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Leukocyte Telomere Length and Mortality in the National Health and Nutrition Examination Survey, 1999–2002

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Abstract

Background—This study examined the association between leukocyte telomere length – a marker of cell aging – and mortality in a nationally representative sample of US adults aged 50–84. We also examined moderating effects of age, sex, race/ethnicity, and education.

Methods—Data were from the National Health and Nutrition Examination Survey (NHANES), 1999–2002 (n=3,091). Cox proportional hazards regression was used to estimate the risk of all-cause and cause-specific mortality adjusting for sociodemographic characteristics, smoking, body mass index, and chronic conditions.

Results—870 deaths occurred over an average of 9.5 years of follow-up. In the full sample, a decrease of 1 kilobase pair in telomere length at baseline was marginally associated with a 10% increased hazard of all-cause mortality (HR: 1.1, 95% CI: 0.9, 1.4) and a 30% increased hazard of death due to diseases other than cardiovascular disease or cancer (HR: 1.3, 95% CI: 0.9, 1.9). Among African-American but not white or Mexican-American respondents, a decrease of 1 kilobase pair in telomere length at baseline was associated with a two-fold increased hazard of

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cardiovascular mortality (HR: 2.0, 95% CI: 1.3, 3.1). There was no association between telomere length and cancer mortality.

Conclusions—The association between leukocyte telomere length and mortality differs by race/ethnicity and cause of death.

Telomeres are the protective caps at the ends of eukaryotic chromosomes. Each time a somatic cell divides, a portion of the telomeric DNA fails to replicate; thus, telomeres naturally shorten with mitosis.[1,2] Telomerase, the cellular enzyme that can counteract shortening by elongating and protecting telomeres, is kept at low levels in normal human cells.[3] When telomeres become too short, cells lose the ability to grow and divide.[4,5] Human genetic mutations that result in short telomeres are associated with a group of conditions collectively called “telomere syndromes” that resemble premature onset of diseases of aging, [6] consistent with a role of telomere shortening in human aging in the general population.[7]

Recent studies have found that shorter leukocyte telomere length is associated with numerous age-related diseases, including cardiovascular disease,[8–11] type 2 diabetes,[12,13] dementia,[14–16] and cancer,[17,18] independent of chronological age. While a number of studies have also reported that shorter telomeres are associated with increased mortality,[17,19–30] others have failed to find an association between telomere length and survival [31–34] (see the appendix for a summary of findings). In general, studies that have not found an association between telomere length and mortality have examined older populations. Inconsistencies in the literature may be due to differences in sample size and measurement techniques, the use of population versus clinical samples, or unknown biologic differences between those who survive to extreme old age and those with earlier mortality.[35,36]

Using data from the National Health and Nutrition Examination Survey (NHANES) 1999–2002, the current study examined the association between leukocyte telomere length and mortality in a large, nationally representative, socioeconomically and ethnically diverse sample of US adults. This study addressed the following research questions: (1) Is telomere length associated with all-cause mortality in adults aged 50–84? (2) Is telomere length associated with cause-specific mortality? (3) Do associations between telomere length and mortality vary according to age, sex, race/ethnicity, or socioeconomic status (SES)? Although prior research has shown that older age, male sex, white race, and low SES are associated with shorter telomere length,[37,38] it is not known whether the relationship between telomere length and mortality differs according to sociodemographic characteristics. Answering this question could help determine whether telomere length is a comparable indicator of mortality risk across population subgroups.

METHODS

Sample and Procedures

Since 1960, the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC) has conducted The National Health and Nutrition Examination Survey (NHANES) to provide national estimates of the health and nutritional status of the US civilian non-institutionalized population. NHANES 1999–2002 is a cross-sectional,

nationally representative sample of more than 20,000 individuals aged 2 months and older. NHANES 1999–2002 utilized a 4 stage sampling design: 1) primary sampling units (PSUs) consisting primarily of single counties, 2) area segments within PSUs, 3) households within segment areas, and 4) persons within households. On average, 2–3 individuals per household were sampled. NHANES 1999–2002 oversampled low-income persons, persons aged 12–19, persons aged 60 and over, African-Americans, and Mexican-Americans in order to obtain more accurate estimates in these populations.

All NHANES 1999–2002 respondents aged 20 and over were asked to provide DNA samples. Of the 10,291 respondents who were eligible to provide samples of DNA, 7,825 (76%) both provided DNA and consented specifically to future genetic research. We excluded 653 respondents whose self-reported race/ethnicity was “other” or “other Hispanic,” since a goal of this study was to examine race/ethnic differences in the association between telomere length and mortality, and these groups are too diverse for our purposes. Given the possibility of survival bias among the extreme elderly,[36] we also excluded 225 respondents aged 85+. Next, we excluded 3,747 respondents under age 50 since we were interested in mortality due to chronic age-related diseases, which are rare among individuals under 50 years of age. Finally, we excluded an additional 109 respondents from the analytic sample due to missing data on one or more covariates (final n=3,091). Human subjects approval for this study was provided by the Institutional Review Board at the CDC.

Mortality

NHANES 1999–2002 survey data have been linked to death certificate data from the National Death Index, which uses a well-documented and validated method of matching deaths to population data sets.[39,40] Codes for the underlying cause of death have been validated to have a discrepancy rate of approximately five percent.[41] Mortality follow-up data are available from the date of survey participation until December 31, 2011. Person-years of follow-up from the interview date ranged from 0.08 to 12.7, with a mean of 9.5. We examined all-cause mortality, as well as mortality due to cardiovascular disease, cancer, and other diseases (including infectious disease, cerebrovascular disease, diabetes, Parkinson’s disease, Alzheimer’s disease, liver disease, and kidney disease). World Health Organization International Classification of Diseases, Tenth Revision (ICD-10) codes for the underlying causes of death included in these categories can be found in the eAppendix in the electronic version of the journal.

Telomere Length Assay

Aliquots of purified DNA were provided by the laboratory at the Division of Health and Nutrition Examination Surveys, National Center for Health Statistics, Centers for Disease Control and Prevention. Using standardized procedures, DNA was extracted from whole blood and stored at −80°. The telomere length assay was performed in the laboratory of Dr. Elizabeth Blackburn at the University of California, San Francisco, using the quantitative polymerase chain reaction (PCR) method to measure telomere length relative to standard reference DNA (T/S ratio), as described in detail elsewhere.[42,43] Each sample was assayed 3 times on 3 different days. The samples were assayed on duplicate wells, resulting in 6 data

points. Sample plates were assayed in groups of three plates, and no two plates were grouped together more than once. Each assay plate contained 96 control wells. Any assay runs with 8 or more invalid control wells were considered a failed run and were excluded from further analysis (>99% of runs passed this criterion). The mean of the T/S ratio values was calculated, and the largest or the smallest T/S ratio value in the set (whichever deviated most from the mean) was marked as a potential outlier. Then the mean of the T/S ratio value was calculated without the potential outlier. If the absolute value of the log of the ratio between the recalculated mean (excluding the potential outlier) to the value of the potential outlier was greater than 0.4, then the value was marked as an outlier (98.7% of all samples contained no outliers).

The conversion from T/S ratio to kilobase pairs (kb pairs) was calculated based on comparison of telomeric restriction fragment length from Southern blot analysis and T/S ratios using DNA samples from the human diploid fibroblast cell line IMR90 at different population doublings. The formula to convert T/S ratio to kb pairs was (3,274 + 2,413 * (T/S))/1000. DNA samples were coded and the lab was blinded to all other measurements in the study. The CDC conducted a quality control review before linking the telomere data to the NHANES 1999–2002 public use data files. The quality control protocol is available at http://www.cdc.gov/nchs/data/nhanes/genetics/Quality_Control_Public.pdf.

Covariates

All models included controls for the following potential confounders: age (in years), sex (female=1; male=0), race/ethnicity (dummy variables for African-American and Mexican-American, with white as the reference category), education (dummy variables for less than high school, high school, and some college, with college degree as the reference category), smoking (dummy variables for current smoker and former smoker, with never smoker as the reference category), and body mass index (BMI) (the ratio of weight/height^2 in kg/m^2). All models also included an age-squared term to account for potential nonlinearity in the association between age and mortality.

It is not clear whether chronic health conditions are a predictor or an outcome of reduced telomere length, or both. If they are, in fact, a predictor of shorter telomeres, then chronic conditions could potentially confound the association between telomere length and mortality. For this reason, we examined models with and without controls for the following chronic health conditions: cardiovascular disease (participant reported being told by their physician that they ever had a heart attack or stroke, or participant reported being told by their physician that they had coronary heart disease=1; no heart attack, stroke, or coronary heart disease=0), diabetes (participant reported physician diagnosis of diabetes or participant reported current use of medication for diabetes=1; no diabetes or diabetes medication=0), hypertension [participant reported being told by their physician that they had high blood pressure, or participant reported current use of medications to treat high blood pressure, or average measured blood pressure (the average of all measurements taken after dropping the first measurement) was 140 mmHg systolic or 90 mmHg diastolic=1; no high blood pressure or blood pressure medication=0], and high cholesterol (participant reported physician diagnosis of high cholesterol, or participant reported current use of medication to treat high

cholesterol, or participant had a total cholesterol level of 240 mg/dL or higher=1; no high cholesterol or cholesterol medication=0).

Data Analysis

We used Cox proportional hazards regression to estimate the risk of all-cause and cause-specific mortality. Censoring was done at the date of death or December 31, 2011. For the analysis of cause-specific mortality, deaths due to causes other than the cause of interest were treated as censored at the date of death. The time-scale was time-on-study. We verified the proportionality assumption by testing a model for each mortality outcome that included interactions of all the predictors with time. We examined models with telomere length as a continuous predictor and as a categorical predictor (dummy variables for the first, second, and third quartiles of telomere length, with the fourth quartile as the reference category). In these models, the continuous telomere length measure was multiplied by −1 to reflect increased risk of mortality associated with shorter telomeres. To determine whether the association between telomere length and mortality was moderated by age, sex, race/ethnicity, or SES we also examined interactions between age and telomere length, sex and telomere length, race/ethnicity and telomere length, and education and telomere length. All regression models accommodated the complex sampling design of NHANES by incorporating strata and primary sampling unit indicators, as well as sample weights for the genetic subsample.[44] The use of sample weights, which account for oversampling and non-response bias, helps ensure that estimates are representative of the general US population. Analyses were conducted on-site at the CDC Research Data Center in Atlanta and remotely using ANDRE, the CDC's remote access system for the analysis of restricted data.

RESULTS

Table 1 shows mean leukocyte telomere length by selected characteristics of study participants. Age was inversely associated with telomere length; men had shorter telomeres than women; African-Americans had longer telomeres than whites and Mexican-Americans; and education was positively associated with telomere length. Telomere length did not vary by smoking status or body mass index. Telomere length was shorter by 13.5 base pairs per year of age; and approximately six percent of the variation in telomere length was explained by age (R^2=.06; results not tabulated).

A total of 870 deaths occurred during the follow-up period. The results of the Cox proportional hazards models for all-cause mortality, cardiovascular mortality, cancer mortality, and other disease mortality are shown in Table 2. In the full sample, aged 50–84, the continuous measure of telomere length was not associated with cardiovascular mortality or cancer mortality; however, a decrease of 1 kilobase pair in telomere length at baseline was marginally associated with a 10% increased hazard of all-cause mortality (HR: 1.1, 95% CI: 0.9, 1.4) and a 30% increased hazard of death due to diseases other than cardiovascular disease or cancer (HR: 1.3, 95% CI: 0.9, 1.9). Compared to respondents in the longest quartile of telomere length, those in the shortest quartile had a 20% increased hazard of all-cause mortality (HR: 1.2, 95% CI: 1.0, 1.5); those in the second quartile had a 20% increased hazard of all-cause mortality (HR: 1.2, 95% CI: 1.0, 1.5); and those in the third

quartile had a 10% increased hazard of all-cause mortality (HR: 1.1, 95% CI: 0.9, 1.4). For cardiovascular mortality, those in the second (HR: 1.4, 95% CI: 0.9, 2.0) and third (HR: 1.5, 95% CI: 1.0, 2.3) quartiles of telomere length had an increased hazard of death compared to those in the longest quartile. Finally, compared to respondents in the longest quartile of telomere length, those in the shortest quartile had a 50% increased hazard of death due to diseases other than cardiovascular disease or cancer (HR: 1.5, 95% CI: 1.0, 2.1). Results were substantively equivalent regardless of the inclusion of controls for chronic conditions.

The next step in the analysis was to examine age, sex, race/ethnicity, and SES as potential moderators of the association between telomere length and mortality. For all-cause mortality, cancer mortality, and mortality due to diseases other than cardiovascular disease or cancer, there was no evidence of moderating effects of age, sex, race/ethnicity, or education; however, we found an interaction between race/ethnicity and telomere length for cardiovascular mortality (see Table S1 in the electronic version of the journal). As shown in Table 3, neither measure of telomere length was associated with cardiovascular mortality among white or Mexican-American respondents. Among African-Americans, a decrease of 1 kb pair in telomere length at baseline was associated with a two-fold increased hazard of death due to cardiovascular disease (HR: 2.0, 95% CI: 1.3, 3.1); and those in the second (HR: 2.8, 95% CI: 1.0, 7.4) and third (HR: 2.7, 95% CI: 1.0, 7.7) quartiles of telomere length had a nearly three-fold increased hazard of death compared to those in the longest quartile. We found no evidence of interactions between age and telomere length, sex and telomere length, or education and telomere length for cardiovascular mortality (see Table S1 in the electronic version of the journal).

DISCUSSION

Although evidence suggests that telomere shortening contributes to aspects of human aging,[7] previous studies have not always found an association between telomere length and mortality. Conflicting findings may reflect several problems that have plagued research on telomere epidemiology, including small sample sizes, survival bias among the extreme elderly, and the use of different methods of telomere measurement.[35,36] The current study, which used the well-validated and now widely-accepted PCR technique to measure telomere length, examined the association between leukocyte telomere length and mortality over an average of 9.5 years of follow-up in a large, nationally representative sample of US adults aged 50–84. We found limited support for the hypothesis that shorter telomere length is associated with increased risk of death. In the full sample, there was some evidence that shorter telomere length was associated with increased risk of all-cause mortality, cardiovascular mortality, and death due to diseases other than cardiovascular disease or cancer. Among African-American but not White or Mexican-American participants, shorter telomere length at baseline was associated with increased risk of cardiovascular mortality.

Limitations and Directions for Future Research

Despite the strengths of this study, there were several limitations. First, the follow-up period was relatively short (an average of 9.5 years). As a result, we only observed 870 deaths in the sample, which limited the power to detect associations between telomere length and

mortality, particularly for cause-specific mortality. This may explain why we failed to replicate the results of a recent study examining the association between telomere length and cancer mortality that used similar data (a large, nationally representative Danish sample) and method of telomere measurement (PCR) but had up to 20 years of follow-up.[30] Given the small number of deaths attributable to causes other than cardiovascular disease or cancer, we were unable to examine deaths due to infectious disease, cerebrovascular disease, diabetes, Parkinson's disease, Alzheimer's disease, liver disease, and kidney disease in separate models. The CDC will continue to link data from the National Death Index to the NHANES 1999–2002 data, which will provide greater power in the future to examine the hypothesis that reduced telomere length is associated with specific causes of death. Additional mortality data will also provide greater power to detect possible moderation effects of age, sex, race/ethnicity, and education in the association between telomere length and all-cause and cause-specific mortality.

Next, the accuracy of the cause-specific mortality data from the National Death Index depends on the accuracy of the death certificate data submitted to the National Center for Health Statistics by state vital statistics offices, and previous research has found evidence of problems with the reliability and accuracy of cause-of-death statements.[45] Another potential limitation of the cause-specific mortality analysis was the assumption that competing risks of death were independent of one another. This assumption is only valid if the probability of death from one cause (e.g., cancer) is not altered by the probability of death from another cause (e.g., cardiovascular disease).[46] Cox proportional hazards regression does not account for competing risks of death and, therefore, may overestimate the risk of death from a specific cause. However, given the short follow-up period in this study, the difference between traditional survival analysis and the competing risk approach is likely to be minimal.[47] After the CDC has linked additional mortality follow-up data, researchers should consider examining competing risk models to ensure that results for cause-specific mortality analyses are not biased.

Another limitation of the current study was the use of telomere length data measured at only one point in time. To determine whether the rate of change in telomere length influences mortality risk, it will be necessary for future longitudinal studies to obtain repeated measures of telomere length. Finally, leukocytes are composed of many cell types, including neutrophils, eosinophils, basophils, lymphocytes, and monocytes. Within the same individual, telomere length in different cell types varies.[48] Given that prior infection and other factors, such as chronic stress exposure, affect the percentage of each cell type within an individual,[48] this could potentially bias estimates of the association between overall leukocyte telomere length (an average of telomere length across all leukocyte cell types) and mortality.

Conclusions

This study found that the association between telomere length and mortality differs by race/ethnicity and cause of death. Because we examined data from a large, nationally representative data set, the results of this work are generalizable to US adults aged 50–84. The findings suggest that telomere length may be a more useful indicator of cardiovascular

mortality risk for African-Americans compared to whites and Mexican-Americans. This finding will be particularly important if telomere length is used in clinical settings.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Appendix. Summary of the Main Study Findings Regarding the Association between Telomere Length and Mortality

Study	Sample	Method	Follow-up Period	Number of Deaths	Major Findings
Support Null Hypothesis					
Bischoff et al. 2006	812 white women and men, aged 73–101	Southern blots	Up to 8 years	412	Telomere length was not associated with mortality.
Harris et al. 2006	190 white women and men, aged 79	PCR	5 years	36	Telomere length was not associated with mortality.
Houben et al. 2011	203 white males, aged 73–91	PCR	7 years	105	Telomere length was not associated with mortality.
Martin-Ruiz et al. 2005	598 white women and men, aged 85+	PCR	Up to 12.9 years	598	Telomere length not a predictor of mortality.
Njajou et al. 2009	2,721 white and black women	PCR	Average of 8.2 years	975	Telomere length was not

Study	Sample	Method	Follow-up Period	Number of Deaths	Major Findings
	and men, aged 70–79				associated with mortality.
Strandberg et al. 2011	622 white men, mean age 75.7	Southern blots	10 years	130	Telomere length was not associated with mortality.
Reject Null Hypothesis					
Astrup et al. 2010	157 white female and male type 1 diabetic patients with diabetic nephropathy and 116 controls with type 1 diabetes and normoalbuniria, aged 33–53	Southern blots	12.9 years	75	Telomere length was inversely associated with all-cause mortality in patients and controls.
Bakaysa et al. 2007	350 white female and male twins, mean age 78.8	Southern blots	Up to 9.3 years	176	Twins with shorter telomeres more likely to die than their co-twins with longer telomeres.
Cawthon et al. 2003	143 white women and men, over age 60	PCR	15 years	101	Telomere length was inversely associated with all-cause mortality, heart disease mortality, and infectious disease mortality (but not cancer or cerebrovascular mortality) in people aged 60–74.
Epel et al. 2009	236 white women and men, aged 70–79	PCR	12 years	102	Among women, baseline telomere length was inversely associated with cardiovascular mortality. Among men, telomere shortening over 2.5 years was associated with increased cardiovascular mortality.
Farzaneh-Far et al. 2008	780 white, black, Asian, and other race/ethnicity female and male patients with stable CAD, aged 65–80	PCR	4.4 years	166	Telomere length was inversely associated with mortality.
Fitzpatrick et al. 2011	1,136 white, black, and other race/ethnicity women and men, aged 65+	Southern blots	Up to 8.1 years	468	Those in the shortest quartile of telomere length were 60% more likely to die than those in

Study	Sample	Method	Follow-up Period	Number of Deaths	Major Findings
					the longest quartile.
Honig et al. 2012	1,983 white, African-American, Hispanic, and other race/ethnicity women and men, aged 65+	PCR	Up to 16 years	863	Telomere length was inversely associated with mortality.
Kimura et al. 2008	548 white female and male same-sex twins, aged 73–94	Southern blots	9–10 years	289	Short telomeres predicted mortality.
Lee et al. 2012	4,271 mostly (~97%) white female and male subjects with mild to moderate COPD, aged 40–65	PCR	7.5 years	399	Telomere length was inversely associated with mortality.
Martin-Ruiz et al. 2006	195 white female and male non-demented stroke survivors, over age 75	In-gel hybridization	5 years	44	Telomere length was inversely associated with mortality.
Weischer et al. 2012	19,838 white women and men, aged 36–74	PCR	Up to 19 years	4,342	Telomere length was inversely associated with mortality.
Weischer et al. 2013	47,102 white women and men, aged 20–100	PCR	Up to 20 years	1,730	Telomere length was positively associated with survival after cancer.
Willeit et al. 2010	787 white women and men, aged 40–79	PCR	10 years	44	Telomere length was inversely associated with cancer mortality.
Willeit et al. 2011	787 white women and men, aged 40–79	PCR	15 years	137	Confirmed previous finding that telomere length was inversely associated with cancer mortality.

Table 1

Mean Leukocyte Telomere Length by Selected Characteristics (n=3,091)[a]

Characteristic	n	Mean telomere length in kb pairs (SE)
Age		
50–59	901	5.67 (.04)
60–74	1554	5.54 (.04)
75–84	636	5.33 (.04)
Sex		
Female	1485	5.59 (.04)
Male	1606	5.54 (.04)
Race/ethnicity		
White	1888	5.55 (.04)
African-American	511	5.68 (.05)
Mexican-American	692	5.49 (.03)
Education		
Less than high school	1164	5.49 (.04)
High school	711	5.57 (.05)
Some college	634	5.56 (.04)
College	582	5.63 (.05)
Smoking		
Current	494	5.55 (.04)
Former	1226	5.57 (.04)
Never	1371	5.56 (.04)
BMI quartiles		
<24.7	775	5.56 (.05)
24.7–28.0	771	5.56 (.04)
28.1–31.8	773	5.56 (.03)
>31.8	772	5.56 (.04)

[a] kb pairs = kilobase pairs; SE = standard error.

Table 2

Associations Between Leukocyte Telomere Length and All-Cause Mortality and Cause-Specific Mortality (n=3,091)[a]

	Deaths (n)	HR (95% CI) Minimally Adjusted[b]	HR (95% CI) Fully Adjusted[c]
All-Cause Mortality			
Telomere Length (kb pairs)[d]	870	1.1 (0.9, 1.4)	1.1 (0.9, 1.4)
Telomere Length Quartiles (kb pairs)			
<5.15	284	1.2 (1.0, 1.6)	1.2 (1.0, 1.5)
5.15–5.45	230	1.3 (1.0, 1.5)	1.2 (1.0, 1.5)
5.46–5.82	208	1.1 (0.9, 1.4)	1.1 (0.9, 1.4)
>5.82	148	1.00	1.00
Cardiovascular Mortality			
Telomere Length (kb pairs)	230	1.0 (0.7, 1.4)	1.0 (0.7, 1.4)
Telomere Length Quartiles (kb pairs)			
<5.15	60	0.9 (0.6, 1.6)	0.9 (0.5, 1.5)
5.15–5.45	70	1.5 (1.0, 2.2)	1.4 (0.9, 2.0)
5.46–5.82	62	1.4 (0.9, 2.1)	1.5 (1.0, 2.3)
>5.82	38	1.00	1.00
Cancer Mortality			
Telomere Length (kb pairs)	217	1.1 (0.7, 1.6)	1.1 (0.7, 1.5)
Telomere Length Quartiles (kb pairs)			
<5.15	71	1.2 (0.7, 1.9)	1.2 (0.7, 1.9)
5.15–5.45	49	1.1 (0.7, 1.6)	1.1 (0.7, 1.6)
5.46–5.82	56	1.1 (0.8, 1.5)	1.1 (0.8, 1.5)
>5.82	41	1.00	1.00
Other Disease Mortality			
Telomere Length (kb pairs)	315	1.3 (0.9, 1.8)	1.3 (0.9, 1.9)
Telomere Length Quartiles (kb pairs)			
<5.15	121	1.4 (1.0, 2.0)	1.5 (1.0, 2.1)
5.15–5.45	80	1.1 (0.7, 1.8)	1.1 (0.7, 1.7)
5.46–5.82	64	1.0 (0.6, 1.5)	1.0 (0.7, 1.5)
>5.82	50	1.00	1.00

[a] kb pairs = kilobase pairs; CI = Confidence Interval; HR = hazard ratio.

[b] Models include controls for age, age squared, sex, race/ethnicity, education, smoking, and body mass index.

[c] Models include controls for age, age squared, sex, race/ethnicity, education, smoking, body mass index, cardiovascular disease, diabetes, hypertension, and high cholesterol.

[d] The continuous measure of telomere length was multiplied by −1 to reflect increased risk of mortality associated with shorter telomere length.

Table 3

Association Between Leukocyte Telomere Length and Cardiovascular Mortality, By Race/Ethnicity[a]

	White (n=1,888)		African-American (n=511)		Mexican-American (n=692)	
	Deaths (n)	**HR (95% CI)**	**Deaths (n)**	**HR (95% CI)**	**Deaths (n)**	**HR (95% CI)**
Telomere Length (kb pairs)[b]	138	0.9 (0.6, 1.3)	44	2.0 (1.3, 3.1)	48	1.1 (0.5, 2.3)
Telomere Length Quartiles (kb pairs)						
<5.15	36	0.8 (0.4, 1.4)	10	2.2 (0.8, 5.8)	14	0.7 (0.3, 1.7)
5.15–5.45	42	1.2 (0.8, 2.0)	15	2.8 (1.0, 7.4)	13	0.9 (0.4, 2.3)
5.46–5.82	39	1.4 (0.8, 2.4)	14	2.7 (1.0, 7.7)	9	0.8 (0.3, 2.4)
>5.82	21	1.00	5	1.00	12	1.00

[a] kb pairs = kilobase pairs; CI = Confidence Interval; HR = hazard ratio. Models include controls for age, age squared, sex, education, smoking, body mass index, cardiovascular disease, diabetes, hypertension, and high cholesterol.

[b] The continuous measure of telomere length was multiplied by −1 to reflect increased risk of mortality associated with shorter telomere length.