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ORIGINAL ARTICLE

Actigraphy-derived sleep health profiles and mortality in older men and women

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Abstract

Study Objectives: To identify actigraphy sleep health profiles in older men (Osteoporotic Fractures in Men Study; N = 2640) and women (Study of Osteoporotic Fractures; N = 2430), and to determine whether profile predicts mortality.

Methods: We applied a novel and flexible clustering approach (Multiple Coalesced Generalized Hyperbolic mixture modeling) to identify sleep health profiles based on actigraphy midpoint timing, midpoint variability, sleep interval length, maintenance, and napping/inactivity. Adjusted Cox models were used to determine whether profile predicts time to all-cause mortality.

Results: We identified similar profiles in men and women: High Sleep Propensity [HSP] (20% of women; 39% of men; high napping and high maintenance); Adequate Sleep [AS] (74% of women; 31% of men; typical actigraphy levels); and Inadequate Sleep [IS] (6% of women; 30% of men; low maintenance and late/variable midpoint). In women, IS was associated with increased mortality risk (Hazard Ratio [HR] = 1.59 for IS vs. AS; 1.75 for IS vs. HSP). In men, AS and IS were associated with increased mortality risk (1.19 for IS vs. HSP; 1.22 for AS vs. HSP).

Conclusions: These findings suggest several considerations for sleep-related interventions in older adults. Low maintenance with late/variable midpoint is associated with increased mortality risk and may constitute a specific target for sleep health interventions. High napping/inactivity co-occurs with high sleep maintenance in some older adults. Although high napping/inactivity is typically considered a risk factor for deleterious health outcomes, our findings suggest that it may not increase risk when it occurs in combination with high sleep maintenance.

Statement of Significance

We used a flexible clustering approach to identify three actigraphy sleep health profiles in older men and women: High Sleep Propensity (high maintenance and high napping/inactivity), Adequate Sleep (typical levels), and Inadequate Sleep (late/variable midpoint, low maintenance). Inadequate Sleep was associated with increased mortality risk. Sleep health interventions may consider targeting the combination of late/variable midpoint and low maintenance (Inadequate Sleep) in older adults; such efforts can improve sleep and may also have important health benefits. High Sleep Propensity was associated with decreased mortality risk. Although high napping/inactivity is typically considered a risk factor for deleterious health outcomes, these findings suggest that it may not be associated with increased risk when it occurs in the context of high maintenance.

Key words: actigraphy; clustering; sleep health; mixture model; mortality; older adult; skewed data

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Introduction

Habitual sleep health characteristics can be captured across multiple established domains, including regularity, alertness/sleepiness, timing, efficiency, and duration [1, 2]. This "multidimensional sleep health perspective" emphasizes that characteristics across these domains occur simultaneously in context of one another, regardless of the presence or absence of a sleep disorder [2]. An individual can have "poor" levels on one sleep characteristic and simultaneously "good" levels on another, and identifying common within-subject combinations of sleep health characteristics (i.e. sleep health profiles) can yield novel insights. Determining whether these profiles subsequently predict relevant health outcomes – such as mortality in older adults – can motivate targeted treatments and interventions.

We recently showed that actigraphy characteristics map onto the established sleep health domains in samples of older adults [1]. Actigraphy uses wrist-worn accelerometry to continuously monitor 24-hour rest–activity patterns, which correlate with polysomnographically-defined sleep–wake states and sleep patterns. In older adults, individual actigraphy features predict adverse health outcomes including mortality, with the most consistent effects observed from poor sleep efficiency (or conversely, high sleep fragmentation), irregularity of sleep rhythms and timing, and higher napping/inactivity [3–6]. The predictive nature of individual actigraphy characteristics in older adults – combined with the unique insights that the sleep health perspective can provide – offer promise that identification of actigraphy sleep health profiles could suggest innovative ways in which sleep-related treatments may be tailored to enhance effectiveness.

Some prior studies have used clustering-related methods to identify sleep profiles in older adults. For example, clustering was applied to actigraphy data in children and their parents to suggest sleep profiles [7]. However, given developmental changes in sleep health across the lifespan [8], these profiles are not necessarily relevant for older adults. Latent classes of activity rhythms in older men have also been identified [9], but these models did not assess core domains of sleep health. We also recently used latent class analysis to identify self-report sleep health profiles in large cohorts of older men and women [10], but retrospective self-report sleep measures do not necessarily track with objective measures of sleep, such as actigraphy [11]. Thus, we do not yet know which actigraphy sleep health profiles are common in older adults, and whether these profiles might relate to key health outcomes such as mortality.

In this secondary data analysis, our objective is to use clustering to reveal actigraphy sleep health profiles in older men and women, considering specific measures that empirically represent five established actigraphy sleep health domains in these cohorts: Alertness/Sleepiness, Efficiency, Duration, Timing and Regularity [1]. Because many actigraphy measures follow non-normal distributions, even in highly homogenous samples, mixture model approaches allowing for asymmetric cluster shapes are advantageous for actigraphy data [12]. After identifying profiles using novel and flexible mixture models in men and women separately [13], we characterize them and determine whether the identified profiles are associated with time to mortality – an outcome that is unequivocally important for patients and society.

Methods

Sample

Data are from the Study of Osteoporotic Fractures (SOF) and Osteoporotic Fractures in Men (MrOS) Sleep studies, multi-site studies of older women and men that were established in 1997 and 2000, respectively. The SOF study was designed to determine risk factors for osteoporotic fractures in community-dwelling older women aged ≥ 65 [14, 15]. The MrOS Sleep study was a sleep-focused study within the larger Osteoporotic Fractures in Men (MrOS) Study [16, 17], originally designed to assess risk factors for osteoporotic fractures in community-dwelling older men aged ≥ 65. Participants in both studies were identified through a variety of population-based listings and invited to enroll through mass mailings. In year 3 of MrOS and year 16 of SOF, participants provided written informed consent to participate in longitudinal studies of sleep.

The SOF and MrOS studies have similarities that facilitate cohort comparisons, including overlapping scientific teams, study procedures, and measures. However, there are two prominent differences in study design. First, because of the different timing of the sleep questionnaires within the course of the parent cohorts, SOF women are generally older than MrOS men at the time of the sleep study. Second, because of the addition of an African American ancillary study, SOF women are more likely to be African American than MrOS men. In contrast, MrOS recruited more participants who identified as races other than White or Black. However, the percentages of non-White individuals in both cohorts are low (Table 1).

Primary analytic samples. In primary analyses, the MrOS and SOF samples are analyzed separately. For consistency with our prior work in these samples [10], we include participants in the analytic samples if they are Black or White and have complete self-reported sleep, sociodemographic and clinical characteristics, and follow-up for all-cause mortality. We also require participants to have valid actigraphy measures, defined as at least three valid "in-bed" and three valid "out-of-bed" intervals. These criteria result in $N = 2640$ men (MrOS) and $N = 2430$ women (SOF) for our two primary analytic samples. See Supplement Section 1 for detailed sample derivations.

Secondary Sample. Because of the differences between MrOS and SOF, we previously used propensity score matching to develop a sample of 1722 men and women who are comparable on selected sociodemographic and non-sleep clinical characteristics (no sleep characteristics were used for matching) [10]. Full details of the development of the matched sample are provided elsewhere [10] with additional details provided in the Supplement Section 1. $N = 1418$ (658 women and 760 men) from this matched sample also have valid actigraphy. In the present analysis, we use the matched sample as a secondary sample to further evaluate reproducibility of the profiles identified in the MrOS and SOF samples.

Measures

Because of the overlapping investigative and data management teams, most measures required for analysis could be easily harmonized across the MrOS and SOF cohorts. This harmonization

Table 1. Cross sectional characteristics in women and men

	Women (*N* = 2430)	Men (*N* = 2640)
Sociodemographic, %(*N*)		
Age	83 (81, 86)	76 (72, 80)
Race (Black vs. White)	8.11 (197)	3.86 (102)
Marital status		
Married	27.37 (665)	84.28 (2225)
Widowed	61.44 (1493)	7.84 (207)
Other	11.19 (272)	7.88 (208)
Education		
<High school degree	13.21 (321)	5.19 (137)
High school degree	67.33 (1636)	38.9 (1027)
≥College degree	19.47 (473)	55.91 (1476)
Health-related measures, %(*N*) or median (quartile 1, quartile 3)		
Past or current smoker	35.31 (858)	60.72 (1603)
Any alcohol use	42.22 (1026)	66.21 (1748)
Body mass index		
Underweight or normal	35.8 (870)	29.55 (780)
Overweight	41.15 (1000)	49.92 (1318)
Obese	23.05 (560)	20.53 (542)
#Functional limitations (range 0–5)	1 (0, 2)	0 (0, 0)
Self-rated health (1 = excellent, 5 = poor)	2 (2, 2)	2 (1, 2)
Number of Rx. medications	4 (2, 6)	3 (2, 6)
Number of chronic conditions (range 0–9)	2 (1, 3)	1 (1, 2)
Goldberg anxiety scale (GAS)	0 (0, 1)	0 (0, 1)
Anxiety (GAS ≥ 5)	13.83 (336)	8.64 (228)
Geriatric depression scale (GDS)	2 (1, 3)	1 (0, 2)
Depression (GDS ≥ 6)	10.78 (262)	6.55 (173)
Cognition 23-Item modified Mini Mental State Exam (mMMSE)	25 (24, 26)	25 (24, 25)
Cognitive impairment (mMMSE ≤ 21)	4.86 (118)	4.51 (119)
Calories burned from walking	280 (112, 672)	–
Physical activity scale for the elderly (PASE)	–	141.27 (95.74, 186.14)
Self-report sleep and sleep disturbances %(*N*) or median (quartile 1, quartile 3)		
Hours napping per week	0 (0, 3.5)	0 (0, 2.5)
Epworth sleepiness scale	5 (3, 5)	6 (3, 8)
Medication with sleep effects	23.46 (570)	17.05 (450)
Difficulty staying asleep	63.99 (1555)	76.73 (2025)
Difficulty falling asleep	35.51 (863)	22.39 (591)
Frequent snoring	4.86 (118)	20.98 (554)
Ever stop breathing during sleep	2.39 (58)	14.96 (395)

process largely consisted of re-naming variables and, in some instances, recoding them to reflect identical categories. Unless otherwise noted, the measures are the same in the MrOS and SOF cohorts.

Actigraphy measures

Actigraphs are wrist-worn devices that capture and store accelerometry data occurring within pre-specified time windows (every 60 s in SOF and MrOS). Participants in SOF and MrOS were directed to wear a Sleepwatch-O actigraph (Ambulatory Monitoring, Inc, Ardsley, NY) on their non-dominant wrist for at least four consecutive 24-hour periods, although some participants had fewer days of valid data (e.g. if they removed the watch). These data were then downloaded and scored to estimate characteristics of the sleep/wake cycle. Actigraphy data were scored using Action W-2 software with Proportional Integration Mode and the University of California, San Diego scoring algorithm [18]. Details related to MrOS and SOF actigraphy methods were published previously [19–21]. In the SOF sample, there was a median of 5 (range of 3–13) nights of actigraphy. However, 98.6% of women had between 4 and 6 nights. In the MrOS sample, there was a median of 5 (range of 3–9) nights of actigraphy. However, 98.7% of men had between 4 and 7 nights of actigraphy.

We recently used factor analysis to show that actigraphy measures in MrOS and SOF reflect five underlying factors: [1] Timing, Regularity, Alertness/Sleepiness, Efficiency, and Duration. For the current study, we selected the actigraphy measure with the highest loading on each factor to be used for clustering. These five measures are: *Midpoint* (mean of the midpoint of onset and wake-up time), *Variability* (standard deviation [SD] of the midpoint), *Napping* (mean minutes of napping or inactivity per day, requiring a minimum of 5 consecutive minutes per bout), *Sleep Maintenance* (Nighttime Sleep Duration/Sleep Interval × 100), and *Sleep Interval* (mean time from sleep onset to wake-up), respectively. We also consider two additional actigraphy measures to assist with characterizing the profiles after they are identified: *Nighttime Sleep Duration* and *24-hour Sleep Duration* (i.e. Nighttime Sleep Duration + Napping).

Prospective outcomes

Our primary outcome is time to all-cause mortality, selected because it is a definitive outcome that is easily harmonized across

the two studies. All-cause mortality was adjudicated using death certificates. In MrOS and SOF, participants were contacted every 4–5 months during follow-up via postcard. Initial death information was ascertained through the return of a postcard by the participant's family or by direct contact by study staff if a postcard was not received. These deaths were then adjudicated through central examination of death certificates plus additional medical records when available.

Our secondary outcome is time to cardiovascular mortality. Cardiovascular mortality was determined by a MrOS or SOF physician adjudicator and was based on the underlying cause of death, i.e. the disease or injury that initiated the train of morbid events leading directly to death as determined by the primary cause of death listed on the death certificate, ICD-9 codes from hospital discharge summaries, and/or physician contact.

In MrOS, there is a median of 12.2 and a maximum of 14.9 years of follow-up, with 52.5% of participants with deaths from all causes (1386 deaths). Among these deaths, 404 are attributed primarily to cardiovascular disease. In SOF, there is a median of 6.7 and a maximum of 8.1 years of follow-up, with 31.7% of participants with deaths from all causes (771 deaths). Of the 2430 women, only 2233 have observed cardiovascular mortality data, with 254 deaths attributed primarily to cardiovascular disease.

Sociodemographic, health, and self-report sleep covariates

We used prior literature to identify sociodemographic factors, health behaviors, mental health symptoms, medications and physical health conditions, and additional self-report sleep characteristics that may be relevant for actigraphy sleep health and/or mortality. These are measured at the same time point as actigraphy.

Sociodemographic characteristics. Age, sex, college education (≥16 years vs. < 16 years), race (Black vs. White), and marital status (married, widowed, or other marital status).

Health behaviors. Smoking status (ever smoked vs. never smoked), alcohol use (drink any alcohol versus non-drinker), the Physical Activity Scale for the Elderly [22] (MrOS only), and the estimated number of calories burned per week from walking (SOF only).

Mental and cognitive health. Depression and anxiety symptoms are measured using the Geriatric Depression Scale [23] (GDS) and Goldberg Anxiety and Depression Scale [24, 25] (GAS). Clinically significant depression and anxiety symptoms are defined as GDS ≥ 6 and GAS ≥ 5, respectively. Cognition is measured using the modified Mini Mental State Exam (mMMSE; range 0–26), with a score ≤ 21 indicating clinically significant cognitive impairment.

Physical health. Total number of prescription medications per participant, body mass index (underweight/normal weight, overweight, obese), self-reported health status (1 = excellent, 2 = good, 3 = fair, 4 = poor, 5 = very poor), number of instrumental activities of daily living that could not be performed (range 0–5), and the number of chronic conditions (considering stroke, heart attack, angina, heart failure, high blood pressure, diabetes, chronic obstructive pulmonary disease, osteoporosis, and rheumatoid or osteoarthritis). Comorbid medical conditions were assessed by participant self-report, which is well-established in epidemiological studies but may reduce precision and increase variability compared to using method such as medical record review [26].

Self-report sleep. Daytime sleepiness, number of naps per week, frequent snoring, ever stopping breathing during sleep, difficulty falling asleep, difficulty staying asleep, and use of medications with recognized effects on sleep. The latter is defined as: (1) use of prescription or non-prescription sleep aids at least once in the past month; or (2) use of prescription sedative-hypnotics (benzodiazepines, benzodiazepine receptor agonists) or other benzodiazepines in the past two weeks; or (3) use of any tricyclic antidepressants, trazodone, mirtazapine, or nefazodone in the past two weeks.

Data analysis

Clustering to identify sleep health profiles

Clustering with actigraphy data presents a methodological challenge because many actigraphy measures follow skewed distributions [12] (see Supplement Section 2 for distributions). This skewness typically occurs a result of the underlying measurement process – for example, counting the number of minutes awake after onset or the number of minutes of napping during the day. When elliptical clusters are imposed upon such data (e.g. from standard clustering approaches such as k-means or multivariate normal mixture modeling), more clusters than necessary may be required to explain the skewness [12]. Therefore, clustering approaches that allow the clusters themselves to potentially be skewed and/or asymmetric, and which are more accommodating of outliers, are beneficial for actigraphy data. Mixture models based on the Multiple Coalesced Generalized Hyperbolic Distribution (MCGHD) provide this flexibility [13].

In the MrOS ($N = 2640$) and SOF ($N = 2430$) samples separately, we applied MCGHD mixture models to reveal clusters based on the five selected actigraphy variables. This was accomplished using the MixGHD package [27] in R, considering models with one through five clusters. To ensure stability in the clustering solution, we used multiple random initializations based on k-medoids and selected the initialization with the optimal log-likelihood. To determine the number of clusters that best represented the data, we examined plots of the Bayesian Information Criteria (BIC), Akaike Information Criteria (AIC), and Integrated Complete-data Likelihood (ICL) for models with one through five clusters. These criteria penalize the number of parameters differently, and as a group can help to guide the optimal number of clusters, with higher values indicating a better fit for the data. As recommended for this approach [13], we prioritized clustering solutions that created an "elbow" in the AIC and BIC and/or which preceded a drop in ICL. Secondarily, we applied these same methods to the matched sample ($N = 1418$), thereby allowing us to potentially replicate profile findings in a sample of both men and women who are similar with regards to several key sociodemographic and health measures.

Characterizations of the sleep health profiles

We characterized profiles based on actigraphy and cross-sectional characteristics. We computed effect sizes with

95% bootstrap confidence intervals to evaluate whether differences across profiles were clinically meaningful. Effect sizes for continuous or ordinal measures were computed using the non-parametric Standardized Median Absolute Difference (SMAD), computed as the difference in the medians divided by a robust pooled estimate of the standard deviation [28]. SMAD was selected over a more common Cohen's *d* because of our emphasis on robustness to skewed data. Effect sizes for categorical measures were computed using Cohen's *h*. Given the exploratory nature of these analyses, we only considered a difference to be meaningful if the effect size was at least medium (magnitude of SMAD or Cohen's $h \geq 0.50$) [29]. We use the expression "effect size" to denote the magnitude of difference between profiles. However, the use of this term does not infer causality.

Time to mortality

We examined whether profile predicted time to all-cause mortality (primary outcome) and cardiovascular mortality (secondary outcome) in men and women separately using fully adjusted Cox proportional hazards models. We also fit fully adjusted Cox models including the five clustering variables simultaneously in lieu of the cluster indicator. In these models the clustering variables were coded as categorical, with cut-offs based on tertiles to allow for potentially non-linear associations. All Cox models were adjusted for age, sex, race, education, alcohol use, smoking status, physical activity (walking for women, PASE for men), functional limitations, self-rated health, number of prescription medications, number of chronic conditions, anxiety symptoms, depression symptoms, cognition, napping, daytime sleepiness, sleep-related medication, difficulty staying/falling asleep, frequent snoring, and stopping breathing during sleep. Within samples and modeling strategies (i.e. men versus women; actigraphy profiles versus the set of five actigraphy variables), we used the Benjamini-Hochberg correction [30] for multiple comparisons when assessing statistical significance.

Results

Sample descriptions

Cross-sectional and actigraphy characteristics of the MrOS and SOF samples are provided in Tables 1 and 2. Relative to men, women were older, more likely to be widowed, and less likely to report ever smoking, alcohol use, or frequent snoring. Women had worse physical functioning, higher depressive symptoms, more chronic diseases, and lower education. Details of all effect sizes between women and men and characteristics of the secondary matched sample are provided in Supplement Section 3.

Actigraphy Profiles

Primary samples (MrOS and SOF)

After examining the AIC, BIC, and ICL, we determined that three profiles (i.e. clusters) provide the best model fit for women and men. See Supplemental Section 4 for plots displaying the AIC, BIC, and ICL. Table 2 summarizes the actigraphy characteristics by profile (median [quartile 1, quartile 3]) and highlights comparisons that have at least a moderate effect size. Supplement Section 5 provides additional effect size details. Figure 1 depicts median quantile rankings of each actigraphy clustering variable by profile, which provide a visualization of the relative central distributions of each profile. Based on these characterizations, actigraphy profiles in both men and women are named: "High Sleep Propensity", "Adequate Sleep", and "Inadequate Sleep".

High Sleep Propensity ***(HSP)***. In women (20%; *N* = 486) and men (39%, *N* = 1029), HSP is characterized by high maintenance (median 90% in women and men) and high napping/inactivity (median minutes per day of 119 in women and 71 in men); together these characteristics result in a long 24-hour sleep duration (median 08:43 in women and 08:05 in men). However, the nighttime sleep interval length is moderate (median 07:23 in women; 07:37 in men). Although HSP characterizations are similar in men and women, it is notable that napping/inactivity is almost 70% higher in women than that in men.

Adequate Sleep (AS). In women (74%, *N* = 1807) and men (31%, *N* = 826), AS is characterized by a longer nighttime sleep interval length (median 08:03 in women; 07:47 in men) coupled with typical maintenance (median 86% in women and 82% in men) and moderate midpoint variability (median 00:25 in women and men). Taken together, these characteristics result in a moderate 24-hour duration (median 07:37 in women and 07:14 in men). Despite these similarities, napping/inactivity and midpoint timing differ between men and women with this profile. Among women with AS, napping/inactivity is lower than the median (median 36 min/day in AS vs. 49 in all women) and midpoint timing is moderate (median 03:13 in AS vs. 03:14 in all women). Conversely, among men with AS, napping/inactivity is moderate (median 45 min in AS vs. 41 min in all men) and midpoint timing is earlier than the median (median 02:40 in AS vs. 03:00 in all men).

Inadequate Sleep (IS). In women (6%, *N* = 137) and men (30%, *N* = 785), IS is characterized by poor sleep health across several domains: later midpoint timing (median 04:27 in women; 03:12 in men), higher midpoint variability (median 01:12 in women; 00:36 in men), and low sleep maintenance (median 62% in women; 79% in men). Both men and women with the IS profile had a short sleep interval length (median 07:03 in women; 07:32 in men), although it was only meaningfully lower in the women. Taken together, these characteristics result in a short 24-hour sleep duration (median 05:37 in women; 06:31 in men) and short nighttime duration (04:36 in women; 06:02 in men). In women, IS has higher-than-average napping/inactivity (median 64 min/day); however, in men, IS has low napping/inactivity (median 17 min/day). The sleep health features for women with IS are much more extreme than those in men with IS.

Profile shapes. Figures 2 and 3 show contour plots for visualizing the estimated shapes of the profiles. For both men and women, the three profiles visually differ most on napping, variability, and maintenance. It is noteworthy that the profile shapes are asymmetric and skewed (i.e. non-elliptical); this feature underscores the importance of using MCGHD mixture models that allow for this flexibility. Had symmetric/elliptical shapes been observed, a normal mixture model may have been a more parsimonious model selection. In women, the IS profile distribution is notable for its large scale and minimal overlap with other

Table 2. Actigraphy characteristics in women and men, overall and by profile

Women (*N* = 2433)

	Full sample (*N* = 2430)	High sleep propensity (*N* = 486)	Adequate sleep (*N* = 1807)	Inadequate sleep (*N* = 137)	Effect size comparisons (|SMAD| ≥ 0.50)
Clustering characteristics					
Sleep midpoint (HH:MM)	03:14 (2:41, 3:52)	03:07 (2:34, 3:46)	03:13 (2:40, 3:47)	04:27 (3:55, 5:04)	IS > (HSP, AS)
Sleep maintenance	86.63 (80.46, 90.92)	90.21 (87.06, 92.77)	86.01 (80.31, 90.4)	62.28 (56, 73.73)	HSP > AS > IS
Sleep Interval (HH:MM)	07:53 (07:07, 08:36)	07:23 (06:40, 08:16)	08:03 (07:19, 08:41)	07:03 (06:05, 08:04)	AS > (HSP, IS)
SD of sleep midpoint (HH:MM)	00:26 (00:16, 00:41)	00:22 (00:14, 00:33)	00:25 (00:16, 00:39)	01:12 (00:54, 01:36)	IS > (HSP, AS)
Mean napping per day (minutes)	48.67 (22.33, 89.33)	118.80 (88.54, 163.5)	35.67 (16.5, 63.00)	63.67 (33.2, 113.60)	HSP > IS > AS
Additional characteristics					
24-Hour sleep duration	07:44 (06:54, 08:41)	08:43 (07:49, 09:52)	07:37 (06:53, 08:25)	05:37 (04:55, 07:00)	HSP > AS > IS
Nighttime sleep duration	06:51 (06:02, 07:33)	06:45 (06:04, 07:28)	06:57 (06:13, 07:38)	04:36 (03:46, 05:26)	(AS, HSP) > IS

Men (*N* = 2640)

	Full sample (*N* = 2640)	High sleep propensity (*N* = 1029)	Adequate sleep (*N* = 826)	Inadequate sleep (*N* = 785)	Effect size comparisons (|SMAD| ≥ 0.50)
Clustering characteristics					
Sleep midpoint (HH:MM)	03:00 (02:26, 03:36)	03:02 (02:34, 03:33)	02:40 (02:00, 03:24)	03:12 (02:38, 03:52)	IS > AS
Sleep maintenance	85.17 (77.94, 89.99)	89.73 (86.98, 92.23)	82.34 (75.64, 87.58)	78.50 (70.45, 84.06)	HSP > (AS, IS)
Sleep interval (HH:MM)	07:38 (06:58, 08:15)	07:37 (07:00, 08:10)	07:47 (07:10, 08:32)	07:32 (06:52, 08:07)	
SD of sleep midpoint (HH:MM)	00:29 (00:19, 00:42)	00:27 (00:18, 00:39)	00:25 (00:17, 00:36)	00:36 (00:23, 00:53)	IS > (HSP, AS)
Mean napping per day (minutes)	40.75 (19.00, 72.27)	70.75 (40.75, 111)	44.75 (27.5, 65.44)	16.75 (7.86, 28.8)	HSP > AS > IS
Additional characteristics					
24-Hour sleep duration	07:18 (06:29, 08:10)	08:05 (07:27, 08:58)	07:14 (06:31, 07:58)	06:21 (05:32, 06:57)	HSP > IS
Nighttime sleep duration	06:32 (05:46, 07:13)	06:53 (06:19, 07:25)	06:28 (05:36, 07:20)	06:02 (05:05, 06:41)	HSP > IS

Cells show the median (quantile 1, quantile 3). SMAD = Standard Median Absolute Difference, with values ≥0.50 noted as being clinically meaningful.

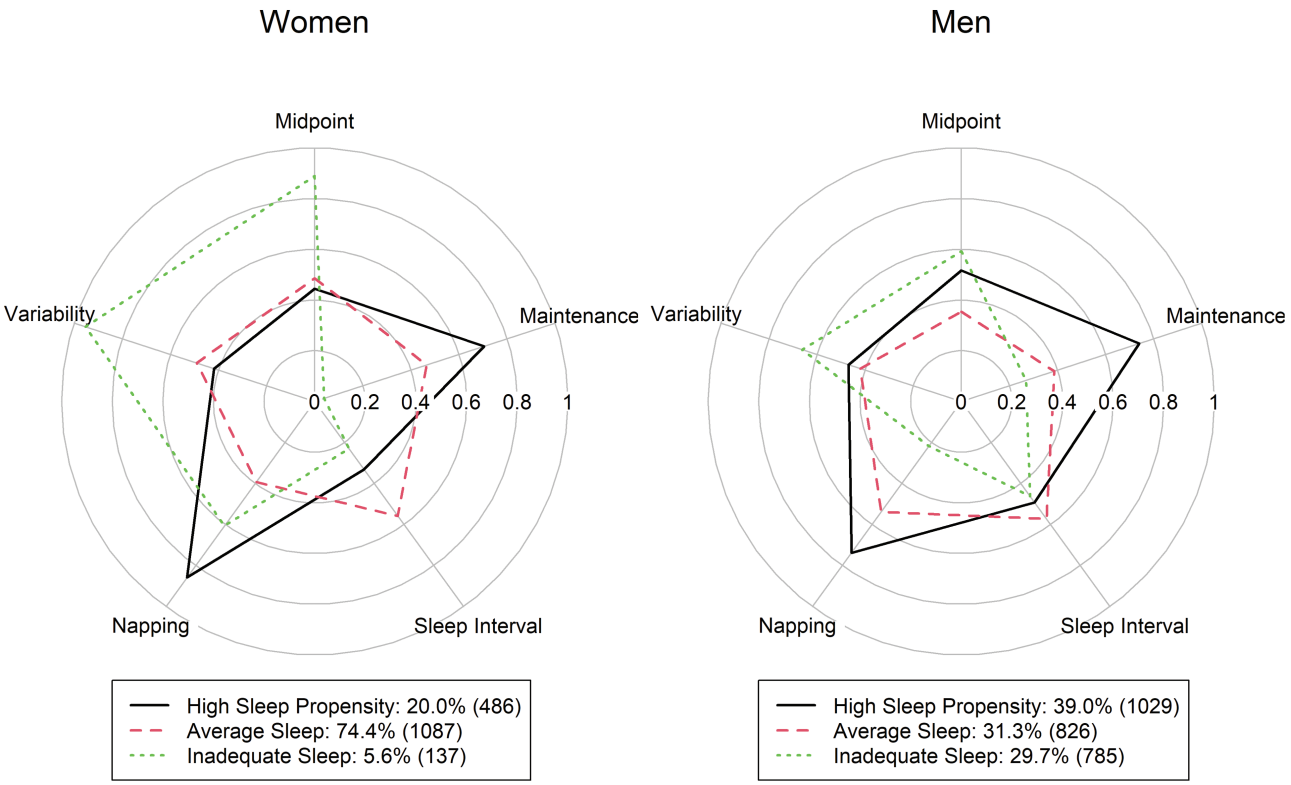

Figure 1. Radial plots showing the median quantile rankings for each sleep health characteristic by profile in women and men. The maximum value 1 reflects the highest ranked value in the sample, 0.50 reflects the median ranked value in the sample, and the minimum value 0 reflects the lowest ranked value in the sample.

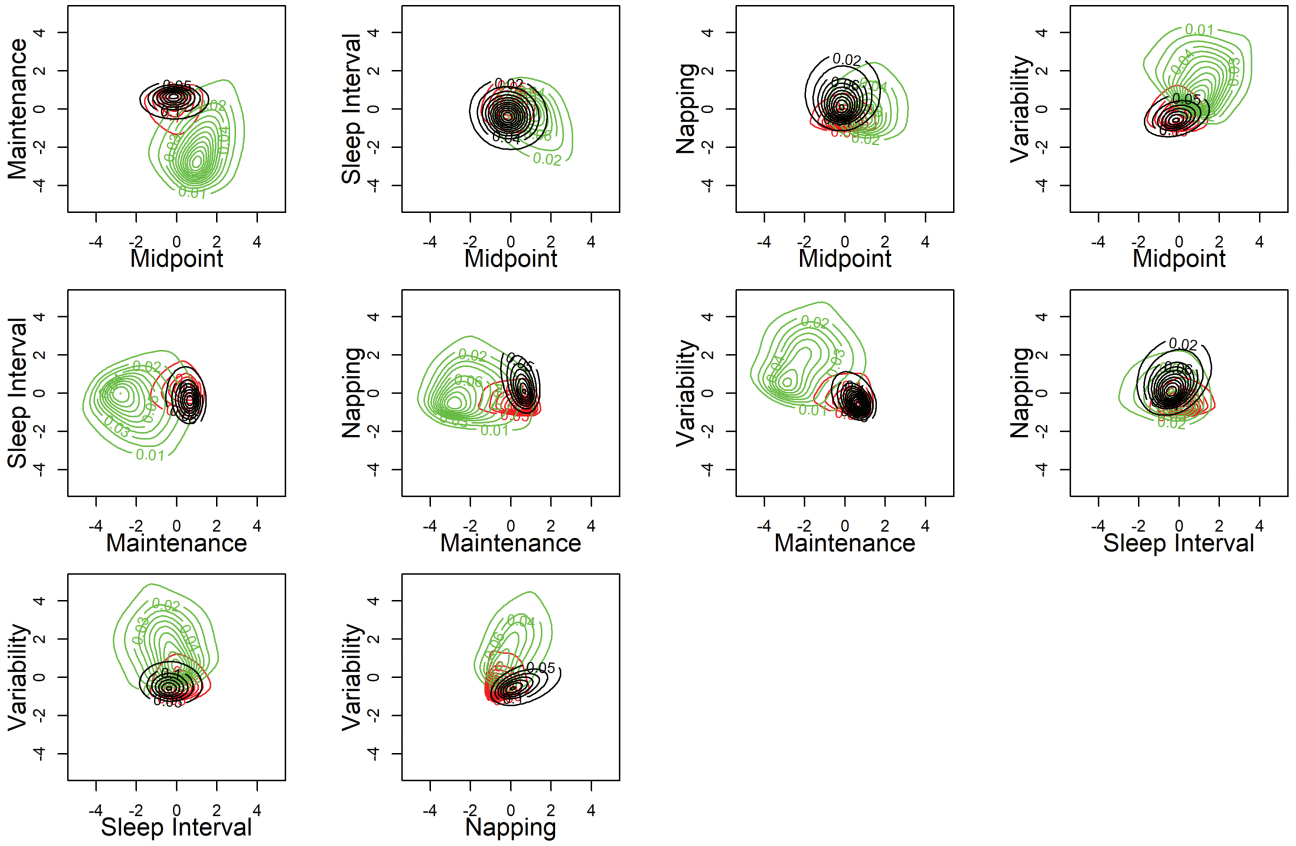

Figure 2. Contour plots of actigraphy profile distributions in women. Black = High Sleep Propensity; Red = Adequate Sleep; Green = Inadequate Sleep.

profiles. In men, the three profiles overlap more and have relatively similar scales.

Secondary matched sample

Information criteria indicate three profiles for the matched sample (Supplement Section 4). Based on profile summary characteristics (Supplement Section 6), these three profiles are consistent with the HSP, AS, and IS profiles observed in the full samples of women and men. HSP (N = 140, 10%) is characterized by high sleep maintenance (median 90%) and high napping/inactivity (median 131 min/day). AS (N = 853, 60%) is characterized by relatively moderate actigraphy characteristics. IS (N = 425, 30%) is characterized by low maintenance (median 80%), high variability (median 00:45), late midpoint (median 03:33), and low napping/inactivity (median 28 min). While this profile is consistent with findings from both men and women, the observation that the IS group has low napping/inactivity is most consistent with the findings in the men.

Supplement Section 6 graphically displays the profiles in the matched sample using radial and contour plots. Like the full samples of men and women, the contour plots show profiles that are asymmetric and which differ most on combinations of napping, variability, and maintenance. Like the full sample of men, the three profiles are similar in scale.

Cross-sectional profile characterizations

Cross-sectional characteristics of the actigraphy profiles in women and men are shown in Tables 3 and 4. We emphasize pairwise profile comparisons with at least moderate effect sizes (SMAD ≥ 0.50) to focus on clinically meaningful differences; however, all effect sizes with 95% bootstrap confidence intervals are provided Supplement Section 5.

Among women, the IS profile is generally associated with worse health characteristics, while the AS profile is associated with better health characteristics. All three profiles differ on functional limitations, such that IS has higher-than-average functional limitations (median of 2), HSP has a moderate number of functional limitations (median of 1), and AS has lower-than-average functional limitations (median of 0). IS has less walking activity than AS (median 112 kCals burned walking for IS versus 280 for AS). IS also has lower cognition relative to AS and HSP, with a median mMMSE of 24 for IS and medians of 25 for HSP and IS. Both IS and HSP have more depressive symptoms than AS with median GDS scores of 2 for HSP and IS versus 1 for AS. Finally, HSP and IS have the most self-reported hours of napping per day (median 1 h for HSP and IS vs. 0 h in AS); this is consistent with the actigraphy characterizations of HSP and IS having the most napping. Profiles in men did not differ meaningfully on any measures (i.e. all effect sizes were <0.50).

Time to mortality

Actigraphy profile predicts time to both all-cause mortality (X^2 = 24.54, p < 0.001 in women; X^2=18.87, p < 0.001 in men) and cardiovascular mortality (X^2 = 19.19, p < 0.001 in women; X^2 = 14.54, p < 0.001 in men). Table 5 provides Hazard Ratios [HRs] with 95% confidence intervals for pairwise profile comparisons. Among women, the IS profile is associated with increased risk for all-cause mortality (HRs = 1.59–1.75) and cardiovascular

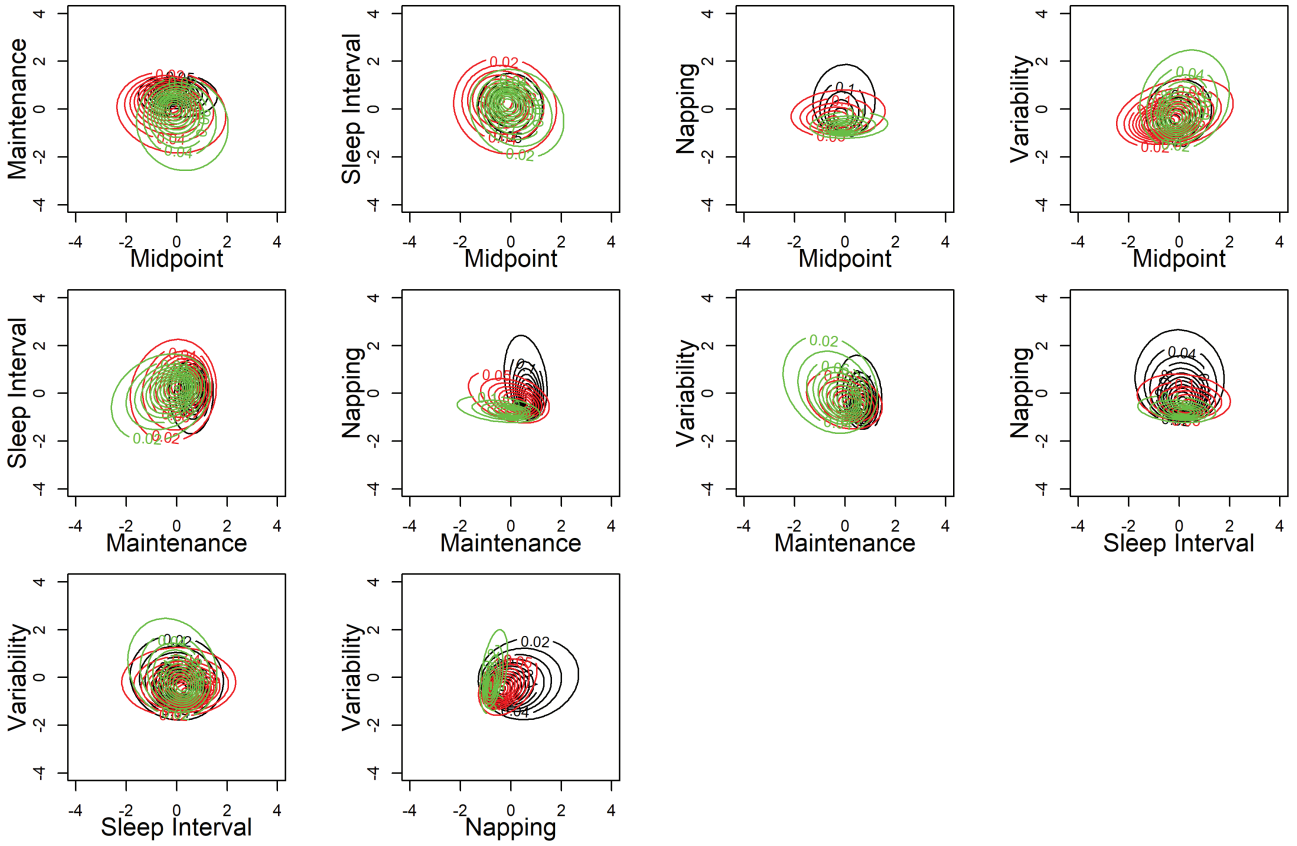

Figure 3. Contour plots of actigraphy profile distributions in men. Black = High Sleep Propensity; Red = Adequate Sleep; Green = Inadequate Sleep.

mortality (HRs = 2.38–2.46) relative to the other two profiles. AS and HSP do not significantly differ in mortality risk. Among men, IS and AS profiles are associated with increased risk for all-cause mortality relative to HSP (HRs = 1.19–1.22). AS also increases risk for cardiovascular mortality relative to HSP (HR = 1.33).

Table 5 displays mortality risk and 95% confidence intervals for individual actigraphy clustering characteristics when included simultaneously in the same model. In women, low maintenance increased risk for all-cause mortality relative to high maintenance (HR = 1.43). In men, low maintenance increased risk for all-cause mortality relative to moderate and high maintenance (HRs = 1.25–1.37); and low and moderate maintenance increased risk for cardiovascular mortality relative to high maintenance (HR = 1.45–1.47). Also in men, high napping/inactivity increased risk for mortality (HR = 1.28 for all-cause; 1.43 for cardiovascular) relative to low napping/inactivity; high variability also increased risk for all-cause mortality relative to moderate variability (HR = 1.20).

Discussion

We identified actigraphy sleep health profiles in large samples of older men and women from MrOS and SOF studies. In both samples, we observed a High Sleep Propensity profile with the hallmark combination of high sleep maintenance and high napping/inactivity. We also observed Adequate Sleep and Inadequate Sleep profiles in both samples; these two profiles were largely consistent across men and women with regards to nighttime sleep but differed in their napping/inactivity. Importantly, we also replicated the hallmark features of these profiles in a smaller matched sample of men and women from MrOS and SOF.

The High Sleep Propensity profile may appear counterintuitive, as one might expect efficient nighttime sleep to be associated with less daytime napping/inactivity. However, this profile occurred in substantial proportions of men (40%) and women (20%), suggesting that it reflects a relatively common combination of actigraphy characteristics in older adults. This profile was also clearly replicated in the matched sample, albeit in a smaller percentage of older adults (10%). The High Sleep Propensity profile was protective against all-cause and cardiovascular mortality in both men and women, a finding that is notable because high napping/inactivity is typically considered to increase risk for mortality, while high efficiency is protective [5, 31–33]. In line with this prior literature, when we examined the relationship of individual sleep features with mortality (i.e. not in the context of the profile), high napping/inactivity was associated with increased mortality risk in men while high efficiency was protective in both men and women. These findings highlight the importance of considering combinations of sleep features in relation to health outcomes.

Inadequate Sleep was characterized by low maintenance, late/variable timing, and shorter sleep interval length in both men and women – although these features were more extreme in women. This profile was associated with increased all-cause mortality risk in both women and men, although the effect was again more extreme in women (HR = 1.75) relative to men (HR = 1.19). Low sleep maintenance outside the context of the profile (defined as the lower third of the distribution; <81% in men and <83% in women) also increased mortality

Table 3. Cross-sectional measures in women by actigraphy profile

	High sleep propensity (*N* = 486)	Adequate sleep (*N* = 1807)	Inadequate sleep (*N* = 137)
Sociodemographic, %(*N*)			
Age	83 (81, 86)	83 (81, 86)	83 (81, 86)
Race (Black vs. White)	5.35 (26)	8.14 (147)	17.52 (24)
Marital status			
Married	25.72 (125)	28.17 (509)	22.63 (31)
Widowed	60.91 (296)	61.32 (1108)	64.96 (89)
Other	13.37 (65)	10.51 (190)	12.41 (17)
Education			
<High school degree	11.52 (56)	13.89 (251)	10.22 (14)
High school degree	68.93 (335)	66.80 (1207)	68.61 (94)
≥College degree	19.55 (95)	19.31 (349)	21.17 (29)
Health-related measures, %(*N*) or median (quartile 1, quartile 3)			
Past or current smoker	32.72 (159)	35.31 (638)	44.53 (61)
Any alcohol use	35.39 (172)	44.44 (803)	37.23 (51)
Body mass index			
Underweight or normal	35.19 (171)	37.13 (671)	20.44 (28)
Overweight	42.39 (206)	41.01 (741)	38.69 (53)
Obese	22.43 (109)	21.86 (395)	40.88 (56)
#Functional limitations (range 0–5)	1 (0, 2)	0 (0, 2)	2 (1, 3)
Self-rated health (1 = excellent, 5 = poor)	2 (2, 3)	2 (2, 2)	2 (2, 3)
Number of Rx. medications	4 (2, 6)	4 (2, 6)	5 (3, 8)
Number of chronic conditions (range 0–9)	2 (1, 3)	2 (1, 3)	2 (1, 3)
Goldberg anxiety scale (GAS)	0 (0, 1)	0 (0, 1)	0 (0, 1)
Anxiety (GAS ≥ 5)	13.37 (65)	14.11 (255)	11.68 (16)
Geriatric depression scale (GDS)	2 (1, 3.75)	1 (0, 3)	2 (1, 4)
Depression (GDS ≥ 6)	14.2 (69)	9.68 (175)	13.14 (18)
Cognition 23-item modified Mini Mental State Exam (mMMSE)	25 (24, 26)	25 (24, 26)	24 (23, 25)
Cognitive impairment (mMMSE ≤ 21)	5.14 (25)	4.59 (83)	7.30 (10)
Calories burned from walking	224 (56, 672)	280 (112, 672)	112 (0, 336)
Self-report sleep and sleep disturbances, %(*N*) or median (quartile 1, quartile 3)			
Hours napping per week	1 (0, 4.5)	0 (0, 3)	1 (0, 6)
Daytime sleepiness	6 (3, 8)	5 (3, 7)	6 (4, 9)
Medication with sleep effects	21.40 (104)	23.35 (422)	32.12 (44)
Difficulty staying asleep	62.14 (302)	64.42 (1164)	64.96 (89)
Difficulty falling asleep	34.57 (168)	35.53 (642)	38.69 (53)
Frequent snoring	3.50 (17)	4.93 (89)	8.76 (12)

risk in women (HR = 1.43) and men (HR = 1.37). Given the relative strengths of these hazard ratios across, we theorize that low maintenance is a key driver of the risk associated with the Inadequate Sleep profile. However, in women especially, the other characteristics that tended to "ride along" with low maintenance (i.e. moderate napping, late/variable timing, short sleep interval) may further increase the risk beyond low sleep maintenance alone.

The actigraphy self-report profiles we observed are noteworthy in the context of our prior work on self-report sleep health profiles in the same samples [10]. Using self-report sleep, we also observed a High Sleep Propensity profile (long nighttime sleep duration, high efficiency/quality, high sleepiness), which was associated with *increased* risk for mortality relative to other profiles. Post-hoc exploratory analyses suggested that the self-report High Sleep Propensity and actigraphy High Sleep Propensity profiles did not align in either men or women. Prior studies have observed that subjective–objective discrepancies can stem from a number of sleep, psychiatric, and medical disorders, and that this discrepancy can vary in both its level and direction depending on specific patient profiles [11].

Our findings focused on combinations of sleep characteristics suggest several important considerations for sleep-related interventions. First, in both men and women, Inadequate Sleep was primarily characterized by combinations of low maintenance and late/variable timing. Interventions aimed at improving sleep health in older adults may consider targeting this combination of measures. These are already key features of Cognitive Behavioral Therapy for Insomnia (CBT-I), Brief Behavioral Therapy for Insomnia (BBTI), and Transdiagnostic Sleep and Circadian Intervention (TranS-C) [34]. Thus, not only are these behavioral treatments on track for treating insomnia, but they may also have important health effects – something important to examine in future studies.

A second interesting treatment-relevant speculation is that napping may not constitute a single phenotype. In the High Sleep Propensity profile, "dispositional" napping co-occurs with high sleep maintenance but a relatively moderate nighttime sleep interval length, as is often the case in siesta cultures. The High Sleep Propensity profile was protective in older men and women, despite napping being an independent risk factor. One potential implication of this finding is that dispositional napping in combination with a shorter time in bed may potentially provide a way to get more 24-hour sleep duration while maintaining high efficiency at night. On the other hand, "compensatory" napping may result from a poor night's sleep

Table 4. Cross-sectional measures in men by actigraphy profile

	High sleep propensity (*N* = 1029)	Adequate sleep (*N* = 826)	Inadequate sleep (*N* = 785)
Sociodemographic factors, %(*N*)			
Age	76 (72, 80)	76 (72, 81)	75 (71, 79)
Race (Black vs. White)	3.11 (32)	3.03 (25)	5.73 (45)
Marital status			
Married	85.13 (876)	84.75 (700)	82.68 (649)
Widowed	7.39 (76)	7.51 (62)	8.79 (69)
Other	7.48 (77)	7.75 (64)	8.54 (67)
Education			
<High school degree	4.76 (49)	5.45 (45)	5.48 (43)
High school degree	38.48 (396)	40.19 (332)	38.09 (299)
≥College degree	56.75 (584)	54.36 (449)	56.43 (443)
Health-related measures, median(SD) or %(*N*)			
Past or current smoker	56.17 (578)	62.35 (515)	64.97 (510)
Any alcohol use	65.79 (677)	64.41 (532)	68.66 (539)
Body mass index category			
Underweight or normal	31.20 (321)	29.9 (247)	27.01 (212)
Overweight	49.66 (511)	50.24 (415)	49.94 (392)
Obese	19.14 (197)	19.85 (164)	23.06 (181)
#Functional limitations (range 0–5)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Self-rated health (1 = excellent, 5 = poor)	2 (1, 2)	2 (1, 2)	2 (1, 2)
Number of Rx. medications	3 (2, 5)	3 (2, 6)	3 (1, 5)
Number of chronic conditions (range 0 – 9)	1 (1, 2)	1 (1, 2)	1 (1, 2)
Geriatric anxiety scale (GAS)	0 (0, 1)	0 (0, 1)	0 (0, 1)
Anxiety (GAS ≥ 5)	7.19 (74)	9.08 (75)	10.06 (79)
Geriatric depression scale	1 (0, 2)	1 (0, 2.83)	1 (0, 2)
Depression (GDS ≥ 6)	6.41 (66)	8.47 (70)	4.71 (37)
Cognition 23-item modified Mini Mental State Exam (mMMSE)	25 (24, 25)	25 (23, 25)	25 (24, 26)
Cognitive impairment (mMMSE ≤ 21)	3.30 (34)	5.33 (44)	5.22 (41)
Physical activity (PASE)	141.75 (95.04, 184.64)	136.5 (92.64, 183.42)	146.71 (100.21, 189.86)
Self-reported sleep and sleep disturbances, median (quartile 1, quartile 3) or %(*N*)			
Hours napping per week	0 (0, 3)	0 (0, 3.5)	0 (0, 1.5)
Daytime sleepiness	6 (3, 8)	6 (4, 8)	5 (3, 8)
Medication with effects on sleep	15.84 (163)	17.68 (146)	17.96 (141)
Difficulty staying asleep	74.34 (765)	78.45 (648)	78.06 (612)
Difficulty falling asleep	20.51 (211)	23.12 (191)	24.08 (189)
Frequent snoring	21.77 (224)	19.25 (159)	21.78 (171)
Stop breathing	14.19 (146)	14.65 (121)	16.31 (128)

characterized by poor sleep maintenance. The Inadequate Sleep profile in women suggests a pattern of compensatory napping (i.e. napping with very low maintenance, late/variable timing, and shorter duration) and conferred high risk for both all-cause and cardiovascular mortality.

This work has several strengths and innovations. Our findings are based on large and well-characterized samples of older men and women. These samples allowed us to assess replicability and generalizability of our findings, which is critical in clustering. Overall, our findings were highly consistent across men, women, and a matched sample of men and women, which adds confidence to the potential replicability of our findings in other samples of older adults. We also used novel clustering methods that allow for flexible assumptions related to cluster distributions, which is an important methodological advancement in sleep research, as well as health research more broadly.

There are limitations to note regarding the analytic samples. The samples are primarily white, affording limited generalizability to more racially/ethnically diverse samples. Furthermore, the distributions of several key confounders differ between the male and female samples, making it difficult to directly compare their findings. The matched sample findings provide additional assurances regarding the constancy of the trademark features of the identified profiles in a sample of men and women who are similar on the specific measures included in the propensity score. However, the matched sample is not a "cure" for confounding.

Another limitation relates to our secondary outcome of cardiovascular mortality, which was included because it may provide more insight into specific mechanisms. However, this outcome may be less reliable given that it is rare for older adults to have a single attributable cause of death [35]. As such, determining the primary cause of death can be challenging and subject to misclassification.

There are also caveats concerning the measures used to characterize sleep. In older adults, actigraphy-measured "napping" reflects periods of inactivity in addition to periods of daytime sleep, making it relatively non-specific to actual sleep. We required at least five minutes of inactivity for a period to be indexed as a "nap" although in older adults it is possible that longer periods of inactivity do not include actual sleep. Correlations

Table 5. Hazard ratios (95% confidence intervals) for actigraphy characteristics in fully adjusted Cox models

	Women		Men	
	All-cause mortality	Cardiovascular mortality	All-cause mortality	Cardiovascular mortality
Actigraphy profile in women[*]				
High sleep propensity vs. adequate sleep	1.10 (0.93, 1.32)	1.03 (0.76, 1.42)	–	–
Inadequate sleep vs. adequate sleep	**1.75 (1.33, 2.31)**	**2.46 (1.59, 3.81)**	–	–
Inadequate sleep vs. high sleep propensity	**1.59 (1.17, 2.15)**	**2.38 (1.46, 3.87)**	–	–
Actigraphy profile in men[†]				
Adequate sleep vs. high sleep propensity	–	–	**1.22 (1.08, 1.37)**	**1.33 (1.06, 1.69)**
Inadequate sleep vs. high sleep propensity	–	–	**1.19 (1.04, 1.36)**	1.06 (0.82, 1.37)
Inadequate sleep vs. adequate sleep	–	–	0.98 (0.85, 1.12)	0.79 (0.62, 1.02)
Individual actigraphy characteristics				
Sleep interval				
Short vs. medium sleep interval	0.83 (0.69, 0.99)[‡]	0.81 (0.58, 1.12)	1.03 (0.90, 1.18)	1.11 (0.86, 1.44)
Long vs. medium sleep interval	1.00 (0.84, 1.19)	1.06 (0.78, 1.43)	1.13 (0.99, 1.29)	1.26 (0.98, 1.61)
Long vs. short sleep interval	1.21 (1.01, 1.46)	1.3 (0.95, 1.80)	1.10 (0.95, 1.26)	1.13 (0.88, 1.46)
Napping				
Low vs. medium napping	0.96 (0.79, 1.17)	0.89 (0.63, 1.25)	0.91 (0.79, 1.05)	0.91 (0.70, 1.20)
High vs. medium napping	1.16 (0.97, 1.38)	1.13 (0.84, 1.53)	1.16 (1.02, 1.33)[‡]	1.30 (1.02, 1.66)[‡]
High vs. low napping	1.20 (0.99, 1.46)	1.28 (0.90, 1.80)	**1.28 (1.11, 1.48)**	**1.43 (1.09, 1.86)**
Sleep maintenance				
Low vs. medium maintenance	1.17 (0.98, 1.40)	1.29 (0.95, 1.75)	**1.25 (1.09, 1.43)**	1.02 (0.80, 1.29)
Low vs. high maintenance	**1.43 (1.19, 1.72)**	1.51 (1.10, 2.22)[‡]	**1.37 (1.19, 1.72)**	**1.47 (1.12, 1.92)**
Medium vs. high maintenance	1.23 (1.02, 1.49)[‡]	1.19 (0.85, 1.67)	1.10 (0.96, 1.27)	**1.45 (0.89, 1.12)**
Midpoint timing				
Early vs. middle midpoint	1.02 (0.85, 1.22)	0.92 (0.67, 1.27)	1.03 (0.90, 1.18)	1.05 (0.82, 1.35)
Late vs. middle midpoint	1.07 (0.90, 1.28)	1.22 (0.90, 1.65)	1.08 (0.94, 1.24)	1.15 (0.89, 1.48)
Late vs. early midpoint	1.05 (0.88, 1.27)	1.32 (0.96, 1.83)	1.05 (0.92, 1.20)	1.10 (0.85, 1.41)
Variability of midpoint				
Low vs. medium variability	0.98 (0.82, 1.17)	1.05 (0.76, 1.46)	1.01 (0.88, 1.15)	0.87 (0.68, 1.11)
High vs. medium variability	1.04 (0.87, 1.25)	1.22 (0.89, 1.67)	**1.20 (1.04, 1.37)**	0.94 (0.73, 1.20)
High vs. low variability	1.06 (0.89, 1.27)	1.15 (0.85, 1.57)	1.19 (1.03, 1.36)[‡]	1.08 (0.83, 1.41)

[*]Omnibus test for profile in women: $X^2 = 24.54$, $p < .001$ for all-cause mortality; $X^2 = 19.10$, $p < .001$ for cardiovascular mortality.
[†]Omnibus test for profile in men; $X^2 = 18.87$, $p < .001$ for all-cause mortality; $X^2 = 14.54$, $p < .001$ for cardiovascular mortality.
[‡]Not significant after multiple comparison adjustment.
All models were adjusted for age, sex, race, education, alcohol use, smoking status, physical activity, functional limitations, self-rated health, number of prescription medications, number of chronic conditions, anxiety symptoms, depression symptoms, cognition, self-report of napping, daytime sleepiness, sleep-related medication, difficulty staying/falling asleep, frequent snoring, and stopping breathing during sleep. Bold findings are statistically significant after multiple comparison adjustment.

of actigraphy and self-report napping were moderate in both women and men (Spearman $r = 0.30–0.31$), indicating that the measures are reasonably well-aligned, and profiles with greater actigraphy napping/inactivity also typically had greater self-reported daytime sleepiness and napping. Additionally, profiles are not characterized by information from a polysomnography sleep study. Post-hoc analyses in men (Supplement Section 8) indicated that adjusting for the Apnea-Hypopnea Index (AHI) did not alter our findings. However, only 17% of women had the AHI, which precluded a similar examination in this sample. An important next step will be to develop profiles that incorporate self-report, actigraphy, and polysomnography measures to reveal comprehensive multidimensional sleep profiles. This type of analysis would provide a better understanding of which older adults tend to have consistent versus inconsistent sleep profiles across modalities. Such information will be valuable for advancing interventions.

In conclusion, this work presents an important step forward for understanding actigraphy sleep health profiles in older adults, especially with regards the importance of considering whether napping may be dispositional versus compensatory, and the finding that high napping co-occurring with high efficiency may not be inherently problematic in older adults. Our findings may help to reinforce and improve sleep-related interventions in older adults and suggest future research focused on combinations of sleep characteristics in older adults.

Supplementary Material

Supplementary material is available at *SLEEP* online.

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