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Self-reported sleep disordered breathing as risk factor for mortality in the elderly

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Abstract

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Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study.

Background/Aims—To examine the association between self-reported sleep disordered breathing (‘awaken short of breath or with a headache’) and mortality in a large and ethnically diverse group of community-dwelling elderly people.

Methods—1288 participants, 65 years and older, were examined longitudinally. Sleep problems were estimated using the Medical Outcomes Study Sleep Scale examining: sleep disturbance, snoring, sleep short of breath or with a headache, sleep adequacy, and sleep somnolence. Cox regression analysis was used to examine the association between sleep problems and mortality. Age, gender, education, ethnicity, and body mass index were included as covariates. In further analyses we included hypertension, diabetes, heart disease, and stroke as additional covariates.

Results—The participants were followed for up to 6 years (mean 2.9, SD: 1.1), and 239 (18.6%) participants died during the follow-up. In unadjusted models, SDB at the initial visit was associated with mortality HR=1.37; 95% CI 1.21-1.55; $p<0.0001$. After adjusting for all the covariates, the relationship between SDB and mortality remained significant HR=1.48; 95% CI 1.29-1.70; $p<0.0001$. Participants with Caribbean-Hispanic ancestry have higher risk for mortality.

Conclusion—Our results suggest that SDB is a risk factor for mortality in a large and ethnically diverse group of older adults, independent of demographic and clinical factors. Further research is needed in order to examine the underlying mechanisms of this association.

Keywords

sleep disordered breathing; mortality; elderly; self-reported sleep problems; longitudinal study

Introduction

Sleep problems are common among the elderly population [1] and have been linked to many disorders in the specific age group [2-4]. In particular, sleep disordered breathing (SDB) – including difficulties breathing during sleep- has a high prevalence among older adults, and often occurs even with atypical symptoms [5, 6]. Obstructive sleep apnea (OSA) is the most salient symptom of SDB, and has a prevalence rate of 30-80% in the elderly [7]. Given that SDB has been associated with increased risk of both cardiovascular disorders [8] and dementia [9], understanding whether SDB can be linked to mortality in older adults is of a paramount importance.

A number of studies have shown that, of all sleep problems, sleep duration is the most predictive of mortality [10-24]. Sleep duration has been linked to mortality in older, but not middle aged adults [13]. Longer durations of sleep in older adults have been shown to increase the risk of dementia mortality [10]. Further, daytime napping, which is factored into measures of the total sleep duration, has been also associated with an elevated risk of cardiovascular disease mortality [25] and with all-cause mortality [26]. Similarly, excessive daytime sleepiness seems to be an independent risk indicator for cardiovascular mortality in older adults [27]. Finally, insomnia symptoms, especially difficulty initiating asleep and nonrestorative sleep have been linked to a higher risk of mortality [28].

In contrast, much less is known about the association between SDB and mortality. One recent 10-year-follow-up study suggests that OSA is associated with a higher risk of

mortality [29]. A different study reported that OSA is specifically associated with cancer mortality [30]. However, even though untreated SDB seems to be a strong risk factor for mortality [31, 32], the results of other studies examining the association between SDB and mortality have produced discrepant results [33-35].

There are some significant limitations in the present literature exploring the association between SDB and mortality. First, the sample size of some of the existing studies is relatively small [36-39]. Likewise, most of the studies to date, have not specifically focused on the impact of SDB in older adults, and instead, have included a wide range of ages in their population samples [29-32, 40]. Furthermore, other studies have limited their sample to include either male or female participants, and/or do not adequately represent an ethnically diverse population sample [41-43]. All of these factors may contribute to the mixed findings present in the current body of literature surrounding this topic and also may limit the generalizability of their findings.

Thus, there is a relative paucity of longitudinal research examining the specific association in the older adults, and the existing results are often discrepant. To help reconcile these issues, in the present study, we aimed to examine the association between SDB and mortality, in a large and ethnically diverse sample of older adults.

Methods

Study participants

Participants were selected from the Washington Heights-Inwood Community Aging Project (WHICAP) at Columbia University Medical Center [44, 45]. WHICAP is a longitudinal community based research study aimed at identifying risk factors and biomarkers for aging and Alzheimer's disease in a multi-ethnic cohort that includes Caucasian, African-American and Hispanic participants [46]. The age range of the participating pool that took part in the project was 65 years and older. Informed consent approved by the Internal Review Board (IRB) of the College of Physicians and Surgeons of Columbia University and the New York State Psychiatric Institute, was obtained prior to study participation for each participant.

Each participant underwent a structured in-person interview including an assessment of health and physical function, as well as a neuropsychological assessment in their preferred language (i.e., English or Spanish). Participants were followed at intervals of approximately 1.5 years, repeating the baseline examination and consensus diagnosis at these time points.

From 2007 onwards, sleep information was gathered from the participants. In the current study, we define the baseline visit as the visit when the sleep questionnaire was first administered to the participants.

The initial sample was consisted of 2358 participants. By the time when sleep questionnaire was first introduced to the cohort, 1838 participants remained alive. Among these, we excluded 550 participants who had no sleep information or follow-up data. Thus, the final sample consisted of 1288 participants.

Information about mortality was tracked through follow-up interviews and submission of identifying information to the National Death Index.

Sleep measures

Sleep quality was assessed using the Sleep Scale from the Medical Outcomes Study. This scale is a self-report 12-item questionnaire which asks the following questions [47]: 1. How long did it usually take for you to fall asleep during the past 4 weeks? 2. On average, how long did you sleep each night during the past 4 weeks? How often during the past 4 weeks did you: 3. Feel that your sleep was not quite (moving restlessly, feeling tense, speaking, etc.) while sleeping? 4. Get enough sleep to feel rested upon waking in the morning? 5. Awaken short of breath or with a headache? 6. Feel drowsy or sleepy during the day? 7. Have trouble falling asleep? 8. Awaken during your sleep time and have trouble falling asleep again? 9. Have trouble staying awake during the day? 10. Snore during your sleep? 11. Take naps (5 minutes or longer) during the day. 12. Get the amount of sleep you needed?

Each of the questions has a possible rating of 0-6, based on the frequency of the sleep problem (See Appendix), with a higher score indicating greater sleep dysfunction. We used response to the question ‘awaken short of breath or with a headache’ as a marker for self-reported SDB.

Covariates

Age (years), education (years), and body mass index (BMI) were used as continuous variables. Ethnicity was ascertained based on self-report using the format of the 1990 census [48]. Participants were then assigned to one of four ethnic groups: African-American (non-Hispanic), Hispanic, White (non-Hispanic), and Other. Ethnicity was used as a dummy variable with White (non-Hispanic) as the reference. In further analyses, we added hypertension, diabetes, heart disease, and stroke as covariates.

Statistical analysis

Analyses were performed using SPSS 22 (SPSS, Chicago, Illinois). Baseline characteristics of subjects were compared using t-test or ANOVA models for continuous variables (i.e., age, education), and with chi-square test for categorical baseline characteristics (i.e., gender, ethnicity).

In order to examine the association between SDB and mortality we used Cox proportional hazards model, with death as the dichotomous outcome. The time-to-event variable was the time from recording of baseline sleep quality reports to death for those who died, and from baseline to the last follow-up for those who survived. The sleep question: ‘awaken short of breath or with a headache’, as a continuous variable was used as the predictor.

Adjustments were made initially for age (years), gender, education (years), ethnicity, and BMI, and then for hypertension, diabetes, heart disease, and stroke, in order to estimate the association between sleep problems and mortality. The predictor of interest was the sleep question score as a continuous variable.

Results

In the sample, there were more females than males, and more participants with an Hispanic ancestry (see Table 1). From the total of 1288 participants, 239 (18.6%) died, over a mean of 2.9 (SD= 1.1; range: 0.2-6) years of follow-up. The average age at death was 87.4 (SD: 7.0) (see Table 1).

In the unadjusted models, self-reported SDB, was associated with mortality (HR=1.37; 95% CI 1.21-1.55; $p<0.0001$).

After controlling for age, gender, education, ethnicity, and BMI, the association between self-reported SDB and mortality remained highly significant (HR=1.47; 95% CI 1.29-1.69; $p<0.0001$).

We then added hypertension, diabetes, heart disease, and stroke as covariates to our model. The association between SDB and mortality remained significant (HR=1.48; 95% CI 1.29-1.70; $p<0.0001$) (see Table 2 and Figure 1).

We ran further analysis in order to examine whether the association would remain significant in a model that included all 12 sleep questions. After adding all of the questions and controlling for all covariates, SDB remained significantly associated with mortality (HR=1.39; 95% CI 1.20-1.61; $p<0.0001$). None of the other sleep problems was associated with mortality (see Table 2).

Finally, after stratifying the adjusted analyses by ethnicity, and adding the above covariates, our results suggest that participants with Caribbean-Hispanic ancestry have higher risk for mortality (HR=1.51; 95% CI 1.26-1.82; $p<0.0001$), followed by Caucasians (HR=1.61; 95% CI 1.19-2.17; $p=0.002$).

Discussion

In the present study, we examined the association between SDB and mortality, in a large and ethnically diverse sample of older adults. Although some previous studies have found a significant association between SDB and mortality, most of these studies included varied age groups, focused only one gender, or had relatively small sample size. According to our results, SDB was significantly linked to mortality in our large group of elderly men and women.

In an attempt to explain the present results, we initially hypothesized that cardiovascular problems may play an important role in the participant's health outcome [31, 49]. Metabolic syndrome is a clustering of cardiovascular risk factors characterized by insulin resistance [50] which has been linked to SDB in the general population [51]. Furthermore, metabolic syndrome has also been associated with cardiovascular mortality in the elderly by increasing the risk for stroke, diabetes, and hypertension [50, 51]. Thus, increased blood pressure, high blood sugar levels, and/or abnormal cholesterol levels may explain the association between SDB and mortality. However, as we did include diabetes, heart disease, stroke, and

hypertension as covariates in the model, our results suggest that these factors do not seem to mediate the association between SDB and mortality.

Another explanation could be that SDB can be the cause of lower oxygenation of the brain because of the motor regulation that occurs in the upper airway [52]. Hypoxia has a broad effect on the brain's function including changes in cognition such as deficits in learning, and short-term memory [53]. Apart from cognitive dysfunction, hypoxia affects -directly or indirectly- most of the neural systems of the brain, as it is mostly used for the oxidation of the glucose [53]. Thus, SDB could be linked to hypoxia and thus, to the death of brain cells, as well as to gray matter loss [52] and thereby drive mortality.

Sleep disturbances, and especially sleep disordered breathing has been connected to cerebrovascular diseases [54]. Apnea duration has also been linked to induced variations in cerebral blood flow velocity and arterial blood pressure [55]. In a recent study, it has been suggested the association between a specific peptide and the adverse outcomes of OSA [56]. As the risk of mortality in patients with cerebrovascular disease is high and can increase even more the possibility of new stroke or vascular events to take place [57-59], people suffering from sleep disordered breathing could drop in that clinical pathology, and have increased risk for mortality.

Dementia may also play an important role in the association between SDB and mortality. SDB has been linked to cognitive decline and dementia in older adults [60-62]. There is also an association between dementia and mortality [63]. Thus, it is possible that participants who were demented at baseline or became demented through the follow-up period are the ones who primarily died. However, the question as to whether SDB is a cause of mortality, a consequence of poor health, or a symptom of an underlying neurodegenerative disease, remains open. The association between sleep problems and mortality could include all three of the above, as cause, consequence, and symptom can interact [64, 65].

The present study has some limitations. First, we did not use an objective measure of sleep problems, such as actigraphy/ polysomnography. Moreover, the answers in the sleep questionnaire refer to the previous four weeks, and may not accurately represent a participant's chronic sleep pattern. Finally, the study had a relatively short follow-up period.

However, the present study has strengths that are noteworthy. This is a large study examining the association between SDB and mortality in the elderly including both men and women, thus, having a great ecological validity. Furthermore, to the best of our knowledge, this study is the first to include a large number of ethnically diverse participants, counting African-Americans and Hispanics.

In conclusion, our results suggest that SDB is significantly associated with incident mortality, in older adults, over and above numerous demographic and clinical factors. The meaning of the study is great as early detection and treatment of the SDB symptoms may reduce the risk of mortality in older adults. Further research is needed in order to understand the exact underlying mechanisms involved in this association.

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Appendix

Sleep Scale from the Medical Outcomes Study

1. How long did it usually take for you to fall asleep during the past 4 weeks?

(Circle One)

0-15 minutes……..…1

16-30 minutes……..2

31-45 minutes……..3

46-60 minutes……..4

More than 60 minutes …….5

_____

2. On the average, how many hours did you sleep each night during the past 4 weeks?

Write in number of hours per night:

_____

How often during the past 4 weeks did you…

3. Feel that your sleep was not quiet (moving restlessly, feeling tense, speaking, etc., while sleeping)?

4. Get enough sleep to feel rested upon waking in the morning?

5. Awaken short of breath or with a headache?

6. Feel drowsy or sleepy during the day?

7. Have trouble falling asleep?

8. Awaken during your sleep time and have trouble falling asleep again?

9. Have trouble staying awake during the day?

10. Snore during your sleep?

11. Take naps (5 minutes or longer) during the day?

12. Get the amount of sleep you needed?

Possible answers: 1= All of the time, 2= Most of the time, 3= A good bit of the time, 4= Some of the time, 5= A little of the time, 6= None of the time, -1= Not asked, -2= Too impaired to respond, -3= Refused

Hays, R. D., & Stewart, A. L. (1992). Sleep measures. In A. L. Stewart & J. E. Ware (eds.). Measuring functioning and well-being: The Medical Outcomes Study approach (pp. 235-259), Durham, NC: Duke University Press.

References

1. Foley DJ, et al. Sleep complaints among elderly persons: an epidemiologic study of three communities. Sleep. 1995; 18(6):425–32. [PubMed: 7481413]
2. Spiegel K, Leproult R, Van Cauter E. Impact of sleep debt on metabolic and endocrine function. Lancet. 1999; 354(9188):1435–9. [PubMed: 10543671]
3. Tsapanou A, et al. Daytime Sleepiness and Sleep Inadequacy as Risk Factors for Dementia. Dement Geriatr Cogn Dis Extra. 2015; 5(2):286–95. [PubMed: 26273244]
4. Tsapanou A, et al. Daytime somnolence as an early sign of cognitive decline in a community-based study of older people. Int J Geriatr Psychiatry. 2015
5. Janssens JP, et al. Sleep disordered breathing in the elderly. Aging (Milano). 2000; 12(6):417–29. [PubMed: 11211951]
6. Russell T, Duntley S. Sleep disordered breathing in the elderly. Am J Med. 2011; 124(12):1123–6. [PubMed: 21906711]
7. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002; 165(9):1217–39. [PubMed: 11991871]
8. Linz D, et al. The importance of sleep-disordered breathing in cardiovascular disease. Clin Res Cardiol. 2015
9. Yaffe K, et al. Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. JAMA. 2011; 306(6):613–9. [PubMed: 21828324]
10. Benito-Leon J, et al. Long sleep duration in elders without dementia increases risk of dementia mortality (NEDICES). Neurology. 2014; 83(17):1530–7. [PubMed: 25253755]
11. Cappuccio FP, et al. Sleep duration and all-cause mortality: a systematic review and meta-analysis of prospective studies. Sleep. 2010; 33(5):585–92. [PubMed: 20469800]
12. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. J Sleep Res. 2009; 18(2):148–58. [PubMed: 19645960]
13. Gangwisch JE, et al. Sleep duration associated with mortality in elderly, but not middle-aged, adults in a large US sample. Sleep. 2008; 31(8):1087–96. [PubMed: 18714780]
14. Grandner MA, et al. Mortality associated with short sleep duration: The evidence, the possible mechanisms, and the future. Sleep Med Rev. 2010; 14(3):191–203. [PubMed: 19932976]
15. Heslop P, et al. Sleep duration and mortality: The effect of short or long sleep duration on cardiovascular and all-cause mortality in working men and women. Sleep Med. 2002; 3(4):305–14. [PubMed: 14592192]
16. Ikehara S, et al. Association of sleep duration with mortality from cardiovascular disease and other causes for Japanese men and women: the JACC study. Sleep. 2009; 32(3):295–301. [PubMed: 19294949]
17. Kripke DF, et al. Mortality associated with sleep duration and insomnia. Arch Gen Psychiatry. 2002; 59(2):131–6. [PubMed: 11825133]
18. Kronholm E, et al. Self-reported sleep duration, all-cause mortality, cardiovascular mortality and morbidity in Finland. Sleep Med. 2011; 12(3):215–21. [PubMed: 21317033]
19. Mesas AE, et al. Sleep duration and mortality according to health status in older adults. J Am Geriatr Soc. 2010; 58(10):1870–7. [PubMed: 20840460]

20. Patel SR, et al. A prospective study of sleep duration and mortality risk in women. Sleep. 2004; 27(3):440–4. [PubMed: 15164896]
21. Shankar A, et al. Sleep duration and coronary heart disease mortality among Chinese adults in Singapore: a population-based cohort study. Am J Epidemiol. 2008; 168(12):1367–73. [PubMed: 18952563]
22. Zhong G, et al. Daytime napping and mortality from all causes, cardiovascular disease, and cancer: a meta-analysis of prospective cohort studies. Sleep Med. 2015; 16(7):811–819. [PubMed: 26051864]
23. Stone KL, et al. Self-reported sleep and nap habits and risk of mortality in a large cohort of older women. J Am Geriatr Soc. 2009; 57(4):604–11. [PubMed: 19220560]
24. Amagai Y, et al. Sleep duration and mortality in Japan: the Jichi Medical School Cohort Study. J Epidemiol. 2004; 14(4):124–8. [PubMed: 15369129]
25. Tanabe N, et al. Daytime napping and mortality, with a special reference to cardiovascular disease: the JACC study. Int J Epidemiol. 2010; 39(1):233–43. [PubMed: 19900974]
26. Pollak CP, et al. Sleep problems in the community elderly as predictors of death and nursing home placement. J Community Health. 1990; 15(2):123–35. [PubMed: 2355110]
27. Empana JP, et al. Excessive daytime sleepiness is an independent risk indicator for cardiovascular mortality in community-dwelling elderly: the three city study. Stroke. 2009; 40(4):1219–24. [PubMed: 19246707]
28. Li Y, et al. Association between insomnia symptoms and mortality: a prospective study of U.S. men. Circulation. 2014; 129(7):737–46. [PubMed: 24226807]
29. Jennum P, et al. All-cause mortality from obstructive sleep apnea in male and female patients with and without continuous positive airway pressure treatment: a registry study with 10 years of follow-up. Nat Sci Sleep. 2015; 7:43–50. [PubMed: 25914563]
30. Nieto FJ, et al. Sleep-disordered breathing and cancer mortality: results from the Wisconsin Sleep Cohort Study. Am J Respir Crit Care Med. 2012; 186(2):190–4. [PubMed: 22610391]
31. Young T, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep. 2008; 31(8):1071–8. [PubMed: 18714778]
32. Punjabi NM, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med. 2009; 6(8):e1000132. [PubMed: 19688045]
33. Ancoli-Israel S, et al. The relationship between congestive heart failure, sleep apnea, and mortality in older men. Chest. 2003; 124(4):1400–5. [PubMed: 14555572]
34. Ancoli-Israel S, et al. Sleep apnea in female patients in a nursing home. Increased risk of mortality. Chest. 1989; 96(5):1054–8. [PubMed: 2805836]
35. Bliwise DL, et al. Sleep apnea and mortality in an aged cohort. Am J Public Health. 1988; 78(5): 544–7. [PubMed: 3354738]
36. Campos-Rodriguez F, et al. Mortality in obstructive sleep apnea-hypopnea patients treated with positive airway pressure. Chest. 2005; 128(2):624–33. [PubMed: 16100147]
37. Gami AS, et al. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med. 2005; 352(12):1206–14. [PubMed: 15788497]
38. Gooneratne NS, et al. Sleep disordered breathing with excessive daytime sleepiness is a risk factor for mortality in older adults. Sleep. 2011; 34(4):435–42. [PubMed: 21461321]
39. Marshall NS, et al. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep. 2008; 31(8):1079–85. [PubMed: 18714779]
40. Yaggi HK, et al. Obstructive sleep apnea as a risk factor for stroke and death. N Engl J Med. 2005; 353(19):2034–41. [PubMed: 16282178]
41. He J, et al. Mortality and apnea index in obstructive sleep apnea. Experience in 385 male patients. Chest. 1988; 94(1):9–14. [PubMed: 3289839]
42. Lavie P, Lavie L. Herer, All-cause mortality in males with sleep apnoea syndrome: declining mortality rates with age. Eur Respir J. 2005; 25(3):514–20. [PubMed: 15738297]
43. Marin JM, et al. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet. 2005; 365(9464):1046–53. [PubMed: 15781100]

44. Tang MX, et al. Incidence of AD in African-Americans, Caribbean Hispanics, and Caucasians in northern Manhattan. Neurology. 2001; 56(1):49–56. [PubMed: 11148235]
45. Manly JJ, et al. Implementing diagnostic criteria and estimating frequency of mild cognitive impairment in an urban community. Arch Neurol. 2005; 62(11):1739–46. [PubMed: 16286549]
46. Tang MX, et al. The APOE-epsilon4 allele and the risk of Alzheimer disease among African Americans, whites, and Hispanics. JAMA. 1998; 279(10):751–5. [PubMed: 9508150]
47. Spritzer, KHR. MOS Sleep Scale: a manual for use and scoring, Version 1.0. Los Angeles, CA: 2003.
48. Census of population and housing. Summary tape file 1, technical documentation. Washington, DC: Bureau of the Consensus; 1991.
49. Mokhlesi B, Pamidi S, Yaggi HK. Sleep disordered breathing and subjective sleepiness in the elderly: a deadly combination? Sleep. 2011; 34(4):413–5. [PubMed: 21461318]
50. Wang J, et al. The metabolic syndrome predicts cardiovascular mortality: a 13-year follow-up study in elderly non-diabetic Finns. Eur Heart J. 2007; 28(7):857–64. [PubMed: 17303589]
51. Heinzer R, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med. 2015; 3(4):310–8. [PubMed: 25682233]
52. Macey PM, et al. Brain morphology associated with obstructive sleep apnea. Am J Respir Crit Care Med. 2002; 166(10):1382–7. [PubMed: 12421746]
53. Gibson GE, et al. Brain dysfunction in mild to moderate hypoxia. Am J Med. 1981; 70(6):1247–54. [PubMed: 6112879]
54. Gurnell M, Powlson AS. Cardiovascular Disease and Sleep Disordered Breathing in Acromegaly. Neuroendocrinology. 2015
55. Alex R, et al. Effect of apnea duration on apnea induced variations in cerebral blood flow velocity and arterial blood pressure. Conf Proc IEEE Eng Med Biol Soc. 2014; 2014:270–3. [PubMed: 25569949]
56. Durgan DJ, et al. Increased cerebrovascular sensitivity to endothelin-1 in a rat model of obstructive sleep apnea: a role for endothelin receptor B. J Cereb Blood Flow Metab. 2015; 35(3):402–11. [PubMed: 25425077]
57. Weijmans M, et al. Incremental value of a genetic risk score for the prediction of new vascular events in patients with clinically manifest vascular disease. Atherosclerosis. 2015; 239(2):451–8. [PubMed: 25687271]
58. Weijmans M, et al. The relation between the presence of cardiovascular disease and vascular risk factors in offspring and the occurrence of new vascular events in their parents already at high vascular risk. Am Heart J. 2015; 170(4):744–752 e2. [PubMed: 26386798]
59. Weijmans M, et al. Prevalence and risk of cardiovascular risk factors and events in offspring of patients at high vascular risk and effect of location of parental vascular disease. Int J Cardiol. 2015; 195:195–202. [PubMed: 26046422]
60. Blackwell T, et al. Associations between sleep-disordered breathing, nocturnal hypoxemia, and subsequent cognitive decline in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc. 2015; 63(3):453–61. [PubMed: 25803785]
61. Manni R, Terzaghi M. Sleep-disordered breathing in dementia with Lewy bodies. Curr Neurol Neurosci Rep. 2015; 15(3):7. [PubMed: 25663033]
62. Osorio RS, et al. Sleep-disordered breathing advances cognitive decline in the elderly. Neurology. 2015; 84(19):1964–71. [PubMed: 25878183]
63. Roehr S, et al. Mortality in incident dementia - results from the German Study on Aging, Cognition, and Dementia in Primary Care Patients. Acta Psychiatr Scand. 2015
64. Cappucio, FP.; M, M.; Locker, SW., editors. Sleep, health and society From aetiology to public health. Oxford University Press; 2010. p. 1-471.
65. Cappuccio FP, Miller MA. Sleep and mortality: cause, consequence, or symptom? Sleep Med. 2013; 14(7):587–8. [PubMed: 23684937]

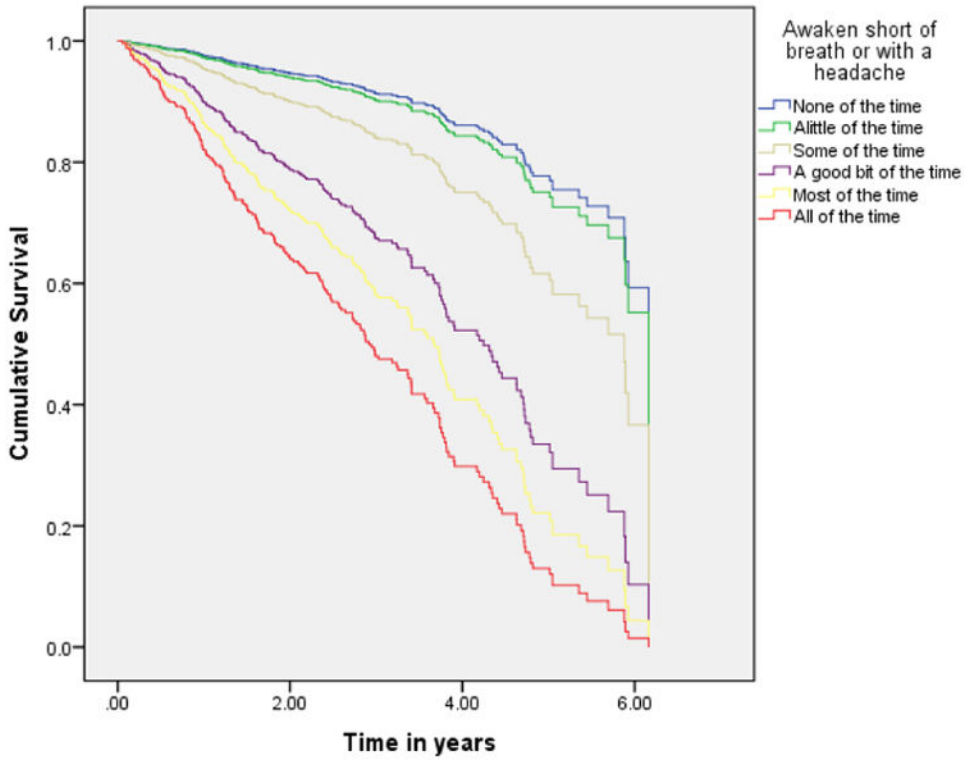

Figure 1.
Survival plot for mortality, with SDB as the predictor.

Table 1
Demographic and clinical characteristics of the participants

Characteristics	Death			Total
	No	Yes	*p* value	
Total (n) (%)	1049 (81.4)	239 (18.6)		1288
Age at evaluation, M(SD)	79.5 (6.5)	85.5 (7.0)	<0.0001	80.6 (7.0)
Age at death, M (SD)	82.2 (6.6)(last visit)	87.4 (7.0)	<0.0001	83.1 (7.0)
Gender, N (% Female)	745 (71.0)	152 (63.6)	0.024	897 (69.6)
Education, M (SD)	10.0 (5.1)	10.0 (5.1)	0.915	10.0 (5.1)
Ethnicity, N (%)			0.026	
Whites	234 (22.3)	68 (28.5)		302 (23.4)
Hispanics	568 (54.1)	109 (45.6)		677 (52.6)
African-Americans	236 (22.5)	58 (24.3)		294 (22.8)
Other	11 (1.0)	4 (1.7)		15 (1.2)
BMI, M (SD)	29.1 (5.7)	27.2 (5.8)	<0.0001	28.8 (5.7)
Hypertension	826 (79.3)	173 (73.3)	0.042	999 (78.2)
Diabetes mellitus	293 (28.1)	79 (33.5)	0.104	372 (29.1)
Heart disease	282 (27.1)	96 (40.7)	<0.0001	378 (29.6)
Stroke	97 (9.3)	47 (19.7)	<0.0001	144 (11.2)

Table 2

Association between SDB and mortality. Unadjusted model.

Sleep variable	HR (95% CI), *p* value
SDB*	HR=1.37; 95% CI 1.21-1.55; $p<0.0001$

*SDB: sleep disordered breathing: 'Awaken short of breath or with a headache'.

Association between SDB and mortality. Model used SDB as a separate question adjusted for: age, gender, education, ethnicity, BMI.

Sleep variable	HR (95% CI) *p* value
SDB	HR=1.47; 95% CI 1.29-1.69; $p<0.0001$

Association between SDB and mortality. Model used SDB as a separate question adjusted for: age, gender, education, ethnicity, BMI, hypertension, diabetes, heart disease, and stroke.

Sleep variable	HR (95% CI) *p* value
SDB	HR=1.48; 95% CI 1.29-1.70; $p<0.0001$

Association between SDB and mortality. Model included all 12 sleep questions, age, gender, education, ethnicity, BMI, hypertension, diabetes, heart disease, and stroke.

Sleep variable	HR (95% CI), *p* value
1. Duration to fall asleep [a]	HR=1.11; 95% CI .970-1.27; $p=0.130$
2. Duration of sleep (h) [a]	HR=.925; 95% CI .838-1.02; $p=0.123$
3. Sleep not quite [a]	HR=1.00; 95% CI .892-1.12; $p=0.981$
4. Feel rested in the morning [a]	HR=.985; 95% CI .857-1.13; $p=0.829$
5. SDB [a]	HR=1.39; 95% CI 1.20-1.61; $p<0.0001$
6. Drowsiness/ sleepiness [a]	HR=1.00; 95% CI .877-1.15; $p=0.959$
7. Trouble falling asleep [a]	HR=.901; 95% CI .768-1.06; $p=0.198$
8. Awakening and trouble falling asleep again[a]	HR=.976; 95% CI .854-1.12; $p=0.719$
9. Daytime sleepiness[a]	HR=1.10; 95% CI .942-1.29; $p=0.223$
10. Snoring[a]	HR=.973; 95% CI .880-1.07; $p=0.587$
11. Taking naps [a]	HR=1.09; 95% CI .985-1.21; $p=0.095$
12. Sleep adequacy [a]	HR=1.08; 95% CI .925-1.26; $p=0.325$

Cox proportional Hazard Ratios (HRs) for mortality by sleep problems.

[a]1. How long did it usually take for you to fall asleep during the past 4 weeks? 2. On average, how long did you sleep each night during the past 4 weeks? How often during the past 4 weeks did you: 3. Feel that your sleep was not quite (moving restlessly, feeling tense, speaking, etc.) while sleeping? 4. Get enough sleep to feel rested upon waking in the morning? 5. Awaken short of breath or with a headache? 6. Feel drowsy or sleepy during the day? 7. Have trouble falling asleep? 8. Awaken during your sleep time and have trouble falling asleep again? 9. Have trouble staying awake during the day? 10. Snore during your sleep? 11. Take naps (5 minutes or longer) during the day. 12. Get the amount of sleep you needed?

A *p* value of less than 0.05 was considered statistically significant.