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Abstract

Negative early-life exposures have been linked to a host of poor adult health outcomes, but are such early exposures associated with cellular senescence decades later? This study uses data from the Health and Retirement Study to examine the association between six childhood exposure domains (e.g., socioeconomic disadvantage, risky parental behavior) and a biomarker of aging, telomere length, among 4,935 respondents. Telomere length is obtained from DNA of cells found in saliva and is measured as the telomere repeat copy number to single gene copy number ratio (T/S). Men who as children were exposed to risky parental behaviors or who reported risky adolescent behaviors have shorter telomeres ($b = -0.031$, $p = .052$; $b = -0.041$, $p = .045$, respectively); however, these relationships are attenuated after adjusting for adult risks and resources. Among women, parental substance abuse is associated with shorter telomeres even after adjusting for adult risks and resources ($b = -0.041$, $p = .005$). In addition, men and women whose mother lived

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at least until the age of 85 have longer telomeres than those without a long-lived mother (b = 0.021, p = .045; b = 0.032, p = .005, respectively). Taken together, the ways in which early-life exposures are associated with adult telomeres vary for men and women.

Keywords: Telomere length, Biological age, Adverse childhood experiences

Over the past few decades, researchers in gerontology and developmental biology have built a convincing case that adverse childhood experiences have deleterious effects on health and longevity. Negative early-life exposures such as socioeconomic disadvantage and parental abuse increase the risk of many leading causes of death including cancer (1) and cardiovascular disease (2). However, it is unclear whether early-life exposures influence cellular aging per se or simply disease onset. If childhood disadvantage is associated with premature aging, this may be one mechanism by which early exposures shape morbidity.

To examine the biological mechanisms of stress and detect premature aging, researchers increasingly turn to biomarkers of aging. Although some biomarkers are useful for linking social stressors to certain biological responses such as inflammation (e.g., C-reactive protein), telomere length is thought to reflect the cumulative damage of the genome and likelihood of cellular senescence (3). As cells replicate, telomeres—chromosomal end caps that protect from DNA degradation— shorten until a critically short telomere triggers cellular senescence (3,4). The accumulation of senescent cells, moreover, is hypothesized to play a pivotal role in the pathogenesis of age-related diseases (4). As McFarland and colleagues describe, telomeres are thought to act as markers *and* mechanisms of cellular aging (5).

Shorter telomeres have been linked to some diseases of aging such as coronary heart disease (6); however, there is inconclusive evidence that telomere length is a predictor of cancer or mortality, with some studies reporting no or even an inverse association (7–10). Telomeres may be associated with the pathogenesis of some diseases but not others, yet the precise mechanisms of telomere regulation remain a matter of debate. Adding to the complexity are differences by sex; women tend to have longer telomeres than men (10,11). The biological theses that describe sex differences center on the role of hormones in stimulating the production of telomerase as well as women having a compensatory allele on a sister × chromosome in the case that one × chromosome has a deleterious recessive allele associated with

telomere maintenance (12). Despite the incomplete understanding of telomere regulation, multiple scholars point to the relationship between stressful life events and telomere length as evidence for the utility of telomere length as a meaningful biomarker for accumulated challenges (5,13).

In describing the antecedents of telomere shortening, it is hypothesized that severe and cumulative stressors potentially alter biochemical parameters within the body (4). For instance, scholars suggest that lifestyle factors associated with inflammation may increase oxidative stress, resulting in telomeric replication stress and telomere erosion (14). An emerging literature indicates that adversity experienced during childhood can heighten vulnerability to biological risk. Research has revealed that children who spend more time in an institutionalized setting (15), have experienced family violence (16), or live in neighborhoods characterized by high levels of disorder have shorter telomeres than their counterparts (17), and these studies examine telomeres from buccal cells (15,16) and cells in saliva (17).

Evidence from samples of adults (age 21–80) indicates that cumulative negative exposure during childhood is associated with shorter adult telomeres obtained from cells in blood and saliva, respectively (18,19). For instance, Kiecolt-Glaser and colleagues (20) found that two or more adversities were associated with shorter telomeres from peripheral blood mononuclear cells. Studies also reveal shorter lymphocyte telomeres with each additional childhood adversity reported (21). Using the Health and Retirement Study, Puterman and colleagues (19) found that cumulative childhood adversity, but no single adversity, was associated with shorter adult telomeres from cells in saliva. These studies suggest a graded relationship and perhaps a threshold effect of two or more instances of childhood negative exposures on telomere length.

Drawing from the notable adverse childhood experience study by Felitti and colleagues, studies that examine the association between early-life exposures and telomere length often focus on maltreatment (20–23). However, recent research points to the importance of considering different types or *domains* of negative exposures (24). Failing to account for multiple childhood domains may lead to an overestimation of the domain under study especially because domains of life are often interrelated (e.g., socioeconomic status, diet, educational performance) (25). Also, some types of childhood exposures may be

protective, whereas others are harmful and may elicit different responses among men and women. For instance, women are more likely to partake in internalizing behaviors or rumination, whereas men are more likely to cope through externalizing or outward behaviors (26). There also are notable differences in health behaviors by men and women that may lead to men's higher morbidity and shorter telomeres (25). Studying the relationships between early-life exposures and telomere length may help identify avenues to enhance health among men and women.

Method

Sample Description

This study uses data from the Health and Retirement Study (HRS), a panel survey of adults 51 years of age and older with oversamples of Black adults, Hispanic adults, and residents of the state of Florida (27). The present study uses the sample of adults with telomere data, who are age eligible (i.e., 54 years and older at their 2008 interview), and excludes those who used proxies for childhood indicators (n = 217) and individuals who reported non- Hispanic other race (n = 114) resulting in an analytic sample size of 4,935.

Telomere Length

Saliva was collected via cheek swabs using an Oragene Collection Kit, and telomere length from cells in saliva (e.g., buccal epithelial cells, leukocytes) was measured using quantitative polymerase chain reaction. The assay procedure is outlined in greater detail in HRS documentation (28). Average telomere length is reported as the ratio of the respondent's sample telomere sequence copy number (T) to a single-copy gene copy number (S); human beta-globin served as the single-copy reference sequence. After examining outliers and following the work of Puterman and colleagues (19), respondents with telomere length above 2 are treated as missing (n = 257). We are cautious when comparing results across samples because telomere length varies across cell types and assay methods.

Childhood Exposures

Six domains of childhood exposures are constructed from survey waves 1996–2008: socioeconomic (SES) disadvantage, risky parental behavior, infectious diseases, chronic diseases, impairments, and risky adolescent behavior. Multiple indicators are used for each domain, and each domain is coded 1 if any exposure in that domain was reported, 0 otherwise.

The SES domain is made up of four indicators: father's education or mother's education if father's was unknown (1 for <8 years and 0 for ≥8 years), perceived family finances (1 for poor, 0 otherwise), father's occupation (1 for nonskilled manual, 0 otherwise), and whether the respondent ever moved due to financial difficulties. The risky parental behavior domain includes three indicators: physical abuse by a parent, a parent who abused alcohol or substances, and a parent/guardian who smoked. Risky adolescent behavior includes four indicators: substance abuse, trouble with the police, depressive symptoms, and other psychological problems.

Infectious diseases during childhood include chickenpox, measles, and mumps. Chronic diseases during childhood consist of asthma, diabetes, respiratory disorder, seizures, migraines, stomach problems, allergies, heart disease, ear problems, high blood pressure, and self-rated childhood health (poor or fair health coded as 1, 0 otherwise). The childhood impairment domain consists of five indicators: head injury, disability for six or more months, vision impairment even with corrective lenses, speech impairment, and learning problems.

Parental Longevity

Along with environmental stressors (physical, social, and psychological), research suggests that heritability accounts for an appreciable portion of variability in telomere length (29). Few studies that investigate the effects of childhood negative exposures on telomere length account for heritable influences, probably due to limited information in data sets on both genetic factors and social stressors. This study uses parental longevity as an indicator of family lineage. Mother's and father's age (currently or at time of death) is coded dichotomously, so that 85 years or older is 1, 0 otherwise. Given the age of the sample,

parents of the respondents were probably born before the 1940s. Life expectancy at birth in the 1940s was around 65–70 years (30); thus, the cutoff at age 85 is intended to indicate notable longevity.

Adult Risks and Resources

Smoking, heavy alcohol consumption, and obesity have been associated with shorter telomere length (9,31). In the present study, smoking is assessed by pack-years—the total number of years smoked multiplied by the average number of packs smoked daily. Those who have never smoked are coded as 0. Heavy alcohol drinking is coded as 1 for women who drink more than four drinks per day or men who drink more than five drinks per day when they drink (32). Body mass index is measured in kilogram per square meter, and bottom and top coded at 15 and 50 kg/m2, respectively. Physical activity is coded as 1 if the respondent reported exercising once or more per week, 0 otherwise.

Among SES factors, education is measured in years and top coded at 17. In addition, wealth—an appropriate SES measure for older adults—is included. Marital status has been considered health protective, especially for men, and included in the models as a nominal variable: married or partnered (reference), divorced or separated, widowed, and never married.

Demographics

Several studies find differences in the lengths of telomeres for men and women (10,12). This suggests that telomere length could be sex linked, have varying rates of shortening, or both. We recognize that there may be sex and gender differences in telomere length, but given our focus on early-life experiences rather than innate characteristics, we refer to any potential differences as those by gender herein. Given gender (and/or sex) differences found in previous studies, we stratify our analyses for men and women. The models also adjust for age measured in years as well as race and ethnicity: non-Hispanic White (reference), non-Hispanic Black, and Hispanic adults.

Analysis

Preliminary analyses and descriptive statistics are conducted in Stata version 14. Final estimates are completed with ordinary least squares regression and obtained in Mplus version 7. We use full-information maximum likelihood estimation with robust *SE* to handle missing data. Item missing is most prevalent for the SES domain at 29.69% followed by chronic diseases at 11.98%. Models adjust for the complex survey design. Including the assay plate number did not alter conclusions; thus, plate number was removed from models for parsimony.

Multiple group analysis in Mplus is used to estimate the models by gender, and differences in coefficients are tested across models. Analyses were conducted in three stages. First, we examine partially adjusted models for men and women that include the covariates: age, race, ethnicity, parental longevity, and the six childhood exposure domains (which we describe as Model 1). Second, we examine fully adjusted models that add education, wealth, marital status, smoking, alcohol consumption, body mass index, and physical activity (Model 2). Third, we completed two types of supplementary analyses to examine (a) potential confounding of domains and (b) whether an individual indicator within a domain is responsible for that domain being significantly associated with telomere length.

To illustrate the association between selected modifiable exposures and telomere length, we also present a figure displaying these effects as comparable to the effect of chronological age on telomere length. For instance, we divide the effect of an exposure by the effect of age in a given model. We caution that this illustration does not translate to conclusions about accelerated aging or telomere shortening over time, but is a useful heuristic for envisioning the magnitude of an effect.

Results

Descriptive statistics for men and women are presented in **Table 1**; *p* values for differences by gender are shown in the far right column. On average, women had longer telomeres than men. Men reported more impairments and risky adolescent behaviors, and fewer chronic

Table 1. Descriptive Statistics for Men and Women From the Health and Retirement Study

	Men		Women		
	Range[a]	(*n* = 1,983)	Range	(*n* = 2,952)	*p*[b]
Telomere length (mean ± *SD*)	0.2–2.0	1.3 (0.3)	0.2–2.0	1.3 (0.3)	.000
Demographics					
Non-Hispanic Black, *n* (%)		1,983 (11.0)		2,952 (14.1)	.002
Non-Hispanic White, *n* (%)		1,983 (80.4)		2,952 (75.7)	.000
Hispanic, *n* (%)		1,983 (8.6)		2,952 (10.3)	.048
Age (mean ± *SD*)	54–97	70.3 (9.3)	54–100	69.9 (9.6)	.128
Parental longevity					
Mom age, ≥85, *n* (%)		1,911 (34.9)		2,906 (33.7)	.420
Dad age, ≥85, *n* (%)		1,900 (20.8)		2,855 (20.4)	.703
Childhood exposures					
SES disadvantage, *n* (%)		1,417 (70.1)		2,053 (72.1)	.203
Risky parental behavior, *n* (%)		1,789 (71.5)		2,651 (69.7)	.211
Chronic disease, *n* (%)		1,715 (31.8)		2,629 (36.0)	.004
Infectious disease, *n* (%)		1,941 (91.0)		2,896 (95.2)	.000
Impairment, *n* (%)		1,981 (22.1)		2,944 (15.7)	.000
Risky adolescent behavior, *n* (%)		1,796 (11.7)		2,672 (5.3)	.000
Adult risks and resources					
Education (mean ± *SD*)	0–17	12.9 (3.3)	0–17	12.3 (3.0)	.000
Pack-years smoking (mean ± *SD*)	0–248	21.5 (30.7)	0–188	11.0 (20.5)	.000
Body mass index (mean ± *SD*)	15–50	28.1 (4.9)	15–50	28.1 (6.2)	.730

SES = socioeconomic status.

a. Range of values for continuous variables.

b. *p* Value of difference between men and women based on analysis of variance or χ^2 tests.

diseases and infectious diseases during childhood than women, on average. Roughly 34% and 20% of respondents reported mother's and father's age to be 85 and older, respectively.

Results for Men

Multiple regression results for men are shown in **Table 2**. As seen in Model 1, Black men had longer telomeres than White men (b = 0.062, p = .005) and, as expected, age was negatively associated with telomere length (b = −0.004, p < .001). Men whose mothers lived to age 85 and older had longer telomeres than men without a long-lived mother (b = 0.021, p = .045). Shorter telomeres were observed among those who reported risky adolescent behavior, even after adjusting for parental longevity (b = −0.041, p = .045). Risky parental behavior also was potentially associated with shorter telomeres among men

Table 2. Regression of Telomere Length on Childhood Exposures and Covariates for Men

	Model 1		Model 2	
	Coefficient	*SE*	Coefficient	*SE*
Black	0.062**	0.022	0.069**	0.023
Hispanic	0.030	0.023	0.043	0.027
Age	−0.004***	0.001	−0.003***	0.001
Parental longevity				
Mom age ≥ 85	0.021*	0.010	0.019	0.011
Dad age ≥ 85	−0.011	0.014	−0.009	0.014
Childhood exposures				
SES disadvantage	−0.017	0.015	−0.015	0.014
Risky parental behavior	−0.031*	0.016	−0.028	0.015
Chronic disease	−0.012	0.012	−0.013	0.011
Infectious disease	0.013	0.020	0.013	0.021
Impairment	0.001	0.015	0.002	0.015
Risky adolescent behavior	*−0.041*[a,]*	0.020	*−0.036*	0.021
Adult health lifestyle				
Pack-years smoking			0.000	0.000
Heavy drinking			−0.006	0.041
Physical activity			0.004	0.013
Body mass index			*0.005***	0.001
R^2	.028		.038	

Model 2 also adjusts for education, wealth, and marital status.
a. Italicized coefficients indicate significant differences between men and women at $p < .05$.
* $p \leq .05$; ** $p < .01$; *** $p < .001$

($b = -0.031$, $p = .052$). Preliminary analyses that examined one domain at a time, adjusting for the covariates in Model 1, revealed that risky parental behavior was associated with shorter telomeres for men ($b = -0.032$; $p = .042$; not shown), and results for all other domains were similar to results seen in Model 1 of Table 2.

Model 2 added adult SES, health, and lifestyle factors to Model 1, and maternal longevity was no longer directly associated with telomeres. Risky parental behavior and risky adolescent behavior were also no longer significant after inclusion of adult SES, health, and lifestyle. Each kg/m2 increase in body mass index was associated with 0.005-unit increase in telomere length ($p < .001$). All estimates from fully adjusted models are presented in Supplementary Table S1.

We draw on the work of Epel and colleagues (33) to offer a visual representation of the effects of selected modifiable exposures on telomere length as comparable to the effect of each additional year of age. For instance, Figure 1A shows that the effect of risky adolescent

Table 3. Regression of Telomere Length on Childhood Exposures and Covariates for Women

	Model 1		Model 2	
	Coefficient	*SE*	Coefficient	*SE*
Black	0.086***	0.016	0.078***	0.016
Hispanic	0.047	0.025	0.031	0.023
Age	−0.004***	0.001	−0.004***	0.001
Parental longevity				
Mom age ≥ 85	0.032**	0.011	0.031**	0.011
Dad age ≥ 85	0.009	0.011	0.008	0.011
Childhood exposures				
SES disadvantage	−0.010	0.014	−0.003	0.014
Risky parental behavior	0.002	0.011	0.007	0.011
Chronic disease	0.003	0.013	0.006	0.013
Infectious disease	−0.018	0.023	−0.019	0.023
Impairment	0.007	0.014	0.013	0.014
Risky adolescent behavior	*0.025*[a]	0.023	*0.031*	0.022
Adult health lifestyle				
Pack-years smoking			−0.002***	0.000
Heavy drinking			0.017	0.047
Physical activity			−0.001	0.011
Body mass index			*0.001*	0.001
R^2	0.039		0.054	

Model 2 also adjusts for education, wealth, and marital status.
a. Italicized coefficients indicate significant differences between men and women at $p < .05$.
**$p < .01$, ***$p < .001$.

behavior ($b = -0.041$, $p = .045$; Model 1 in Table 2) is roughly equivalent to ten years of men's chronological age (0.004 × 10 = 0.040); however, this association was attenuated in Model 2 after including adult SES, health, and lifestyle (see Table 2). Figure 1B shows that the effect of risky adolescent behavior as visualized in chronological years was no longer significant after adjusting for adult risks and resources.

Results for Women

Model 1 in **Table 3** shows the regression results for women. Black women had longer telomeres than White women by 0.086 units ($p < .001$). Similar to men, age was negatively associated with telomere length ($b = -0.004$, $p < .001$), and maternal longevity was associated with longer telomeres ($b = 0.032$, $p = .005$). In contrast to the findings for men, Model 1 in Table 3 reveals that none of the domains of childhood exposures were associated with women's telomere length. Model 2 added adult SES, health, and lifestyle to Model 1 in Table 3.

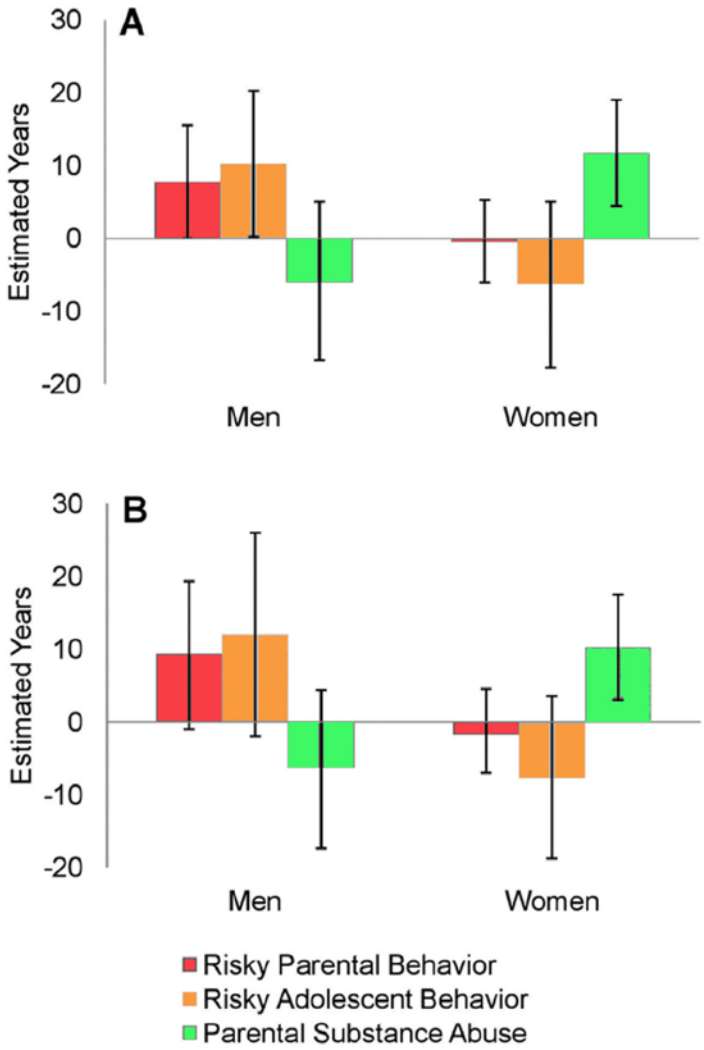

Figure 1. Visualizing the effect of selected modifiable early-life exposures as estimated years of age. (A) Partial adjustment: models adjust for age, race, ethnicity, parental longevity, and the other childhood exposure domains. (B) Full adjustment: models adjust for age, race, ethnicity, parental longevity, the other childhood exposure domains, smoking, heavy drinking, body mass index, physical activity, marital status, education, and wealth. 95% confidence intervals are shown.

The net difference by race decreased slightly; roughly, 9% of the Black–White difference in telomere length in Model 2 was due to adult health lifestyle ($b = 0.078$, $p < .001$). Differences in telomere length by age and mother's longevity remained relatively stable from Model 1. Among adult health lifestyle factors, pack-years of smoking was associated with shorter telomere length ($b = -0.002$, $p < .001$). As shown in **Figure 1**, the effects of risky parental and adolescent behaviors as

Table 4. Regression of Telomere Length on Indicators of Risky Parental Behaviors for Men and Women

	Men				Women			
	Model 1[a]		Model 2[b]		Model 3[a]		Model 4[b]	
	Coefficient	*SE*	Coefficient	*SE*	Coefficient	*SE*	Coefficient	*SE*
Risky parental behaviors[c]								
Physical abuse	−0.026	0.023	−0.027	0.021	−0.030	0.016	−0.022	0.016
Substance abuse	*0.018*[d]	0.017	*0.019*	0.017	*−0.047***	0.015	*−0.041***	0.015
Smoking	−0.021	0.013	−0.018	0.013	0.008	0.010	0.013	0.011

a. Partial adjustment: models adjust for age, race, ethnicity, parental longevity, and the other childhood exposure domains.
b. Full adjustment: models adjust for age, race, ethnicity, parental longevity, the other childhood exposure domains, marital status, education, wealth, heavy drinking, smoking, body mass index, and physical activity.
c. Indicators are examined separately.
d. Italicized coefficients indicate significant differences between men and women at $p < .01$.
**$p < .01$

visualized as chronological age were not associated with telomere length for women in the partially adjusted (Figure 1A) or fully adjusted models (Figure 1B).

Supplementary Analyses

To ensure that domains were not confounding in the models, we examined each domain separately in partially adjusted and fully adjusted models and found similar results. Moreover, given that one of the risky parental behaviors and one of the risky adolescent behaviors were associated with shorter telomere length among men in Model 1, we sought to identify if a single indicator within each of these domains was responsible for this relationship. We examined indicators separately in models that adjust for the covariates seen in Model 1 of Tables 2 and 3. None of the individual indicators for the risky parental behavior domain were significant for men as seen in Model 1 of **Table 4**, suggesting that it is the accumulation of exposures that matters. For women, however, parental substance abuse was associated with shorter telomeres, and this association was significantly different for men and women ($b = -0.047$, $p = .002$; Model 3 of Table 4). The association remained significant for women in the fully adjusted model as seen in Model 4 of Table 4 ($b = -0.041$, $p = .005$). Figure 1

shows the effects of parental substance abuse visualized as chronological years in partially adjusted (Figure 1A) and fully adjusted models (Figure 1B). None of the individual indicators of the risky adolescent behavior domain were significant for men or women.

Discussion

To our knowledge, this is the first study to examine which, if any, domains of negative childhood exposures are associated with shorter adult telomere length. By studying a wide range of exposures—from parental behaviors to childhood diseases—in a national sample, two conclusions are noteworthy. First, exposure to risky parental behavior and manifesting risky adolescent behavior during childhood were associated with shorter telomeres among men. These associations were attenuated, however, after adjusting for adult risks and resources. Although we did not test mediation, a recent study found that adult stressors completely mediate the association between early-life stressors and telomere length (13). Perhaps early-life events and experiences that lead to adult stressors or risky behaviors and lifestyles shape processes associated with cellular senescence, especially among men.

Second, and in contrast to men, parental substance abuse, including alcohol and/or drugs, was directly associated with shorter telomeres among women, even after adjusting for adult health and lifestyle factors. Parental alcohol or drug abuse could have direct effects such as abnormal growth or indirect effects including neglect, maltreatment, or development of maladaptive behaviors by the child (34). Taken together, there is compelling evidence that risky parental behaviors have an enduring influence on biological health for men and women, but the association is gender specific. Two domains were associated with shorter telomeres in the partially adjusted model for men, suggesting that accumulation of these certain types of exposures matters; however, only one individual indicator was associated with shorter telomeres among women. The results also add to the accumulated evidence that health risks may be transmitted across generations but distinctly for men and women. Unfortunately, we do not have information on which parent exhibited the risky behavior, which may offer insight to why we found these differences for men and women, but hope that future studies can differentiate parental influence.

The findings herein corroborate other studies that examine childhood exposures and adult telomere length; that is, psychosocial stressors related to risky and violent behaviors are associated with shorter telomeres (16,20). We did not, however, find that childhood socioeconomic disadvantage or health was associated with telomeres for men or women. It is possible that arguably more severe exposures lead directly to alterations in the stress response process, thereby creating systemic biological vulnerability, rather than chronic or infectious diseases per se. Another potential explanation is that risky parental behaviors heighten the probability of their children's risky behaviors, both during adolescence and during adulthood, which may lead to shorter telomeres, particularly in men. In a study investigating different life-course models in explaining how early-life exposures are associated with adult telomeres, evidence suggests that this association is completely mediated by adult stressors (13).

Moreover, evidence suggests the importance of considering multiple domains (24). Using the HRS, Puterman and colleagues (19) found that no individual childhood exposure was associated with telomere length, but the cumulative measure of childhood adversity was associated with shorter telomeres. Although other authors summed several types of exposures, we found that two domains— risky behaviors by the parent or by the adolescent—were probably the factors influencing telomere length, specifically for men. Moreover, we found that no childhood exposure domain was associated with telomeres for women and no single indicator was associated with telomeres for men. Several studies investigate accumulated adversity (18,19,21), but the results presented herein show that it is important to examine domains of childhood exposures because they are probably interrelated. Analyzing domains also helps identify plausible avenues of intervention.

Although we focused on negative early exposures, the study also contributes to our understanding of resources that protect against telomere shortening. By integrating maternal and paternal longevity into our analysis, we found that maternal longevity was associated with longer telomeres. We chose the cutoff of 85 years of age for the parents to indicate notable longevity and reflect an advantageous family lineage. Few studies have examined this association; however, in a study of Amish families, *paternal* longevity was weakly correlated with daughter's telomere length (29). We uncovered that *maternal* longevity is related to telomere length for both men and women,

and the association persists for women even after adjusting for adult characteristics. Our results imply that mothers who live to advanced ages may be a resource for their adult child's—especially their daughter's—biological health and aging, somewhat reflective of a mother or grandmother effect (35). It should be noted, however, that although stressors are often associated with shorter telomeres, evidence that shorter telomeres are associated with mortality and some diseases such as cancer is inconclusive (7,9).

These findings should be interpreted in light of several study limitations. First, recall bias is a potential issue in all studies that use retrospective data. To address this issue, models were adjusted for measures associated with recall bias such as adult socioeconomic resources (36). Models adjusting for cognition score did not alter conclusions. Second, the results from this study may not be easily compared with other studies that use a different telomere measure (i.e., measured from blood samples) or assay method. Telomere samples from saliva and from blood reveal similar results in studies that investigate the effect of childhood stress; however, caution is still warranted as telomere lengths vary by cell type (15–17). Similarly, different assay methods may provide distinct results. Although quantitative polymerase chain reaction is a commonly used method, it tends to have greater measurement error compared with other methods such as Southern blot (37).

Third, this study is cross-sectional, and therefore, we cannot make inferences about telomere shortening over time. Despite current data limitations, there are a few studies that have examined telomere length at multiple time points revealing that some individuals' telomeres lengthen (38). One potential explanation for telomere lengthening is telomerase—an enzyme typically only found in fetal tissue, adult germ cells, and some tumor cells that elongates telomeres. Unfortunately, the HRS collected telomere data at one time point only and does not have information on telomerase activity.

Despite these limitations, this study advances the literature in several ways. First, prior studies have examined an overall count of early-life stressors, but we investigated domains of various early-life exposures to identify specific pathways for intervention. With national data from the HRS, we found that two of the six domains— risky parental and adolescent behaviors—were related to shorter telomeres among men in partially adjusted models. Although none of the childhood

exposure domains were associated with women's telomeres, one of the risky parental behavior indicators—parental substance abuse—was associated with shorter telomeres for women. Second, this study is among the first to show that the types of childhood exposures that are associated with shorter adult telomeres vary for men and women. Third, although one study reported that stressful exposures are related to telomere length in younger, but not older adults (5), this study provides evidence that some types of exposures are related to telomere length among older adults. Taken together, we build on past studies by identifying which types of exposures are associated with adult telomeres and for whom, noting differences by gender.

Supplementary Table S1 follows the **References**.

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Supplementary Table S1. Regression of Telomere Length on Childhood Exposures and Covariates for Men and Women

	Men (n=1,983)			Women (n=2,952)		
	Coef.[a]		S.E.[b]	Coef.		S.E.
Black	0.069	**	0.023	0.078	***	0.016
Hispanic	0.043		0.027	0.031		0.023
Age	-0.003	***	0.001	-0.004	***	0.001
Parental Longevity						
Mom Age 85+	0.019		0.011	0.031	**	0.011
Dad Age 85+	-0.009		0.014	0.008		0.011
Childhood Exposures						
SES Disadvantage	-0.015		0.014	-0.003		0.014
Risky Parental Behavior	-0.028		0.015	0.007		0.011
Chronic Disease	-0.013		0.011	0.006		0.013
Infectious Disease	0.013		0.021	-0.019		0.023
Impairment	0.002		0.015	0.013		0.014
Risky Adolescent Behavior	*-0.036*	[c]	0.021	*0.031*		0.022
Adult SES Factors						
Education	0.002		0.002	-0.002		0.002
Wealth[d]	0.002		0.002	0.002		0.002
Marital Status (ref. is married)						
Divorced/Separated	-0.008		0.023	0.001		0.013
Widowed	0.000		0.019	-0.006		0.015
Never Married	0.077	*	0.033	0.043		0.028
Adult Health Lifestyle						
Pack-Years Smoking	0.000		0.000	-0.002	***	0.000
Heavy Drinking	-0.006		0.041	0.017		0.047
Physical Activity	0.004		0.013	-0.001		0.011
Body Mass Index	*0.005*	***	0.001	*0.001*		0.001
R^2	0.038			0.054		

[a] Coef. is coefficient
[b] S.E. is standard error
[c] Italicized coefficients indicate significant differences between men and women at $p<0.05$
[d] Cube root of wealth in $1,000s
* $p<0.05$; ** $p<0.01$; *** $p<0.001$