Sleep Duration Patterns in Early to Middle Adulthood and Subsequent Risk of Type 2 Diabetes in Women

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OBJECTIVE

To identify sleep duration trajectories from early to middle adulthood and their associations with incident type 2 diabetes.

RESEARCH DESIGN AND METHODS

Using a group-based modeling approach, we identified sleep duration trajectories based on sleep duration in ages 20–25, 26–35, 36–45, and 46+ years, which were retrospectively assessed in 2009 among 60,068 women from the Nurses' Health Study II (median age 54.9 years) who were free of diabetes, cardiovascular disease, and cancer. We investigated the prospective associations between sleep duration trajectories and diabetes risk (2009–2017) using multivariable Cox proportional hazards models.

RESULTS

We documented 1,797 incident diabetes cases over a median follow-up of 7.8 years (442,437 person-years). Six sleep duration trajectories were identified: persistent 5-, 6-, 7-, or 8-h sleep duration and increased or decreased sleep duration. After multivariable adjustment for diabetes risk factors, compared with the persistent 7-h sleep duration group, the hazard ratio was 1.43 (95% CI 1.10, 1.84) for the 5-h group, 1.17 (1.04, 1.33) for the 6-h group, 0.96 (0.84, 1.10) for the 8-h group, 1.33 (1.09, 1.61) for the increased sleep duration group, and 1.32 (1.10, 1.59) for the decreased sleep duration group. Additional adjustment for time-updated comorbidities and BMI attenuated these associations, although a significantly higher risk remained in the decreased sleep duration group (1.24 [1.03, 1.50]).

CONCLUSIONS

Persistent short sleep duration or changes in sleep duration from early to middle adulthood were associated with higher risk of type 2 diabetes in later life. These associations were weaker after obesity and metabolic comorbidities were accounted for.

Chronic sleep loss is common in the "24/7" society, with 32% of the U.S. adult population reporting <7 h of sleep in a 24-h period (1). As sleep plays a central role in the regulation of metabolism, energy balance, and the general rejuvenation of various biologic systems (2,3), the importance of sleep duration for health has attracted considerable research interest. Numerous epidemiologic studies have documented that both short and long sleep duration are associated with the risk of type 2 diabetes (4–7). A recent review suggested that the diabetes risk associated with sleep duration is comparable with that of traditional risk factors, such as obesity or physical inactivity

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(8), leading to recommendations of considering sleep duration and sleep disturbances in clinical diabetes screening.

Notably, most prior prospective studies were limited by their reliance on a single sleep duration measurement at baseline (4), which did not adequately reflect sleep duration patterns, which is a more relevant exposure for diabetes development than a single assessment. To our knowledge, only two studies evaluated changes in sleep duration by calculating differences in sleep duration between two time points and reported that increase in sleep duration was associated with increased diabetes risk (5,6). This approach, however, is still prone to misclassification, given that it assumes a linear change between two time points, is sensitive to measurement error in either measurement, and may not well characterize sleep duration changes resulting from altered physical health prior to diabetes onset (e.g., fatigue). Therefore, the observed associations may be partly attributed to reverse causation from subclinical or undetected morbidity (9–11), which might explain why increase in sleep duration was more strongly positively associated with diabetes risk compared with decrease in sleep duration or persistent short sleep duration (5,6).

In the current study, we tackled these limitations from a life course perspective by identifying the trajectories of recalled sleep duration from early to middle adulthood and evaluating their associations with subsequent type 2 diabetes risk. We hypothesized that individuals with sleep duration patterns deviating from persistent 7–8 h of sleep per night were at higher risk of developing diabetes and that these associations were attenuated after adjustment for time-updated BMI and comorbid metabolic disorders, which we considered as potential intermediates between sleep duration and type 2 diabetes risk (12).

RESEARCH DESIGN AND METHODS

Study Population and Design

The Nurses' Health Study II (NHSII) was established in 1989 among 116,429 U.S. female registered nurses aged 25–42 years. All women completed a baseline questionnaire and updated their information on health behaviors and medical histories by biennial follow-up questionnaires. The cumulative follow-up rate exceeds 90% (13).

The baseline of the current study was 2009, when participants recalled their habitual sleep duration in different age periods from early to middle adulthood. Participants were prospectively followed until 2017. We included participants with complete sleep duration data and excluded those with a history of diabetes ($n = 4,188$), cardiovascular disease ($n = 1,736$), or cancer ($n = 7,091$) prior to 2009, resulting in a total of 60,068 women. The study protocol was approved by the institutional review boards of the Brigham and Women's Hospital and Harvard T.H. Chan School of Public Health. The completion of self-administered questionnaires was considered to imply informed consent.

Exposure Assessment

In 2009, participants reported their average sleep duration over a 24-h period in different age periods (ages 20–25, 26–35, 36–45, and 46+ years) in the following categories: <5, 5, 6, 7, 8, 9, and 10+ h/day. To aid recall, we had participants simultaneously report their employment status, work schedules, and frequency of rotating night shifts in each period. In a subset of 54,021 women who also reported their current sleep duration in 2001, we evaluated the reliability of recalled sleep duration in 2009 by comparison with prospectively assessed sleep duration in 2001. For each participant, sleep duration reported in 2001 was compared with sleep duration recalled in 2009 for a specific age period corresponding to her age in 2001. The intraclass correlation coefficient between the two measurements was 0.52 (95% CI 0.51, 0.53), suggesting moderate reproducibility of recalled sleep duration.

Ascertainment of Incident Type 2 Diabetes

Incident diabetes cases were identified by self-reports on every biennial questionnaire and were further confirmed via a supplemental questionnaire regarding symptoms, diagnostic tests, and diabetes treatment. This method has previously been validated; >97% of cases confirmed by the supplemental questionnaire were ascertained by medical record review (14,15). Type 2 diabetes was confirmed if more than one of the following criteria by the American Diabetes Association (16) were met: *1*) elevated plasma glucose levels (fasting glucose ≥126 mg/dL or random glucose ≥200 mg/dL) with one or more classic symptoms (polyuria, polydipsia, unexpected weight loss, or coma), *2*) elevated plasma glucose on at least two occasions (fasting glucose ≥126 mg/dL, random glucose ≥200 mg/dL, or glucose ≥200 mg/dL after an oral glucose test) with no symptoms, and *3*) hypoglycemic therapy with insulin or oral medications.

Assessment of Covariates

Birth date, height, and race/ethnicity were self-reported in 1989. Body weight, smoking status, menopausal status, postmenopausal hormone use, recent physical examination, duration of rotating night shift work, medication use, and clinical diagnosis of hypertension, hypercholesterolemia and depression were assessed every 2 years. BMI was calculated as weight in kilograms divided by the square of the height in meters, and self-reported weight and height in nurses have previously been validated with high accuracy (17). Lifetime duration of rotating night shift work was calculated by summing duration of rotating night shift work (defined as at least three nights/month in addition to other days and evenings in that month) reported on every questionnaire. Parity, defined as pregnancies lasting longer than 6 months, was assessed every 2 years from baseline until 2009, when the majority of women underwent menopause. Chronotype was queried in 2009 using a single question from the Morningness-Eveningness Questionnaire (18). Starting in 1991, dietary data were collected every 4 years using a semiquantitative food-frequency questionnaire. The reliability and validity of the food-frequency questionnaire have previously been described (19,20), based on which alcohol consumption (grams/day) and the Alternate Healthy Eating Index-2010 (AHEI-2010) were derived (21). Physical activity was assessed every 2–4 years by MET h/week derived from a validated questionnaire (22). Participants who reported both antidepressants use and physician-diagnosed depression were considered to have clinical depression. Physician-diagnosed sleep apnea was retrospectively assessed in 2013 (23).

Statistical Analysis

We used latent class growth modeling, a group-based modeling approach (SAS Proc Traj), to identify subgroups that shared a similar sleep duration trajectory from ages 20–25 to age 46+ years (24,25). This

method has previously been implemented to identify trajectory of body shape (26). Briefly, the recalled sleep duration information in different age periods was fitted by a maximum likelihood method as a mixture of multiple latent trajectories in a censored normal model with a polynomial function of age (24). The categories of sleep duration <5 h and 10+ h were approximated as 4 h and 10 h, respectively. We used the Bayesian information criterion to determine the optimal number and shapes of trajectory groups (27). The model with six trajectories and a cubic function of age showed the best fit to the data, including persistent sleep duration of 5, 6, 7, and 8 h; increased sleep duration from 6 to 7.5 h; and decreased sleep duration from 8 to 6 h. We then calculated the posterior predicted probability for each participant of being a member of each of the six trajectory groups and assigned participants to the trajectory group with the greatest posterior probability of membership. Average posterior probabilities for all trajectory groups were ≥0.70 (0.89, 0.85, 0.84, 0.96, 0.70, and 0.74, respectively), indicating high internal reliability within each trajectory and sufficient discrimination of individuals with different sleep duration patterns between trajectory groups (25).

We used Cox proportional hazards models to estimate the hazard ratios (HRs) and 95% CIs for type 2 diabetes risk according to sleep duration trajectory groups. Person-years were calculated from the date of return of the 2009 questionnaire to the date of diabetes diagnosis, death, loss to follow-up (i.e., return of the most recent questionnaire), or the end of follow-up (June 2017)—whichever occurred first. We used calendar year (in months) as the underlying time scale and presented age-adjusted and multivariable-adjusted (MV) models. MV1 further adjusted for race, family history of diabetes, menopausal status, postmenopausal hormone use, smoking status, cumulative average of alcohol consumption, AHEI-2010 and physical activity (28), marital status, parity, physical exam, duration of rotating night shift work (29), and chronotype. All covariates except race, family history of diabetes, parity, and chronotype were modeled as time varying. Because sleep duration is closely associated with metabolic dysregulation, depression, sleep disorders, and weight change, all of which could serve as potential intermediates leading to diabetes, as reported previously (3,11,12,30,31), we further considered these factors, which were time updated after baseline sleep assessment, in two separate models—consistent with previous studies (5,6). MV2 additionally adjusted for time-updated hypertension, hypercholesterolemia, depression, and sleep apnea, and MV3 further adjusted for time-varying BMI. We conducted sensitivity analyses to test the robustness of our findings. First, we conducted 2-year lag analyses by excluding incident diabetes cases diagnosed in the first 2 years of follow-up to address potential reverse causation. Second, we performed subgroup analyses according to age (<60 or ≥60 years), BMI (<30 or ≥30 kg/m^2), chronotype (morning, evening, or neither), history of night shift work (ever or never), parity (nulliparous or parous), family history of diabetes (yes or no), physical activity (< or ≥16.9 MET h/week [the median]), and AHEI-2010 score (< or ≥53.0 [the median]). Statistical interactions were assessed by likelihood ratio tests comparing the models with and without the multiplicative interaction terms. Third, we examined the associations of recalled sleep duration in each age period with diabetes risk separately.

Secondarily, to provide further insights into how chronotype may be associated with chronic sleep duration patterns, we compared the distribution of sleep duration trajectory groups by chronotype using χ^2 tests, and estimated the odds ratios and 95% CIs of sleep duration trajectories according to chronotype using multinomial logistic regression, with adjustment for the same baseline covariates as described in MV3.

All analyses were executed using SAS for UNIX, version 9.4 (SAS Institute, Cary, NC), and *P* values <0.05 were considered statistically significant.

RESULTS

Trajectory of Sleep Duration From Early to Middle Adulthood

Using latent class growth modeling, we identified six distinct sleep duration trajectories from ages 20–25 to age 46+ years (Fig. 1). Of 60,068 participants, 1,410 (2.3%) had persistent 5-h sleep duration, 11,551 (19.2%) had persistent 6-h sleep duration, 26,960 (44.9%) had persistent 7-h sleep duration, 13,289 (22.1%) had persistent 8-h sleep duration, 3,374 (5.6%) had increased sleep duration from ~6 to 7.5 h, and 3,484 (5.8%) had decreased sleep duration from ~8 to 6 h. Of note, 5,197 (8.7%) women reported ≥9 h sleep duration on at least one occasion and only 438 (0.7%) women reported ≥9 h sleep on all four occasions. Owing to underrepresentation of long sleepers in this sample, the data-driven algorithm did not identify a separate trajectory for these women and incorporate them into other trajectory groups with the most similar sleep duration pattern.

Participant Characteristics

Participants with persistent 7- and 8-h sleep duration showed similar baseline characteristics (Table 1). Compared with the participants with persistent 7-h sleep duration, participants with shorter sleep duration (persistent 5 or 6 h) were less likely to be currently married and more likely to currently smoke, be physically active, and have greater BMI, comorbidities, and evening chronotype. Participants with persistent shorter sleep duration also had longer lifetime duration of rotating night shift work and were more likely to identify themselves as evening chronotype. Further, compared with the participants with persistent 7-h sleep duration, participants with changes in sleep duration (increased or decreased sleep duration) were less likely to be married and more likely to have greater BMI, comorbidities, and evening chronotype. Postbaseline BMI changes also differed by sleep trajectory groups ($P < 0.009$), whereas changes in physical activity or AHEI-2010 did not ($P > 0.35$) (Supplementary Table 1). Specifically, decreased and persistent 6-h sleep duration were associated with the largest BMI increases, while persistent 5-h sleep duration was not associated with BMI change, possibly because this group already had the highest baseline BMI (Table 1).

When we compared the distribution of sleep duration trajectory groups according to chronotype, participants with evening chronotype were more likely to report persistent short or decreased sleep duration patterns compared with those with morning chronotype ($P < 0.001$) (Supplementary Fig. 1). After adjustment for sociodemographic, lifestyle, and comorbid factors, individuals with evening chronotype compared with morning

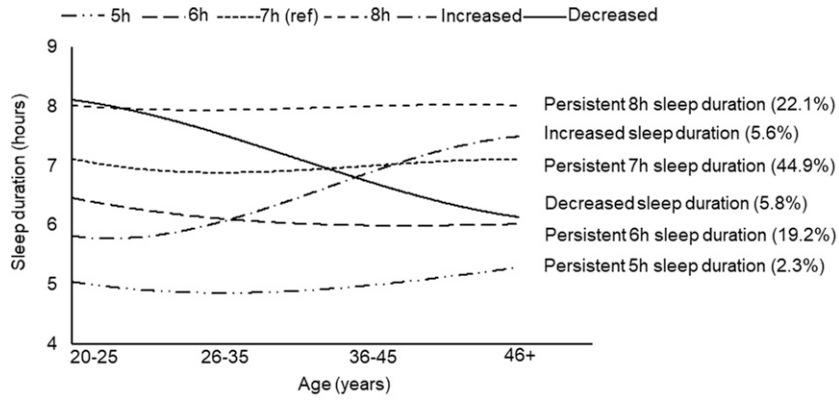

Figure 1—Trajectories of sleep duration from early to middle adulthood in the NHSII. The numbers in parentheses are the percentages of participants in the trajectories.

chronotype had 26% higher odds for persistent 5 h sleep duration (95% CI 13, 42), 27% higher odds for persistent 6 h sleep duration (21, 33), and 34% higher odds for decreased sleep duration from 8 to 6 h (24, 44) (Table 2).

Trajectory of Sleep Duration and Risk of Type 2 Diabetes

We documented 1,797 incident diabetes cases over 442,437 person-years of follow-up.

Compared with the persistent 7-h sleep duration trajectory group, the HRs for diabetes after adjustment for demographic, lifestyle, and sleep-related factors (MV1) were 1.43 (95% CI 1.10, 1.84) for the persistent 5-h sleep duration group, 1.17 (1.04, 1.33) for persistent 6-h group, 0.96 (0.84, 1.10) for persistent 8-h group, 1.33 (1.09, 1.61) for increased sleep duration group, and 1.32 (1.10, 1.59) for decreased sleep duration group (Table 3). These associations were attenuated but remained statistically significant after additional adjustment for development of comorbidities over follow-up including hypertension, hypercholesterolemia, depression, and sleep apnea (MV2). Further adjustment for time-updated BMI attenuated the associations for all trajectory groups (MV3), although a significantly increased diabetes risk persisted in the decreased sleep duration group (HR 1.24 [95% CI 1.03, 1.50).

Sensitivity Analyses

Similar associations between sleep duration trajectory and type 2 diabetes risk were observed when we excluded type 2 diabetes cases diagnosed in the first 2 years of follow-up (Supplementary Table 2), albeit the estimates were less precise due to smaller case numbers. When we stratified the analysis by age, BMI, chronotype, history of night shift work, parity, family history of diabetes, physical activity, and AHEI-2010 score, the associations were not statistically different due to the small number of cases in each subgroup and high degree of freedom of the test ($P_{interaction} > 0.11$) (Supplementary Table 3). However, the increased diabetes risk associated with persistent short sleep duration appeared larger in participants who were older, obese, nulliparous, of morning chronotype, and exposed to night shifts and had family history of diabetes or better diet quality, whereas the increased diabetes risk associated with changes in sleep duration was more apparent in participants who were younger, of evening chronotype, parous, and physically active. When we assessed the associations of recalled sleep duration with diabetes risk in each age period separately, shorter sleep duration tended to associate with higher diabetes risk in all age periods, although the associations appeared to be stronger at age 46+ years than for earlier age periods (Supplementary Table 4).

CONCLUSIONS

In the current analyses, we found that compared with participants with persistent 7-h sleep duration from their early to middle adulthood, those with persistent shorter sleep duration or changes in sleep duration had significantly higher risk of type 2 diabetes. Persistent 8-h sleep duration was not associated with diabetes risk compared with persistent 7-h sleep duration. Consistent with our hypothesis and substantial prior evidence (12) that development of obesity and metabolic comorbidities may be intermediate factors linking sleep duration and diabetes risk, adjustment for these factors attenuated the associations, particularly for the persistent 5-h sleep duration group and the increased sleep duration group. However, the higher diabetes risk associated with decreased sleep duration remained statistically robust after adjustment for time-updated BMI and comorbidities. In support of our earlier findings on chronotype and diabetes risk (18), we found that evening chronotypes compared with morning chronotypes were more likely to follow metabolically unhealthy chronic sleep duration patterns, such as persistent short or decreased sleep duration over time. To our knowledge, this is the first study that evaluated sleep duration patterns in relation to risk of type 2 diabetes.

Previous studies based on a single measurement of sleep duration consistently reported a U-shaped relationship between sleep duration and the incidence of diabetes (4,7). In a dose-response meta-analysis, every 1 h shorter sleep duration was associated with 9% higher diabetes risk among short sleepers—similar to the graded relationships that we observed for persistent 6-h and 5-h sleep duration groups (4). This meta-analysis also reported 14% higher risk associated with every 1 h longer sleep duration among individuals sleeping >7 h, which was not observed in the current study. Two recent studies from The Whitehall II study and the NHS (a sister cohort of the NHSII) examined changes in sleep duration in relation to diabetes risk; both reported increased diabetes risk associated with ≥2 h increase in sleep duration (5,6). In the Whitehall II study, persistent short sleepers were also at higher diabetes risk, but this association weakened and did not reach statistical significance after adjustment for BMI and weight change, suggesting that short sleep may precipitate diabetes development through effects on weight change (5). Misclassification due to the reliance on only two measures and potential reverse causation (e.g., short sleepers may increase their sleep duration due to changes in physical health prior to diabetes onset) may explain why these studies only detected an association with increased sleep duration and did not observe associations with short or

Table 1—Population characteristics of participants according to trajectories of sleep duration

	Sleep duration trajectory group					
	Persistent sleep duration of 5 h	Persistent sleep duration of 6 h	Persistent sleep duration of 7 h	Persistent sleep duration of 8 h	Increased sleep duration from 6 to 7.5 h	Decreased sleep duration from 8 to 6 h
N	1,410	11,551	26,960	13,289	3,374	3,484
Age, years	55.0 (4.5)	54.9 (4.5)	54.8 (4.6)	54.8 (4.6)	54.4 (4.6)	54.6 (4.4)
Follow-up, years*	7.7 (7.4, 7.9)	7.8 (7.6, 7.9)	7.8 (7.6, 7.9)	7.8 (7.6, 7.9)	7.8 (7.6, 7.9)	7.8 (7.5, 7.9)
Range of follow-up, years	0.3–8.0	0.1–8.0	0.1–8.0	0.1–8.0	0.1–8.0	0.1–8.0
White race	92	95	98	97	97	94
Currently married	71	77	82	81	78	76
Premenopausal	31	32	33	33	33	32
Postmenopausal hormone use†	18	22	23	24	24	20
Family history of diabetes	38	36	34	33	35	36
BMI, kg/m^2	28.9 (7.1)	27.8 (6.4)	26.9 (5.8)	26.7 (5.8)	27.9 (6.4)	27.7 (6.2)
AHEI-2010	51.9 (10.3)	51.9 (9.9)	52.7 (9.9)	53.0 (10.1)	52.5 (9.8)	51.8 (10.1)
Alcohol intake, g/day	3.6 (5.8)	4.1 (6.2)	4.7 (6.6)	4.9 (7.4)	5.1 (7.5)	4.0 (6.3)
Smoking status						
Never	62	65	67	68	60	67
Past	28	28	28	27	33	27
Current	10	7	5	5	8	6
Physical activity, MET h/week	25.7 (25.7)	22.5 (21.6)	21.7 (19.8)	21.4 (20.2)	23.7 (24.6)	20.8 (18.8)
Parous	79	83	84	79	81	80
Parity‡	2.4 (1.1)	2.3 (1.0)	2.3 (0.9)	2.2 (0.9)	2.3 (1.0)	2.2 (0.9)
Physical examination	91	92	94	93	93	91
Medical history						
Hypertension	29	27	24	22	29	27
High cholesterol	34	33	33	32	35	35
Sleep apnea	5	3	3	3	4	4
Depression	15	12	14	17	18	13
Ever had night shift	84	77	70	65	79	70
Lifetime duration of rotating night shift work, years§	7.3 (6.2)	5.8 (5.5)	4.8 (4.6)	4.3 (4.2)	5.8 (5.1)	5.2 (5.1)
Chronotype						
Morning type	54	56	63	63	61	55
Evening type	39	38	32	31	34	39
Neither	7	6	5	5	5	5

Data except for follow-up years are means (SD) for continuous variables and percentages for categorical variables at baseline (2009). All variables except age and follow-up years are age standardized. *Values are median (lower quartile, upper quartile). †Calculated among participants with postmenopausal status. ‡Calculated among parous participants. §Calculated among participants who ever had rotating night shift work.

decreased sleep duration. In the current study, we leveraged the unique data on sleep duration in different life periods from early to middle adulthood and observed that all chronic sleep duration patterns that deviated from persistent 7-h or 8-h sleep duration conferred an increased risk of type 2 diabetes. Our findings provide novel evidence on the relationships between sleep duration and diabetes risk using a life course approach and corroborated the metabolic benefits of 7–8 h of sleep per night as recommended by American Academy of Sleep Medicine (32).

Interestingly, there were few participants with persistent sleep duration ≥9 h in our study sample. Indeed, while 8.7% of the sample reported ≥9 h sleep duration in at least one of the four age periods, only 0.7% reported persistent long sleep duration at all four age periods, suggesting that long sleep may be a short-term phenotype induced by changes in mood or physical health. This was supported by prior evidence that long sleep duration may be an epiphenomenon of metabolic disorders, depression, or low socioeconomic status (9–11). It is likely that chronically long sleep duration is determined by multiple factors, and in our sample of middle-aged nurses, we did not have sufficient power to fully characterize risk associated with persistent long sleep. By contrast, we identified two trajectory groups of persistent sleep duration shorter than 7 h, which together constituted 21.5% of the study population. This is consistent with the increasing trend of chronic sleep deprivation in the U.S. across different racial/ethnic populations (1,33). Further, we identified two groups characterized by changes in sleep duration, each representing about 6% of the study sample. Such changes in sleep duration could possibly result from aging, menopausal transition, changes in working status and living arrangements, or altered health states that we have adjusted for in the analyses.

Table 2—Adjusted multinomial logistic regression odds ratios (95% CI) of trajectory of sleep duration by chronotype, with persistent 7-h sleep duration as a reference category

Chronotype	Persistent sleep duration of 5 h	Persistent sleep duration of 6 h	Persistent sleep duration of 8 h	Increased sleep duration from 6 to 7.5 h	Decreased sleep duration from 8 to 6 h
Morning type					
Age adjusted	1.00	1.00	1.00	1.00	1.00
MV*	1.00	1.00	1.00	1.00	1.00
Evening type					
Age adjusted	1.43 (1.28, 1.60)	1.33 (1.27, 1.40)	1.00 (0.95, 1.04)	1.13 (1.04, 1.22)	1.41 (1.31, 1.52)
MV*	1.26 (1.13, 1.42)	1.27 (1.21, 1.33)	0.99 (0.94, 1.03)	1.05 (0.97, 1.13)	1.34 (1.24, 1.44)
Neither					
Age adjusted	1.61 (1.29, 2.02)	1.33 (1.21, 1.47)	1.07 (0.97, 1.18)	1.02 (0.85, 1.21)	1.22 (1.04, 1.44)
MV*	1.39 (1.10, 1.74)	1.27 (1.15, 1.41)	1.05 (0.96, 1.16)	0.96 (0.81, 1.14)	1.17 (1.00, 1.39)

*Adjusted for age (continuous), race (nonwhite or white), family history of diabetes, menopausal status (pre- or postmenopausal), postmenopausal hormone use (never, past, or current), smoking status (never, past, or current), alcohol intake (0, 0 to <5, 5 to <15, 15 to <30, or ≥30 g/day), AHEI-2010 dietary score (in quintiles), physical activity (<3, 3 to <9, 9 to <18, 18 to <27, or ≥27 MET h/week), marital status (yes or no), parity (nulliparous, 1, 2, or ≥3), physical exam (yes or no), duration of rotating night shift work (years), development of hypertension (yes or no), hypercholesterolemia (yes or no), depression (yes or no), sleep apnea (yes or no), and BMI (<20, 20 to <25, 25 to <30, 30 to <35, 35 to <40, or ≥40 kg/m^2). All the covariates were based on baseline information in 2009.

We also noted that the participants with evening chronotype were more likely to report persistent short or decreased sleep duration patterns compared with those with morning chronotype. This novel finding suggests that chronotype may be an important determinant of chronic sleep duration patterns and that individuals with evening chronotype may experience more chronic circadian misalignment due to their shortened sleep duration that poses them at even higher diabetes risk (18). Given that chronotype reflects individual preferences of the synchronization between inherent circadian rhythm and the environment, future investigation is needed to understand the genetic basis as well as gene-environment interactions for chronic sleep duration patterns, which may provide further insights into the mechanisms leading to diabetes development (2,34,35).

Several potential mechanisms may explain the associations of persistent short sleep duration or decreased sleep duration with diabetes risk. First, laboratory studies reported that experimental reduction of sleep duration was linked to glucose dysregulation and increases in hunger and appetite, with downregulated leptin (the satiety hormone), upregulated ghrelin (the appetite-stimulating hormone), and altered brain mechanisms involved in the hedonic aspects of appetite (3,36). A recent randomized control pilot study found that sleep extension in adult short sleepers led to reduced intakes of fat, carbohydrates, and free sugars (37). Second, activation of inflammatory pathways due to chronic insufficient sleep may promote diabetes development (38). Experimental sleep restrictions in animals and humans were associated with an evolving proinflammatory state (39–43). Third, melatonin, a pineal hormone under the control of the circadian clock, was involved in glucose regulation and energy metabolism (44). Reduced melatonin secretion were independently associated with a higher diabetes risk (45). Finally, high night-to-night variations in sleep duration, which are more commonly present in short and poor sleepers and possibly among individuals with changes in sleep duration (46), have recently emerged as a risk factor for metabolic health that could lead to diabetes development (47–49).

The strengths of this study included prospective study design, large sample size, high rates of follow-up, repeated assessments of diabetes risk factors, and the life course trajectory approach that added novel and complementary findings to prior studies (26,50). However, several limitations should be noted. First,

Table 3—HR (95% CI) of type 2 diabetes according to trajectories of sleeping duration

	Persistent sleep duration of 5 h	Persistent sleep duration of 6 h	Persistent sleep duration of 7 h	Persistent sleep duration of 8 h	Increased sleep duration from 6 to 7.5 h	Decreased sleep duration from 8 to 6 h
Case subjects/ person-years	66/10,049	408/84,276	725/199,928	341/98,419	119/24,541	138/25,224
Age adjusted	1.79 (1.39, 2.30)	1.32 (1.17, 1.50)	1.00	0.96 (0.84, 1.09)	1.39 (1.14, 1.69)	1.53 (1.27, 1.84)
MV1	1.43 (1.10, 1.84)	1.17 (1.04, 1.33)	1.00	0.96 (0.84, 1.10)	1.33 (1.09, 1.61)	1.32 (1.10, 1.59)
MV2	1.34 (1.04, 1.74)	1.16 (1.02, 1.31)	1.00	0.98 (0.86, 1.11)	1.24 (1.02, 1.51)	1.29 (1.08, 1.55)
MV3	1.17 (0.90, 1.52)	1.09 (0.96, 1.23)	1.00	1.02 (0.90, 1.17)	1.12 (0.92, 1.36)	1.24 (1.03, 1.50)

HRs were estimated from age-stratified Cox proportional hazards models. MV1 model was adjusted for race (nonwhite or white), family history of diabetes, menopausal status (pre- or postmenopausal), postmenopausal hormone use (never, past, or current), smoking status (never, past, or current), alcohol intake (0, 0 to <5, 5 to <15, 15 to <30, or ≥30 g/day), AHEI-2010 dietary score (in quintiles), physical activity (<3, 3 to <9, 9 to <18, 18 to <27, or ≥27 MET h/week), marital status (yes or no), parity (nulliparous, 1, 2, or ≥ 3), physical exam (yes or no), duration of rotating night shift work (years), and chronotype (morning type, evening type, neither type, or missing). All covariates, except race, family history, parity, and chronotype, were modeled as time varying. MV2 model was further adjusted for development of hypertension (yes or no), hypercholesterolemia (yes or no), depression (yes or no), and sleep apnea (yes or no). MV3 model was further adjusted for time-updated BMI (<20, 20 to <25, 25 to <30, 30 to <35, 35 to <40, or ≥40 kg/m^2).

our assessment on sleep duration was based on self-reported information, which may produce measurement errors (51). Certain preexisting conditions, such as obesity, hypertension, and depressed mood, may also have influenced how women recalled sleep duration in early life and could have resulted in differential recall bias that might affect the trajectory patterns of sleep duration. Nevertheless, the consistency of our results with previous experimental and epidemiologic studies on sleep duration and metabolic risk factors and diabetes risk suggests that the observed associations were unlikely to be entirely explained by measurement errors (3,4,8). Further, simultaneous recall of other work characteristics along with sleep assessment may help reduce recall bias (e.g., nurses with longer duration of night shift work were more likely to report persistent shorter sleep duration). Second, the trajectory groups were derived from a limited number of sleep duration measurements that may not reflect chronic sleep duration patterns in high resolution (e.g., fluctuating sleep duration patterns). However, the excellent posterior probability for each trajectory group indicated that these trajectories capture the predominant features of sleep duration patterns shared by a group of participants and distinctive from others. Third, we were underpowered to detect potential subgroup heterogeneity using multiplicative interactions, particularly given that the exposure consisted of six categories (52). Lastly, generalizability may be limited because participants in our study were predominantly white female nurses with high exposure to night shift work (65–84% across trajectory groups). However, we observed similar associations among women who had never worked any night shifts. In addition, the homogeneity of our participants, particularly considering their working characteristics and education level, may provide an advantage in the recall of early life sleep duration and in the report of lifestyle and health-related information while minimizing confounding by socioeconomic status. Given potential racial/ethnic disparities in sleep health (33), future studies are warranted to explore these associations in other racial/ethnic populations.

In conclusion, we found that persistent short (5- or 6-h) sleep duration in early to middle adulthood, as well as increased sleep duration (from 6 to 7.5 h) or decreased sleep duration (from 8 to 6 h), was associated with higher subsequent type 2 diabetes risk. These associations weakened after adjustment for time-updated BMI and comorbidities. In conjunction with prior studies, our findings underscore that maintaining a consistent pattern of the recommended daily 7–8 h of sleep is beneficial for the prevention of type 2 diabetes.

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