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Depressive Symptoms and Salivary Telomere Length in a Probability Sample of Middle-Aged and Older Adults

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Abstract

Objective—To examine the association between depressive symptoms and salivary telomere length in a probability sample of middle-aged and older adults, evaluate age and sex as potential moderators of this association, and test whether this association was incremental to potential confounds.

Methods—Participants were 3,609 individuals from the 2008 wave of the Health and Retirement Study. Telomere length assays were performed using quantitative real-time polymerase chain reaction (qPCR) on DNA extracted from saliva samples. Depressive symptoms were assessed via interview, and health and lifestyle factors, traumatic life events, and neuroticism were assessed via self-report. Regression analyses were conducted to examine the associations between predictor variables and salivary telomere length.

Results—After adjusting for demographics, depressive symptoms were negatively associated with salivary telomere length (b = -.003, p = .014). Furthermore, this association was moderated by sex (b = .005, p = .011), such that depressive symptoms were significantly and negatively associated with salivary telomere length for men (b = -.006, p < .001) but not for women (b = -.001, p = .644). The negative association between depressive symptoms and salivary telomere length in men remained statistically significant after additionally adjusting for cigarette smoking, body mass index, chronic health conditions, childhood and lifetime exposure to traumatic life events, and neuroticism.

Conclusions—Higher levels of depressive symptoms were associated with shorter salivary telomeres in men and this association was incremental to several potential confounds. Shortened telomeres may help account for the association between depression and poor physical health and mortality.

Keywords

depression; depressive symptoms; gender difference; sex difference; telomere; telomere shortening

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Introduction

Depression is a common and serious mental health problem. Worldwide, the lifetime and annual prevalence of major depressive episode is estimated at 14.6% and 5.5% in high-income countries and 11.1% and 5.9% in low-income countries, respectively (1). Depression is associated with a variety of physical health problems, including cardiovascular diseases (2) and type 2 diabetes mellitus (3), and with increased risk of mortality (4, 5).

Telomere biology may help to explain the association between depression and physical health and mortality. Telomeres are DNA-protein structures located at the ends of chromosomes that serve to maintain DNA integrity during cell division (6). Telomeres shorten with successive cell divisions, and gradual shortening of telomeres after each cell division eventually can lead to a loss of cellular division capacity and cell death (6). Consequently, telomere length has come to be viewed as a biomarker of cellular aging (7, 8), as well as a potential biomarker for factors that contribute to aging and age-related diseases (6). A meta-analysis of 124 cross-sectional and 5 longitudinal studies evaluating the association between age and telomere length reported a yearly loss of 24.7 base pairs (9). Meta-analytic results further indicate that shorter telomere length from DNA extracted from blood (i.e., leukocyte telomere length) is significantly associated with cancer (10), myocardial infarction, stroke, and type 2 diabetes mellitus (11), as well as with mortality (12). Although much of the research on telomere length and health conditions has been cross-sectional, longitudinal studies have shown that shorter telomeres are associated with the incidence of age-related health conditions (e.g., 13), suggesting that accelerated cell aging, as indexed by shorter telomere length, may be a determinant of early onset of diseases of aging (6, 8). Consequently, understanding factors that may accelerate or ameliorate telomere shortening has become an important focus of researchers interested in understanding aging and age-related illness.

Prior research suggests that depression is associated with leukocyte telomere length. Researchers have examined both depressive symptoms and clinical diagnosis of depression, and a meta-analysis of 30 effect sizes yielded a combined weighted effect size (r) of -.12 between depression and telomere length (14). Furthermore, there were no statistically significant differences in weighted effect sizes between studies that used self-report to measure depression versus those that used an interview or diagnosis, or between studies that examined correlations between telomere length and depressive symptoms versus group comparisons in telomere length.

This study was conducted to expand research examining the association between depression and telomere length in several directions. First, whereas prior studies have evaluated telomere length obtained from DNA extracted from blood leukocytes, we examined the association between depression and telomere length obtained from DNA extracted from saliva. Saliva contains both white blood cells and epithelial cells (15), and therefore has both similarities and differences to previously used sources of DNA in studies examining the association between depression and telomere length. Presumably, the differences in leukocyte telomere length associated with depression (and other health outcomes) would be found in DNA extracted from other cells, but this hypothesis remains to be tested.

Second, we examined demographic moderators of the association between depression and salivary telomere length, as it seems reasonable to expect that the strength of the association may vary among individuals. For example, in the meta-analysis of the association between depression and telomere length, stronger associations were observed in studies that had samples with lower mean age (14), and a study that examined the association between depressive symptoms and telomere length in three age cohorts found that symptoms were associated with telomere length only in the youngest cohort (16). Therefore, we examined whether age moderated the association between depression and salivary telomere length. In addition, we examined whether this association was moderated by sex. A meta-analysis of the association between depression and mortality in community samples found that this association was larger for men than for women (4). If shortened telomeres may partially account for the association between depression and poor health and mortality, then the strength of the association between depression and telomere length would be expected to be greater in men than in women.

Third, we sought to rule out several potential confounds of the association between depressive symptoms and salivary telomere length. It is possible that this association is secondary to confounding factors, as prior research has shown that leukocyte telomere length is associated with a range of demographic, environmental, behavioral, and psychosocial factors (for a review, see 17). For example, leukocyte telomere length is negatively correlated with age (9) and positively correlated with educational attainment (18), and on average, longer telomeres have been found in women relative to men (19) and in African Americans relative to Whites (20). Furthermore, telomere length is associated with lifestyle factors such as cigarette smoking (21) and body mass index (BMI) (22), as well as with indicators of stress (23) and personality factors such as neuroticism (24). Given that many of these same variables are associated with depression, it is possible that the association between depression and telomere length is secondary to these other variables. In the current study, we examined the association between depressive symptoms and salivary telomere length, statistically adjusting for several variables that may account for this association.

In summary, this study was conducted to (a) examine the association between depressive symptoms and salivary telomere length in a probability sample of people 50 years of age; (b) evaluate age and sex as potential moderators of this association; and (c) rule out demographic variables, lifestyle factors, chronic health conditions, traumatic life events, and neuroticism as rival explanations for this association.

Materials and Methods

Participants

Participants were drawn from the Health and Retirement Study (HRS), which is a multistate probability cohort sample of households in the United States including at least one person over the age of 50. In 2008, a random half of HRS households were preselected to additionally participate in an Enhanced Face-to-Face Interview, which included a questionnaire on psychosocial topics and collection of saliva samples. Data were collected from more than one member of the household in nearly half of the remaining households. To

account for nonindependence of household data, we selected for analyses all people for whom data were available for only one household member and, for each multi-participant household, we selected at random one member. We excluded data from 12 people who had missing data on the measure of depressive symptoms, leaving a final sample of 3,609 people. Descriptive information for the sample is provided in Table 1.

Measures

Telomere Length (25)—Telomere length was measured from saliva; prior research has shown that the quality of DNA from saliva samples is comparable with blood samples (26, 27). Salivary telomere length correlates with leukocyte telomere length (28, 29) and positive correlations are observed for telomere length measured in leukocytes, skeletal muscle, skin, and subcutaneous fat (30). In addition, salivary telomere length correlates with (a) other risk factors for adverse health outcomes (e.g., familial risk for depression; 31); (b) known correlates of telomere length as measured by blood leukocytes, including age (32), tobacco smoking (32), perceived stress (32), other measures of adversity and disadvantage (28, 29); and (c) hypothalamic-pituitary axis (HPA) dysregulation (i.e., coritsol reactivity to stress; 31). Saliva samples were obtained using an Oragene[®] Collection Kit, and were sent to a central laboratory for DNA extraction. The average DNA concentration of the Oragene saliva samples was 64.72 µg/mL, and the typical DNA yield was 14.65 µg. DNA samples were sent in 96 well plates to Telome Health, where they were stored in original plates in an -80° freezer upon arrival and assayed within 1 week. Telomere length assays were performed using quantitative real-time polymerase chain reaction (qPCR), adapted from a method by Cawthon (33) and described in detail elsewhere (34). Ratio of telomere sequence copy number in each respondent's sample (T) to a single gene copy number (S) was determined. T/S ratio is proportional to mean telomere length. Genomic DNA from pooled 100 male donors was used as the standard reference. A triplicate serial dilution was made to create a 6-point standard curve containing 5, 1.6667, 0.5556, 0.1852, 0.6173 and 0.02058 ng of DNA respectively in each reaction tube. The accepted quality control criteria of PCR amplification efficiency was >75% for T runs and >80% for S runs (with mean amplification efficiencies of 0.88 [SD = 0.32] and 0.94 [SD = 0.33], respectively), and the inter-assay variability (coefficient of variation) acceptance criterion was <12.5%. Quality control success rate was 98.17%. Coefficients of variation for mean T/S ratios of quality control samples ranged from 3.5% to 6.3%. Because salivary telomere length was not normally distributed in this sample, data were transformed using the natural logarithm to improve normality, which is consistent with other studies on salivary telomere length (32).

Depression—Depressive symptoms were measured with an adapted version of the Center for Epidemiologic Studies Depression Scale (CES-D; 35). The HRS used an abbreviated 8-item version of the scale, which was designed to reduce the length of survey interviews for elderly respondents while measuring the continuum of symptoms captured by the original scale (36). The original four-level response format of the CES-D was changed to a Yes/No response format in the HRS to simplify telephone administration of the measure (37). The CES-D is scored by summing the number of "yes" answers across the eight items (with positive items reverse-scored); scores range from 0 - 8, with higher scores indicating more severe symptoms. The abbreviated scale has comparable reliability, validity, and

dimensionality to the full version (38), and a cutoff of 4 on the HRS 8-item, Yes/No version of the CES-D corresponds to a cutoff of 16 on the 20-item CES-D, typically used for defining clinically elevated levels of symptoms (37). Cronbach's alpha for the current sample was .81.

Body Mass Index—Participants were asked their height and weight, and body mass index (BMI) was based on their self-report using the formula, BMI = [weight in pounds/(height in inches)²] × 703. HRS interviewers measured height and weight for a subset of 3,404 people and BMI derived from self-report was highly correlated (r = .90) with BMI derived from measured height and weight.

Health Conditions—Chronic health conditions were assessed with interview questions, in which participants were asked, "Has a doctor ever told you that you have" (a) diabetes or high blood sugar; (b) cancer or a malignant tumor, excluding minor skin cancer; (c) a heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems; and (d) a stroke. We used dummy coding (0 = no, 1 = yes) to classify lifetime history of each condition.

Childhood Traumatic Life Events—Traumatic events occurring during childhood were measured with a checklist, in which participants were asked to indicate whether each of four events (e.g., *parents drink or use drugs so often that it caused problems in the family; physically abused by either of your parents*) had occurred before they were 18 years old. Items were taken from an ongoing longitudinal study on the health consequences of trauma in older adults (39) and events such as these are common to many measures of traumatic life events. Exposure to traumatic life events before the age of 18 was calculated by summing the number of events checked as having occurred, with scores > 2 recoded as 2, due to the small number of people who experienced more than 2 childhood traumatic life events.

Lifetime Traumatic Life Events—Lifetime exposure to traumatic events was measured with a checklist, in which participants were asked to indicate whether seven traumatic life events (e.g., *major fire, flood, earthquake or other natural disaster; life-threatening illness or accident*) had occurred at any point in their life. Events such as these are common to measures of traumatic life events (39). Lifetime exposure to traumatic life events was calculated by summing the number of events checked as having occurred, with scores >4 recoded as 4, due to the small number of people who experienced more than 4 traumatic life events.

Neuroticism—Personality was measured with an adjective measure developed for the Midlife Development in the United States survey by selecting adjectives that (a) were most consistently identified in the literature as trait markers for Big Five personality traits in existing personality trait lists, and (b) demonstrated the highest factor loadings or item-total correlations during scale construction in 1994 in a United States probability sample of 1,000 people between the ages of 30 and 70 (40). The neuroticism scale consists of four adjectives (*moody, nervous, calm, worrying*) that were rated on a 4-point scale indicating how well each adjective described the respondent (1 = not at all, 4 = a lot). Items were reverse scored as necessary and averaged to create a total score, with higher scores indicating higher

standing on the measure ($\alpha = 74$). This scale significantly correlates with the neuroticism scale from the NEO Personality Inventory Short Form (see http://www.brandeis.edu/departments/psych/lachman/pdfs/revised-midi-scales.pdf).

Demographics—Standard questions were administered to assess for age, sex, race (coded as White, Black, other), ethnicity (Latino/Hispanic, not Latino/Hispanic), and years of education.

Statistical Analysis

The association between depressive symptoms and salivary telomere length was examined using linear regression. In Model 1, we regressed telomere length on the continuous measure of depressive symptoms, statistically adjusting for demographics. Because statistical interactions qualify the interpretation of a main effect, we then evaluated whether the association between depressive symptoms and salivary telomere length was moderated by age or sex (Model 2). Multiplicative interaction terms were created and entered into the regression analyses, controlling for the component terms (and other demographics); age and depressive symptoms were mean deviated prior to creating the interaction terms (41). If the main or moderated association between depressive symptoms and salivary telomere length was statistically significant, we then evaluated the covariation between depressive symptoms and salivary telomere length, additionally accounting for lifetime cigarette smoking (based on participant report), BMI, chronic health conditions, childhood traumatic life events, lifetime traumatic life events, and neuroticism (Model 3). Finally, we conducted parallel analyses using a categorical measure of depressive symptoms (using a cutoff of > 4 on the CES-D) to examine whether clinically elevated levels of depressive symptoms were associated with salivary telomere length. We used HRS sample weights (i.e., the 2008 Biomarker sample weights) for descriptive statistics and all analyses. These weights account for differential selection probabilities, adjust for differential baseline and wave-specific nonresponse, and make the weighted sample representative of non-institutionalized individuals in the United States population in the age-eligible range.

RESULTS

The weighted mean salivary telomere length was 1.37 (SD = 0.58); the mean log transformed salivary telomere length was 0.12 (SD = 0.12) (for a frequency distribution of log transformed scores, see Figure S1, Supplemental Digital Content 1). The mean number of depressive symptoms reported on the 8-item CES-D was 1.47 (SD = 2.02). Descriptive statistics for and bivariate associations between each of the covariates and salivary telomere length are presented in Table 1.

We first examined the multivariate association between depressive symptoms and salivary telomere length, statistically adjusting for demographic variables. As can be seen for Model 1 in Table 2, depressive symptoms were significantly and negatively associated with salivary telomere length in the full sample: higher levels of depressive symptoms were associated with shorter salivary telomeres. We then evaluated whether the association between depressive symptoms and salivary telomere length was moderated by age or sex. After adjusting for the component terms (and other demographics), the association between the

Age × Depressive Symptoms interaction and salivary telomere length was not statistically significant, b = .000, SE = .000, $\beta = .019$, p = .252, whereas the association between the Sex × Depressive Symptoms interaction and salivary telomere length was statistically significant; the result for this interaction term is presented in Model 2 in Table 2; a scatterplot (Figure S2) depicting the interaction can be found in Supplemental Digital Content 1. Because sex was dummy coded, the coefficient for depressive symptoms provides a test of the simple slope between depressive symptoms and salivary telomere length for the reference group (41). As men were the reference group (i.e., the group coded "0") in this analysis, results indicate that the association between depressive symptoms and salivary telomere length was statistically significant for men (Model 2, Table 2, first row of data under the Depressive Symptoms heading). When we re-ran the analysis and reversed coding of sex such that women were coded "0," the coefficient for depressive symptoms was not significant, indicating that the association between depressive symptoms and salivary telomere length was not statistically significant for women (Model 2, Table 2, Table 2, second row of data under Depressive Symptoms heading).

In Model 3, we added lifetime cigarette smoking status, BMI, chronic health conditions, childhood traumatic life events, lifetime traumatic life events, and neuroticism. As can be seen in Table 2, results indicated that after additionally adjusting for these factors, the association between the Sex \times Depressive Symptoms interaction and salivary telomere length remained statistically significant, and that depressive symptom severity was significantly and negatively associated with salivary telomere length for men but not for women.

The CES-D is commonly used for identifying people with clinically elevated depressive symptoms. In this sample, 14.9% of participants scored 4 on the CES-D, which corresponds to the cutoff of 16 on the 20-item CES-D that has been used for defining clinically elevated levels of depressive symptoms (37). We examined whether salivary telomere length differed for people who scored above and below the CES-D cutoff for clinically elevated symptoms. Results indicated that (a) after adjusting for demographic variables, the categorical measure of depressive symptoms was not significantly associated with salivary telomere length in the full sample; (b) sex, but not age, moderated the association between the categorical measure of depression and salivary telomere length, such that the association was statistically significant for men (with men scoring above the cutoff having shorter salivary telomeres than those scoring below the cutoff) but not for women; and (c) the association between clinically elevated depressive symptoms and salivary telomere length remained statistically significant for men when additionally adjusting for lifetime cigarette smoking status, BMI, chronic health conditions, childhood traumatic life events, lifetime traumatic life events, and neuroticism (see Table S1, Supplemental Digital Content 1), although the interaction term was no longer statistically significant (indicating that after adjusting for these other variables, the difference between men and women on the slope of the association between clinically elevated depressive symptoms and salivary telomere length was not statistically significant).

DICSUSSION

This study was conducted to examine the association between depressive symptoms and salivary telomere length in a probability sample of adults 50 years of age, evaluate whether this association was moderated by age or sex, and test whether this association was incremental to several possible confounds. After adjusting for demographic variables, a continuous measure of depressive symptoms was significantly and negatively associated with salivary telomere length. However, the strength of the association obtained in this study is smaller than that found in a meta-analysis of the association between depression and leukocyte telomere length (r = .12) (14), and the association between clinically elevated levels of depressive symptoms and salivary telomere length was not statistically significant for the full sample. It may be that the association found for leukocyte telomere length. Alternatively, it may be that the weaker association obtained in this study relative to those reported in the meta-analysis is due to age of participants in the current sample, who were all

50 years old and were 67 years old on average. Although age did not moderate the association between depressive symptoms and salivary telomere length in this study, because variability in leukocyte telomere length in a population can decrease with increasing age (7), the strength of the association between depression and telomere length in middle-aged and older people would be expected to be smaller than that which would be obtained from a sample that included younger people. Consistent with this interpretation, a meta-analysis of the association between depression and leukocyte telomere length found that stronger associations were obtained for studies with lower mean age (14).

Furthermore, the current results indicate that after adjusting for demographic variables, sex moderated the association between depressive symptoms and salivary telomere length, such that that this association was statistically significant for men but not for women. Evidence for sex moderation was obtained for both the continuous and categorical measures of depressive symptoms. These results are similar to those obtained in another study, which found that for men but not for women, persistence of internalizing disorders (i.e., depression, generalized anxiety disorder, and post-traumatic stress disorder) across repeated assessments from ages 11 to 38 years was associated with shorter telomeres obtained from blood at age 38 years, and incidence of internalizing disorder between two time points (26 and 38 years) was associated with greater telomere shortening for the same time points (42). Similarly, the results from a meta-analysis examining the association between depression and mortality in community samples found that the association was larger for men than for women (4). The finding that sex moderated the strength of the association between depressive symptoms and salivary telomere length in the current study is consistent with the perspective that telomere shortening may contribute to the sex difference in the strength of the association between depression and mortality.

The current study builds on prior studies that have evaluated the association between depressive symptoms and telomere length not only by examining salivary telomere length but also by ruling out several potential confounds of this association. Specifically, the association between depressive symptoms and salivary telomere length for men remained statistically significant when adjusting for demographic variables, (age, race, education

attainment), cigarette smoking, BMI, chronic health conditions, childhood traumatic life events, lifetime traumatic life events, and neuroticism. Because this association remained statistically significant when adjusting for these other variables, greater confidence can be had that the association between depressive symptoms and salivary telomere length is not secondary to these other factors. These findings add to a growing literature demonstrating that the association between mental health and telomere length is incremental to other correlates of telomere length (e.g., 42).

We also evaluated the bivariate association between salivary telomere length and other variables, which were considered as potential confounds of the association between depressive symptoms and salivary telomere length. These results, presented in Table 1, suggest that salivary telomere length was significantly and negatively associated with age, being White, being a cigarette smoker, having cancer or heart disease, and lifetime exposure to traumatic life events, and significantly and positively associated with being Black or of another race. These results replicate prior studies that have shown that salivary telomere length is associated with age (32) and tobacco smoking (32) and suggest that salivary telomere length is also associated with other correlates of leukocyte telomere length, including race (20), cancer (10), heart disease (11), and stress (23). As such, the current results add to the growing body of research suggesting that the correlates of telomere length assessed from saliva show similar patterns of association with correlates of leukocyte telomere length. BMI was positively correlated with salivary telomere length, which is inconsistent with the results from a meta-analysis that found a negative association between BMI and leukocyte telomere length (22). However, there were individual studies included in the meta-analysis that, similar to the current study, found a positive association between BMI and leukocyte telomere length (e.g., 43, 44).

Results from the study should be interpreted in light of several limitations. First, the criteria required for PCR application efficiency (>75% for T runs and >80% for S runs) in this study are lower than those used in more recent studies, in which efficiency values between 90-110% are considered acceptable. Lower efficiencies indicate greater amplification than would be expected in a cycle, which affect the concentration estimates and increase error to the T/S values based on samples from those plates. Second, the design of the study was cross-sectional, and continued research is needed on the longitudinal association between depressive symptoms and salivary telomere length. Third, participants were all 50 years of age. By 2060, it is anticipated that nearly one of every four Americans – 98 million people – will be age 65 or older, which is more than double the number of older adults in the United States in 2014 (45). Although focusing on older adults is important given the growth in the number and proportion of older adults in the United States, because variability in leukocyte telomere length has been shown to decrease with increasing age (7), the restricted age range may have affected results for the Age × Depressive Symptoms interaction. Future research is needed to examine this interaction with a broader age range and whether the incremental association between the Sex × Depressive Symptoms interaction and salivary telomere length, adjusting for potential confounds, is found in younger participants. Fourth, the assessments of traumatic life events and neuroticism were based on relatively short measures. Although brief measures are typically used in large epidemiological surveys due to their lower costs and reduced respondent burden relative to longer measures, the use of

such measures may underestimate the true association between these constructs and telomere length. Therefore, future research is needed to test whether the association between depressive symptoms and salivary telomere length remains statistically significant when statistically adjusting for more comprehensive measures of these constructs. Relatedly, there are a variety of ways of conceptualizing stress, and future research is needed to see whether the association between depressive symptoms and salivary telomere length remains statistically significant when adjusting for other measures of stress, such as perceived stress, which has been shown to covary with leukocyte telomere length in prior studies (23). Fifth, although several potential confounds were included in this study, there may be other constructs that are associated with both depressive symptoms and salivary telomere length that may be potential confounds of observed associations between these variables, and examining these variables in future research would further increase confidence that the association between depressive symptoms and salivary telomere length is not secondary to some other construct. Finally, the study examined only telomere length, which was measured in saliva. In addition to telomere length, researchers have studied other aspects of telomere functioning, such as telomerase – an enzyme that adds nucleotides to and protects telomeric ends (6) - and future research is needed to examine sex differences in the association between depressive symptoms and telomerase activity and whether this association is incremental to potential confounding variables like those assessed in the current study.

CONCLUSION

Results from this probability sample of people 50 years of age suggest that (a) the association between depressive symptoms and salivary telomere length was moderated by sex, and that the association was statistically significant for men but not for women; and (b) the association between depressive symptoms and salivary telomere length in men remained statistically significant when adjusting for several important potential confounds, including demographics, cigarette smoking, BMI, chronic health conditions, childhood and lifetime exposure to traumatic life events, and neuroticism. These results add to our understanding of how depression may be associated with age-related illnesses and shortened life span, which may help to advance understanding of the links between depression on the one hand and health and mortality on the other hand, including potential sex differences in these pathways. Furthermore, because saliva collection is noninvasive, painless, relatively inexpensive, and rapidly renewable (15), the finding that salivary telomere length was associated with depression (and several variables treated as covariates in these analyses) suggests that assessment of the correlates and predictors of salivary telomere length holds considerable promise in understanding telomere biology.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Acronyms

BMI	body mass index
HRS	Health and Retirement Study
qPCR	quantitative real-time polymerase chain reaction

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Table 1

Descriptive Data on Study Variables and Bivariate Associations with Salivary Telomere Length

Variable			ull San	nple			Men			Women		+	χ ²
	W	SD	%	u	'n	Μ	SD	%	W	SD	%		
Age (Years)	67.0	10.0			11	65.9	9.5		67.8	10.3		-5.9 **	
Sex													
Women			56.3	2205	.03								
Men			43.7	1404									
Race													
White			87.7	3017	11			88.1			87.5		0.31
Black			9.7	506	.11			9.1			10.1		1.10
Other			2.6	86	.03*			2.8			2.4		0.53
Ethnicity (Latino)			7.4	340	.03			7.0			7.8		0.67
Education (Years)	12.9	3.0			.01	13.2	3.1		12.7	2.9		5.5 **	
Lifetime Cigarette Smoker			57.4	2036	05 **			66.4			50.3		95.4 **
Body Mass Index (kg/m ²)	28.4	6.0			.06**	28.4	5.4		28.3	6.5		0.5	
Diabetes			19.5	811	.01			21.4			18.1		6.2
Cancer			14.1	595	04 *			13.8			14.3		0.1
Heart Disease			25.0	1024	06			27.7			22.8		11.5**
Stroke			6.4	270	02			7.8			5.3		9.5**
Childhood Traumatic Life Events	0.5	0.7			.02	0.6	0.7		0.4	0.6		8.3 **	
Lifetime Traumatic Life Events	1.2	1.2			04	1.2	1.2		1.2	1.2		1.3	
Neuroticism	2.0	0.6			.02	2.0	0.6		2.1	0.6		-4.7 **	
Depressive Symptoms	1.5	2.0				1.3	1.9		1.6	2.1		-5.4 **	
Salivary Telomere Length b	0.1	0.1				0.1	0.1		0.1	0.1		-1.9	
Note.													
a Bivariate correlation with salivary te	elomere	length.											

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 $b_{\text{Log 10 transformed scores.}}$

Table 2

Multivariate Analysis of the Association between Continuous Assessment of Depressive Symptoms and Salivary Telomere Length

Variable		Mo	del 1			Mo	del 2			Mo	del 3	
	p	SE	β	d	\boldsymbol{q}	SE	β	d	p	SE	β	d
Age (Years)	001	000.	106	<.001	001	000.	107	<.001	001	000.	063	.001
Sex (Women)	.011	.004	.045	.007	.011	.004	.046	.005	600.	.004	.039	.028
Race ^a												
Black	.044	.007	.106	<.001	.044	.007	.106	<.001	.043	.007	.105	<.001
Other	.022	.013	.028	.091	.021	.013	.027	.110	.013	.014	.017	.335
Ethnicity (Latino)	.012	.008	.026	.156	.011	.008	.023	.205	.007	600.	.016	.390
Education (Years)	.001	.001	.012	.498	000.	.001	.010	.590	.001	.001	.021	.278
Lifetime Cigarette Smoker									011	.004	047	.007
Body Mass Index (kg/m ²)									.001	000.	.060	.001
Diabetes									004	.005	014	.442
Cancer									008	.006	024	.159
Heart Disease									010	.005	037	.040
Stroke									000.	600.	001	.973
Childhood Traumatic Life Events									.005	.003	.029	.106
Lifetime Traumatic Life Events									002	.002	017	.327
Neuroticism									900.	.004	.033	.080
Depressive Symptoms	003	.001	042	.014								
Reference Group = Men					006	.002	096	<.001	006	.002	093	.001
Reference $Group = Women$					001	.001	010	.644	001	.001	019	.432
$\mathbf{Sex} \times \mathbf{Depressive} \ \mathbf{Symptoms}$.005	.002	.068	.011	.004	.002	.058	.033

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^aWhite was the reference group.