HHS Public Access

Author manuscript

Sleep Health. Author manuscript; available in PMC 2021 August 01.

Published in final edited form as:

Sleep Health. 2020 August ; 6(4): 513–521. doi:10.1016/j.sleh.2019.12.003.

Association of Sleep Quality to Telomere Length, a marker of cellular aging. A retrospective cohort study of Older Adults in the United States

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Abstract

Background: Sleep quality is a risk factor for age-related diseases, and although the underlying mechanisms remain unclear, the effects of poor sleep quality on telomere length may play a role.

Objective: To evaluate the independent association between sleep quality and salivary telomere length in a large sample of older adults.

Design: We adopted a retrospective cohort design, participants comprised 5,268 adults drawn from the Health and Retirement Study. We used the 2006 (baseline) and 2008 (follow-up) waves. Baseline sleep quality was assessed using 4 Likert scale questions (trouble falling asleep, waking up during the night, waking up too early and not being able to fall sleep again, and feeling well rested in the morning). Telomere length was assessed using T/S ratio, a continuous variable. The associations between sleep quality and T/S were assessed using multivariable ordinary least squares regressions. All analyses were adjusted for demographics, lifestyle characteristics, psychosocial, and other factors.

Results: Overall, 16% reported never feeling well rested in the morning; 25.7% of respondents always had trouble waking during the night, and 12.8% always had trouble waking up too early in the morning. Respondents who never felt rested in the morning had significantly shorter telomere

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All authors contributed to the conception and design of the research. CI/US conducted the statistical analyses. CI wrote the first draft. CI, US and KI worked on successive iterations

Declarations of Interest: None

length compared to those who always felt rested in the morning (adjusted beta = −0.08, SE =0.03, $p < 0.01$). The composite sleep measure was not significantly associated with shorter TL.

Conclusions: In this cohort of older adults, not feeling well rested in the morning was significantly and inversely associated with telomere length; however, the composite measure of sleep quality was not significantly associated with telomere length. These findings suggest a potential connection between one of the measures of impaired sleep and reduction in telomere length, a marker of cellular aging that has been linked to multiple chronic conditions.

Keywords

Biomarkers; Biology of aging; Telomeres; Population health; Sleep quality

1. Introduction

Telomeres are DNA protein structures that function as caps protecting and stabilizing the ends of chromosomes during cell division.[1,2] Increasingly considered a marker of cellular aging and vulnerability to senescence and/or apoptosis, telomere length (TL) has been shown to decline with age and with each cycle of cell division.[3-8] Shorter TL has been associated with cardiovascular disease, stroke, diabetes, cancer and other age-related chronic conditions,[5,9-13] with cardiometabolic risk factors for chronic disease,[12,14] with depression, chronic stress, adverse early childhood experiences, [15-19] and with premature mortality.[20,21] Shorter telomeres and accelerated shortening in TL has also been shown to predict greater disease progression.[6,21-23]

In addition, recent research suggests that telomere length may be altered by certain modifiable life-style factors associated with elevated chronic disease risk, such as inadequate sleep and other factors.[24-28] The prevalence of sleep problems increases with age, and has been rising in all age groups.[29-32] Inadequate sleep has been prospectively linked to increased risk for a range of common chronic conditions, including cardiovascular disease (CVD),[33-35] diabetes,[36] hypertension,[34,35] and other cardiometabolic risk factors,[34] as well as to depression,[37,38] cognitive decline, and Alzheimer's disease.[39-42] Poor sleep quality has also been associated with increased risk for mortality from CVD, diabetes, and other disorders.[43-45] The relationship between inadequate sleep and adverse health outcomes is bidirectional, contributing to a vicious cycle of increasing sleep and metabolic disturbance, declining quality of life, deterioration in mental and physical health, accelerated cognitive decline, neurodegenerative changes, and increasing risk for disability, morbidity and mortality.[46-49]

Sleep quality is a complex construct encompassing several domains, including sleep latency, sleep maintenance and sleep efficiency.[50] Sleep quality declines with age,[31,51] paralleling both the overall age-related decline in TL [21,28] and rise in chronic disease risk.[35,52] Numerous studies have attempted to elucidate the pathway linking sleep quality and disease risk.[53-60] Plausible pathways include biological processes such as cellular injury, DNA damage, inflammation and accelerated cellular aging as indicated by shortened telomere length.[58-60] However, research regarding the potential link between sleep quality and TL remains limited and findings have been inconsistent. Moreover, of the few published studies

that have examined the association between measures of sleep impairment and TL in adults, [25,54-56,61] all have been cross-sectional, and only three included measures of sleep quality. [53,55,61] For example, in a study of 154 older adults aged 44-77 years, both sleep duration and sleep quality - measured by the sleep quality component of the Pittsburgh Sleep Quality Index (PSQI) were significantly related to TL,[25] although specific risk estimates were not provided. In a second investigation using a sample of 283 HIV-positive individuals aged 22-77 y, [61] investigators found an association between reduced telomere length and short sleep duration but not poorer sleep quality. Conversely, Prather et al reported a significant association between short TL and poor sleep quality, but not short sleep duration in their study of 245 healthy community-dwelling middle-aged women.[55] Although reasons for the discordant findings are unclear, the discrepancies may reflect differences in study population, design, and measures used. While collectively, these findings suggest sleep deficits may be linked to TL, conclusions are limited by cross-sectional design, relatively small sample sizes, and/or restricted study population characterizing previous published studies. Designed to help address these limitations, this study examines the association of sleep quality to TL in a large, nationally representative cohort of older adults using data from the Health and Retirement Study (HRS). We hypothesized that TL would be shorter in older adults with poor sleep quality.

2. METHODS

2.1. Study Design

This study used a retrospective cohort design using data from the Health and Retirement Study (HRS), collected in two waves: 2006 and 2008.

2.2. Data Source

The HRS is an ongoing longitudinal survey of over 27,000 non-institutionalized adults over 50 years of age living in the United States.[62] Details regarding the study, including participant eligibility, recruitment and enrollment, study procedures, and data collection are given elsewhere.[62,63] Sponsored by the National Institute on Aging, the HRS began in 1992 and is fielded every two years. The HRS team surveys a nationally representative sample of more than 20,000 older adults during each 2-year cycle and follows the participants until death. The aim is to evaluate the economic and healthcare experiences of older Americans from preretirement into retirement. The survey comprises a core questionnaire and exam that are administered each wave. Data are collected on a broad range of factors including demographics, health status and conditions, health care utilization, health insurance, current employment and employment history, disability, occupation, industry, job and work environment characteristics, earnings and other income, pension and retirement plan, housing, assets, cognitive status, physical functioning, and intergenerational financial transfers. In 2006, the HRS began conducting Enhanced Face to Face (EFTF) interviews, during which physical measures (height, weight, waist circumference, blood pressure) are taken and saliva collected to assay biomarkers and genetic profiles. Physical performance indicators such as grip strength, timed walk, balance tests, and pulmonary function are also measured. In addition, information on subjective well-being, well-being, personality, job characteristics lifestyle and stress are also gathered using a self-report psychosocial

questionnaire that participants receive at the end of the interview and return by mail. The eligibility criteria for the 1992 cohort included the following: at least one age-eligible member from the 1931-1941 birth year cohorts should reside in the household, and must be community dwelling, non-institutionalized individuals in the contiguous United States. In subsequent waves, HRS included other birth year cohorts. We used the 8th wave (2006) and 9th wave of the HRS (2008). These waves contain three birth year cohorts (1931-41; 1942-1947; 1948-1953). Sample weights are supplied to account for the multistage area probability design and were used in the analyses.

In 2006, 50% of the respondents were randomly assigned to enhanced face to face interviews that included collection of additional physical health information, saliva samples and blood to assess specific biomarkers (e.g., cholesterol, C-reactive protein, and hemoglobin A1C); The remaining 50% of participants received only the core questionnaire in 2006, which included all questions on sleep quality. The 50%-samples interchange waves so the other half received enhanced face to face interview in 2008. Thus, expanded data are available on a nationally representative 50% sample every wave. Telomere length was measured using saliva (see 2.4.1, below), and was assessed only in 2008.

2.3. Study Sample

Participants included 5,268 eligible respondents who were alive, did not have missing data on sleep problems (2006 wave, baseline period) and had complete TL data from the 2008 wave (follow-up period).

2.4. Measures

2.4.1. Dependent Variable: Telomere Length (TL) - T/S Ratio—As indicated above, TL was measured only once, in 2008 (9th wave of the HRS). 85% of the respondents consented to providing saliva samples for the measurement of TL; viable samples were collected from 99% of consenting participants. Saliva samples were collected using an Oragene Collection Kit and sent to a central laboratory for processing within 24 hours. The TL assays were conducted by Telome Health using quantitative polymerase chain reaction (qPCR) adapted from a method by Cawthon[64] and described in detail elsewhere.[64-66] qPCR is a widely used and well-validated method for measuring TL.[66] Telomere sequence copy numbers for every respondent's sample (T) were divided by a single-copy gene standardized reference (S), to yield a standardized T/S ratio.[67,68] Although telomere length is frequently assessed in leukocytes, TL measurement using saliva samples has been shown to have high reliability and has been used in a number of recent studies.[69]

2.4.2. Key Independent Variable: Sleep Quality—HRS investigators measured sleep quality using an adapted version of Jenkins Sleep Questionnaire, a validated[70] and broadly used screening questionnaire for evaluating sleep complaints.[71-76] The scale has been used to evaluate sleep quality in a wide range of populations, from healthy adults[77] to those with ankylosing spondylitis,[72] myocardial infarction,[76] COPD,[78] chronic pain and depression.[74] The scale facilitates the assessment of self-reported sleep problems over the past 30 days but does not permit a clinical diagnosis of sleep disorders. We used the sleep quality variables from the 2006 wave of the HRS. In 2006, respondents were asked how

often they had trouble with: 1) “falling asleep” 2) “waking up during the night” 3) “waking up too early and not being able to fall asleep again”. The respondents were also asked “how often they felt really rested when they woke up in the morning.” Responses included “most of the time” “sometimes” and “rarely or never.” We adopted methods used in previous studies to code the sleep quality variable.[79] We created a binary variable for poor sleep quality (yes/no) for each measure. The respondents were categorized as having poor sleep quality if they answered; “most of the time” or “sometimes” to the initial three questions, and “rarely or never” or “sometimes” to the last question regarding “feeling rested in the morning”.

We combined the four items to create a composite variable for overall sleep quality. Overall sleep quality was categorized as both a binary and continuous variable if the respondents reported that “most of the time” they had trouble falling asleep, waking up during the night, or waking up too early and not being able to fall sleep again or answered that they “rarely or never” felt rested in the morning, they were considered to have poor sleep quality. To calculate the continuous composite variable, responses to question 4 were reverse-coded, and responses to all items were summed.

2.4.3. Conceptual Framework and Other Independent Variables—To guide the selection of factors that may affect the relationship between sleep and cellular aging, we reviewed previous studies to identify factors that likely influence sleep and TL [16,24,53,54,61,80] Factors included in multivariable analyses were as follows: age in 2008 (continuous in years), sex, (male, female) race/ethnicity, (non-Hispanic white, African American, Latino and other race), education (< high school, high school diploma, some college, and college.), income level based on the federal poverty line (poor, low income, moderate income, high income), employment status (employed vs. not employed) and insurance status (Medicare and private insurance). Chronic physical conditions (i.e., heart disease, arthritis, stroke, hypertension, diabetes, cancer (excluding non-melanotic skin cancer), pain (none, mild, moderate, severe), and perceived general health status as measured on a self-report 5-item scale (excellent, very good, good, fair and poor). Depression was ascertained using the Center for Epidemiologic Studies Depression scale (CES-D short form) and assessed as a binary variable (< 3 and ≥ 3)[81; 81] childhood health was measured on a 5-item self-report scale (excellent, very good, good, fair and poor). Life-style factors included body mass index (BMI, categorized as normal/underweight (<25), overweight (25-29.9) and obese (≥30)), smoking status (current smoker, nonsmoker) and physical activity (assessed using participant responses to the question ‘How often do you take part in sports or vigorous activity?’ And ‘How often do you take part in sports or activities that are moderately energetic?’ and categorized as yes (> twice/week) or no (< twice/week). Except for sex, race/ethnicity and education, all independent variables included in the analyses were ascertained based on information gathered in 2008, the follow-up year.

2.5. Statistical Analyses

Group differences by sleep problem categories were assessed using Rao-Scott chi-square tests (categorical and ordinal variables), T tests, or F tests (continuous variables). We used separate multivariable ordinary least squares (OLS) regressions to evaluate the independent

association between each sleep quality variable and T/S ratio. Model 1 was the unadjusted model, in model 2, we adjusted for age, sex, race, education, and income. In model we adjusted for the biomedical (pain, chronic conditions, childhood health, and BMI), biosocial (sex, race/ethnicity, education, marital status, employment, and income), and psychosocial/ lifestyle variables (depressive symptoms, physical activity, and smoking) as defined above. Findings of the OLS regression analyses are presented as parameter estimates (beta), with their standard errors, t-values, and probabilities of t-values. As mentioned above, T/S ratio of "1" refers to a reference normal TL Thus T/S = 1 when measured TL is identical to the reference single copy gene. Positive beta coefficients indicate longer TL and negative beta coefficients indicate shorter TL. To assess the robustness of our findings, we conducted ancillary analyses to examine, in separate multivariable regression models, the relation of T/S ratio to each sleep problem, collapsed into two categories ('sometimes/most times' and 'rarely/never'). We also examined the relation between different sleep domains using Chi square analysis, and p-values from Rao-scott chi-square test were reported. In sensitivity analysis, we excluded individuals with TL over 2 (N = 289) as was done in previous studies.[82] TL in this sample was normally distributed. We additionally performed the regression tests using log TL. Because the effects of sleep quality may differ in men and women over 50 years of age, we evaluated the potential interaction of sleep problems and gender in our regression analyses. All analyses were conducted using STATA and SAS v 9.4. and used SAS survey procedures[83] to account for the complex survey design. All observations with missing or non-positive values were excluded from the analysis. Statistical significance was defined as $p < 0.05$.

3. Results

Study participants were predominantly female (55%) and non-Hispanic white (81%); age averaged 67.0 ± 10 years, with almost 20% of participants aged 80 years or older (Table 1). The weighted mean salivary TL (T/S ratio) was 1.37 (SD = 0.58); Unweighted numbers and weighted percentages of respondents by sleep quality domains are given in Table 2. Overall, 12.8% of respondents reported that they always had problems with sleep latency and early awakening, 30.4% and 29.9% indicated sometimes having trouble falling asleep or waking too early respectively, and 57% reported no trouble falling asleep and no problems with early awakening. Twenty-six percent of respondents reported always awakening during the night and not being able to go back to sleep, whereas only 40% of respondents did not indicate trouble waking up during the night. Over 40% indicated that they never (16.2%) or only sometimes (24.8%) felt rested in the morning.

Overall, 80% of participants indicated always or sometimes experiencing at least one sleep problem. Fifteen percent of respondents had trouble in all four sleep quality domains, and 20% had problems in three of the four sleep quality domains. Twenty-one percent of respondents had problems in two of the four sleep quality domains, and 24% reported only one sleep problem. Twenty percent of respondents did not indicate any sleep problems. Only 18% of the survey respondents reported use of sleep medications in the past two weeks.

Weighted percentages of sample characteristics by the sleep quality item "feeling rested in the morning" are reported in Table 3. A lower percentage of women than men (57% vs 62%)

rarely or never felt rested in the morning (p= 0.021). Compared to adults under 65 years of age, participants 65 years and older more commonly reported never or rarely feeling rested in the morning ($p < 0.001$). Relative to single respondents, married people were less likely to indicate feeling rested in the morning ($p < 0.001$). Feeling rested in the morning also varied significantly with level of education and income. (Table 3).

Table 4 summarizes the unadjusted and adjusted associations of sleep quality domains to TL, expressed as T/S ratio. There was no statistically significant association between either the binary or continuous composite variable of overall sleep quality and TL. (Beta = −0.03, SE =0.04, p = 0.33) and (Beta = −0.01, SE =0.007, p = 0.15) respectively. Of the four individual sleep variables assessed, only feeling rested in the morning was significantly associated with TL. In the unadjusted OLS (Model 1), TL was significantly shorter in those who reported never or rarely feeling well rested at baseline relative to those who indicated feeling well-rested in the morning (Beta = −0.04, SE =0.02, $p < 0.05$). Adjustment for age, sex, and race/ethnicity slightly strengthened this association (Beta = −0.05, SE = 0.02, $p < 0.05$). Additional adjustment for lifestyle factors, pain, chronic conditions, childhood health, BMI, depressive symptoms, physical activity, and smoking further strengthened the inverse relationship of this measure of sleep quality to T/S ratio (Beta = −0.08 SE = 0.02, $p < 0.01$). Further adjustment for depressive symptoms did not alter this association, suggesting that depression did not explain the relation of sleep quality to TL in this study. There were negative but statistically insignificant associations between telomere length and trouble falling asleep (beta = −0.01, SE = 0.02, p = 0.60), trouble waking up during the night (beta = −0.01, SE = 0.02, p = 0.56) and trouble waking up too early in the morning (beta = −0.02, SE = 0.04, p = 0.65) and TL.

Other variables significantly associated with shorter TL or shorter T/S ratio after adjustment for other covariates included moderate pain level (beta = −0.03, SE = 0.012 p = 0.014, History of cancer (beta = −0.1, SE = 0.04 $p < 0.01$); and cardiovascular disease (beta = −0.04, SE = 0.02 $p < 0.05$). Factors significantly associated with longer TL (higher T/S ratio) after adjustment for other covariates included obesity (BMI ≥ 30 vs. <25, beta = 0.024 SE = 0.011 p = 0.031); African American race (beta = 0.061, SE = 0.0164 $p < 0.0001$) compared to non-Hispanic white; and history of diabetes (beta = 0.08, SE = 0.03 $p < 0.01$). The interaction term for sleep quality and gender was not significant (beta = 0.02, SE = 0.08 p = 0.83), nor did TL differ by gender among participants either with or without sleep problems $p > 0.8$). We excluded individuals with TL over 2 (N = 289) as part of the sensitivity analysis, as was done in previous studies,[82] removing these individuals did not substantively change the findings. When we used Log TL in our analyses, the findings did not differ.

As detailed in Table 5, scores on the item “well rested in the morning” were significantly and inversely associated with those on other sleep quality items. 51.5% of participants who felt rested in the morning (sometimes/most times) never had trouble with falling asleep, while 11% of respondents who rarely/never felt rested in the morning also had trouble falling asleep (sometimes/most times). Twelve percent of participants who rarely/never felt rested in the morning had trouble waking up during the night (sometimes/most times) and

51% of respondents who felt rested in the morning (sometimes/most times) rarely/never had trouble with waking up too early in the morning.

4. Discussion

This study examined the association between self-reported sleep problems and TL two years later, using data on a representative sample of older U.S. adults. Our estimated percentages of adults with sleep problems were broadly consistent with published studies. More than half of the respondents did not report trouble with falling asleep and early morning awakenings, whereas only 40% did not have trouble maintaining sleep. This is in agreement with previous studies that showed that difficulty maintaining sleep is most prevalent symptom reported by all adults with nighttime insomnia.[84] In our study, we observed a statistically insignificant negative association between the composite sleep quality measure and TL. Oneitem of sleep quality (feeling well rested in the morning) was associated with TL. Those who reported that they never felt rested in the morning had significantly shorter TL, compared to those who felt rested in the morning most of the time or sometimes, an association that was further strengthened after adjustment for multiple demographic, lifestyle, and health-related factors. Although age, childhood health, cancer history, race and income were significantly and inversely associated with both TL and sleep quality, inclusion of these factors in the model did not alter the association of sleep quality to TL.

In contrast with our findings, previous studies in older adults (N=154)[53] and middle-aged women (N=145),[55] suggested significant associations between poor sleep quality and shorter TL. In agreement with our findings using the overall sleep quality item,, Lee et al found no association between sleep quality and TL in their study of 283 adults with HIV.[61]

Of the five studies assessing the association between TL,[53-56,61] and another measure of adequate sleep, i.e., sleep duration, three found evidence for a significant inverse relationship,[54,55,61] while two found evidence of a curvilinear relationship between sleep duration and TL.[53,56] Although we did not have data on sleep duration, it is plausible that being well rested in the morning is a global measure that may capture overall sleep problems better than other sleep variables, and may in part reflect sleep duration as well as provide a marker of overall sleep quality.[85] For example, in a study of 441 white and African American middle-aged to elderly adults, sleep duration was significantly correlated with all three domains of sleep quality measured, with the strongest associations reported for sleep efficiency and sleep latency.[86] Libman et al. found that among three groups of respondents with insomnia disorder, obstructive sleep apnea, and those with no specific sleep related complaint, feeling refreshed in the morning was a strong predictor of good sleep quality.[87] In this study, participants who rarely or never felt rested in the morning were significantly more likely to report having trouble falling asleep, staying asleep, and awakening too early.

In this study TL was not significantly related to the 3 specific measures of sleep latency, maintenance, and early awakening, although the observed associations were in the expected direction.

Potential mechanisms:

Biologically plausible explanations for the relationship between feeling well rested in the morning and TL may involve stress reactivity,[88,89] oxidative stress, and inflammation.[90-92,] Bekaert et al found that elevated serum levels of inflammatory markers: fibrinogen, high sensitive c-reactive protein and IL-6 were negatively associated with TL in a sample of healthy middle age subjects; the authors hypothesized that rapid cell turnover in response to inflammation could account for telomere attrition and therefore shorter TL.[90] Participants who never feel rested in the morning may have higher levels of stress hormones, including cortisol and catecholamines, which have in turn been linked to telomere shortening.[93-95] It has been reported that there may be bidirectional associations between poor sleep quality, stress and worry.[96,97] Specifically, non-restorative sleep, identified by not feeling rested in the morning, a primary symptom of insomnia may increase stress levels.[98] Not feeling well rested in the morning may indicate lower defense against oxidative stress, which may in turn affect TL. Oxidative stress has been found to cause telomere-specific single strand breaks in cultured cells,[6] and to compromise the repair mechanism for telomeric DNA.[4] Numerous studies have reported associations between stress and telomere erosion,[99] stress reactivity may act through elevated stress hormones such as cortisol.[93] For example, in vitro studies of T cells have shown treatment with cortisol to decrease telomerase activity in these cells.[93,94] Tomiyama et al. found that among 23 postmenopausal women comprising caregivers for dementia patients, who were exposed to a modified Trier Social Stress Test (TSST), greater cortisol reactivity and elevated overnight cortisol levels were significantly associated with shorter TL.[100] Clearly, additional research is needed to further elucidate the pathways through which waking up rested in the morning may affect telomere length.

Previous studies have demonstrated significant associations between menopausal symptoms are and sleep problems in women.[101] While we did not have information on menopausal status in this study, we did assess the potential modifying effect of gender on the association between sleep quality to TL. We included an interaction term (sleep quality * gender) in the regression model. In this study, we found no evidence for a modifying effect of gender, nor did inclusion of the interaction term (sleep quality * gender) in the model alter our findings. In addition, there were no significant differences in TL between men and women with either good or poor sleep quality.

Consistent with published studies,[16,26,80,102,103] TL was significantly and positively associated with African American race and BMI, and inversely associated with age, sex,[104] pain, education, and history of cancer or CVD[12] in this study after adjusting for multiple potential confounders. Longer TL among African Americans was previously reported by Needham et al.[103] Further research is needed to understand these seemingly paradoxical findings, given that African-Americans have significantly higher morbidity and mortality rates than whites. One study in newborns found that African-American infants had significantly longer TL at birth than white infants.[105] These variations at birth may account for the observed differences in TL in older age. The observed positive association between BMI and telomere length is not consistent with results from previous studies; including two meta analyses that have shown that BMI is negatively associated with TL.[106,107] However,

the positive association of BMI to TL is consistent with two previous studies using the HRS sample.[102,80]

Strengths of this study include the relatively large sample size and the ethnically diverse study population drawn from a nationally representative sample of older U.S. adults. Additional strengths include the use of longitudinal data from an ongoing national cohort study and the availability of comprehensive information on a broad array of potential confounders, including demographic, lifestyle, health-related, and other factors. Participant compliance with assessment procedures was excellent, with high completion rates for all data elements.

However, this study also has several limitations. We did not have information on sleep duration, a factor that has been previously associated with TL in some,[53,55,61,108] although not other studies.[56] We lacked data on TL at baseline (2006) and on sleep problems at follow-up (2008), limiting conclusions regarding causality. In addition, we could not assess how changes in sleep quality predict change in TL as repeated measures of TL were not available. As data are gathered only every two years, the potential role of short vs. long term sleep impairment in telomere shortening could not be assessed. Follow-up was only two years, precluding evaluation of longer-term effects of sleep quality on TL. In addition, while TL is more commonly measured using DNA extracted from blood leukocytes, in the current study, TL was assayed from saliva, which comprises leukocytes and epithelial cells. TL may vary by cell type, and although salivary TL has been shown to be highly correlated with blood leukocyte TL ($r = 0.72$),[69] the association of sleep and other health outcomes to salivary TL may nonetheless differ from that to TL derived from other sources. Furthermore, we did not have data on menopausal symptoms/reproductive status, both factors that may disrupt sleep. We did not have data on nap time in this study, since individuals in our sample are retired, napping is likely to be common, and thus, may represent an important, contributor to sleep quality not captured in our study. Finally, while we were able to control for a wide range of factors, we cannot rule out the possibility of unmeasured confounding.

Conclusions:

In this large retrospective study, overall sleep quality was not significantly associated with telomere length, but one measure of sleep quality, i.e., feeling well rested in the morning. was significantly and inversely associated with TL after adjustment for multiple demographic, lifestyle, and health-related factors. Further prospective research incorporating objective measures of sleep is needed to confirm and extend these findings, to clarify the relationship of both acute and chronic sleep impairment to TL, and to investigate potential underlying mechanisms.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgement

The HRS (Health and Retirement Study) is sponsored by the National Institute on Aging (grant number NIA U01AG009740) and is conducted by the University of Michigan.

Funding

Research reported in this publication was supported by the National Institutes of Health (NIH), National Institute of General Medical Sciences award number 2U54GM104942-02 and in part by the NIH National Center for Complementary and Integrative Health award number 1 R15 AT008606. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIH.

List of Abbreviations

TL	Telomere length
CVD	Cardiovascular disease
PSQI	Pittsburgh Sleep Quality Index
HRS	Health Retirement Study
EFTF	Enhanced Face to Face
qPCR	Quantitative Polymerase Chain Reaction
CES-D	Center for Epidemiologic Studies Depression scale
BMI	Body mass index

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Table 1

Characteristics of Adults aged 50 Years or Older Health Retirement Study, 2006- 2008

Variable	N	Weighted %
All	**5,268**	**100.0**
Sex		
Female	3,076	56.0
Male	2,192	44.0
Age		
50 - 64 years	886	13.4
65-69 years	1,605	47.6
70-79 years	1,026	15.8
80 years or older	1,751	23.1
Race/Ethnicity		
Non-Hispanic White	3,985	80.8
African American	675	8.7
Hispanic/Latino	496	8.1
Other	112	2.4
Marital Status		
Married	3,228	63.5
Divorced/separated/widowed	1,892	33.1
single	148	3.4
Education		
Less than High school	1,213	19.1
High school	1,768	32.3
Some College	1,110	22.8
College degree	1,173	25.7
Income		
Poor	456	8.2
Low income	969	16.2
Mod income	1,699	29.7
High income	2,144	45.9
Employment Status		
Employed	1,510	36.9
Not employed	3,755	63.0
Medicare Enrollment		
Yes	3,714	55.1
No	1,545	44.8
Private Insurance		
Yes	3,109	64.8
No	2,143	35.0
Childhood Health **		
Excellent	1,942	35.7

Variable	N	Weighted %
All	**5,268**	**100.0**
Very Good	1,143	20.2
Good	660	11.7
Fair	185	3.1
Poor	64	1.0
Pain		
None	3,463	64.7
Mild	552	11.1
Moderate	948	18.7
Severe	298	5.5
General health		
Excellent	504	10.5
Very Good	1,544	30.9
Good	1,711	31.8
Fair	1,094	19.2
Poor	413	7.6
Arthritis		
Yes	3,539	63.4
No	1,727	36.6
Cancer		
Cancer	34	0.5
No Cancer	5,234	99.5
Diabetes		
Yes	1,210	21.4
No	4,058	78.6
Cardiovascular Disease		
Yes	1,540	26.5
No	3,727	73.5
Hypertension		
Yes	3,319	59.1
No	1,944	40.8
Depression		
CES-D >= 3	1,066	20.3
CES-D < 3	4,202	79.7
BMI		
Normal or Underweight	1,241	22.6
Overweight	1,872	35.7
Obese	2,131	41.2
Smoking Status		
Current smoker	657	13.9
Non-smoker	2,327	43.2
Physical activity		

Variable	N	Weighted %
All	**5,268**	**100.0**
>= twice/week	3,001	59.0
< twice/week	2,267	41.0

Note: Based on 5,268 respondents 50 years and older, living in the United States, alive and with complete TL data in 2008, and with complete sleep data in 2006. Depression measured with Center for Epidemiologic Studies-Depression scale scores (Yes CESD >= 3, and "No" CES-D <3) BMI = Body Mass Index. Percentages weighted using weights supplied in the HRS dataset to account for the multistage area probability design.

** Percentage not equal to 100% some respondents did not answer this question.

Table 2

N and Weighted Percentages of Sleep Quality Items Measured in 2006 Adults aged 50 Years or Older Health Retirement Study, 2006 – 2008

Sleep Trouble Questions	N	Wt %
Trouble falling asleep		
Most time	661	12.4
Some time	1,619	30.4
Rare/never	2,988	57.2
Trouble waking up during the night		
Most time	1,368	25.7
Some time	1,876	34.8
Rare/never	2,024	39.5
Trouble waking up too early in the morning		
Most time	683	12.8
Some time	1,597	29.9
Rare/never	2,988	57.2
Feel rested in the Morning		
Rare/never	776	16.2
Some time	1,235	24.6
Most time	3,257	59.2
Take Sleep medication		
Yes	942	18.0
No	4,326	82.0
At least one sleep problem		
One or more	4224	80.2
None	1043	19.8

Note: Based on 5,268 respondents 50 years and older, living in the United States, alive and with complete TL data in 2008, and had no missing data in any of the sleep quality items. At least one sleep problem computed for all respondents who answered sometimes/most times to any of the 4 sleep problems. Percentages weighted using weights supplied in the HRS dataset to account for the multistage area probability design.

Table 3

Selected characteristics of Adults Aged 50 years or Older By Sleep Quality Item (Well-rested in the morning) Measured in 2006 Health Retirement Survey 2006- 2008

Variable	Most of the time Wt%	Sometimes Wt%	Rarely/never Wt%	p-value
Sex				
Women	17.5	25.3	57.3	0.021
Men	14.6	23.7	61.7	
Age				
50 - 64	20.1	28.3	51.7	< 0.001
65-69	12.3	22.7	65.0	
70-79	12.6	20.9	66.5	
Above 80	13.4	19.9	66.7	
Race				
White	16.5	23.9	59.5	0.104
African American	12.5	29.2	58.2	
Other	16.8	25.5	57.7	
Marital status				
Married	14.7	23.9	61.4	< 0.001
Divorced/Separated/widowed	19.6	23.7	56.6	
Single	11.3	44.9	43.9	
Education				
Less than HS	22.4	24.3	53.3	< 0.001
High School	14.9	24.9	60.2	
Some college	15.3	24.8	59.9	
College Degree	14.2	24.2	61.6	
Income (Federal Poverty Line)				
Poor	22.7	28.6	48.7	< 0.001
Low income	19.0	25.2	55.8	
Mod income	15.1	24.6	60.4	
High income	14.8	23.6	61.6	
Childhood Health				
Excellent	14.7	24.0	61.2	< 0.001
Very Good	16.4	26.5	57.1	
Good	18.6	25.8	55.5	
Fair	28.1	23.1	48.8	
Poor	36.1	26.5	37.5	

Note: Based on 5,268 respondents 50 years and older, living in the United States, alive and with complete TL data in 2008, and with complete sleep data in 2006. Depression measured with Center for Epidemiologic Studies-Depression scale scores (Yes CESD >= 3, and “No” CES-D <3) BMI = Body Mass Index. Percentages weighted using weights supplied in the HRS dataset to account for the multistage area probability design. P-values derived from Rao-scott chi-square tests for difference between groups.

Table 4

Regression Coefficient Estimates and Standard Errors of Sleep Quality Items Measured in 2006 From Separate Ordinary Least Squares Regressions on Telomere Length In adults aged 50 years or Older (Health Retirement Survey, 2006 – 2008)

	UNADJUSTED MODEL			PARTIALLLY ADJUSTED MODEL (Age, Sex, Race, Education, SES)			FULLY ADJUSTED MODEL		
	B	SE	P value	B	SE	p value	B	SE	p value
Trouble falling asleep									
Sometimes/Most times	0.00	0.02	0.66	0.01	0.04	0.74	−0.03	0.04	0.49
Rarely/Never	Ref			Ref			Ref		
Trouble waking up during the night									
Sometimes/Most times	−0.02	0.02	0.37	0.01	0.03	0.66	0.01	0.03	0.66
Rarely/Never	Ref			Ref			Ref		
Trouble waking up too early in the morning									
Sometimes/Most times	0.00	0.03	0.99	−0.02	0.03	0.48	−0.02	0.04	0.63
Rarely/Never	Ref			Ref			Ref		
Feel rested in the morning									
Rarely/Never	−0.04	0.02	0.05	−0.05	0.02	0.02	−0.08	0.03	<0.01
Sometimes/Most times	Ref			Ref					Ref

Note: Based on 5,268 respondents 50 years and older, living in the United states, alive and with complete TL data in 2008, and with no missing data in any of the sleep quality items. Model 2 adjusted for Age, Sex, Race, Education and Income. Model 3 adjusted for Age, Sex, Race, Education, Income, childhood health, depression, BMI, smoking status, Medicare insurance, cognition, pain, general health, life satisfaction and exercise,

Table 5.

Feeling Rested in The Morning by Other Sleep Problems Adults Aged 50 Years or Older Health Retirement Study, 2006 – 2008

	FEELING RESTED IN THE MORNING				
SLEEP PROBLEM	**Rarely/Never**		**Sometimes/Most times**		
	N	**Wt %**	**N**	**Wt %**	**p-value**
Trouble falling asleep					
Sometimes/Most times	492	10.5	1,788	32.5	<0.0001
Rarely/Never	284	6.0	2,704	51.5	
Trouble waking up during the night					
Sometimes/Most times	571	12.1	2,673	48.7	<.0001
Rarely/Never	205	4.2	1,819	35.4	
Trouble waking up too early in the morning					
Sometimes/Most times	455	9.9	1,825	33.0	<.0001
Rarely/Never	321	6.4	2,667	50.8	

Note: Based on 5,268 respondents 50 years and older, living in the United States, alive and with complete TL data in 2008, and with complete sleep data in 2006. Percentages weighted using weights supplied in the HRS dataset to account for the multistage area probability design.