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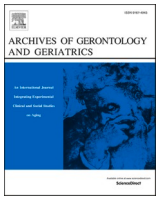

Related risk factors for age-dependent telomere shortening change with age from the perspective of life course

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HIGHLIGHTS

- Related risk factors of telomere attrition differ contribute to different at different age stages.
- Modification of telomere length by behavioral, environment, and social factors changed with age.
- Education levels, family income, marital status, physical activity, and self-reported greatest weight were associated with telomere length at different age stages.

ARTICLE INFO

Keywords:
Telomere attrition
Risk factors
Age stratified assessment
Heterogeneity
A nationally representative survey

ABSTRACT

Background: Many related factors can accelerate the age-dependent telomere shortening, but some problems remain unresolved. This study aimed to assess the risk factors of telomere attrition at different age stages.
Methods: This study was a population-based nationally representative survey study. All data were collected using a standard methodology by the national surveillance system. Quantitative polymerase chain reaction was used to measure relative leukocyte telomere length. Multiple linear regression analysis with age stratification was used to estimate the association of shortened telomere length with risk factors at the different age stages. Covariance analysis was used to compare the telomere length of category variables, and the model was adjusted for potentially confounders.
Results: A total of 7,659 eligible participants aged 20 years or older with DNA specimens participated in the study. Related risk factors for age-dependent telomere shortening included gender, race-ethnicity, education levels, family income, health insurance, marital status, physical activity, smoking status, alcohol use, and self-reported greatest weight, which were associated with change in telomere length at different age stages.
Conclusions and implications: Related risk factors of telomere attrition were changed with age in life course. The evaluation of related risk factors for telomere attrition in terms of age may be a more accurate evaluation comparison with the specific age.

1. Introduction

Over the past two decades, there has been a growing focus among researchers worldwide on studying telomeres. Specifically, telomere length, a significant biological marker that has been linked to cellular senescence and life expectancy, has been studied (Turner et al., 2019; Aguado et al., 2020).

Aging is the foremost risk factor for the development of human diseases and mortality (Gude et al., 2018; Loaiza & Demaria, 2016; Martin-Ruiz et al., 2005). However, the aging process varies among individuals, and there are interindividual variations within different populations (Carmona & Michan, 2016). Telomeres, which are nucleoprotein complexes consisting of six nucleotide DNA repeats and associated proteins, play a crucial role in maintaining chromosome end stability and preventing DNA damage (Harley et al., 1990). Telomeres undergo age-related shortening with cell division after an individual's birth. Consequently, telomere length has long been recognized as the most effective biomarker for predicting aging, and disorders in telomere

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length maintenance can accelerate aging in humans (Gil, 2019).

At the cellular level, telomere attrition can result in cell cycle arrest and senescence, thereby contributing to aging-related biology and pathology (Blackburn et al., 2015; Bountziouka et al., 2022). Telomere shortening is influenced by genetic factors, epigenetic factors, and other modifiable factors. Generally, women tend to have longer telomeres than men. This difference is attributed to the earlier stages of growth and development in females. Unlike in men, in women, age does not appear to be associated with telomere length after accounting for menopausal status. Additionally, race and ethnicity have been found to be associated with telomere length (Rewak et al., 2014; Vyas et al., 2020), which may be influenced by lifestyle and behavioral factors (Vyas et al., 2021). On an individual level, higher levels of physical activity have been linked to longer telomeres (Fretts et al., 2018), while heavy drinking and smoking have been associated with shorter telomeres (Latifovic et al., 2016). The Mediterranean dietary pattern has been shown to be associated with longer telomeres (Nilsson, 2014), whereas overweight and obesity are considered major risk factors for shorter telomeres due to the impact of inflammation and oxidative stress on telomeres (An & Yan, 2017; Correia-Melo et al., 2014). At the population level, telomere attrition has been linked to increased all-cause mortality and morbidity associated with age-related diseases (Wang et al., 2018; Okamoto & Seimiya, 2019).

In recent years, our understanding of the effects of various factors on telomere length has improved through numerous basic, clinical, and epidemiological studies. However, some studies have reported inconsistent results, likely due to small sample sizes, weak research designs, and a lack of control for confounding variables. Additionally, previous studies have focused primarily on the cellular, individual, or population levels, neglecting the influence of the social environment and the life course perspective on telomere length. The identification of modifiable factors that contribute to telomere attrition is still ongoing to slow or prevent telomere shortening. Although telomere length can provide only an approximate estimate of aging and cannot be used as a clinically precise tool for assessing age-related pathologies and mortality, it remains a valuable marker for predicting individual health status and disease risk (Mather et al., 2011).

Telomeres are widely recognized as “biological clocks” associated with an individual’s lifespan, and previous studies have focused predominantly on older age and age-related diseases such as cancer and chronic degenerative diseases. Consequently, there is insufficient evidence regarding telomere dynamics in early life stages and life processes. In this study, we hypothesized that the risk factors associated with telomere attrition differ across different age groups. Our aim was to investigate these risk factors in a large sample size and to consider additional relevant factors. We propose that exploring the determinants of telomere length from a life course perspective will enhance our understanding of the important role that telomeres play in aging. The findings of this study can serve as a basis for guiding self-health management planning and intervention strategies at various phases of the life cycle.

2. Materials and methods

2.1. Study population

We utilized data from the National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention, which included the years 1999–2000 and 2001–2002. The NHANES is a nationally representative survey of individuals residing in the U.S. Participants were selected from 15 different locations using a four-stage sampling design. Sample weights for the 1999–2000 data were calculated based on the 1990 U.S. census, while the 2001–2002 sample weights were based on the 2000 census. Our study included 10,291 eligible participants from 1999 to 2002, 7826 of whom were aged >20 years and consented to participate in genetic research and provided DNA specimens. Participants with missing data on important covariates were excluded from the analysis, resulting in a final sample size of 7659 participants. Written informed consent was obtained from all participants, and the study was approved by the institutional review board at the U.S. Centers for Disease Control and Prevention.

2.2. Data collection

The survey was conducted through home interviews and health examinations at a mobile examination center (MEC). During the home interviews, participants provided self-reported information on their demographic characteristics, lifestyle behaviors, medical history, and social and psychological status. Physical measurements, dental examinations, and blood specimen collection were performed at the MEC.

Regarding lifestyle behaviors such as smoking, drinking, and physical activity, participants were asked about the frequency, duration, and quantity of these behaviors in the past month or day. Physical activity was assessed using the question “Over the past 30 days, did you perform any moderate or vigorous physical activity for at least 10 min?”, and the responses were classified into two groups: “yes” and “no”. Smokers were identified as participants who reported having smoked at least 100 cigarettes in their lifetime. Individuals who reported consuming at least 12 alcoholic drinks per year were defined as drinkers. Participants were asked to provide their highest self-reported weight in pounds. Family income was classified as “Under $20,000″ or “Over $20,000″. Marital status was categorized as “married”, “widowed”, “divorced”, “separated”, “never married”, or “living with partner”.

2.3. Telomere length measurement

All participants whose blood samples were collected were eligible for DNA purification. Telomere length in leukocytes was measured relative to that of standard reference DNA using the quantitative polymerase chain reaction method (Cawthon, 2022). The concentration of each sample was measured three times on different days, resulting in six data points. A 96-well plate included eight control samples. Measurements with more than four control values exceeding 2.5 standard deviations from the mean for all measurements were excluded from further analysis. Potential outliers were identified for each sample, and less than 2 % of the samples were excluded from the calculations of the mean and standard deviation of the telomere-to-single copy gene (T/S) ratio.

2.4. Statistical analysis

The statistical analysis was limited to participants with validated telomere length data and no missing important covariates. All analyses were conducted following the methods of Johnson et al. (Johnson et al., 2013), and a weighted sampling approach was used. Descriptive statistics were utilized to present the demographic characteristics of the participants. Weighted percentages were calculated for sex-specific categories of variables.

The telomere length means were compared based on different participant characteristics. Differences between two groups were determined using the Mann–Whitney U test, and participant characteristics are expressed as the means and standard deviations. One-way analyses of variance were conducted to compare telomere length means among multiple groups. Prior to intergroup comparisons, normality tests and variance homogeneity tests were performed for each group’s measurements. An analysis of covariance was further conducted to evaluate changes in telomere length means across different age groups, as well as the effects of important covariates on telomere length. The covariates included sex, race-ethnicity, education level, family income, marital status, physical activity, smoking status, alcohol use, and self-reported greatest weight.

Multiple linear regression analyses were performed, stratified by age, to estimate the association between shortened telomere length and risk

factors across different age groups. Standardized regression coefficients and standard errors were calculated to determine the relative importance of each factor related to telomere length. All variables with a significance level of $p \leq 0.1$ were included in the model. Categorical variables such as race-ethnicity and marriage were also included in the age-stratified covariance analysis to compare telomere length means across different variable categories, accounting for potentially important confounders. All analyses were conducted using SAS for Windows (version 9.4).

3. Results

Table 1 displays the demographic characteristics of the participants by sex. A total of 7659 participants with a mean age of 49.5 years were included in the analysis. Among the participants, 48.3 % were male and 51.7 % were female. Approximately 20.1 % of the participants were 60 years old and older. Non-Hispanic whites accounted for a significantly larger proportion of participants than did other participants. Among the participants, 42.2 % of the men and 30.9 % of the women engaged in moderate or vigorous intensity physical activity. The smoking rate was 57.2 % among men and 42.6 % among women. Approximately 15.9 % of men and 36.1 % of women reported consuming no more than 12 drinks per year.

A comparison of telomere length based on various participant characteristics is displayed in Table 2. The means of telomere length significantly varied among the subgroups of each variable, including sex, race-ethnicity, education level, family income, marital status, physical activity, smoking status, alcohol use, and self-reported greatest weight ($P < 0.01$). Compared with men, women exhibited notably longer telomeres. Non-Hispanic black had the longest telomere, and Mexican American had the shortest telomere length. Telomere length increased with education level. Participants with higher family incomes had longer telomeres than did those with lower family incomes.

Table 1
Characteristics of participants by gender in the study.

Variable	Men (n = 3701)	Weighted %	Women (n = 3958)	Weighted %
Characteristic variables				
Age groups (yr)				
20–29	577	(20.0)	759	(20.1)
30–39	588	(22.2)	722	(23.1)
40–49	662	(22.8)	632	(20.8)
50–59	513	(16.2)	466	(14.7)
60–69	604	(10.2)	570	(10.3)
70–79	443	(6.3)	394	(7.1)
80 +	267	(2.3)	292	(3.9)
Race-ethnicity				
Mexican American	858	(7.2)	902	(6.5)
Other Hispanic	182	(6.6)	213	(7.3)
Non-Hispanic White	1914	(73.7)	1949	(71.9)
Non-Hispanic Black	603	(8.7)	651	(10.2)
Other Race	97	(3.8)	120	(4.1)
Education levels				
Less than 9th Grade	595	(6.7)	550	(6.4)
9 – 11th Grade	670	(14.6)	657	(13.8)
High School Grade	827	(25.7)	920	(26.5)
College	824	(26.8)	1040	(30.8)
College Graduate or above	738	(26.2)	668	(22.5)
Physical activity				
Yes	1252	(42.2)	932	(30.9)
No	2402	(57.8)	2903	(69.1)
Smoking status				
Yes	2181	(57.2)	1477	(42.6)
No	1473	(42.8)	2358	(57.4)
Alcohol use				
Yes	3019	(84.1)	2183	(63.9)
No	635	(15.9)	1652	(36.1)

Table 2
The means and standard deviations of telomere length by characteristics of participants.

	Telomere length				
		95 % CI		Standard	
Variable	Mean	Lower	Upper	Deviation	p value
Gender					
Male	1.009	0.999	1.019	0.296	<0.001
Female	1.045	1.037	1.054	0.265	
ace-ethnicity					
Mexican American	1.003	0.989	1.017	0.272	<0.001
Other Hispanic	1.070	1.044	1.097	0.268	
Non-Hispanic White	1.015	1.007	1.024	0.284	
Non-Hispanic Black	1.083	1.068	1099	0.235	
Other Race	1.046	1.015	1.077	0.272	
Education levels					
Less than 9th Grade	0.950	0.937	0.963	0.230	<0.001
9 – 11th Grade	1.022	1.003	1.040	0.349	
High School Grade	1.040	1.027	1.052	0.275	
College	1.051	1.039	1.063	0.263	
College Graduate or above	1.053	1.039	1.066	0.263	
Family income					
Under $20,000	1.015	1.004	1025	0.276	0.003
Over $20,000	1.034	1.026	1042	0.283	
Marital status					
Married	1.006	0.999	1.014	0.255	<0.001
Widowed	0.896	0.880	0.913	0.221	
Divorced	0.993	0.973	1.014	0.257	
Separated	1.039	1.010	1.069	0.235	
Never married	1.159	1.137	1.182	0.373	
Living with partner	1.091	1.065	1.116	0.258	
Physical activity					
Yes	1.045	1.027	1.073	0.256	<0.001
No	1.009	1.001	1.016	0.299	
Smoking status					
Yes	1.009	1.035	1054	0.259	<0.001
No	1.045	1.001	1.018	0.299	
Alcohol use					
Yes	1.034	1.027	1.042	0.289	<0.001
No	1.012	1.001	1.022	0.259	
Self-reported greatest weight (pounds)					
Less than or equal to155	1.036	1.025	1.048	0.272	<0.001
156 to180	1.029	1.014	1.044	0.324	
181 to 210	1.017	1.006	1.029	0.259	
Greater than 210	1.027	1.015	1.038	0.257	

CI: confidence interval.

Individuals engaging in moderate or higher physical activity, as well as drinkers, had longer telomeres than did both physically inactive participants and nondrinkers. Patients exposed to smoke had shorter telomeres than nonsmokers did. Self-reported greatest weight was negatively associated with telomere length.

The analysis of covariance determined that telomere length decreased with age, presenting a significant linear trend after adjusting for relevant risk factors (Table 3). Important covariates, such as sex, race-ethnicity, education level, family income, marital status, physical activity, and self-reported greatest weight, exhibited significant associations with telomere length. Smoking status and alcohol use, however, were no longer found to be associated with telomere length.

The risk factors associated with shortened telomere length at different age stages are summarized in Table 4 and Fig. 1. In the 20–49 years age group, there was a negative association between weight and telomere length. In the 30–59 years age group, education level was positively associated with telomere length. In the 50–59 years age group, sex was associated with telomere length ($p = 0.081$), with women having significantly longer telomeres than men among participants aged 60 years and older. In the 60–69 years and ≥80 years age groups, family income was positively associated with telomere length. In the 70–79 years age group, individuals with health insurance had significantly

Table 3
The means and standard errors of telomere length by age groups using analysis of covariance.

Variable	Telomere length Mean	95 % CI Lower	Upper	Standard Deviation	*p* value
Age groups					
20−29	1.171	1.165	1.202	0.007	<0.001
30−39	1.099	1.097	1.124	0.007	<0.001
40−49	1.054	1.046	1.073	0.007	<0.001
50−59	0.984	0.978	1.007	0.008	<0.001
60−69	0.948	0.931	0.956	0.007	<0.001
70−79	0.883	0.865	0.896	0.009	<0.001
80 +	0.836	0.819	0.854	0.011	<0.001

Covariates	β	SE	*p* value
Gender	0.018	0.006	0.008
Race-ethnicity	0.018	0.003	<0.001
Education levels	0.006	0.002	0.018
Family income	0.002	0.001	0.048
Marital status	0.006	0.002	0.002
Physical activity	0.012	0.005	0.038
Smoking status	0.012	0.006	0.055
Alcohol use	−0.011	0.006	0.101
Self-reported greatest weight (pounds)	−0.008	0.002	0.005

β: Standardized β-coefficients.
SE: standard error.

Table 4
β coefficients of telomere length and related factors by age-stratified analysis.

Variables by age groups (yr)	Telomere length (Mean T/S ratio) Standardized β-coefficients	Standard Error	t value	*p* value
20−29				
Race-ethnicity	0.016	0.008	1.86	0.063
Physical activity	0.047	0.019	1.68	0.092
Marital status	0.080	0.004	2.85	0.004
Weight (kg)	−0.068	0.001	−2.41	0.017
30−39				
Race-ethnicity	0.089	0.006	3.00	<0.001
Physical activity	0.023	0.015	1,78	0.085
Education levels	0.064	0.006	2.07	0.038
Weight (kg)	−0.077	0.001	−2.67	0.016
40−49				
Race-ethnicity	0.033	0.006	5.18	<0.001
Education levels	0.073	0.005	2.42	0.015
Alcohol use	−0.053	0.015	−1.89	0.059
Weight (kg)	−0.102	0.001	−3.59	<0.001
50−59				
Race-ethnicity	0.091	0.008	2.62	0.009
Education levels	0.067	0.006	1.98	0.049
Gender	0.057	0.015	1.74	0.041
60−69				
Race-ethnicity	0.078	0.005	2.6	0.009
Physical activity	0.058	0.012	2.77	0.005
Family income	0.075	0.002	2.36	0.018
Smoking status	0.032	0.014	1.98	0.072
Gender	0.122	0.013	4.03	<0.001
70−79				
Race-ethnicity	0.054	0.007	1.76	0.086
Physical activity	0.058	0.012	1.62	0.906
Smoking status	0.092	0.015	2.47	0.013
Health insurance	0.094	0.002	2.65	0.008
Gender	0.095	0.015	2.51	0.012
80 +				
Family income	0.096	0.003	2.17	0.030
Alcohol use	0.131	0.014	2.88	0.004
Gender	0.117	0.020	2.56	0.011

longer telomeres than did those without health insurance. Smokers exhibit shortened telomeres, similar to what occurs during the general aging process. In the ≥80-year-old age group, individuals who consumed at least 12 alcoholic drinks per year had longer telomeres than did nondrinkers. In the 30–69 year age group, race and ethnicity played a role in the change in telomere length. The telomere length of Mexican American was the shortest compared with other Hispanic, Non-Hispanic White, and Non-Hispanic Black participants. Marital status had a notable impact on telomere length. In the ≥70 years age group, widowed and divorced participants had longer telomeres than married participants, while participants living with a partner had shorter telomeres than all the other groups. In the 40–49 years age group, married participants had significantly longer telomeres than divorced participants. In the 20–29 year age group, married participants had shorter telomeres than participants living with a partner.

4. Discussion

The results indicate that the influence of behavioral, environmental, and social factors on telomere length varies across different age groups. This finding supports our hypothesis that the risk factors associated with telomere attrition are complex and dynamic across different age groups.

While previous studies have reported the risk factors associated with telomere attrition, conflicting and inconsistent results have emerged due to disparate sample sizes and study designs. The strength of some risk factors varied across different time periods, introducing potential evaluation bias. For instance, studies exploring the relationship between telomere length and obesity have yielded mixed findings. A study summarizing 63 relevant studies revealed that while 24 studies showed no significant difference in the association between obesity and telomere length, one study showed a positive association. These discrepancies can be attributed to the small sample sizes, study heterogeneity, and the inclusion of obesity as an adjusting variable in many studies.

In the present study, the weight did not retain statistical significance, while the two variables, namely, body weight and self-reported greatest weight were included into model. The telomere length was more significantly associated with historical body weight compared with current body weight. Age stratification further revealed a negative association between body weight and telomere length exclusively in the 20–49 years age group. Similarly, another study revealed that the association between body weight and telomere length is strongest in younger individuals and gradually weakens, particularly among those approaching 60 years of age. These findings highlight the influence of age on telomere attrition risk factors and emphasize the importance of conducting age-stratified analyses to identify effective interventions for preventing and delaying telomere shortening.

Sex and race are commonly considered inherent risk factors associated with certain diseases that cannot be modified. Telomere length is related to parental telomere length, and it is similar between male and female infants at birth (Vasu et al., 2017; Okuda et al., 2002). Although studies have shown no difference in telomere length between females and males or have suggested that any sex difference is a result of methodological bias, other studies have shown that white blood cell telomeres are longer in women than in men (Barrett & Richardson, 2011). Several hypotheses have been proposed to explain this association, including the antioxidant properties of estrogen, which can stimulate telomerase and add telomere repeats to the ends of chromosomes (Nawrot et al., 2004; Fitzpatrick et al., 2007). In the present study, women aged 50 years and older had significantly longer telomeres than men did. Additionally, the mean age at menopause was greater in female participants (49 years). One study revealed no difference in telomere length between younger women and men but found that in older individuals, telomere length was longer (Hunt et al., 2008). However, the underlying mechanism requires further investigation. Furthermore, age-associated changes in telomere length are almost six times in black and Hispanic women than in white women and three times in black and Hispanic women than in white men. However, whether estrogen plays a potential role in causing these significant sex and race-ethnicity effects is unknown. Limited information is available regarding the associations

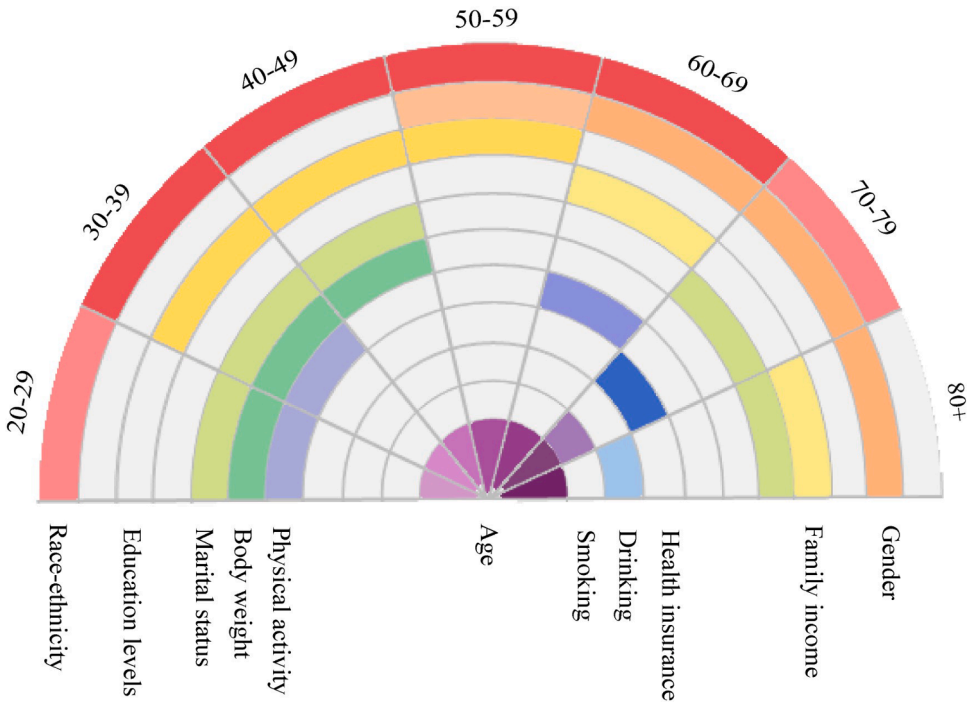

Fig. 1. Changes in risk factors related to telomere attrition at different age stages.

between race-ethnicity factors and telomere length across different age groups. We further analyzed the association between race and ethnicity and between telomere length and age. In the 30–69-year-old group, different race-ethnicity groups exhibited variations in telomere length. Compared with non-Hispanic White individuals, non-Hispanic Black individuals, and Other Hispanics had longer mean telomere lengths, and the telomere lengths of individuals of other races were shorter than those observed in the 30–49 year group. Environmental factors such as inflammation, increased oxidative stress, and behavioral and psychosocial factors are likely contributors to differences in telomere length according to race (Steptoe et al., 2007; Irie et al., 2003).

Numerous studies have investigated the correlation between socioeconomic status and telomere length. However, the inclusion of different measures of socioeconomic status, such as social class, income, and education levels, has led to varied findings. Education level serves as a crucial indicator of socioeconomic status during early adulthood, setting the stage for an individual's future socioeconomic trajectory. Understanding the effects of socioeconomic status, including education, on telomeres may take considerable time (Steptoe et al., 2011; Robertson et al., 2013). Therefore, education may offer a more reliable indicator of socioeconomic status throughout early and mid-life than measures taken at the time of study. Our findings strongly support this notion, as education levels at 30 to 59 years of age were significantly associated with telomere length. This period represents a critical stage where in education exerts the greatest influence on an individual's career, social status, economic circumstances, and family life. The longer the exposure to risk factors is, the greater their impact will be. Nonetheless, with advancing age and changes in the social environment, the effect and intensity of these exposure factors on individuals also change. Environmental stressors resulting from differing educational experiences in terms of occupation, income, and social relationships diminish or weaken significantly in old age. This study's design and implementation are crucial for identifying the most significant risk factors contributing to telomere attrition across different age groups and implementing more effective interventions.

Income is another common marker of socioeconomic status. Studies have shown positive, null, and negative associations between telomere length and income (Cherkas et al., 2006; Adams et al., 2007; Woo et al., 2009). These inconsistent findings are likely due to the small sample sizes, methodological disparities, and subject reporting biases. A multiethnic study demonstrated no significant association between income and telomere length among participants aged 45–84 years (Diez et al., 2009; Needham et al., 2019). However, individuals with higher incomes exhibited longer telomeres than did those with lower incomes (Yen & Lung, 2013). A population-based longitudinal study with a follow-up period of more than 10 years revealed that participants with higher incomes had longer telomeres than did those with lower incomes, but no noteworthy difference was observed in baseline telomere length or 10-year telomere attrition (Shiels et al., 2011). These results support the notion that higher incomes are associated with longer telomere length in older adults aged 60–69 and above 80 years. In the 70–79 age group, health insurance replaced income within the model. Thus, income significantly impacts telomere attrition in older individuals.

The findings of clinical and epidemiological studies indicate that an active lifestyle has protective effects on preventing age-related diseases and telomere attrition. Physical activity not only enhances telomerase activity but also reduces inflammation and oxidative stress levels. However, the available evidence regarding the relationship between physical activity and telomere length is highly varied. In this study, participants who engaged in moderate or vigorous physical activity over the past 30 days exhibited longer telomere lengths than did inactive participants, but only among those aged 60–69 years. No statistical significance was observed among participants aged >20–29 years, although moderate or vigorous physical activity was included in the analysis. We utilized the metabolic equivalent of a task to assess the association between physical activity level and telomere length. The results revealed a significant positive association between physical activity level and telomere length. The differences in measurement instruments contributed to the heterogeneity of the results. Individuals are exposed to different levels of risk factors at various stages, and the effect of the environment on an individual is also subject to constant change. Therefore, risk factors should be evaluated during different periods of exposure.

Marriage is advantageous for an individual's health. Unmarried individuals tend to have shorter telomeres, which corresponds to an increased risk of disease. We further investigated the effect of various

unmarried statuses on telomere length at different ages. Between the ages of 20 and 29, married individuals had longer telomeres than did separated individuals. Between the ages of 30 and 39, individuals who had never married had longer telomeres than did married and divorced individuals. Between the ages of 40 and 49 years, married individuals had longer telomeres than did divorced individuals. No significant effect of marriage on telomere length was observed among individuals aged 50–69 years after adjusting for other factors. Among individuals aged 70 and above, those who were divorced had longer telomeres than did those living with a partner, widowed individuals, or married individuals. Theories on marriage suggest that having a spouse or partner provides benefits such as social support as a buffer against life stressors (Schone & Weinick, 1998). Healthy individuals tend to choose marriage, while unhealthy individuals tend to remain unmarried (Molloy et al., 2009). The results of our study indicated that individuals living with a partner had shorter telomeres than others. Marriage may offer social support as a coping mechanism for stress (Simon et al., 2006; Epel et al., 2004), but under normal circumstances, if stress levels are low, the significance of social support may diminish.

In the present study, smoking was shown to be associated with shortened telomere length, while drinking was associated with longer telomeres in individuals aged 70 years and older. The potential reason behind the impact of smoking on telomere length could be cellular damage, which significantly increases the risk of gene mutations. However, studies on the relationship between alcohol use and telomere length have not yielded conclusive results (Weischer et al., 2014). Although alcohol use is generally considered a risk factor, the present study showed that light drinking was associated with longer telomeres. This could be because individuals who consume wine or follow a Mediterranean diet have a reduced risk of mortality.

It is important to note that we accounted for other factors when analyzing various risk factors. However, studying the risk factors for telomere attrition in large populations is complex due to confounding factors that are difficult to adjust for. Among these factors, race-ethnicity was the most significant risk factor associated with telomere attrition, and we controlled for this factor when analyzing other risk factors. However, the effects observed in older age groups are influenced more by changes in health and population factors (Perls et al., 2002). It has been reported in other studies that if a factor affects telomere length and survival rate, we cannot observe any associations between the interesting factor and this factor among survivors, as individuals exposed to this factor would have died (Pavanello et al., 2021; Crocco et al., 2021). Additionally, a time effect analysis demonstrated that older age is associated with a greater rate of telomere attrition. Although oxidative stress and inflammation likely play a role, the molecular mechanisms linking older patients to faster telomere attrition have not been elucidated. A hypothesis that age-dependent shortening is the general trend in this field is emerging. The mechanism behind the presumed oscillating telomere length of the circulating leukocyte pool is still unknown, but the theory of transient telomerase activation has been proposed.

The main strength of the present study is that it was based on a national survey. In comparison to previous studies, this study had a relatively large sample size. The data were collected using a standardized methodology through a national surveillance system. This allows for the analysis of additional risk factors for telomere attrition and the control of important confounding factors. Additionally, this study was the first to explore the related risk factors for telomere attrition across different age groups. By stratifying the data by age, we were able to evaluate the associated risk factors under varying exposure intensities and environmental effects at different stages of life. These findings partially explain the contradictory results of previous studies. This study has several limitations. First, the exploration of related risk factors for telomere attrition at different ages was conducted using a cross-sectional study design. This means that an age-period-cohort analysis cannot be carried out. Therefore, only associations between telomere length and related risk factors can be determined, while causality and the intensity of interaction with environmental factors cannot be established. Second, the weight measurements relied on self-reports from the participants, introducing the possibility of self-reported bias. Last, participants reported their activity only over the last 30 days, which limits our ability to evaluate the dose–response relationship between physical activity and telomere attrition.

In conclusion, telomere length is an important predictor of health that varies with age. This study revealed that telomere attrition is associated with risk factors at different stages of life. The effect of individual and environmental factors on changes in telomere length at different ages. In particular, middle-aged individuals experience significant positive associations between telomere length and education level, which affects their economic status; career, family, and stress levels. However, the effect of education level on telomere length gradually weakens or disappears in the elderly population. Furthermore, family income significantly affects telomere length in elderly individuals, while self-reported weight is associated with telomere length only in young and middle-aged individuals. Reduced physical activity is associated with an increased risk of telomere shortening in the early stages of old age. Marital status may also impact telomere length across different age groups. Consequently, evaluating telomere-attrition-related factors based on age is more accurate than evaluating them across all ages.

Ethics approval and consent to participate

All participants provided informed consent before participation. The study was approved by the institutional review board at the U.S. Centers for Disease Control and Prevention.

CRediT authorship contribution statement

Yin Chen: Writing – original draft, Software, Formal analysis. **XiWen Ding:** Writing – original draft, Software, Project administration. **Ayizuhere Aierken:** Writing – review & editing, Software, Project administration, Formal analysis. **Yuan Chen:** Writing – review & editing, Validation, Software. **Ying Li:** Writing – review & editing, Writing – original draft, Software, Formal analysis, Data curation, Conceptualization.

Declaration of competing interest

The authors declare no conflict of interest.

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