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Aging reduces the association between sleepiness and sleep-disordered breathing

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Abstract

Aim—To investigate age-related changes in sleepiness symptoms associated with sleep disordered breathing (SDB).

Methods—Wisconsin Sleep Cohort participants were assessed with polysomnography, Epworth Sleepiness Scale (ESS) and Multiple Sleep Latency Test (MSLT). SDB was defined as an apnea/hypopnea index≥15 events/hour, sleepiness as ESS≥10 and MSLT≤5 minutes. Odds ratios were calculated using generalized estimating equations associating sleepiness with SDB, and conditional logistic regression examining changes in longitudinal sleepiness status (ESS only). Models were, a priori, stratified by gender.

Results—ESS was measured in 1281 participants and MSLT in 998, at multiple time points (ESS n=3695; MSLT n=1846). Significant interactions were found between SDB and age in men, but not women. The odds ratios (OR) modeled for sleepiness in a 40 year old male with SDB were significant, compared to a male without SDB (OR: ESS 2.1; MSLT 2.9); however, these associations were not significant at 60 years. The within-subject odds ratio for sleepiness was also significant at 40 years (OR: 3.4), but not at 60 years.

Conclusion—The age-related reductions in the association between sleepiness and SDB may have clinical implications for the diagnosis and treatment of SDB in older people since sleepiness is often used as a therapeutic marker.

Keywords

Sleep disordered breathing; Obstructive sleep apnea; Aging; Sleepiness

INTRODUCTION

The prevalence of sleep disordered breathing (SDB) in older people (>65 years) is almost double that in younger people, with approximately 20% having moderate to severe SDB when measured in a community sample [1]. Using a more liberal measure of SDB (apnea/hypopnea index (AHI) cutoff of >5 events/hour) estimates range up to 56% in community populations, and 70% in clinics and nursing homes [2]. Despite this high prevalence, the symptoms and consequences of SDB in older people are poorly understood. For example

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sleepiness is the cardinal symptom of SDB in younger people; whereas its role as a diagnostic marker in older people is unclear.

In some studies older people with SDB have been found to have minimal symptoms of subjective and objective sleepiness [3], while others have reported excessive sleepiness [4–5], and in the Sleep Heart Health Study the strength of the association between SDB and sleepiness was similar in older and younger people [6]. If sleepiness is reduced in older people with SDB, this could have wider implications for the planning of health care services, since sleepiness is currently a therapeutic target for the treatment of SDB using continuous positive airway pressure (CPAP) [7].

In a recent study, SDB was predictive of cardiovascular mortality in participants with and without sleepiness [8]. These authors concluded that the high cardiovascular risk in untreated severe SDB, suggested that SDB treatment should not be contingent on symptoms of daytime sleepiness. Others have also argued that SDB without daytime symptoms should be treated to reduce cardiovascular risk [9]. This may be particularly relevant in older people, in whom the cardiovascular risk is greater. Older patients with SDB could also benefit from improvements in cognitive function associated with the treatment of OSA; especially if they are at greater risk of cognitive decline, independent of daytime sleepiness [10]. Therefore, the appropriateness of using sleepiness to guide treatment choices, in populations with a higher absolute risk for cardiovascular events, cognitive impairment, and mortality is questionable. The overall aim of this study was to investigate the strength of the association between symptoms of daytime sleepiness and SDB across the age spectrum, using data from the Wisconsin Sleep Cohort. We hypothesized that the symptom of sleepiness would be less in older people with SDB.

METHODS

Participants

In 1988, employees of four Wisconsin state agencies, ages 30–60 years, were surveyed by mail regarding their sleep habits. From these data, a sampling frame was constructed and 3170 randomly-selected respondents were invited to participate in the Wisconsin Sleep Cohort. Participants were studied overnight. Repeat studies occur at four-year intervals. In August 2011, there were 1521 (48%) participants with at least one adequate sleep study. The primary reason for non-participation was the burden of an overnight sleep study. One to six sleep studies per participant were available for analysis. Follow-up rates (calculated from average rates of refusal to participate in follow-up studies) are approximately 80%, although recruitment for follow-up studies continues to accrue. Consent documents for the ongoing Wisconsin Sleep Cohort Study were approved by the University of Wisconsin-Madison Health Sciences Institutional Review Board. All participants gave written, informed consent.

Polysomnography

Overnight polysomnography (Polygraph model 78, Grass Instruments, Quincy, MA) plus other clinical assessments were carried out on each participant. Sleep state was determined by electroencephalography (EEG), electrooculography (EOG) and electromyography (EMG). SDB events were assessed using arterial oxyhemoglobin saturation (SaO_2; Ohmeda 3740, Englewood, CO.), oral and nasal airflow monitored by thermocouples (ProTec, Hendersonville, TN), nasal air pressure measured (Validyne Engineering Corp., Northridge, CA), and thoracic and abdominal respiratory motion recorded by respiratory inductance plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, NY).

Sleep state and respiratory events were scored by trained sleep technicians using the conventional Rechtschaffen criteria. An apnea was defined as the cessation of airflow lasting

≥10 seconds, and a hypopnea being a discernable reduction in the sum of thoracic plus abdomen respiratory inductance plethysmography amplitude associated with a ≥4% reduction in oxyhemoglobin saturation. The average number of apnea plus hypopnea events per hour of sleep defined the AHI.

Assessment of Sleepiness

The sleepiness assessments used in this study were the subjective Epworth Sleepiness Scale (ESS) questionnaire [11] and objective Multiple Sleep Latency Test (MSLT) [12]. These tests were added to the Wisconsin Sleep Cohort study protocol at different times. The ESS was first used in October 1993 and data were available in 1281 participants (693 men, 588 women), with 3695 total sleep studies (270 participants with one study, 211 with two, 310 with three, 373 with four studies, and 117 with five studies). Subjective sleepiness was defined as an ESS ≥10, alternative cutpoints were examined to determine if our results were sensitive to the choice of cutpoint.

The MSLT research protocol was performed between June 1989 and August 2003. Data were available in 998 participants (551 men, 447 women), with 1846 total sleep studies (404 participants with one study, 376 with two, 182 with three, and 36 with four studies). Participants were allowed four nap-opportunities during the day, at 2 hourly internals, in a darkened room. The nap-opportunity was stopped if the EEG showed the participant had fallen asleep, or after 20 minutes if sleep did not occur. Objective sleepiness was defined as an MSLT ≤5 minutes.

Covariate measurements

All participants were interviewed at each visit regarding their usual sleep time (average hours of sleep/day including naps), medical history (including self-report of physician diagnosed comorbidities: congestive heart failure, myocardial infarction, revascularization procedures, and stroke), medication use (coded into pharmacologic categories), alcohol use (drinks/week), smoking habits (current and past) and caffeine use (daily consumption of coffee and other caffeinated beverages). Age and body mass index (BMI; kg/m^2) were also measured. The Zung self-report depression scale was completed, which is a 20-item survey assessing depressive symptoms on a scale ranging from 25–100; scores ≥50 were taken as mild or worse depressive symptomatology [13].

Statistical analyses

Analyses were performed with SAS software, V 9.2 (SAS Institute, Inc., Cary, NC). Two types of regression models estimated odds ratios associating the presence of sleepiness with the presence of SDB; ESS ≥10 or MSLT ≤5 minutes were modeled separately. Generalized estimating equation models were fitted to all data, including multiple sleep studies per participant, if available. The resulting odds ratios represent the weighted averages of the cross-sectional and longitudinal associations, between sleepiness and SDB, while accounting for within-subject correlation due to the use of multiple sleep studies per participant [14].

Conditional (intrasubject) logistic regression was used to estimate the odds of changing sleepiness status between visits (i.e. having ESS <10 at a study visit, and ESS ≥10 at a subsequent visit, or vice versa) associated with SDB status at each study visit [14]. This purely longitudinal approach was used only with ESS, as there were insufficient participants with multiple MSLT's. The within-subject approach accommodated the participants that were initially identified as sleepy, but were no longer sleepy at a later visit. The conditional model implicitly controls for fixed within-person characteristics, such as sex and genetic profile [14].

All models were, a priori, stratified by gender. Within gender-stratified models the interaction terms for SDB*age were fitted to test the primary hypothesis that the association between sleepiness and SDB reduces with age. A significantly negative interaction coefficient would provide evidence consistent with a diminishing association between sleepiness and SDB with increasing age.

SDB was categorized as either absent (AHI <15) or present (AHI ≥15 or use of CPAP therapy). The primary outcome variables were the presence or absence of excessive daytime sleepiness defined as: ESS ≥10, or MSLT ≤5 minutes. Supplemental analyses were performed to examine alternative outcome characterizations for sleepiness (ESS cutpoint of 9 or 11; ESS and MSLT modeled as a continuous outcomes;) and SDB (AHI modeled as a continuous outcome; exclusion of subjects using CPAP from analyses). We found no meaningful differences in the alternative models, compared to the results presented here. Covariates (BMI, comorbidities, alcohol and cigarette use, caffeinated beverage consumption, depressive symptomology, and self-reported usual sleep time) which substantially altered regression coefficients for SDB were retained in final models.

RESULTS

The characteristics of the participants in whom we examined the symptom of sleepiness using the ESS and the MSLT are described in Tables 1 and 2, respectively. There were no substantial differences between the samples in which ESS and MSLT were measured. In both samples, participants with SDB were older, and had higher BMI, compared to those without SDB. The participants with SDB also had a higher prevalence of depressive symptomology and cardiovascular diseases.

Both subjective and objective sleepiness symptoms were more prevalent in participants with SDB compared to those without. The partial correlation ($r_{partial}$) between age and ESS, adjusting for gender, BMI and AHI was $r_{partial}$ =0.04 (p=0.04). A stronger partial correlation was found with age and MSLT, $r_{partial}$ =0.10 (p<0.001). These results show that aging is associated with a decrease in both subjective and objective sleepiness. Thestronger correlation with objective sleepiness, supports the notion that older participants are less sleepy than younger ones.

In mixed longitudinal-cross-sectional models, a significant interaction was found between SDB and age, predicting sleepiness in men but not in women. In men, the association between both subjective and objective sleepiness and SDB diminished significantly with age, adjusting for comorbidities, depressive symptomology, and BMI. Further adjustments for other covariates had no effect and were not included in the final models. The modeled associations between sleepiness and SDB, calculated for participants aged 40 and 60 are given in Table 3. Our data show that a man aged 40 years with SDB has a 2.1 times greater odds of being subjectively sleepy, than a man without SDB. However, for a man aged 60 years the association between subjective sleepiness and SDB is diminished, and no longer statistically significant. Similarly, a man aged 40 years with SDB has a 2.9 times greater odds of being objectively sleepy, than a man without SDB; however, for a man aged 60 years the association is reduced and not significant. Women at both 40 and 60 years with SDB had slightly elevated odd ratios of subjective and objective sleepiness, relative to women without SDB, but these were not statistically significantly.

In the purely longitudinal models that examined the relationship of sleepiness (among participants observed to change their sleepiness status between visits) and SDB status, similar results to the mixed longitudinal-cross-sectional models were found. Specifically, a significant interaction was found between SDB and age predicting subjective sleepiness in

men, but not in women. Estimates of the association between subjective sleepiness and SDB for males and females, aged 40 and 60 years are presented in Table 4. As with the models presented in Table 3 adjustment for comorbidities, depressive symptomology, and BMI had no effect on the associations. A man aged 40 years, had a 3.4 times greater odds of having excessive subjective sleepiness at the study visits where they also had SDB, compared to the visits at which they did not have SDB. There was no significant association between SDB and changing ESS-sleepiness status for a man aged 60 year old, nor women of any age. Note, however, that women with SDB had 1.4 to 1.5 times greater subjective sleepiness in the purely longitudinal models. Although these values are not statistically significant, this may be an important elevation in the odds of sleepiness measured using ESS. Our study was underpowered to identify an elevated risk of this magnitude with statistical significance. Also of note, among persons classified as having SDB, was that men tended to have more severe SDB (median AHI among participants with AHI≥15: Men 24 vs, Women 21 events/hour); this may, in part, explain why stronger associations between SDB and sleepiness were detected in men compared to women.

Participants who reported using CPAP therapy were categorized as having SDB and grouped with participants with AHI >15, regardless of measured AHI (see models presented in Tables 3 and 4). This was done because it was not possible to estimate SDB in participants who were using CPAP during the study, and it was assumed participants were more likely to have been prescribed CPAP treatment if they were sleepy (for a given level of SDB severity). To assess the impact of CPAP use on our findings, the analyses were repeated with the participants that were using CPAP excluded. For males the modeled coefficients (presented in the footnotes of Tables 3 and 4) did not changed more than 10% for the females the results remained non-significant.

DISCISSION

The main finding of this large study, incorporating more than 3,000 measurements of subjective sleepiness and nearly 2,000 objective measurements, was that the association between sleepiness and SDB reduces with age. A 2-fold increase in subjective sleepiness was present in men with moderate to severe SDB at 40 years, but not at 60 years. In women, SDB was not associated with statistically significant increases sleepiness at any age, although a clinically significant association cannot be ruled out. Objective sleepiness measurements showed an even greater 3-fold increase in the odds of sleepiness in younger people with SDB, compared to those without SDB; again in older people no relationship was found between SDB and objective measures of sleepiness. The fact that both subjective and objective measures of daytime sleepiness reduced with age in people with moderate to severe SDB strengthens our findings, and supports the suggestion that aging *per se* is associated with a reduction in sleepiness symptoms in SDB. Current clinical practice recommends CPAP as an effective treatment for SDB, reducing symptoms of sleepiness in middle-aged patients with moderate to severe disease [7]. The results of our study imply that sleepiness may not be a salient target for SDB therapy in an older population, and other factors such as quality of life or cognitive impairment may be found to be more appropriate targets for therapeutic intervention.

Sleepiness as a symptom of SDB

The age-related reduction in sleepiness that we found in participants with SDB is consistent with previous studies that have shown reduced sleepiness in older people with SDB [3, 15]. This leads us once again to explore the notion of treating SDB based on symptoms of sleepiness. In younger people with SDB and little or no sleepiness, mortality remains high [8], supporting the argument that SDB patients who are not sleepy should be offered treatment to reduce possible cardiovascular mortality. However, in older people the evidence

base for this treatment strategy is less clear [7]. Resolving this issue will require further studies in older people, adequately powered to establish the effect of SDB on both sleepiness and cardiovascular outcomes.

SDB in older people may lead to cognitive decline, independent of sleepiness [10]; as with cardiovascular sequli this could be mediated by intermittent hypoxia [16]. The study by Ayalon *et al.*, 2010 has recently shown that the combined effects of SDB and aging produced significant impairments in cognitive function and neural activation, greater than either variable acting independently [17]. These data are also in accordance with the findings obtained from an aging animal model of OSA, where exposure to chronic intermittent hypoxia produced impaired special learning and increased neural apoptosis in older rats [18]. If the older brains are is more susceptible to intermittent hypoxia, then SDB in older people could be associated with cerebral atrophy, leading to accelerate cognitive decline, and treatment strategies would need to be developed accordingly.

Symptoms of SDB in women

In our study females with SDB did not have statistically significantly elevated odds of sleepiness, and the relationship between sleepiness and SDB was not influenced by aging. In previous studies, females with SDB have reported more symptoms of sleepiness than males [19]. This may (in part) reflect differences in the perception of sleepiness between males and females; with women often reporting more fatigue or tiredness [20]. In our study neither subjective nor objective measures of sleepiness were significantly elevated in females with SDB. This suggests that there are gender differences in the symptoms of SDB in men and women. It is notable that in a recent large cross-sectional study of older people, females with OSA perceived themselves to be less sleepy than males with OSA, but more anxious and depressed [21].

Mechanism for the age related reduction in sleepiness in older people with SDB

Age-related changes in the causes of SDB may be responsible for the reduced symptoms of sleepiness in older people with SDB. For example, aging is associated with a lengthening of the upper airway [22] and descent of the hyoid bone [23]. The response of the genioglossus muscle to negative pressure is reduced in older people, compared to younger people [24], and less negative pressure is required to collapsible the upper airway, independent of body mass index in older people [25]. These changes in the structure and function of the upper airway are likely to increase collapsibility, and the subsequent number of apneas or hypopneas in older poeple. Furthermore, if the amount of negative intra-luminal pressure required to collapse the upper airway is less, a smaller perturbation in sleep state may be required to re-open the airway. This could lead to SDB with minimal sleep disturbance in older people.

The frequency of arousals from sleep is increased in older people [26]. Each arousal leads to hyperventilation and relative hypocapnia, which can give rise to central sleep apnea (CSA) during the subsequent sleep onset. This type of CSA may be associated with fewer symptoms of sleepiness because the intrinsic frequency of arousals is not increased.

SDB is prevalent in many age-related diseases such as chronic heart failure [27] and stroke [28]. When SDB occurs with these co-morbidities the symptoms of sleepiness are reduced despite profound sleep disruption [29]. The suppressed symptoms of sleepiness may be due to factors associated with the disease processes such as increased sympathetic nervous system activity in CHF patients. However, in the present study we corrected for self reported cardiovascular co-morbidity.

The perception of sleepiness may be confounded by expectations; or habituation to the increased sleep fragmentation that occurs with aging. However the age-related reduction in objective sleepiness with SDB does not support this suggestion. Daytime napping could also be a factor in reducing the symptom of sleepiness. Older people are less likely to be employed full-time; thus may have more nap opportunities, whereas younger people in full-time employment may have less nap opportunity for a given level of nocturnal sleep disruption (due to SDB or other causes). We have previously shown a reduction in daytime activity associated with a reduction in sleepiness, in CHF patients with SDB [30]. Such life style modifications are likely to reduce the impact of nocturnal sleep disturbances on the symptom of sleepiness in SDB.

Critique of methods

To interpret the results of this study it is necessary to consider several factors. As with many cross sectional studies, the natural history of the disease is unknown in our cohort. Therefore, the temporal relationship between the development of the sleepiness and the duration of the SDB is unknown. In the Wisconsin Sleep Cohort, participants are invited to return every 4 years. At 4 and 8 years the response rate was 74 and 84%, respectively. In later years the dropout rate may be greater in people who develop severe sleepiness or co-morbidities, potentially making the sample less representative of older people.

At any age, CPAP treatment of severe, symptomatic SDB may mask associations between sleepiness and SDB. In our analysis we categorized participants with CPAP as having SDB, regardless of measured AHI (if available), we also had to take measured sleepiness in these people at face value, i.e. we were unable to adjust for what their sleepiness would have been if their SDB was untreated. Although, our re-analyses excluding the CPAP users did not alter our findings, this does not preclude the possibility that we have underestimated the association between sleepiness and SDB by excluding people with both severe sleepiness and severe SDB (in the untreated state). However, this bias would likely operate in both younger and older participants, so should not affect our comparison of associations in older vs. younger persons.

Conclusion

Our analysis of this large data set from the Wisconsin Sleep Cohort study has shown a reduction in the association between SDB and symptom of sleepiness in older men, but not women. These findings may explain (in part) why the reported increased prevalence of SDB in older people is not reflected in clinical populations. The lack of sleepiness in older people with SDB also implies that other consequences of SDB, such as reduced cognitive function, are relatively more important for health. Our findings lead us to speculate that in future composite scores may be needed to identify the risks, and determine treatment responses to SDB in older people.

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Table 1

Characteristics of sample used to examine subjective sleepiness using the Epworth Sleepiness Scale (n=3695)

Characteristic	**Females (n=1683 studies)**		**Males (n=2012 studies)**		**All**
	AHI < 15	**AHI ≥15 or CPAP**	**AHI < 15**	**AHI ≥15 or CPAP**	
Sample size	1472	211	1617	395	**3695**
Age (years) mean (range)	55 (32–81)	57 (35–77)	55 (33–80)	59 (34–78)	**56 (32–81)**
Body Mass Index (Kg/m^2)	31 (7)	41 (10)	29 (5)	35 (7)	**31 (7)**
Epworth Sleepiness Score	8 (4)	9 (4)	9 (4)	10 (4)	**9 (4)**
Epworth ≥ 10, n (%)	525 (36)	93 (44)	683 (42)	211 (53)	**1512 (41)**
MSLT* **(mins)**	11 (5)	10 (6)	9 (5)	9 (5)	**10 (5)**
MSLT ≤ 5 mins, n* **(%)**	109 (15)	19 (24)	181 (22)	53 (27)	**362 (20)**
Habitual sleep time (hours)	7 (1)	7 (1)	7 (1)	7 (1)	**7 (1)**
Nap per week (hours)	1 (2)	2(2)	2 (2)	2 (3)	**2 (2)**
Depression** **, n (%)**	450 (31)	102 (48)	273 (17)	85 (22)	**910 (25)**
Comorbid conditions, n (%)	74 (5)	15 (8)	162 (10)	84 (21)	**335 (9)**
Stroke, n (%)	25 (2)	5 (2)	14 (1)	12 (3)	**56 (2)**
Heart Failure, n (%)	10 (1)	2 (1)	8 (0.5)	8 (2)	**28 (1)**
Cardiovascular disease***, n (%)	44 (3)	10 (5)	150 (9)	74 (19)	**278 (8)**
Current Smoker, n (%)	175 (12)	21 (10)	190 (12)	42 (11)	**428 (12)**
Alcoholic drinks per week, median (range)	1 (0–36)	0 (0–17)	3 (0–42)	2 (0–32)	**2 (0–42)**
Caffeinated drinks per day	2 (2)	2 (2)	3 (2)	3 (3)	**3 (2)**
CPAP use, n (%)	NA	87 (41)	NA	144 (36)	**231 (6)**

These data are reported on number of sleep studies, with most subjects contributing multiple studies. Variables are reported as mean (sd) unless otherwise stated.

*Sample Size, n=1846

**Defined as: participants using antidepressant medication and/or ZUNG depression scale ≥ 50

***Defined as: heart attack, coronary artery disease, or cardiovascular surgical procedure

Table 2

Characteristics of sample used to examine objective sleepiness using the Multiple Sleep Latency Test (n=1846)

Characteristic	Females (n=814 MSLT studies)		Males (n=1032 MSLT studies)		All
	AHI < 15	AHI ≥15 or CPAP	AHI < 15	AHI ≥15 or CPAP	
Sample size	735	79	836	196	**1846**
Age (years) mean(range)	51 (31–73)	54 (35–68)	52 (31–72)	55 (33–71)	**52 (31–73)**
Body Mass Index (Kg/m^2)	31 (7)	42 (9)	29 (5)	35 (7)	**31 (7)**
MSLT (mins)	11 (5)	10 (6)	9 (5)	9 (5)	**10 (5)**
MSLT ≤5 mins, n (%)	109 (15)	19 (24)	181 (22)	53 (27)	**362 (20)**
Habitual sleep time (hours)	7 (1)	7 (1)	7(1)	7 (1)	**7 (1)**
Nap per week (hours)	1 (3)	2 (3)	2 (2)	2 (3)	**2 (3)**
Depression*, n (%)	217 (30)	27 (35)	142 (17)	38 (20)	**424 (23)**
Comorbid conditions, n (%)	30 (4)	4 (5)	58 (7)	30 (15)	**122 (7)**
Stroke, n (%)	9 (1)	2 (3)	1 (0.1)	7 (4)	**19 (2)**
Heart Failure, n (%)	5 (1)	0 (0)	4 (0.5)	2 (1)	**11 (1)**
Cardiovascular disease**, n (%)	19 (3)	3 (4)	55 (7)	23 (12)	**100 (5)**
Current Smoker, n (%)	108 (15)	6 (8)	134 (16)	26 (16)	**274 (15)**
Alcoholic drinks per week, median (range)	1 (0–36)	0 (0–14)	2 (0–98)	2 (0–29)	**2 (0–98)**
Caffeinated drinks per day, mean (sd)	3 (2)	2 (2)	3 (3)	4 (3)	**3 (3)**
CPAP use, n (%)	NA	26 (33)	NA	54 (28)	**80 (4)**

These data are reported on number of sleep studies, with most subjects contributing multiple studies. Variables are reported as mean (sd) unless otherwise stated.

*Defined as using antidepressant medication or ZUNG depression scale ≥ 50

**Heart attack, coronary artery disease, or cardiovascular surgical procedure

Table 3

Odds ratios for SDB predicting subjective sleepiness (ESS≥10) and objective (MSLT≤5 minutes) by gender and age, from mixed longitudinal-cross-sectional models

Sleepiness Measure		**Odds ratios for SDB* vs no SDB (95% Confidence Interval)**	
	Age (years)	**Men**	**Women**
Epworth Sleepiness Scale ≥ 10 Men = 2012 studies, Women = 1683 studies	40	2.1 (1.2, 3.8)[a]	1.1 (0.6, 2.2)[b]
	60	1.1 (0.9, 1.4)[a]	1.2 (0.9, 1.7)[b]
Multiple Sleep Latency Test ≤ 5 mins Men = 1032 studies Women = 814 studies	40	2.9 (1.3, 6.4)[c]	1.2 (0.4, 3.7)[d]
	60	0.7 (0.4, 1.3)[c]	2.1 (0.9, 4.6)[d]

*SDB: Defined as an apnea hypopnea index ≥ 15 events/hour, or self-reported CPAP use and adjusted for comorbidities, depressive symptoms, and BMI.

[a]In men, the OR for SDB predicting subjective sleepiness (ESS≥10) as a function of age can be expressed as OR = $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$, where α (the estimated SDB-ESS≥10 OR at age 30) is 1.05 (95% C.I.=0.22 to 1.88) and β (the coefficient for the SDB-age interaction term in men) is estimated to be −0.031 (95% C.I.= −0.057 to −0.004)

[b]In women, the OR for SDB predicting subjective sleepiness (ESS≥10) is $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$: α=0.04 (95% C.I.= −0.94 to 1.03); β=0.005 (95% C.I.= −0.03 to 0.04)

[c]In men, the OR for SDB predicting objective sleepiness (MSLT≤5) is $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$: α=1.77 (95% C.I.=0.58 to 2.96); β= −0.069 (95% C.I.= −0.12 to −0.02)

[d]In women, the OR for SDB predicting objective sleepiness (MSLT≤5) is $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$: α= −0.081 (95% C.I.= −1.73 to 1.57); β=0.026 (95% C.I.= −0.039 to 0.091);

Table 4

Odds ratios for SDB predicting subjective sleepiness (ESS≥10) by gender and age from longitudinal models using subjects who were observed to change sleepiness status between visits

Sleepiness Measure		Odds ratio for SDB* vs no (95% Confidence Interval)	
	Age (years)	Males (n= 266 studies)	Females (n = 211 studies)
Epworth Sleepiness Scale ≥ 10	40	3.4 (1.2, 9.7)	1.4 (0.3, 5.7)
	60	1.1 (0.6, 1.8)	1.5 (0.8, 3.0)

*SDB: Defined as an apnea hypopnea index ≥15 or self-reported CPAP use and adjusted for comorbidities, depressive symptoms, and BMI.

[a]In men, the OR for SDB predicting subjective sleepiness (ESS≥10) as a function of age can be expressed as OR = $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$, where α (the estimated SDB-ESS≥10 OR at age 30) is 1.8 (95% C.I.=0.34 to 3.3) and β (the coefficient for the SDB-age interaction term in men) is estimated to be −0.058 (95% C.I.= −0.11 to −0.011);

[b]In women, the OR for SDB predicting subjective sleepiness (ESS≥10) is $e^{\{\alpha + \beta^* (\text{age in years} - 30)\}}$: α=0.26 (95% C.I.= −1.8 to 2.4); β=0.005 (95% C.I.= −0.069 to 0.078);