Published in final edited form as:

Sleep Med. 2011 January ; 12(1): 28–33. doi:10.1016/j.sleep.2010.04.016.

Mortality Related to Actigraphic Long and Short Sleep

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Abstract

Background—The folk belief that we should sleep 8 hours seems to be incorrect. Numerous studies have shown that self-reported sleep longer than 7.5 hours or shorter than 6.5 hours predicts increased mortality risk. This study examined if prospectively-determined objective sleep duration, as estimated by wrist actigraphy, was associated with mortality risks.

Methods—From 1995–1999, women averaging 67.6 years of age provided one-week actigraphic recordings. Survival could be estimated from follow-up continuing until 2009 for 444, with an average of 10.5 years before censoring. Multivariate age-stratified Cox regression models were controlled for history of hypertension, diabetes, myocardial infarction, cancer, and major depression.

Results—Adjusted survival functions estimated 61% survival (54%–69%, 95% C.I.) for those with sleep less than 300 min and 78% survival (73%–85%, 95% C.I.) for those with actigraphic sleep longer than 390 min, as compared with survival of 90% (85%–94%, 95% C.I.) for those with sleep of 300–390 min. Time-in-bed, sleep efficiency and the timing of melatonin metabolite excretion were also significant mortality risk factors.

Conclusion—This study confirms a U-shaped relationship between survival and actigraphically measured sleep durations, with the optimal objective sleep duration being shorter than the self-report optimums. People who sleep five or six hours may be reassured. Further studies are needed to identify any modifiable factors for this mortality and possible approaches to prevention.

Keywords

Sleep; Epidemiology; Duration; Mortality; Survival; Time-in-bed; Melatonin

1. Introduction

People often wonder if they are getting enough sleep, reflecting the ancient folk belief that adults should sleep 8 hours. In 1964, Hammond reported that among men participating in

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Disclosure

We state that there were no conflicts of interest.

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the Cancer Prevention Study I (CPSI), those who reported 7 hours of sleep had survived longer than those who slept 8 hours or more [1], casting doubt on the 8-hour belief. In addition, men who reported less than 7 hours sleep had shorter survival. A subsequent analysis strengthened these findings using a more complete sample of the CPSI men and women [2]. More than two decades later, after the Cancer Prevention Study II (CPSII) was completed, an extensive analysis of the new sample of 1.1 million participants who were followed for 6 years, with control for 32 covariates, continued to show that those with 6.5 – 7.4 hours of sleep had lower mortality than those with shorter or longer self-reported sleep durations [3]. Somewhat to the surprise of many observers, this analysis showed that reported insomnia was not a mortality risk factor after control for confounding covariates, but reported sleeping pill use was associated with substantial increased risk after controlling for sleep duration, insomnia, and other covariates. Moreover, there was a greater proportion reporting long sleep >7.5 hours than the proportion with short sleep <6.5 hours, and a greater attributable mortality risk was associated with long sleep than with short sleep.

Mainly in the last decade, numerous studies have replicated the general findings from the Cancer Prevention Studies. A large representative sample from Japan showed a similar mortality minimum at approximately the same reported sleep duration and likewise showed the more impressive risk associated with the longer sleep durations [4]. A recent meta-analysis confirmed these findings among the increasing body of available self-report studies, estimating that the risk ratio associated with short sleep was 1.10 (1.06–1.15, 95% CI), whereas that associated with long sleep was 1.23 (1.17–1.30, 95% CI) [5].

Reported sleep is only loosely associated with objectively-recorded sleep duration, especially in the age group above 60 years in which most sleep-associated deaths are observed [6;7]. Whether mortality associated with reported sleep durations effectively represents mortality associated with objective physiologic sleep is a lingering question [8]. A well designed polysomnographic study was unable to verify any association of sleep durations less than 6 hours with excess mortality, but only 66 participants had died among 184 recorded [9]. Since long sleep latency and poor sleep efficiency were associated with decreased survival in that study, a new question emerged whether excessive time spent in bed was associated with excess mortality [9]. The larger issue is whether the associated mortality is caused or mediated by long or short sleep, or whether sleep duration is merely a comorbid marker associated with other yet-to-be-defined causal processes.

To determine if objective sleep duration is associated with mortality, from October, 1995 through June, 1999, we collected actigraphic sleep recordings of women who were participating in the Observational Study of the Women's Health Initiative (WHI), University of California, San Diego Clinical Center. These observations were funded independently as an ancillary study of the WHI. Several previous analyses of the initial data from our participants have appeared, as described in Appendix 1, but the excellent survival of these women has required up to 14 years of follow-up to ascertain sufficient deaths so that the pre-planned mortality analyses could be performed.

2. Methods

As described in our previous publications in more detail, 459 women who were already participating in the Women's Health Initiative as part of the Observational Study at the San Diego Clinical Center were recruited to participate in ancillary recordings of sleep. Subsample recruitment was deliberately structured to include as many older women as possible to increase the power of mortality analyses. Likewise, the subsample was structured to over-represent women subjectively reporting sleep durations of 6 hours or less or 8 hours

or more, to increase the power of analyses of short and long sleep. Informed consent was obtained under supervision of the UCSD Human Research Protections Program.

Almost all of the women completed sleep questionnaires and underwent SCID research psychiatric interviews to determine any history of affective or sleep disorders [10]. With permission, data from previously-completed questionnaires and examinations, which were part of the main WHI study, were merged with the ancillary study questionnaires to enrich the available covariate information, e.g., BMI, systolic blood pressure, history of diabetes, stroke or cancer, etc. This provided questionnaire estimates of the participant's sleep duration both at entry to the WHI (Form 37, question 120, available at <http://whiscience.org/data/forms.php>) and generally a few months later on entry to the sleep ancillary study. Subjective estimates of sleep duration were also provided in sleep diaries completed for 7 nights in conjunction with the actigraphic studies, and then averaged. Sleep-wake state was recorded objectively with a wrist actigraph (see Appendix 1).

The majority of participants collected 24-hour fractional urine specimens for analyses of aMT6s (the major metabolite of melatonin), described in more detail elsewhere [11]. The majority also wore a finger pulse oximetry probe for 3 nights, which provided the 4% oxygen desaturations index (ODI4, i.e., desaturation events per hour of sleep, a metric of sleep respiratory disturbance). Since ODI4 is highly skewed, $\log_{10}$ ODI4 was the preferred indicator of severity of sleep apnea.

At the outset of the study, in 1995, the Principal Investigator and collaborating statistician prospectively planned to test the main hypothesis: that a U-shaped curve in mortality would be related to actigraphic sleep duration, as it is to questionnaire sleep duration. The primary preplanned test was a Cox Proportional Hazards model for mortality, testing deviation from that sleep duration with minimum mortality (absolute value deviation, either longer or shorter sleep, combined) as the main predictor. Since previous studies had suggested that minimal mortality might be associated with sleep durations somewhat shorter than the median duration, the investigators prospectively predicted that the minimum mortality would be associated with an actigraphic sleep duration 30 minutes less than the actigraphic median. The prospectively defined risk factor was, therefore, the absolute value of the observed in-bed actigraphic sleep duration minus the median group actigraphic nocturnal sleep time of 363.6 min less 30 min or 333.6 min. This risk factor was abbreviated ASDM-30 (actigraphic sleep duration median less 30 min). Age, body mass index (BMI), and health history items similar to those proven useful in the Cancer Prevention Study analyses [3;12] were planned as additional covariates in the analyses. In addition, the investigators planned to control for depression, melatonin excretion, and ODI4 as possible risk factors which might be confounded with sleep duration.

Until 2005, WHI staff followed the women with yearly mailed questionnaires and telephone calls, when necessary, to trace each participant's address and vital status. Deaths were ascertained when possible. In June, 2009, Social Security Death Index (SSDI) data were interrogated to ascertain any additional deaths, but 15 subjects could not be checked in the SSDI due to problems matching WHI and sleep study records for social security numbers or names, so their observations were censored at the last available follow-up. Presumably-valid ascertainment of vital status or date lost to follow-up (censored) was recorded for 444 women, but some deaths may not have been detected.

Statistical analyses were based on Cox Regression, computed by SPSS 12.0 (SPSS, Inc., Chicago, Illinois), modeling ascertained deaths as the hazard over the interval until the participant died or was lost to follow-up. The models were generally stratified by 3 age groups: <60, 60–69.9, and ≥ 70 years. In addition, age² (age in years * age in years, a better

mortality predictor than age) was entered into the age-stratified models, but was usually removed during backwards stepwise elimination. Likelihood ratio criteria were used with 0.05 to enter and 0.10 for stepwise removal from the models. The relative risk associated with each variable was modeled by $\text{Exp}(B)$ in Cox Regression, for which the 95% confidence interval (C.I.) was estimated.

3. Results

Some usable data were obtained for 459 participants. The women's ages at intake ranged from 50 to 81 years with a mean of 67.6 (SD 7.9) years. Of the 444 participants for whom follow-up vital status could be estimated, 86 deaths were recorded over a mean observation of 10.5 (SD 2.8) years before censoring. Thus, the utilized N for each analysis was never greater than 444 (96.7% of all participants) and was often reduced to about 350 (76.3%) in analyses which required adequate urine collections and technically satisfactory oximetry recordings.

Interrelationships among sleep variables

Table 1 displays the main measures of sleep duration. The initial WHI-questionnaire-reported hours of sleep (questionnaire choices of "5 or less," "6 hours," "7 hours," "8 hours," "9 hours," or "10 or more hours") and the responses to the same question on the ancillary sleep questionnaire obtained months later were both close to 6.75 hours and were moderately well correlated ($r = 0.60$). The mean of next-morning sleep diary estimates of total sleep was only a few minutes longer, but the diaries were better correlated to the sleep questionnaire estimates of total sleep time completed the same week than to the prior WHI questionnaire responses. Actigraphic in-bed sleep times of 6 hours (mean 359.6 min, median 363.6 min) were substantially less than the sleep diary estimates recorded for the same nights and were not as well correlated with the subjective estimates of sleep duration as the subjective estimates were correlated with each other. Actigraphic time-in-bed (TIB) was greater than questionnaire-estimated sleep times, and actigraphic TIB was better correlated with actigraphic sleep than with subjective sleep. Actigraph-estimated out-of-bed sleep durations (nap times) averaged 0.53 hr and were only very weakly (negatively) correlated with any measure of in-bed sleep.

The inter-correlations of various measures of sleep duration are given in Table 2. The prospectively-defined sleep risk factor was ASDM-30, the absolute value of actigraphic sleep duration minus 333.6 min. ASDM-30 was somewhat correlated with actigraphic sleep duration ($r = 0.40$, $P < 0.001$), and sleep efficiency was also correlated with sleep duration ($r = 0.47$, $P < 0.001$). Actigraphic time-in-bed (TIB) correlated $r = 0.70$ ($P < 0.001$) with actigraphic sleep duration, and ASDM-30 correlated $r = 0.52$ ($P < 0.001$) with the analogous deviation from 30 min less than the median TIB (TIBM-30). Body mass index (mean BMI = $27.0 \pm \text{SD } 6.0$) was negatively correlated with actigraphic total sleep time ($r = -0.17$, $P = 0.001$) but was not significantly correlated with ASDM-30 or with sleep diary sleep time ($P > 0.05$). Reflecting the sleep disturbances of sleep apnea, the oxygen desaturation index ODI4 (mean = 9.7/hr. $\pm \text{SD } 9.5$) was negatively correlated with actigraphic sleep time ($r = -0.27$, $P < 0.001$) and with sleep efficiency ($r = -0.31$, $P < 0.001$) but was not significantly correlated with ASDM-30 or with sleep diary total sleep time. Reflecting obesity as a risk factor for sleep apnea, the ODI4 and BMI were positively correlated ($r = 0.27$, $P < 0.001$). A Bland-Altman plot (not shown) indicated no trend for the difference between sleep diary and actigraphic total sleep time to vary with their mean ($r = 0.07$, NS), but the disparity increased with increasing $\log_{10}\text{ODI4}$ ($r = 0.19$, $P = 0.001$). This was because actigraphic sleep time was reduced when $\log_{10}\text{ODI4}$ was higher (more actigraphic sleep disturbance from sleep apnea).

Fully controlled multivariate models

The development of the multivariate models is described in supplementary tables 1–4 in Appendix 2 (please see supplementary material). Table 3 below lists Model 4, combining ASDM-30 (the prospectively-defined actigraphic sleep duration risk factor), medical risk factors, and potential mediators or moderators of sleep effects. When major depression and aMT6s-sleep phase were included in Model 4, ASDM-30 and the medical risk factors were retained, confirming the prospective hypothesis. The aMT6s-sleep phase angle and major depression were also significant risk factors in this final model, but they did not reduce the significance of ASDM-30, despite the reduction in available N, since this model removed participants for whom adequate aMT6s data were not available.

To visualize the durations of long and short actigraphic sleep associated with elevated risk, Figure 1 and Table 4 present a variation of model 4 where actigraphic sleep duration was categorized into 8 ranges. There were far more participants with actigraphic sleep >390 min than participants with sleep <300 min. A roughly U-shaped distribution of risk ratios was seen, with the minimum risk ratio locations statistically indistinguishable between 300–330, 330–360, and 360–390 min of actigraphic sleep. From the same model, Table 4 presents the covariate-adjusted terminal survival fractions at the end of follow-up for each actigraphic sleep deviation category, estimated from the Cox Regression survival curves. These were survival estimates adjusted for multiple risk factors. Though the risk ratio and survival estimates were unstable when the participants were subdivided into 8 sleep duration categories, when retrospectively divided into 3 categories (Table 4, right side), it became clear that both short sleep ($P = <0.001$) and long sleep ($P = 0.005$) were associated with significantly reduced survival as compared to a reference of 300–390 min. Figure 2 illustrates the marked differences in survival of those with actigraphic sleep of 300–390 min from those with shorter or longer sleep durations.

In this sample, biased towards those with long or short sleep, participants with actigraphic sleep durations <300 min or >390 min were 42.4% of the sample, but they experienced 50 of the 86 deaths observed.

4. Conclusions

These results confirmed our prospective hypothesis that objective actigraphic sleep would be associated with a U-shaped mortality risk, with both short sleep and long sleep associated with excess mortality. The mortality ratios associated with actigraphic short and long sleep were surprisingly large, as much as 2–4 fold. Moreover, in this sample, objectively measured sleep durations predicted significant mortality risk, whereas subjectively reported sleep durations did not, implying that the risk was greater when associated with objective sleep duration as compared to self-reported duration. We are aware that a WHI writing committee is analyzing the mortality predicted by questionnaire sleep duration for the entire national WHI Observational Study. With close to 100,000 participants, subjective self-reported long and short sleep may also be found to be significant mortality risk factors in WHI women, but the hazards associated with questionnaire-measured sleep durations may prove weaker than those associated with objectively-measured actigraphic sleep durations.

The current analyses are consistent with our prospective hypothesis that the minimal mortality risk might be associated with actigraphic sleep durations somewhat shorter than the median of 363.6 min. The categories of 300–330 min, 330–360 min and 360–390 min were not statistically distinguishable for locating the minimal risk. It is not surprising that when the boundaries for short sleep and long sleep were optimized retrospectively (as in Fig. 1 and 2 and Table 4), the statistical significance of the findings appeared even greater than with our prospective definition of ASDM-30. The difference in adjusted survival between

the 90% for the 300–390 min group and 61% for the short sleep group was remarkable. The estimated mortality for those sleeping <300 min was almost 4 times as great as for the group with minimal risk ratios. Considering that 50 of the 86 deaths in the total sample were in the long and short sleep groups (42.4% of a total sample in which long and short sleep groups were over-represented), one could crudely estimate that 16% of sample deaths would not have occurred were the mortality rate the same in long and short sleep groups as in the intermediate optimal group. After adjusting for age and other risk factors, the adjusted survival curves computed for a portion of the sample (Table 4) suggested that as many as 30% of all sample deaths would not have occurred were the survival rate in the long and short groups as high as that of the intermediate group. Replications and larger samples will be needed to clarify the risks associated with objective sleep durations. The current data suggest that this risk is much higher than previously expected.

Whether mortality appeared elevated more among those with short sleep or with long sleep depended entirely upon what arbitrary boundaries were selected for short and long sleep (data not shown.) With the retrospective categories illustrated on the right side of Table 4, the increase in mortality risk associated with sleep >390 min was just over half as great as the increased mortality among those with sleep <300 min, but there were more than twice as many participants with long sleep as with short sleep. Using those retrospective boundaries would suggest that short and long sleep were associated with about equal numbers of excess deaths.

It may seem surprising to regard objective sleep exceeding 6.5 hours (390 min) as long sleep. However, our average values for actigraphic and subjective sleep duration were quite similar to those of the CARDIA study [7]. Validation of our actigraphic scoring indicated that our actigraphic methodology often over-estimates the amount of wake within sleep [13]. With polysomnographic recording, a somewhat longer recorded sleep length might be indicated as the threshold where excess mortality is associated with longer sleep. On the other hand, since the minimal reported sleep durations in the largest recent population samples have been about 6.5–7.5 hours, and we found that actigraphic sleep durations were as much as 52 min shorter than reported sleep durations, an upper boundary of 6.5 hours for optimal objective sleep would not be inconsistent with the recent population studies.

These results are consistent with the observation of Dew et al. that low sleep efficiency was associated with excess mortality [9]. Since reduced sleep efficiency was associated both with our short sleep category and with long time-in-bed, which were mortality risk factors, it was impossible to distinguish in our data whether sleep efficiency, short sleep, or excessive time-in-bed might be the process most closely associated with excess mortality. Moreover, since the relationship of TIB to mortality risk was U-shaped in parallel to that for sleep duration, it was impossible to distinguish in these data whether TIB or time actually asleep was more associated with mortality hazard.

We were not surprised that the oxygen desaturations index (ODI4 or $\log_{10}$ ODI4), an indicator of the respiratory disturbance index, did not prove to be a significant mortality risk factor in our sample of modest size. In an aging sample of similar size from the same community [14], we had previously found that the respiratory disturbance index was not significantly related to mortality after control for comorbidities. More recently, the Sleep Heart Health Study found that sleep apnea did not predict excess mortality in women [15]. These WHI data do add to the skepticism that sleep apnea confers any important mortality risk for older women.

We were quite interested in the outcome of our urinary aMT6s assays. Many observers have speculated that low total melatonin production contributes to mortality risk. This study

found no significant relationship between total 24 hr melatonin excretion and survival, but the trend was toward higher mortality when melatonin excretion was higher. The estimated risk ratio [Exp(B) = 1.625 (95% C.I. 0.803–3.289)] excluded any large risk associated with low melatonin.

An unexpected risk was associated with the circadian timing of aMT6s excretion. In previous analyses of this same WHI data set, we have found that a delayed offset of aMT6s excretion was associated with current major depression [11]. Somewhat similar mood findings with blood melatonin concentrations have been reported among patients with seasonal affective disorder [16] and with patients with major depression [17;18], but we are not aware that the phase timing of melatonin production has previously been found to be a mortality predictor. In these data, the phase of melatonin excretion as referenced to clock time was associated with mortality hazard, but the phase or the offset of the excretion peak may be a stronger predictor when referenced to sleep timing. Specifically, the melatonin excretion offset was more strongly associated with relative risk than the excretion onset earlier in the night. In model 4, the risk associated with aMT6s-sleep phase was controlled for comorbidity with major depression, with which it might otherwise have been confounded. One possibility is that the aMT6s-sleep phase delay is a harbinger of the circadian sleep disruption observed in Alzheimer's disease [19]. Another possibility is that aMT6s timing and offset are markers of a photoperiodic endocrine disturbance. Further replication of these aMT6s findings is needed.

In summary, this study was able to confirm the association of short sleep and long sleep with mortality hazard using objective recording. Sleep efficiency and time-in-bed were inter-related and somewhat overlapping mortality risk factors. An unexpected measure, melatonin excretion timing, was a risk factor. Control for depression, sleep disturbed breathing, and several other risk factors could not explain these associations. Those with short or long sleep represented 42.4% of the sample and had 2 to 4 times greater mortality, corrected for multiple risk factors, compared to those with optimal sleep durations. These data with objective recording indicate an even larger risk associated with long and short sleep than that previously suggested by self-reported sleep durations and underline the importance of identifying the causal mechanisms and any potential preventive options. A clinical implication may be to reassure those who sleep only five or six hours if they feel their function is unimpaired.

Deviations in objective sleep duration may pose a more important public health risk than previously understood, but, as yet, we have no proven methods of prevention or treatment. Since sleeping pill use was associated with increased mortality risk in epidemiologic studies of sleep duration [3], and since the increases in objective sleep time produced by modern sleeping pills are almost negligible [20], they offer no promise for the challenge of short sleep. Cognitive-behavioral treatment of insomnia, though more effective for the subjective complaint of insomnia, may also provide at best only modest increases in sleep duration. Only avoidance of voluntary or socially-imposed sleep restriction appears promising for the person with sleep short enough to be associated with excessive risk. For people with long sleep, early studies are examining the feasibility of voluntary sleep restriction, but much more research is needed to determine if restricting long sleep would control the associated excess mortality [21]. Were it shown that restricting long sleep would reduce mortality, that benefit would have to be weighed against possible increases in accidents, impairments of performance, or problems in metabolism which might be induced by sleep restriction.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Supported by NIH HL55983, HL071123, and NO1-WH-3-2120.

References

1. Hammond EC. Some preliminary findings on physical complaints from a prospective study of 1,064,004 men and women. *Am J Public Health* 1964;54:11–24.
2. Kripke DF, Simons RN, Garfinkel L, Hammond EC. Short and long sleep and sleeping pills: Is increased mortality associated? *Arch Gen Psychiatry* 1979;36:103–16. [PubMed: 760693]
3. Kripke DF, Garfinkel L, Wingard DL, Klauber MR, Marler MR. Mortality associated with sleep duration and insomnia. *Arch Gen Psychiatry* 2002;59:131–6. [PubMed: 11825133]
4. Tamakoshi A, Ohno Y. JACC Study Group. Self-reported sleep duration as a predictor of all-cause mortality: Results from the JACC Study, Japan. *Sleep* 2004;27:51–4. [PubMed: 14998237]
5. Gallicchio L, Kalesan B. Sleep duration and mortality: a systematic review and meta-analysis. *J Sleep Res* 2009 Jun;18(2):148–58. [PubMed: 19645960]
6. van den Berg JF, Van Rooij FJ, Vos H, Tulen JH, Hofman A, Miedema HM, Neven AK, Tiemeier H. Disagreement between subjective and actigraphic measures of sleep duration in a population-based study of elderly persons. *J Sleep Res* 2008 Sep;17(3):295–302. [PubMed: 18321246]
7. Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? *Epidemiology* 2008 Nov;19(6):838–45. [PubMed: 18854708]
8. Patel SR. Invited Commentary: Understanding the Role of Sleep. *Am J Epidemiol.* 2009 Aug 3;
9. Dew MA, Hoch CC, Buysse DJ, Monk T, Begley AE, Houck PR, Hall M, Kupfer DJ, Reynolds CFI. Healthy older adults' sleep predicts all-cause mortality at 4 to 19 years of followup. *Psychosom Med* 2003;65:63–73. [PubMed: 12554816]
10. First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. Structured Clinical Interview for DSM-IV Axis I Disorders - Non-patient Edition (SCID-I/NP, Version 2.0). New York City: New York State Psychiatric Institute; 1996.
11. Tuunainen A, Kripke DF, Elliott JA, Assmus JD, Rex KM, Klauber MR, Langer RD. Depression and endogenous melatonin in postmenopausal women. *J Affect Dis* 2002;69:149–58. [PubMed: 12103461]
12. Kripke, DF.; Marler, MR.; Calle, EE. Epidemiologic Health Impact of Sleep. In: Kushida, C., editor. *Sleep Deprivation: Clinical Issues, Pharmacology, and Sleep Loss Effects*. New York: Marcel Dekker; 2005. p. 195–209.
13. Jean-Louis G, Kripke DF, Cole RJ, Assmus JD, Langer RD. Sleep detection with an accelerometer actigraph: comparisons with polysomnography. *Physiol Behav* 2001;72:21–8. [PubMed: 11239977]
14. Ancoli-Israel S, Kripke DF, Klauber MR, Fell R, Stepnowsky C, Estline E, Khazeni N, Chinn A. Morbidity, mortality and sleep disordered breathing in community dwelling elderly. *Sleep* 1996;19(4):277–82. [PubMed: 8776783]
15. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, Rapoport DM, Redline S, Resnick HE, Robbins JA, Shahar E, Unruh ML, Samet JM. Sleep-disordered breathing and mortality: a prospective cohort study. *PLoS Med* 2009 Aug;6(8):e1000132. [PubMed: 19688045]
16. Wehr TA, Duncan WC, Sher L, Aeschbach D, Schwartz PJ, Turner EH, Postolache TT, Rosenthal NE. A circadian signal of change of season in patients with seasonal affective disorder. *Arch Gen Psychiatry* 2001;58(12):1108–14. [PubMed: 11735838]
17. Sekula LK, Lucke JF, Heist K, Czambel K, Rubin RT. Neuroendocrine aspects of primary endogenous depression XV: mathematical modeling of nocturnal melatonin secretion in major depressives and normal controls. *Psychiatry Res* 1997;69:143–53. [PubMed: 9109182]
18. Emens J, Lewy A, Kinzie JM, Arntz D, Rough J. Circadian misalignment in major depressive disorder. *Psychiatry Res* 2009 Jun 11;168:259–61. [PubMed: 19524304]

19. Oosterman JM, van Someren EJ, Vogels RL, Van HB, Scherder EJ. Fragmentation of the rest-activity rhythm correlates with age-related cognitive deficits. *J Sleep Res* 2009 Mar;18(1):129–35. [PubMed: 19250179]
20. Buscemi N, Vandermeer B, Friesen C, Bialy L, Tubman M, Ospina M, Klassen TP, Witmans M. The efficacy and safety of drug treatments for chronic insomnia in adults: A meta-analysis of RCTs. *J Gen Intern Med* 2007 Jul 10;22:1335–50. [PubMed: 17619935]
21. Youngstedt SD, Kline CE, Zielinski MR, Kripke DF, Devlin TM, Bogan RK, Wilcox S, Hardin JW. Tolerance of chronic 90-minute time-in-bed restriction in older long sleepers. *Sleep* 2009;32(11):1467–79. [PubMed: 19928386]

Figure 1.

Above: the distribution of the durations of actigraphic sleep for this sample enriched with those reporting long or short sleep. **Below:** the relative risk ratios (with 95% confidence bars) are shown for each actigraphic sleep duration, using 360–390 min. as the reference (black.) The minimum mortality was observed between 300–390 min. (5–6.5 hours), but statistical variability did not permit more precise localization of the minimum.

Figure 2.

The estimated survival curves (adjusted for covariates in Model 4) are shown with the standard errors (SE). Those with actigraphic sleep durations shorter than 300 min. or longer than 390 min. had markedly reduced survival.

TABLE 1

Different measures of participant's sleep.

SLEEP MEASURE	N	Mean	SD	Minimum	Maximum
WHI questionnaire: "About how many hours of sleep did you get on a typical night during the past 4 weeks?"	443	6.79 hr	1.17	5	10
Sleep study questionnaire, "About how many hours of sleep did you get on a typical night during the past 4 weeks?"	431	6.72 hr	0.99	5	9
Mean of week's sleep diary TST: "About how long did you sleep last night?"	435	6.88 hr	0.98	3.5	9.92
Actigraphic in-bed sleep	434	5.99 hr	0.91	2.75	8.37
Actigraphic out-of-bed sleep	434	0.53 hr	0.57	0.0	3.48
Actigraphic time in bed	434	7.88 hr	0.99	3.82	11.66
Actigraphic sleep latency	434	0.48 hr	0.35	0.08	2.63
Actigraphic sleep efficiency (sleep/time-in-bed)	434	76%	8%	45%	94%
Actigraphic sleep efficiency sleep/(onset-to-offset time)	434	80%	7%	51%	97%

TABLE 2

Pearson correlations examining inter-relationships of sleep measures.

SLEEP MEASURE	WHI Quest.	Sleep Quest.	Sleep Diary	Act. time in bed	Actigraphic sleep in-bed
Sleep Questionnaire	.60**				
Sleep Diary	.59**	.84**			
Actigraphic time in bed	.35**	.47**	.53**		
Actigraphic sleep in-bed	.37**	.48**	.53**	.70**	
Actigraph sleep out-of-bed	−0.04/NS	−0.11**	−0.16**	−.016**	−0.09*

** P<0.01 one-tailed.
* P<0.05 one-tailed.
NS Not Significant.

Table 3

Cox regression Model 4: Mortality hazard of ASDM-30, fully controlled for age and medical risk factors, plus mediators/moderators.

RISK FACTOR	P	Exp(B)	95.0% CI for Exp(B)
systolic BP, reference ≤ 120	0.012		
120–140	0.013	2.349	1.196–4.616
≥ 140	0.011	2.746	1.261–5.980
diabetes	0.049	2.508	1.006–6.255
myocardial infarct	0.001	4.099	1.745–9.630
cancer ever	0.008	2.152	1.219–3.798
ASDM-30	0.035	1.008	1.001–1.015
aMT6s-sleep phase	0.001	0.812	0.715–0.923
Lifetime MDD, reference: never	0.011		
subthreshold	NS	1.160	0.235–5.712
Hx, not at intake	0.035	0.373	0.149–0.933
MDD at intake	0.025	3.110	1.153–8.391

ASDM-30 (yellow): actigraphic sleep deviation from the median minus 30 minutes. MDD: major depressive disorder. NS: not significant. Exp(B) is the estimated risk ratio. Categorical risk factors are shaded blue. N = 349.

Estimated survival at the end of follow-up versus Actigraphic Sleep minutes: From Cox regression model estimated survival curves

Table 4

Sleep min.	N	Survival	95% C.I.	Survival*	95% C.I.*
<270	19	0.86	0.80–0.91		
270–300	24	0.54	0.40–0.68	0.61	0.54–0.69
300–330	48	0.91	0.87–0.95		
330–360	72	0.90	0.87–0.94	0.90	0.85–0.94
360–390	89	0.91	0.88–0.95		
390–420	55	0.78	0.70–0.86		
420–450	31	0.58	0.45–0.71	0.78	0.73–0.85
>450	15	0.89	0.84–0.93		
MEAN	349	0.86	0.81–0.91	0.85	0.80–0.90

The left hand columns provide data for subjects divided by actigraphic sleep duration into 8 categories. Survival with its 95% confidence interval was the estimated fraction surviving at the end of follow-up. Besides 8 sleep duration categories, covariates retained in the left-hand model were age squared, systolic blood pressure, major depression, diabetes, history of myocardial infarction, and history of cancer, sleep efficiency, and aMT6s-sleep phase angle. In the right-hand columns model, covariates retained were age squared, systolic blood pressure, major depression, diabetes, history of myocardial infarction, and history of cancer and aMT6s-sleep phase angle. See also Fig. 1.

* The two columns on the right represent a similar model with sleep duration divided into 3 categories, as indicated. See also Fig. 2. The slight discrepancies in the mean values for the left and right hand models resulted from slightly different numbers of subjects entering into the models.