs that limited the assessment of causality (7, 32). Our study expands the current literature by investigating the associations of SDB and insomnia with incident hypertension and diabetes in a prospective large cohort of U.S. Hispanic/Latino individuals, showing that SDB was an antecedent risk factor for the development of both hypertension and diabetes and that insomnia, particularly in men, was associated with incident hypertension.

Table 1. Descriptive Characteristics of HCHS/SOL (2008–2017)

	All Panel Participants			Incident Hypertension Analyses Sample			Incident Diabetes Analyses Sample		
	Overall	Women	Men	Overall	Women	Men	Overall	Women	Men
n	10,106	6,434	3,672	6,965	4,405	2,560	8,023	5,105	2,918
Age, yr, mean (SD)	41.1 (14.9)	41.7 (15.0)	40.3 (14.6)	36.9 (13.0)	37.2 (13.1)	36.5 (13.0)	39.0 (14.1)	39.5 (14.3)	38.4 (13.9)
Sex, %									
F	52.6	100.0	0.0	52.4	100.0	0.0	52.1	100.0	0.0
M	47.4	0.0	100.0	47.6	0.0	100.0	47.9	0.0	100.0
Ethnic background, %									
Mexican	40.7	41.8	39.4	44.8	46.4	43.0	40.8	41.8	39.7
Dominican	9.8	11.0	8.4	9.2	10.4	8.0	9.8	11.1	8.4
Central American	7.5	7.5	7.5	7.9	7.9	7.9	7.7	7.7	7.6
Cuban	18.0	16.3	20.0	15.2	13.8	16.8	18.1	16.5	19.8
Puerto Rican	15.3	14.9	15.9	13.4	12.3	14.6	14.3	13.6	15.1
South American	4.7	5.0	4.4	5.0	5.2	4.7	5	5.3	4.7
More than one/other heritage	4.0	3.5	4.4	4.4	4.0	5.0	4.3	3.9	4.7
Marital status, %									
Married or living with a partner	50.3	48.4	52.5	50.0	50.5	49.4	49.3	48.2	50.5
Single	34.1	30.8	37.9	38.0	33.9	42.7	36.7	32.8	40.8
Separated, divorced, or widowed	15.6	20.9	9.7	12.0	15.7	7.9	14	18.9	8.7
Education, %									
No high school diploma or GED	32.3	32.8	31.8	30.0	29.6	30.5	29.8	29.6	30.1
At most a high school diploma or GED	28.0	26.8	29.2	29.2	28.1	30.3	28.8	27.4	30.3
Greater than high school diploma or GED	39.7	40.4	39.0	40.8	42.3	39.2	41.4	43	39.7
Smoking status, %									
Never	64.0	72.3	54.8	65.6	73.7	56.7	64.8	72.8	56.1
Former	17.1	12.8	21.9	14.8	11.3	18.6	15.8	12	20
Current	18.9	14.9	23.3	19.6	15.0	24.7	19.4	15.2	23.9
Drinking status, %									
Never	18.7	25.8	10.7	17.1	22.9	10.7	18.1	24.4	11.2
Former	30.1	33.5	26.4	29.3	33.0	25.2	28.7	32.3	24.7
Current	51.2	40.7	62.9	53.6	44.1	64.0	53.3	43.3	64.1
BMI, kg/m^2, %									
<25 (underweight and normal)	23.4	23.4	23.3	27.2	27.7	26.7	25.5	26.0	24.9
25–30 (overweight)	37.1	33.9	40.6	37.1	34.0	40.5	38.1	35.1	41.2
⩾30 (obese)	39.5	42.7	36.0	35.7	38.2	32.8	36.5	38.9	33.8
Waist circumference, cm, mean (SD)	97.3 (14.2)	96.5 (14.6)	98.1 (13.7)	95.5 (13.9)	94.8 (14.4)	96.3 (13.3)	95.9 (13.5)	95.0 (13.8)	96.9 (13.2)
Time between visits, yr, mean (SD)	6.1 (0.8)	6.1 (0.9)	6.1 (0.8)	6.2 (0.9)	6.1 (0.9)	6.2 (0.8)	6.1 (0.9)	6.1 (0.9)	6.1 (0.8)
SDB, %									
No	73.9	80.2	66.9	80.9	87.5	73.7	77.9	84.3	70.9
Yes	26.1	19.8	33.1	19.1	12.5	26.3	22.1	15.7	29.1
Insomnia, %									
No	67.4	62.4	72.9	70.1	65.9	74.8	68.7	63.6	74.3
Yes	32.6	37.6	27.1	29.9	34.1	25.2	31.3	36.4	25.7
Incident hypertension, %									
No	89.1	89.2	89.0	85.7	85.8	85.7	90.0	89.8	90.2
Yes	10.9	10.8	11.0	14.3	14.2	14.3	10.0	10.2	9.8
Incident diabetes, %									
No	92.4	92.8	92.0	94.0	93.9	94.1	91.1	91.4	90.7
Yes	7.6	7.2	8.0	6.0	6.1	5.9	8.9	8.6	9.3

Definition of abbreviations: BMI = body mass index; GED = General Educational Development credential; HCHS/SOL = Hispanic Community Health Study/Study of Latinos; SDB = sleep-disordered breathing.

The numbers of participants were unweighted. The percentages were weighted. Weighted descriptive statistics of the following three samples are presented: all participants who participated in both examinations, participants in the incident hypertension analyses sample (excluding those with prevalent hypertension at visit 1 or those who had missing data on hypertension), and participants in the incident diabetes analyses sample (excluding those with prevalent diabetes at visit 1 or who had missing data on diabetes).

Table 2. Effect Estimates from Survey Logistic Regression Models for the Association between Sleep Disorders and 6-Year Incident Hypertension ($n = 6{,}965$)/Diabetes ($n = 8{,}023$) in HCHS/SOL (2008–2017)

	Model 1		Model 2		Model 3	
	OR	95% CI	OR	95% CI	OR	95% CI
Hypertension						
SDB	**3.19***	**2.60–3.90**	**1.93***	**1.52–2.45**	**1.54†**	**1.18–2.00**
Insomnia	**1.73***	**1.44–2.08**	**1.43†**	**1.15–1.76**	**1.37†**	**1.11–1.69**
Diabetes						
SDB	**2.97***	**2.41–3.66**	**2.06***	**1.66–2.56**	**1.33‡**	**1.05–1.67**
Insomnia	**1.39‡**	**1.12–1.74**	1.22	0.96–1.55	1.13	0.89–1.45

Definition of abbreviations: CI = confidence interval; HCHS/SOL = Hispanic Community Health Study/Study of Latinos; OR = odds ratio; SDB = sleep-disordered breathing.
Model 1 included only SDB and insomnia. Model 2 further controlled for sociodemographics, health behaviors, time between visits, and indicators for field centers. Model 3 further controlled for body mass index and waist circumference. Statistically significant ($P < 0.05$) effect estimates are bolded.
*$P < 0.001$.
†$P < 0.01$.
‡$P < 0.05$.

The plausibility for a causal relationship between SDB and cardiometabolic diseases is supported by evidence from intervention studies. Prior research showed that SDB treatment reduces nighttime and daytime blood pressure in patients with SDB (51). Some experimental and small clinical intervention data also showed that SDB treatment improves insulin sensitivity and glucose levels, although more data from large trials are needed (52). For instance, one randomized controlled trial involving 39 individuals with prediabetes showed that 2 weeks of 8-hour nightly continuous positive airway pressure (CPAP) treatment improved glucose metabolism compared with placebo (17). Two 6-month randomized controlled trials reported inconsistent findings on the effect of CPAP on glycemic control in patients with diabetes; a study involving 298 patients found no effect of CPAP treatment on HbA1c, whereas a study involving 50 patients did find an effect (18, 19). SDB, which is characterized by repetitive airflow interruptions during sleep, results in intermittent hypoxia and arousals that cause sleep fragmentation and increased SNA, a mechanism for hypertension and diabetes (53, 54). SDB also induces inflammatory and hormonal responses, including insulin resistance, elevations of inflammatory cells, and endothelial dysfunction. Wide intrathoracic swings in systemic blood and arterial pulmonary pressures could further contribute to vascular damage (49, 55). In addition, although obesity is an established risk factor for SDB, individuals with SDB are also prone to more weight gain (56), which might increase their risk of hypertension and diabetes (57, 58).

Insomnia has been associated with increases in markers of systematic inflammation, known risk factors for hypertension and diabetes (1, 59, 60). Furthermore, patients with insomnia have increased heart rate and chronic activation of the hypothalamic–pituitary–adrenal axis, which have been linked to metabolic disorders such as diabetes (61). Although there are strong biological bases linking insomnia to adverse cardiometabolic health, prior literature has not consistently shown associations between insomnia with incident hypertension or diabetes. A recent

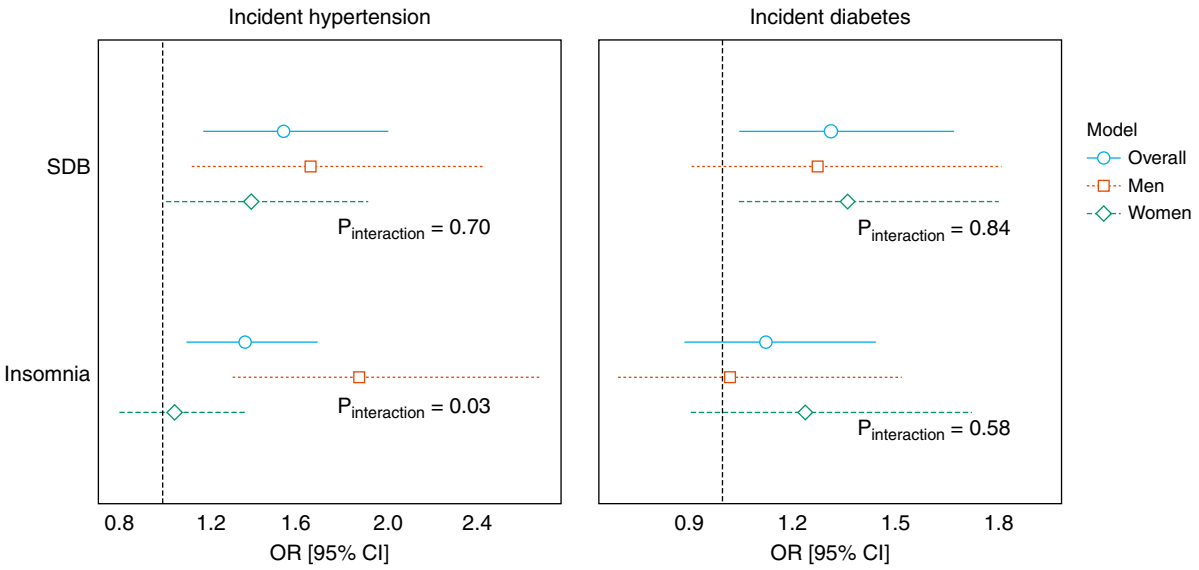

Figure 1. Sex-stratified analyses on the associations between sleep disorders and 6-year incident hypertension ($n = 6{,}965$) or diabetes ($n = 8{,}023$) from the Hispanic Community Health Study/Study of Latinos (2008–2017). *P* values of interaction terms between the respective sleep disorder and sex are presented. Survey logistic regression analyses adjusted for sociodemographics, health behaviors, body mass index, waist circumference, time between visits, and indicators for field centers. CI = confidence interval; OR = odds ratio; SDB = sleep-disordered breathing.

systematic analysis found that insomnia with short sleep duration or arousal is associated with hypertension. However, based on a majority of case–control studies, those with and without insomnia did not differ in blood pressure (62). Similarly, although meta-analyses show consistent associations between short sleep duration and incident diabetes (63), associations between insomnia in the absence of short sleep with diabetes are less clear (50). Findings from the current large prospective study provide new data showing that insomnia in U.S. Hispanic/Latino individuals was associated with incident hypertension but not diabetes and that these associations were not modified by self-reported sleep duration. It is possible that objectively measured sleep duration may have allowed an improved phenotypic characterization of an "insomnia–short sleep" risk factor (50). The severity of insomnia symptoms in a community-based cohort may also not reflect the extent of metabolic disfunction in clinical settings where patients seek help for more severe sleep disorders and are better characterized with clinical interviews.

As discussed earlier, there are multiple potential mechanisms linking sleep disorders to cardiometabolic disease. Although the aim of this study was not to identify physiological mechanisms, we conducted several *post hoc* exploratory analyses modeling change in BMI, baseline heart rate during sleep (a marker of SNA), and CRP level. These analyses did not change the significance of the associations between the sleep disorders and the cardiometabolic outcomes and only slightly to modestly decreased magnitude of the associations. Our findings provide a framework for designing future research to address which physiological mediators link sleep disorders to later cardiometabolic diseases.

Sex differences abound in human health and diseases, possibly because of hormonal factors, gene expression, and behavioral and sociocultural factors. Our data found that the association between insomnia and incident hypertension was stronger among men than women despite a higher prevalence of insomnia in women. Although small experimental studies indicated that acute inflammatory responses to sleep disruption may be stronger in women (64, 65), prior epidemiological studies reported a stronger relationship between insomnia and higher levels of CRP and a stronger relationship between insomnia and mortality among men (66, 67). Self-rated health has been reported to associate more strongly with mortality in men than women (68) despite women usually reporting worse self-rated health (69). It is possible that women, the primary consumers of health services and information, might be more likely to know about their health and report health concerns/problems (69). Men, on the other hand, might only report symptoms with a high level of disturbance. Thus, insomnia, based on self-reported symptoms, might reflect a greater severity of sleep disturbance in men compared with women despite comparable scores. Our data suggest a need for further studies of sex differences that address potential reporting differences and link perceived symptoms with objective changes in sleep.

Recent data suggested that sleepiness reported by predominantly white, older individuals with SDB marked individuals at increased cardiovascular risk (70). Our exploratory analysis did not support differences in the associations between SDB and cardiometabolic outcomes in the presence of sleepiness. This suggests that in middle-aged U.S. Hispanic/Latino individuals, sleepiness should not be relied on to identify individuals at high risk for SDB-associated hypertension and diabetes. On the other hand, comorbid SDB and insomnia was associated with a higher OR of hypertension compared with insomnia only, suggesting increased hypertension risk among individuals with both intermittent desaturation (SDB) and a hyperarousal phenotype (insomnia), supporting further work to identify susceptibility to chronic diseases by SDB subphenotypes.

Our data did not show evidence of a dose–response association between SDB severity and incident hypertension, suggesting that mild levels of SDB confer increased hypertension risk in this sample. In contrast, risk for incident diabetes was highest among those with severely elevated AHI levels, consistent with prior research suggesting that more severe levels of hypoxemia confer greater metabolic dysfunction (15).

Strengths of the study include the large and diverse Hispanic/Latino sample, which was representative of four distinct and diverse geographical areas; the prospective design; the objective measure of SDB and standardized measure of insomnia; standardized assessments of hypertension and diabetes; and the consideration of multiple potential confounders.

This study also has several limitations. First, the home sleep apnea test device did not allow the evaluation of arousal or sleep architecture, which may lead to an underestimation of disease severity both because of overestimation of sleep time and underrecognition of hypopneas unassociated with desaturation. Another limitation is that the current insomnia analyses were based on validated assessment of insomnia symptoms but not on a clinical diagnosis (which uses symptoms and a diagnostic interview). The WHIIRS was developed in a sample of postmenopausal women, and the results should be interpreted cautiously with other age groups and with men. Prior research has suggested that minority populations might underreport sleep disturbances (71), possibly because of social desirability (a tendency not to encode a negative event), stress, stereotype threat, acculturation, attitudes, *et cetera*. If there was underreporting of insomnia symptoms unrelated to study outcomes, the results may be biased toward the null. However, the WHIIRS was developed in a racially/ethnically diverse group, and psychometric work on a sample of almost 70,000 participants demonstrated that the scale has excellent reliability and validity. Factor analysis revealed that the scale has a highly stable factor structure across age and racial/ethnic groups. WHIIRS items correspond with the majority of insomnia characteristics noted in the major nosologies, and differences in sleep latency, sleep efficiency, and waking after sleep onset measured by a wrist activity monitor were reflected by corresponding differences in WHIIRS scores (41, 72). Short sleep was also based on self-report, which might be subject to misclassification (73). Third, although the analyses used prospective data and carefully controlled for potential confounders, the observational design constrained our ability to identify causality and to detect mediating mechanisms. Future research that includes more detailed information on the time of onset of incident hypertension and diabetes would help quantify the extent to which individuals with sleep disorders have an accelerated rate of developing new hypertension or diabetes.

Furthermore, the HCHS/SOL participants were largely recruited from urban areas, and thus, the results might not generalize to populations in rural areas. On a related note, the ethnic background distribution of individuals in HCHS/SOL does not mirror that in the United States. For instance, 41% of the individuals in HCHS/SOL are of Mexican origin, whereas 63% of the Hispanic/Latino population in the United States is of Mexican origin. Because there might be marked heterogeneity and systematic differences in the sleep patterns and cardiovascular risk factors among subgroups of Hispanic/Latino subjects (74, 75), the results might not generalize to the Hispanic/Latino populations outside of the target areas of HCHS/SOL. Additional research with larger numbers of outcomes within each background group is needed to address potential heterogeneity in associations between disturbed sleep and incident cardiometabolic disease. Because there is no non-Hispanic control group, the results might not be directly compared with the observations made in other racial/ethnic groups.

In summary, this study presents some of the first prospective evidence on the associations of SDB and insomnia with incident hypertension and diabetes in U.S. Hispanic/Latino individuals. Results show that SDB was associated with both 6-year incident hypertension and diabetes, whereas insomnia was associated with incident hypertension. Moreover, the association between insomnia and incident hypertension was stronger in men compared with women. Given the fact that sleep disorders are largely undiagnosed and undertreated (7), they might represent modifiable targets for disease prevention and reduction among U.S. Hispanic/Latino populations. Culturally informed interventions focusing on detecting and treating sleep disorders might improve cardiometabolic health among U.S. Hispanic/Latino individuals. ■

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