ORIGINAL ARTICLE

Association Between Sleep Timing, Obesity, Diabetes: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) Cohort Study

Kristen L. Knutson, PhD[1]; Donghong Wu, MS[2]; Sanjay R. Patel, MD[3]; Jose S. Loredo, MD[4]; Susan Redline, MD, MPH[5]; Jianwen Cai, PhD[6]; Linda C. Gallo, PhD[7]; Yasmin Mossavar-Rahmani, PhD, RD[8]; Alberto R. Ramos, MD MSPH[9]; Yanping Teng, MD MSPH[6]; Martha L. Daviglus, MD, PhD[2]; Phyllis C. Zee[1]

[1]Center for Circadian and Sleep Medicine, Department of Neurology, Northwestern University; [2]Institute for Minority Health Research, University of Illinois at Chicago; [3]Division of Pulmonary Allergy and Critical Care Medicine, University of Pittsburgh; [4]Department of Medicine, University of California San Diego; [5]Division of Sleep and Circadian Disorders, Brigham and Women's Hospital; Division of Pulmonary, Critical Care and Sleep, Beth Israel Deaconess Medical Center; Harvard Medical School; [6]Collaborative Studies Coordinating Center, Department of Biostatistics, University of North Carolina at Chapel Hill; [7]Department of Psychology, San Diego State University; [8]Department of Epidemiology & Population Health, Albert Einstein College of Medicine, Bronx, New York; [9]Department of Neurology, University of Miami, Miller School of Medicine

Study Objectives: Recent studies implicate inadequate sleep duration and quality in metabolic disease. Fewer studies have examined the timing of sleep, which may be important because of its potential impact on circadian rhythms of metabolic function. We examined the association between sleep timing and metabolic risk among Hispanic/Latino adults.

Methods: Cross-sectional data from community-based study of 13 429 participants aged 18–74 years. People taking diabetic medications were excluded. Sleep timing was determined from self-reported bedtimes and wake times. Chronotype was defined as the midpoint of sleep on weekends adjusted for sleep duration on weekdays. Other measurements included body mass index (BMI), fasting glucose levels, estimated insulin resistance (HOMA-IR), glucose levels 2 hours post oral glucose ingestion, and hemoglobin A1c. Survey linear regression models tested associations between sleep timing and metabolic measures. Analyses were stratified by diabetes status and age-group when significant interactions were observed.

Results: Among participants with diabetes, fasting glucose levels were positively associated with bedtime (approximately +3%/hour later, $p < .01$) and midpoint of sleep (approximately +2%/hour later, $p < .05$). In participants with and without diabetes combined, HOMA-IR was positively associated with midpoint of sleep (+1.5%/hr later, $p < .05$), and chronotype (+1.2%/hour later, $p < .05$). Associations differed by age-group. Among those < 36 years, later sleep timing was associated with lower BMI, lower fasting glucose, and lower HbA1c, but the opposite association was observed among older participants.

Conclusions: Later sleep timing was associated with higher estimated insulin resistance across all groups. Some associations between sleep timing and metabolic measures may be age-dependent.

Keywords: sleep timing, diabetes, insulin resistance, circadian.

Statement of Significance

Much research has examined associations between sleep duration or quality and metabolic health, but less attention has been paid to sleep timing and metabolism. We examined this association in a large sample of Hispanics/Latinos, a group disproportionately burdened by diabetes and obesity. We found that later sleep timing was significantly associated with higher estimated insulin resistance in both those with and without diabetes combined. In participants with diabetes, later timing was also associated with higher fasting glucose. The relationship between sleep timing and some metabolic measures differed between younger people (< 36 years) and older individuals (36–70 years). This study was cross-sectional, so causality cannot be determined. Future research should test the metabolic effects of manipulating sleep timing at different ages.

INTRODUCTION

Chronic metabolic diseases, such as obesity and diabetes, constitute a significant burden on Americans, and Hispanics/Latinos are disproportionately affected compared to non-Hispanic whites.[1,2] These metabolic diseases can lead to reduced quality of life, lower life expectancy, and increased healthcare costs. Furthermore, the Hispanic/Latino population in the United States is predicted to more than double from 2012 to 2060,[3] and if the disparities in metabolic diseases persist, then a greater proportion of Americans will be afflicted. Clearly, a more thorough understanding of the determinants of metabolic diseases in diverse Hispanic/Latino groups is warranted. The current study explores sleep timing as a potential novel determinant of metabolic disease.

Much attention has been devoted to examining the association between sleep duration and metabolic disease risk,[4–6] although little work has examined this association in Hispanic/Latino populations. The timing of sleep is another distinct characteristic of sleep patterns that may impact metabolic disease risk independent of sleep duration, possibly through the effects of circadian rhythms on metabolism. The timing of sleep is driven by both endogenous circadian rhythms that regulate sleep propensity, energy homeostasis and metabolism as well as by sociocultural factors that influence behavior. A previous observational study reported that individuals who sleep at a later clock time had higher body mass index (BMI), ate more calories after 8:00 PM, and had less healthy diets.[7] In addition, individuals with a preference for later bedtimes were more likely to have diabetes.[8]

Thus, the aim of this study was to examine the association between the timing of sleep and metabolic disease biomarkers in a community-based sample of Hispanic/Latino adults who participated in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL). We hypothesized that later sleep times would be associated with greater metabolic disease risk factors.

METHODS

Sample

The HCHS/SOL is a community-based cohort study of 16 415 self-identified noninstitutionalized Hispanic/Latino adults aged 18–74 years at the time of screening. The primary objectives

of HCHS/SOL are to obtain information about the health status and disease burden of US Hispanics/Latinos and to examine the associations between baseline risk factors and disease incidence on follow-up evaluations. Participants were recruited between 2008 and 2011 from randomly selected households in four US field centers (Bronx, NY; Chicago, IL; Miami, FL; San Diego, CA) using a stratified two-stage probability sample design. In order to obtain an ethnically and socioeconomically diverse and representative sample, HCHS/SOL deliberately oversampled community areas with higher concentrations of Hispanic/Latino households, randomly selected census block groups from these defined community areas and then randomly selected households in these community block groups. Details on study design, including the sleep assessment, have been published previously.[9–11] This study presents data from the baseline examination. The Institutional Review Boards of the participating institutions reviewed and approved the study protocol, and all participants provided written informed consent.

Measurements

The baseline clinical examination[10] included anthropometric measurements, a fasting blood sample, an oral glucose tolerance test, and sociodemographic and behavioral assessments. Questionnaires were administered in Spanish or English based on the participant's language preference.

Weight and height were measured with participants wearing light clothing, and body mass index (BMI) was calculated by dividing weight (kg) by height (m^2). Obesity was defined as a BMI ≥30 kg/m^2. Fasting blood samples were collected soon after arrival and at 120 min after oral glucose ingestion (oral glucose tolerance test). Glucose, insulin, and hemoglobin A1c levels were measured on the fasting blood sample, and glucose was measured again on the 120-min blood sample. The homeostatic assessment of insulin resistance (HOMA-IR) was calculated using the following formula: (fasting plasma insulin (mU/l) × fasting plasma glucose (mmol/l)) / 22.5.[12,13] Diabetes was defined as a fasting glucose value ≥126 mg/dl if fasting time was >8 hr or fasting glucose ≥200 if fasting time was <8 hr, or glucose level ≥200 mg/dl 120 min after oral glucose ingestion, or hemoglobin A1c ≥6.5% or the use of antidiabetes medication. Participants brought all medications to the examination, and medication names and dosages were recorded by study personnel.

The HCHS/SOL sleep questionnaire was adapted from the Sleep Heart Health Study Sleep Habits Questionnaire.[14] Self-reported sleep timing was assessed separately for weekdays (or work/school days) and weekends (or free days) using the following questions: "What time do you usually go to bed?" and "What time do you usually wake up?" Sleep duration was estimated as the interval between bedtime and wake time for weekdays and weekends separately. Weekly average sleep duration was calculated with the following formula: (weekday value × 5 +weekend value × 2)/7. We also calculated the midpoint of the sleep period for both weekdays and weekends. Chronotype was calculated using the method proposed by Roenneberg *et al.*[15] This measure is meant to represent when a person prefers to sleep, an indicator of endogenous circadian phase. It is calculated by determining the average midpoint of the sleep period on weekends but is corrected for average sleep duration on weekdays to account for any accumulated sleep debt during the week that may result in an extended time in bed.

Sleep-disordered breathing was objectively measured using a sleep apnea monitor for overnight recording (ARES Unicorder 5.2; B-Alert, Carlsbad, CA), which measures airflow using a nasal pressure cannula and transducer, hemoglobin oxygen saturation using reflectance oximetry, head movement and position using actigraphy, and a microphone to record snoring levels.[11] Sleep records were scored at a central sleep reading center by registered polysomnographic technologists. Hypopnea was defined as a 50% or greater reduction in airflow lasting ≥10 sec combined with an associated oxygen desaturation ≥3%. The apnea–hypopnea index (AHI) was calculated and dichotomized as AHI ≥15 versus AHI < 15, which is the standard cutoff for moderate sleep apnea.

Sociodemographic variables included in this study were Hispanic/Latino background (i.e., Mexican, Cuban, Puerto Rican, Dominican, Central American, South American, or missing ethnicity), age, gender, income, education, household size, marital status (single, married, or separated), duration of residence in the United States (<10 vs. ≥10 years), employment status, and shift work status. Annual household income was categorized into four groups: <$20 000, $20 000–$50 000, >$50 000, or not reported. Education was also categorized into three groups: <high school, high school or equivalent, and >high school or equivalent. Household size was measured by asking the respondent for the number of people supported by the household income during the past year. Employment status and shiftwork status were combined to create the following categories: (1) retired or not working, (2) part-time nonshift workers, (3) part-time shift workers, (4) full-time nonshift workers, and (5) full time shift workers.

Statistical Analyses

Of the 16 415 HCHS/SOL participants, 1823 were excluded due to use of hypoglycemic medications. Participants taking diabetic medications were excluded from the regression analyses because variability in the type, dosage, and duration of medication use could confound the associations and were not measureable. In addition, 1163 were excluded because of missing data on average sleep duration (n = 791), employment and work shift status (n = 39), or other covariates (n = 333). We compared available variables between those excluded due to missing data and those included in the final analyses. On average, the excluded sample was slightly younger (39.1 vs. 39.8 years), had higher BMI (29.4 vs. 29.1 kg/m^2), had higher fasting glucose (104.7 vs. 97.0 mg/dl), higher HOMA-IR (3.6 vs. 3.1), higher 2-hr glucose (119.3 vs. 118.0 mg/dl), and a higher proportion of participants with diabetes (12.3% vs. 6.9%). The final sample size for these analyses was 13 429 participants. Of note, there were 667 participants without diabetes and 340 participants with diabetes but not taking medication who were missing the 2-hr glucose value. However, these participants were only excluded from analyses of 2-hr glucose levels. Also, there were 20 participants with missing data on the HOMA index of insulin resistance but they were only excluded from analyses of HOMA.

Age and sex-adjusted means (continuous variables) or proportions (categorical variables) were computed by Hispanic/Latino group for each variable. All reported values were weighted for survey design and nonresponse. Survey-specific procedures were used to compute 95% confidence intervals to account for the two-stage sampling design, stratification, and clustering. Comparisons across Hispanic/Latino groups were performed using the overall Wald's test.

To examine the associations between the sleep timing variables and our key outcomes, survey regression models were used. Logistic regression was used for the dichotomous outcomes, including obesity and diabetes. Odds ratios with 95% CIs were computed. Linear regression models were used for the continuous variables, including BMI, fasting glucose, HOMA-IR, 2-hr post-load glucose levels, and hemoglobin A1c levels. Both fasting glucose and HOMA-IR were log transformed due to skewed distributions. Regression coefficients with standard errors were reported. Models were adjusted for age, gender, Hispanic/Latino background, study site, household income, education, household size, marital status, duration of residence in the United States (<10 vs. ≥10 years), sleep duration (except for models that included sleep midpoint and chronotype because sleep duration is part of their calculations), AHI category, employment, and shift work status. We also tested interaction terms between the diabetes status and each sleep timing measure to see if the associations varied by diabetes status. For interaction terms that were significant, analyses were stratified by diabetes status. Finally, we also tested interactions between the sleep timing variables and Hispanic/Latino background, sex, and age. For the interaction terms, age was grouped into four categories: ≤35 years, 36–<55 years, 55–<70 years, and 70 years and older. All statistical tests were two-sided at a significance level of .05. All analyses were performed using complex survey procedures in SAS version 9.3 (SAS Institute).

RESULTS

Table 1 presents age- and sex-adjusted, weighted descriptive statistics for demographic and health variables overall and for each Hispanic/Latino group. Over one-third of the target population was obese and 14% were classified as having diabetes. Table 2 presents age- and sex-adjusted, weighted descriptive statistics for the sleep timing variables overall and for each Hispanic/Latino group. Overall, the average bedtime was 11:24 PM and wake time was 7:24 AM. Comparisons among the Hispanic/Latino groups indicated that individuals of Mexican background had the earliest bedtimes and wake times. Average sleep duration was 8.0 hr. Mean sleep midpoint overall was 3:24 AM and mean chronotype, which adjusts for sleep duration, was 4:00 AM. Chronotype varied substantially with 10.1% having a chronotype before 2:00 AM and 23.4% having a chronotype after 5:00 AM.

In logistic regression models, none of the sleep timing variables was associated with prevalent obesity or diabetes status (results not shown). Table 3 presents results of multivariable linear regression models for associations between sleep timing

Table 1—Descriptive characteristics for HCHS/SOL target population overall and by Hispanic/Latino background groups.

	All	Mexican	Cuban	Puerto Rican	Dominican	Central American	South American	Other
Unweighted *N*	13429	5460	1996	2008	1147	1471	922	425
Age[b]	39.8 (39.3–40.3)	37.5 (36.8–38.3)	45.4 (44.3–46.4)	41.1 (40.0–42.2)	37.8 (36.6–39.1)	38.9 (37.9–39.9)	41.9 (40.4–43.5)	33.2 (31.8–34.6)
BMI[b], kg/m^2	29.1 (28.9–29.3)	29.1 (28.8–29.4)	28.5 (28.1–28.8)	30.3 (29.7–30.8)	29.1 (28.7–29.6)	28.9 (28.6–29.3)	27.8 (27.4–28.3)	29.6 (28.9–30.4)
Obesity[b], %	37.9 (36.5–39.3)	37.7 (34.9–40.4)	35.0 (32.3–37.6)	44.3 (40.6–48.0)	39.2 (35.8–42.7)	36.3 (33.5–39.2)	29.1 (25.2–33.0)	42.0 (35.7–48.3)
Fasting glucose[b], mg/dl	97.0 (96.4–97.6)	98.9 (97.5–100.2)	95.8 (94.9–96.8)	95.8 (94.7–96.8)	94.6 (93.7–95.6)	97.6 (96.1–99.2)	94.9 (94.0–95.9)	95.6 (94.5–96.7)
HOMA_IR[b]	3.1 (3.0–3.2)	3.2 (3.0–3.3)	3.2 (3.1–3.4)	3.2 (3.0–3.4)	2.6 (2.5–2.7)	3.2 (3.1–3.4)	2.7 (2.5–2.8)	3.1 (2.8–3.3)
2-hr glucose[b] (missing *n* = 1007)	118.0 (117.0–119.0)	120.0 (118.2–121.8)	118.0 (115.9–120.1)	113.7 (111.4–116.0)	116.3 (113.6–119.0)	119.7 (117.2–122.2)	117.5 (114.3–120.6)	115.6 (111.3–119.8)
Hemoglobin A1c[b]	5.5 (5.5–5.6)	5.6 (5.6–5.6)	5.4 (5.4–5.5)	5.5 (5.5–5.6)	5.5 (5.5–5.6)	5.6 (5.5–5.6)	5.4 (5.4–5.5)	5.5 (5.4–5.5)
Diabetes[b], %	6.9 (6.3–7.4)	8.2 (7.2–9.1)	6.0 (4.7–7.3)	5.8 (4.6–7.0)	6.3 (4.9–7.6)	7.4 (5.9–8.8)	4.7 (3.1–6.4)	6.3 (4.2–8.4)

Abbreviations: HOMA_IR: HOMA index of Insulin Resistance; CI, confidence interval; HCHS/SOL, Hispanic Community Health Study/Study of Latinos.
[a]Values are presented as means (95% CI) or proportions (95% CI). Values were weighted for survey design and nonresponse and adjusted to mean age and male sex. The mean values of age are sex−adjusted.
[b]$p < .001$; comparisons across Hispanic/Latino groups were performed using the overall Wald's test.
[c]$p < .01$; comparisons across Hispanic/Latino groups were performed using the overall Wald's test.
[d]$p < .05$; comparisons across Hispanic/Latino groups were performed using the overall Wald's test.

Table 2—Description of sleep timing variables for HCHS/SOL target population overall and by Hispanic/Latino background groups.

	All	Mexican	Cuban	Puerto Rican	Dominican	Central American	South American	Other
Weekly average bedtime[d]	23.4 (23.3–23.5)	23.0 (23.0–23.1)	23.6 (23.5–23.7)	23.7 (23.4–23.9)	23.8 (23.6–23.9)	23.4 (23.3–23.5)	23.6 (23.4–23.8)	23.9 (23.6–24.3)
Weekly average wake time[d]	7.5 (7.4–7.5)	7.1 (7.0–7.2)	7.7 (7.6–7.8)	7.8 (7.6–8.1)	7.7 (7.6–7.9)	7.4 (7.2–7.5)	7.4 (7.2–7.6)	7.9 (7.5–8.2)
Weekly average midsleep point[b,d]	3.4 (3.4–3.5)	3.1 (3.0–3.1)	3.7 (3.6–3.8)	3.7 (3.6–3.9)	3.7 (3.6–3.9)	3.4 (3.3–3.5)	3.5 (3.3–3.7)	3.9 (3.6–4.2)
Mean chronotype[c,d]	4.0 (3.9–4.0)	3.6 (3.5–3.6)	4.2 (4.1–4.3)	4.4 (4.3–4.6)	4.3 (4.1–4.5)	4.0 (3.9–4.2)	4.0 (3.8–4.2)	4.6 (4.3–5.0)
Weekly average sleep duration[d]	8.0 (7.9–8.0)	8.0 (8.0–8.1)	8.1 (8.0–8.2)	7.8 (7.7–7.9)	7.9 (7.8–8.0)	8.0 (7.9–8.0)	7.8 (7.7–7.9)	7.8 (7.5–8.0)

Abbreviations: CI, confidence interval; HCHS/SOL, Hispanic Community Health Study/Study of Latinos.
[a]Values are presented as means (95% CI) or proportions (95% CI). Values were weighted for survey design and nonresponse and adjusted to mean age and male sex.
[b]midsleep = waketime−0.5*time in bed.
[c]Average midsleep on weekends minus 0.5 × (sleep duration on weekends − [(5 × sleep duration on weekdays + 2 × Sleep duration on weekends)/7]).
[d]$p < .001$; comparisons across Hispanic/Latino groups were performed using the overall Wald test.

Table 3—Results from linear regression models for associations between 4 different sleep timing variables and 5 metabolic health measures (n = 13 429).

	BMI, kg/m², Regression coefficient (*SE*)	Log of fasting glucose, Regression coefficient (*SE*)	Log of HOMA−Insulin Resistance, Regression coefficient (*SE*)	2−hr glucose, mg/dl, Regression coefficient (*SE*)	HbA1c, Regression coefficient (*SE*)
Weekly bedtime[b] (per clock hour)	−0.0895 (0.046)	Diabetes[c]: 0.0266 (0.009)[d] No diabetes: 0.0010 (0.001)	0.0128 (0.007)	−0.4410 (0.218)[e]	Diabetes: 0.0691 (0.0363) No diabetes: −0.0066 (0.0036)
Weekly wake time[b] (per clock hour)	−0.0008 (0.046)	0.0026 (0.001)[e]	0.0133 (0.007)	−0.1250 (0.212)	0.0032 (0.005)
Weekly sleep midpoint[f] (per clock hour)	−0.0664 (0.041)	Diabetes[c]: 0.0232 (0.009)[e] No diabetes: 0.0012 (0.001)	0.0145 (0.006)[e]	−0.3283 (0.235)	0.0008 (0.005)
Chronotype[f] (per clock hour)	−0.0120 (0.035)	0.0017 (0.001)	0.0118 (0.005)[e]	−0.1740 (0.186)	0.0008 (0.004)

[a]Results are stratified by individuals without diabetes and those with diabetes but who are not taking medication only when interaction terms were significant.
[b]Adjusted for age, sex, Hispanic/Latino background group, study site, income, education, household size, years in US (< 10 vs ≥10 y), marital status, sleep duration, AHI category (< 15 vs ≥15), diabetes, employment/shift work status.
[c]The effect by diabetes status based on the model with interaction term.
[d]$p < 0.01$.
[e]$p < .05$.
[f]Adjusted for age, sex, Hispanic/Latino background group, study site, income, education, household size, years in US (< 10 vs. ≥10 years), marital status, AHI category (<15 vs. ≥15), diabetes, employment/shift work status.
[g]$p < .001$.

variables and metabolic health measures. Among people with diabetes, fasting glucose levels were positively associated with a later bedtime (approximately +3% increase per hour later, $p < .01$) and a later midpoint of the sleep period (approximately +2% increase per hour later, $p < .05$). In participants with and without diabetes combined, a later wake time was associated with higher fasting glucose (approximately +3% increase per hour later, $p < .05$). Estimated insulin resistance (HOMA-IR) was positively associated with later midpoint of the sleep period (approximately +1.5% increase per hour later, $p < .05$), and later chronotype (approximately +1.2% increase per hour later, $p < .05$). There were no significant interactions by diabetes status for HOMA-IR. In participants with and without diabetes combined, a later bedtime was associated with lower 2-hr glucose (approximately −0.4 mg/dl lower per hour later, $p < .05$). BMI and hemoglobin A1c levels were not associated with the sleep timing measures in these analyses. Overall, results were similar in sensitivity analyses excluding shift workers.

None of the interaction terms between the sleep timing variables and Hispanic/Latino background or sex was

significant. There were significant interactions between sleep timing and age-group, however. Age stratified results for significant interactions are presented in Table 4. Among participants ≤35 years of age, a later wake time and sleep midpoint was associated with lower BMI. The association between later bedtime and higher fasting glucose was observed only in those 36–≤55 years and 56–<70 years. Similarly, the associations between higher fasting glucose and later bedtime and sleep midpoint and later chronotype were observed only in the age-groups over 35 years. Of note, however, only a few of these associations reached statistical significance (i.e., the associations between bedtime and fasting glucose in those 36–55 years and those 56–<70 years and the association between chronotype and fasting glucose among the 56–70 year olds). Similar age differences were found when examining HbA1c as the outcome. Among those 35 years or younger, a later wake time, sleep midpoint, and chronotype were associated with lower HbA1c. Among those aged 36–55 years and 56–70 years, later wake times, sleep midpoints, and chronotypes were associated with higher HbA1c, particularly among 56- to 70-year-olds who demonstrated larger effect sizes. There were no significant interactions for the outcomes of HOMA-IR and 2-hr glucose levels.

DISCUSSION

In a large sample of diverse US Hispanics/Latino adults, we found that later sleep timing based on sleep midpoint and chronotype was significantly associated with higher estimated insulin resistance (HOMA-IR) in individuals with and without diabetes combined independent of sleep duration. Furthermore, in individuals with diabetes but not on medication, higher fasting glucose levels were associated with later bedtimes. Some associations were only evident in individuals with diabetes, suggesting that degree of metabolic impairment may modify these associations. We observed no differences in these associations among the Hispanic/Latino backgrounds nor between the sexes; however, there were significant differences among the age-groups. In the younger participants (≤35 years), later sleep timing was associated with lower BMI, lower fasting glucose, and lower HbA1c, whereas the converse association was observed among those aged 36–70 years. These results emphasize that the dynamics of glucose metabolism, as well as circadian rhythms that impact glucose metabolism, varies with age and that optimal sleep timing may vary by age-group.

The effect sizes of these associations may be clinically relevant. A large (n = 5269) prospective study with a median follow-up of 3 years examined the effect of rosiglitazone (an

Table 4—Results from linear regression models for associations between sleep timing variables and metabolic health measures (n = 13 429) stratified by age-groups[a]: (< 35, 36– < 55, 56– < 70, > = 70) for models in which interaction term by age was significant.

	Age Groups	BMI, kg/m^2, Regression coefficient (*SE*)	Log of fasting glucose, Regression coefficient (*SE*)	HbA1c, Regression coefficient (*SE*)
Weekly bedtime[b] (per clock hour)	≤35 years	*Interaction term not significant*	−0.0002 (0.001)	*Interaction term not significant*
	36–55 years		0.003 (0.002)[c]	
	56– < 70 years		0.009 (0.004)[c]	
	≥70 years		0.007 (0.007)	
Weekly wake time[b] (per clock hour)	≤35 years	−0.122 (0.065)	*Interaction term not significant*	−0.007 (0.004)[c]
	36–55 years	0.079 (0.058)		0.003 (0.007)
	56– < 70 years	0.144 (0.113)		0.030 (0.012)[d]
	≥70 years	0.157 (0.193)		−0.013 (0.029)
Weekly sleep midpoint[e] (per clock hour)	≤35 years	−0.142 (0.068)[c]	−0.0002 (0.001)	−0.010 (0.004)[d]
	36–55 years	−0.006 (0.067)	0.003 (0.002)	0.002 (0.008)
	56– < 70 years	−0.043 (0.055)	0.011 (0.006)	0.026 (0.016)
	≥70 years	0.100 (0.223)	0.006 (0.008)	−0.014 2(0.032)
Chronotype[e] (per clock hour)	≤35 years	*Interaction term not significant*	−0.0001 (0.001)	−0.005 (0.003)
	36–55 years		0.0005 (0.002)	−0.002 (0.007)
	56– < 70 years		0.0124 (0.005)[c]	0.032 (0.017)
	≥70 years		0.0053 (0.008)	−0.017 (0.031)

[a]The effect by age group based on the model with interaction term
[b]Adjusted for age groups, sex, Hispanic/Latino background group, study site, income, education, household size, years in US (< 10 vs ≥10 y), marital status, sleep duration, AHI category (< 15 vs. ≥15), diabetes, employment/shift work status.
[c]p < .05.
[d]p < 0.01.
[e]Adjusted for age groups, sex, Hispanic/Latino background group, study site, income, education, household size, years in United States (< 10 vs. ≥10 years), marital status, AHI category (< 15 vs. ≥15), diabetes, employment/shift work status.
[f]p < .001.

antihyperglycemia agent) versus placebo in people with prediabetes.[16] The final fasting glucose level was 0.5 mmol/L lower in those taking rosiglitazone compared to placebo, which represents 8.6% of baseline levels (5.8 mmol/L). They also reported that the rosiglitazone group had a 60% reduction in the risk of a composite indicator of incident diabetes or death. In our study, a 3-hr later bedtime would be associated with an 8.0% higher fasting glucose in those with diabetes.

The biological mechanisms underlying the relationship between sleep timing and metabolic health are not fully understood. One possible explanation for these associations is circadian disruption, which occurs when different endogenous circadian rhythms are not synchronized with one another and/or with the external world. Circadian disruption could occur when the timing of volitional behaviors, including sleeping and eating, are not aligned with the endogenous circadian rhythms of associated physiological processes, such as sleep propensity, insulin sensitivity, or glucose metabolism. For example, eating at night, when the central circadian clock is not expecting meals to occur, could lead to disruption in rhythms. In an animal study, mice with access to high-fat food during the light phase only (the incorrect circadian time for eating in this species) gained significantly more weight than mice fed only during the dark phase despite no difference in caloric intake or activity,[18] which suggests that disturbances in circadian rhythms associated with metabolism may play a role. A well-controlled experimental forced desynchrony study in humans confirmed that eating during the circadian night (i.e., 12 hours out of phase) resulted in more adverse glucose and insulin responses than eating when meals are aligned with endogenous circadian rhythms.[19]

It is also well established that shift work, which is associated with severe circadian disruption, is associated with increased risk of metabolic diseases.[20–23] More recently, however, even less severe differences in timing of behaviors have been associated with metabolic alterations. For example, an observational study in 52 adults (71% white, 8% Black, 12% Asian, 6% Hispanic, and 4% other race/ethnicity) examined the association between sleep timing, dietary patterns, and BMI and found that "late sleepers" (midpoint of sleep at 5:30 am or later) had less healthy diets, including consumption of more calories after 8:00 PM, more fast-food and full-calorie soda, and lower fruit and vegetable consumption.[7] Previous analysis from the HCHS/SOL study reported that participants who did not eat within 3 hr of bedtime had higher overall diet quality.[24] In an experimental study, Japanese medical students followed a "diurnal" lifestyle with bedtimes from 11:30 PM to 6:30 AM and a "nocturnal" lifestyle with bedtimes from 1:30 to 8:30 AM in a randomized crossover design.[25] The so-called nocturnal lifestyle, which involved only a 3-hr delay in bedtime, was associated with significantly higher plasma glucose concentrations from midnight to early morning. Among Spanish adults who participated in a 20-week weight loss program, those who ate their main meal, lunch, after 3:00 PM (the median lunch time) lost less weight than those who ate before 3:00 PM, despite equivalent energy intake, dietary composition, estimated energy expenditure, appetite hormone levels, and self-reported sleep duration.[26] Further, this study found that HOMA-IR was also significantly higher in the late lunch eaters. The timing of sleep was not reported in this study. Other cross-sectional studies have found that people with diabetes tend to go to bed later than people without diabetes.[8,27] Our study did not observe a significant difference in the sleep timing variables between those with and without type 2 diabetes. However, later sleep timing was associated with higher estimated insulin resistance in both persons with and without diabetes, which suggests that later sleep timing may be associated with metabolic abnormalities and is consistent with the literature demonstrating metabolic disruption in late eaters, during a nocturnal lifestyle, and in late sleepers.

Another possible mechanism underlying the association between later sleep timing and metabolic abnormalities could be the exposure to light at night. In animal studies, mice exposed to dim light at night had increased weight gain, reduced glucose tolerance, and altered insulin secretion when compared to mice exposed to a regular light–dark cycle, despite equivalent levels of caloric intake and daily activity levels.[28,29] In a study of older human adults (≥ 60 years), exposure to light at night was associated with higher body weight, BMI, and waist circumference and with significantly higher levels of fasting plasma glucose and hemoglobin A1c.[30] Staying up later could expose a person to artificial light that suppresses melatonin, further altering the endogenous circadian rhythm. Indeed, in a large epidemiologic study, lower melatonin levels were associated with increased risk of incident diabetes,[31] suggesting insufficient melatonin may be associated with metabolic impairment.

Our study also found that some of these associations varied among age-groups. Circadian phase and sleep timing have been demonstrated to occur earlier with increasing age.[32,33] There are other changes in circadian rhythms with aging that have been reported, including reduced amplitude of rhythms as well as changes in alignment between rhythms such as sleep start and melatonin peak.[33] We found that later sleep timing was associated with healthier markers of glucose metabolism (i.e., lower BMI, fasting glucose, and HbA1c) in younger adults (≤35 years), whereas the opposite was true for older adults. We speculate that since younger people are more likely to have a later endogenous circadian phase, sleeping at a later clock time may in fact align more closely with endogenous rhythms, whereas sleeping at a later clock time in older individuals may lead to greater circadian misalignment or disruption. Future research needs to explicitly test how manipulating sleep timing impacts metabolism in both younger and older adults. The results in this analysis highlight the importance of considering how age may modify sleep or circadian effects on health.

There are some important limitations to consider when interpreting our findings. The study was cross-sectional, and as such, these data cannot demonstrate that later sleep timing causes insulin resistance or even circadian disturbances. Our sample included participants with a range of metabolic impairment, including the presence of diabetes, which resulted in a higher average HOMA-IR than would be observed in a sample of healthy subjects. However, inclusion of those with diabetes but not taking medication allowed us to examine whether these associations varied by diabetes status. Furthermore, the timing of sleep and sleep duration was based on self-report, and there is likely misclassification which if random would bias the findings

towards the null. Objective estimates of the timing and duration of sleep could have provided more precise estimates of habitual behavior. Finally, the measurements were not taken with respect to endogenous circadian phase, so it is possible that the fasting blood measures were taken at an earlier circadian time in later sleepers than earlier sleepers. However, since insulin resistance increases across the day,[34] the estimates of insulin resistance would have been lower in later sleepers if the measures were taken at an earlier circadian phase.

In conclusion, later sleep timing was significantly associated with higher estimated insulin resistance in a sample of Hispanic/Latino adults. Among those with diabetes only, fasting glucose levels were also significantly higher in those who with later sleep times. We also observed significant differences among age-groups, emphasizing the importance of examining how risk factors for metabolic disturbances varies by age. Further research is warranted particularly since the timing of sleep a modifiable behavioral factor and may be an area in which to intervene to prevent or manage metabolic disorders. If effective, behavioral interventions addressing sleep timing would add a novel, complementary strategy to existing approaches to prevent and manage diabetes, which currently disproportionally affects Hispanics/Latinos in the United States as well as millions of people worldwide.

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SUBMISSION & CORRESPONDENCE INFORMATION

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Address correspondence to: Kristen L. Knutson, PhD, Department of Neurology, Center for Sleep and Circadian Medicine, Northwestern University Feinberg School of Medicine, 710 N Lakeshore Drive, Room 523, Chicago, IL 60611, USA. Telephone: 312 503 1526, Fax: 312 503 5679; Email: kristen.knutson@northwestern.edu

INSTITUTION AT WHICH WORK WAS PERFORMED

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