Movement-Based Behaviors and Leukocyte Telomere Length among US Adults

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ABSTRACT

LOPRINZI, P. D., J. P. LOENNEKE, and E. H. BLACKBURN. Movement-Based Behaviors and Leukocyte Telomere Length among US Adults. *Med. Sci. Sports Exerc.*, Vol. 47, No. 11, pp. 2347–2352, 2015. **Introduction**: Short leukocyte telomere length (LTL) has become a hallmark characteristic of aging. Some, but not all, evidence suggests that physical activity (PA) may play an important role in attenuating age-related diseases and may provide a protective effect for telomeres. The purpose of this study was to examine the association between PA and LTL in a national sample of US adults from the National Health and Nutrition Examination Survey. **Methods**: National Health and Nutrition Examination Survey data from 1999 to 2002 (n = 6503; 20–84 yr) were used. Four self-report questions related to movement-based behaviors (MBB) were assessed. The four MBB included whether individuals participated in moderate-intensity PA, vigorous-intensity PA, walking/cycling for transportation, and muscle-strengthening activities. An MBB index variable was created by summing the number of MBB an individual engaged in (range, 0–4). **Results**: A clear dose–response relation was observed between MBB and LTL; across the LTL tertiles, respectively, the mean numbers of MBB were 1.18, 1.44, and 1.54 ($P_{trend} < 0.001$). After adjustments (including age) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 3% ($P = 0.84$), 24% ($P = 0.02$), 29% ($P = 0.04$), and 52% ($P = 0.004$) reduced odds of being in the lowest (vs highest) tertile of LTL; MBB was not associated with being in the middle (vs highest) tertile of LTL. **Conclusions**: Greater engagement in MBB was associated with reduced odds of being in the lowest LTL tertile. **Key Words:** AGING, EPIDEMIOLOGY, PHYSICAL ACTIVITY, NHANES

Shortened leukocyte telomere length (LTL) characterizes human aging (5,26,27). Potentially reflecting systemic oxidative stress and inflammation (10,51), short LTL is linked with various cardiometabolic diseases (2,4,13,18,19,21,46,47). Physical activity (PA) may help attenuate age-related diseases, as previous research (8,14,20,23–25,34,37,39,44,49) demonstrates that physically active adults have longer mean LTL. However, some studies show no relation (22,32,33,40,45,48,52), with others reporting an inverted U relation (9,31,43) (review articles, see Ludlow (29,30)).

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Given these mixed findings, coupled with the fact that most of these studies were convenience-based samples or used targeted populations (e.g., postmenopausal women) (29,30), here, we examine the association between PA and LTL in a national sample of US adults. To improve our understanding of associations between PA and LTL, specific attention was focused on data from four movement-based behaviors (MBB). These include moderate-intensity PA (MPA), vigorous-intensity PA (VPA), walking and cycling for transportation, and muscle-strengthening activities (MSA).

METHODS

Design and participants. Data were extracted from the 1999–2002 NHANES (only cycles with LTL data at the time of this writing). Procedures were approved by the National Center for Health Statistics review board. Consent was obtained from all participants. Analyses are based on data from 6503 adults (20–84 yr) who provided complete data for the study variables. In the 1999–2002 NHANES cycles, 9882 participants were between 20 and 84 yr of age. After

excluding those with missing MBB data, 9369 remained. After excluding those with missing covariate data, 7283 remained. Lastly, after excluding those with missing telomere data, 6503 remained (resultant sample) (Fig. 1). When comparing the final analytic sample (n = 6503) with the 780 participants with missing telomere data (7283 − 6503 = 780), there were no differences in age, number of MBB, body mass index (BMI), C-reactive protein (CRP), or smoking (all $P > 0.05$); however, those that were excluded were more likely to be female (60% vs 51.1%; $P < 0.001$), less likely to be non-Hispanic White (38.1% vs 50.4%, $P < 0.001$), and had a lower poverty-to-income ratio (PIR) (2.56 vs 2.71, $P = 0.01$). These are unweighted estimates.

LTL. Detailed methodology of the NHANES procedures for assessing LTL has been previously reported (35). Briefly, DNA was extracted from whole blood and the LTL assay was performed using quantitative polymerase chain reaction to measure LTL relative to standard reference DNA (T/S ratio) (35). Each sample was assayed at least twice, and among samples with a T/S ratio within 7% variability, the average value was used; for samples with variability greater than 7%, a third assay was run and in this case, the average of the two closest T/S values was used. Notably, in NHANES, telomere length in leukocytes was assessed. We acknowledge that LTL is not specific to skeletal muscle tissue; however, it may not be feasible to take muscle biopsies in large epidemiological studies. Previous work suggests that LTL is modestly (r = 0.39) associated with muscle telomere length (1), which is in accordance with other studies (12), providing some justification for continued use of LTL measures, particularly in epidemiological studies.

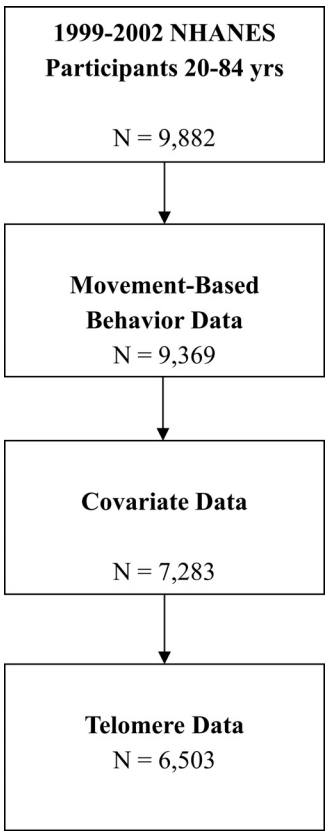

FIGURE 1—Participant flow chart.

MBB. In the 1999–2002 NHANES, four self-report items related to MBB were assessed, including PA participation during transportation and leisure time; notably, objective measures of PA (e.g., accelerometry) were not released until the 2003–2004 NHANES cycle. The four MBB included the degree of participation in *MPA*, *VPA*, *walking/cycling* for transportation, and *MSA* (yes/no responses).

For MPA: "*Over the past 30 d, did you do moderate activities for at least 10 min that cause only light sweating or a slight-to-moderate increase in breathing or HR?*"

For VPA: "*Over the past 30 d, did you do vigorous activities for at least 10 min that caused heavy sweating or large increases in breathing or HR?*"

For walking/cycling for transportation: "*Over the past 30 d, did you walk or bicycle as part of getting to and from work or school or to do errands?*"

For MSA: "*Over the past 30 d, did you do any physical activities specifically designed to strengthen your muscles such as lifting weights, push-ups, or sit-ups?*"

MBB index. An MBB index variable was created by summing the number of MBB an individual engaged in (range, 0–4).

Covariates. Covariates included *age* (continuous), *age squared* (due to nonlinearity between age and LTL), *gender*, *race/ethnicity*, *PIR*, *smoking status* (smokes every day, smokes on some days, no longer smokes, and never smoked), measured BMI ($kg \cdot m^{-2}$), and CRP ($mg \cdot dL^{-1}$).

Analysis. Statistical analyses were performed using procedures from survey data using Stata (version 12). Polytomous regression was used to examine the odds of being in the two lower tertiles (6,53) (vs upper tertile) of LTL based on the degree of engagement in MBB; those with an MBB index score of "0" served as the referent group.

RESULTS

Table 1 displays the characteristics of the sample. The weighted mean numbers of MBB across the LTL tertiles, respectively, were 1.18, 1.44, and 1.54 (Table 1; Fig. 2). The weighted proportions of participants with 2+ MBB across the LTL tertiles, respectively, were 34.7%, 43.6%, and 49.2% (Fig. 2). Table 2 displays the polytomous regression results. After adjustments (including age) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 3% ($P = 0.84$), 24% ($P = 0.02$), 29% ($P = 0.04$), and 52% ($P = 0.004$) reduced odds of being in the lowest (vs highest) tertile of LTL; MBB was not associated with being in the middle (vs highest) tertile of LTL. When changing the referent group to the middle tertile (not shown in the table) and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 MBB, respectively, had a 5%

TABLE 1. Weighted characteristics of the analyzed sample, NHANES 1999–2002 (n = 6503).

	LTL Tertile 1 (n = 2168)	LTL Tertile 2 (n = 2168)	LTL Tertile 3 (n = 2167)	P Value[a]
LTL (T/S ratio)	0.78 (0.77–0.79)	1.01 (1.00–1.02)	1.34 (1.31–1.36)	<0.001
MPA in past 30 d (%)				
Yes	48.3 (44.8–51.8)	53.7 (49.3–58.1)	48.7 (43.7–53.5)	0.03
VPA in past 30 d (%)				
Yes	28.7 (26.1–31.1)	39.2 (34.8–43.5)	45.0 (40.8–49.1)	<0.001
Walked/cycled in past 30 d (%)				
Yes	19.9 (17.6–22.2)	23.7 (20.1–27.3)	27.7 (23.8–31.5)	<0.001
Strengthening activities in past 30 d (%)				
Yes	21.6 (18.2–25.0)	27.6 (24.3–30.9)	33.3 (29.9–36.6)	<0.001
Mean no. of movement behaviors	1.18 (1.11–1.25)	1.44 (1.32–1.56)	1.54 (1.42–1.66)	<0.001
Sum no. of movement behaviors (%)				
0	30.7 (27.0–34.3)	24.8 (21.3–28.3)	22.4 (19.7–25.2)	<0.001
1	34.6 (32.0–37.1)	31.6 (29.3–33.8)	28.4 (25.3–31.6)	
2	21.8 (19.0–24.6)	22.7 (20.4–25.1)	26.1 (23.7–28.4)	
3	10.9 (9.0–12.9)	16.0 (13.5–18.5)	17.8 (14.5–21.0)	
4	1.8 (1.0–2.6)	4.7 (3.0–6.2)	5.1 (3.2–7.0)	
Age (yr)	52.7 (51.4–54.0)	44.6 (43.2–45.9)	38.2 (36.8–39.5)	<0.001
Gender (%)				
Male	51.7 (48.9–54.4)	47.4 (44.5–50.4)	49.0 (47.1–51.0)	0.10
Race/ethnicity (%)				
Mexican American	6.7 (3.9–9.5)	7.7 (5.7–9.8)	6.9 (4.9–8.9)	0.03
Other Hispanic	5.8 (1.2–10.5)	5.6 (2.6–8.6)	7.8 (4.4–11.2)	
Non-Hispanic White	76.4 (71.3–81.6)	75.3 (71.2–79.4)	68.6 (63.8–73.4)	
Non-Hispanic Black	7.0 (4.9–9.1)	7.4 (5.2–9.7)	12.1 (9.1–15.1)	
Other	3.7 (2.0–5.5)	3.6 (2.5–4.8)	4.4 (2.5–6.3)	
Smoking status (%)				
Everyday	19.7 (17.1–22.3)	20.4 (17.3–23.5)	21.8 (19.1–24.6)	<0.001
Some days	2.6 (1.8–3.3)	3.4 (2.4–4.5)	5.5 (4.0–6.9)	
No longer smokes	30.9 (28.0–33.8)	25.3 (22.3–28.4)	19.7 (17.0–22.3)	
Never smoked	46.6 (43.1–50.1)	50.6 (47.5–53.8)	52.9 (48.4–57.3)	
BMI ($kg \cdot m^{-2}$)	28.6 (28.2–29.0)	28.0 (27.7–28.3)	27.4 (26.9–27.8)	<0.001
PIR	3.06 (2.8–3.2)	3.14 (2.9–3.3)	2.97 (2.7–3.2)	0.38
CRP ($mg \cdot dL^{-1}$)	0.49 (0.44–0.54)	0.39 (0.36–0.42)	0.35 (0.31–0.39)	<0.001

[a]Design-based likelihood ratio test was used to determine statistical significance for the categorical variables. Linear regression was used to determine statistical significance for the continuous variables by comparing tertile 3 vs tertile 1.

(P = 0.60), 12% (P = 0.40), 28% (P = 0.02), and 56% (P = 0.009) reduced odds of being in the lowest (vs *middle*) tertile of LTL. Taken together, these findings suggest a dose–response relation between MBB and LTL; greater engagement in MBB was associated with lower odds of being in lowest versus highest LTL tertile and lowest versus middle tertile.

Given that some studies suggest a nonlinear relation between telomere length and morbidity (11,15), in addition to considering tertiles of LTL, further analyses examined the relation between MBB and five quintiles of LTL; across these five quintiles, respectively, the mean LTL values were 0.73, 0.88, 1.01, 1.14, and 1.44; notably, the 90th and 95th percentiles for LTL in this sample were 1.37 and 1.50, respectively. The mean numbers of MBB across the five quintiles of LTL, respectively, were 1.15, 1.27, 1.46, 1.52, and 1.55. This observed monotonic relation suggests that,

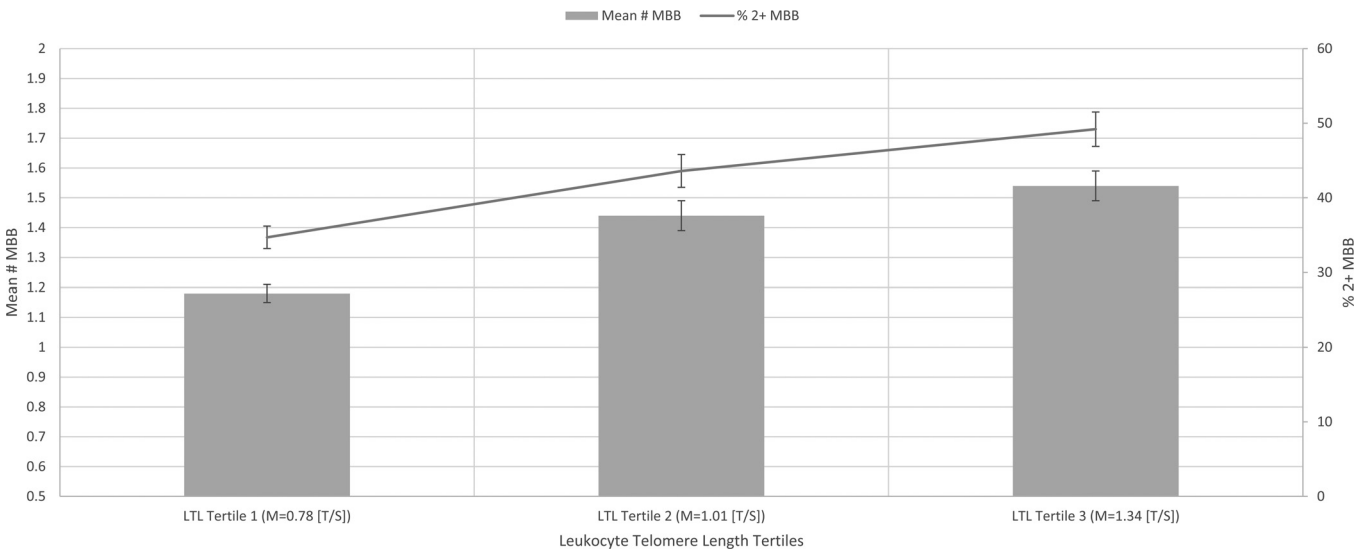

FIGURE 2—Weighted mean number of MBB and the weighted proportion of adults having two or more MBB across LTL tertiles (mean LTL across the LTL tertiles were 0.78, 1.01, and 1.34 T/S). M, mean.

TABLE 2. Weighted multivariable polytomous regression examining the odds of being in the two lower tertiles (vs upper tertile) of LTL based on the degree of engagement in MBB, NHANES 1999–2002 (n = 6503).

	Tertile 1 vs Tertile 3			Tertile 2 vs Tertile 3		
	Odds Ratio	95% CI	*P*	Odds Ratio	95% CI	*P*
No. of movement behaviors						
1 vs 0	0.97	0.78–1.22	0.84	1.02	0.86–1.21	0.73
2 vs 0	0.76	0.61–0.96	0.02	0.86	0.70–1.07	0.18
3 vs 0	0.71	0.52–0.98	0.04	0.98	0.70–1.37	0.92
4 vs 0	0.48	0.29–0.78	0.004	1.08	0.73–1.60	0.67
Covariates						
Age, 1 yr older	1.05	1.01–1.09	0.008	1.04	1.01–1.07	0.004
Age squared	1.00	0.99–1.01	0.53	1.00	0.99–1.01	0.38
Gender						
Female vs male	0.80	0.68–0.94	0.008	1.04	0.88–1.22	0.59
Race/ethnicity						
Mexican-American vs White	1.40	0.84–2.33	0.18	1.29	0.94–1.77	0.10
Other Hispanic vs White	0.86	0.34–2.20	0.76	0.74	0.45–1.23	0.24
Non-Hispanic Black vs White	0.56	0.38–0.84	0.007	0.59	0.43–0.80	0.002
Other vs White	0.98	0.56–1.71	0.96	0.84	0.52–1.36	0.48
Smoking status						
Everyday vs never smoked	1.16	0.95–1.40	0.11	1.03	0.84–1.27	0.70
Some days vs never smoked	0.72	0.46–1.11	0.13	0.78	0.51–1.18	0.23
No longer smokes vs never smoked	1.07	0.90–1.27	0.39	1.03	0.85–1.26	0.69
BMI, 1 $kg \cdot m^{-2}$ increase	1.02	1.01–1.04	0.009	1.01	1.00–1.02	0.04
PIR, 1-unit increase	0.98	0.89–1.08	0.80	1.00	0.94–1.05	0.96
CRP, 1 $mg \cdot dL^{-1}$ increase	1.16	1.00–1.35	0.04	1.02	0.88–1.19	0.69

in this sample, LTL had a linear, rather than an inverted U-shaped, association with mean MBB number.

Additional analyses (not shown in tabular format) were computed to see if age moderated the association between MBB and LTL. Three additional multivariable polytomous regression models were computed for those 20–39, 40–64, and 65–84 yr. Results were not significant for the age groups 20–39 and 65–84 yr (data not shown); among those who were 40–64 yr and compared with those engaging in 0 MBB, those engaging in 1, 2, 3, and 4 behaviors, respectively, had a 15% (P = 0.44), 32% (P = 0.08), 42% (P = 0.01), and 61% (P = 0.03) reduced odds of being in the lowest (vs highest) tertile of LTL.

Furthermore, all four MBB were entered separately into a multivariable polytomous regression model to examine their potential *independent* associations. After adjustments, those engaging in VPA and walking/cycling for transportation, respectively, had a 25% (P = 0.01) and 30% (P = 0.004) lower odds of being in the lowest (vs highest) LTL tertile; MPA [odds ratio (OR), 1.13; P = 0.15] and MSA (OR, 0.92; P = 0.50) were not independently associated with being the in the lowest (vs highest) LTL tertile.

In addition to examining independent associations of the different MBB on LTL, it is of interest to examine whether MBB exclusivity (e.g., only engaging in MPA and not any of the three other MBB) is associated with LTL. Among the 6503 participants, 386 engaged in *only* VPA (i.e., reporting engaging in VPA but not in MPA, MSA, or walking for transportation), 1057 engaged in *only* MPA, 176 engaged in only MSA, and 417 engaged in only walking/cycling for transportation. Results for only VPA, MSA, and walking/cycling for transportation were not statistically significant (data not shown). Interestingly, however, those who engaged in only MPA had a 36% (OR, 1.36; P = 0.01) and 25% (OR, 1.25; P = 0.06) increased odds, respectively, in being in the lowest and middle tertiles (vs highest tertile) after adjustments. This is an unexpected finding, but this association, coupled with our observed finding of a dose–response association between MBB engagement and LTL, suggests that engaging in some MBB in isolation may not be favorable but there may be a combined effect of attenuating the shortening of LTL when multiple MBB are engaged in regularly.

Lastly, given that some studies have demonstrated an inverted U relation between PA and LTL (29,30), we attempted to examine whether such a relation was observed for frequency of MSA; duration and frequency of MPA and VPA were not asked in the 1999–2002 NHANES cycles, and the majority (76%) of participants did not walk/cycle for transportation, so evaluating a dose–response relation between walking/cycling for transportation and LTL was not possible. No dose–response relation was observable for MSA; compared with those in the lowest MSA tertile (mean number of MSA in past 30 d, 5.6) and after adjustments in a linear regression, no association was observed between those in the middle (mean MSA, 12.9; $\beta = -0.02$; P = 0.13) and upper (mean MSA, 27.4; $\beta = -0.002$; P = 0.88) MSA tertiles with LTL.

DISCUSSION

Using a national sample of US adults, we observed a dose–response relation between MBB engagement (i.e., number of MBB they engaged in) and lower LTL. The potential mechanisms to explain a PA–LTL relation are not fully established. Among rodent models, several exercise-specific signaling mechanisms (e.g., TERT, IGF-1, eNOS, and AKT) have been associated with altered telomere biology (29,30) and thus may play an important role in preserving telomere phenotype (30,49,50). Future work is needed

to improve our understanding of the mechanisms underlying this potential relation.

Importantly, the relation between MBB and LTL was observed only among those 40–64 yr old, which suggests that, if confirmed by prospective and experimental work, this may be an important age group in which targeted PA interventions should be developed, implemented, and evaluated. The unexpected finding that those who engaged in only MPA had increased odds of being in the lowest and middle tertiles (vs highest tertile) needs further investigation. Engaging in only MPA may result in an inadequate exercise stimulus to achieve exercise-induced LTL adaptations. The observed findings should be interpreted in the context of the study's limitation, which include, for example, the cross-sectional design and an inability to fully tease out potential intensity/duration effects. In addition, given that the excluded sample due to missing LTL data differed by gender, race/ethnicity, and PIR when compared with the analytic sample, applicability to these subpopulations may be limited.

Owing to the limitations of the MBB items, we were not able to determine the duration and frequency of most of the MBB items but rather whether they engaged in the behavior or not. Previous research, however, suggests that there is likely a range in the amount of PA that provides health benefits without negatively affecting LTL (22,38,40,43). Data in very active adults suggest that if this range is exceeded, PA may result in a detrimental effect on LTL (22,43). For example, high levels of PA may increase demand on the body to repair and regenerate, resulting in shortening of LTL. This may explain why some studies do not always find a dose–response relationship between the amount of PA and LTL (22,32,33,40,45,48,52). Our findings suggest that engaging in more MBB is associated with reduced odds of being in the lowest LTL tertile, suggesting that engaging in multiple MBB may have a combined effect in minimizing LTL shortening.

Future epidemiological studies examining the extent to which MBB duration and frequency influence LTL are needed. Furthermore, future work examining tissue- and cell-specific telomere adaptations from exercise is warranted (30). Given the protective effects of telomerase activity (42), future epidemiological studies examining the effects of MBB on telomerase activity is warranted. Because of the combined effects of multiple health-enhancing behaviors on health (28,41), as well as LTL (16,17,36), future epidemiological work examining the additive and additive interaction effects of multiple health behaviors on LTL is warranted. Lastly, given that it is not entirely certain whether LTL is a cause or consequence of morbidity (e.g., cardiovascular disease), future longitudinal mediational models examining whether LTL mediates the relation between MBB and morbidity/mortality is warranted. However, prospective studies showing that shorter LTL is predictive of premature mortality from an increased risk of various chronic diseases (e.g., cardiovascular disease) are starting to emerge (7), but several issues (e.g., methodology used to assess LTL and potential regression to the mean) need to be carefully considered when examining and interpreting the prospective interrelations among PA, LTL, and morbidity/mortality (3).

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REFERENCES

1. Ahmad S, Heraclides A, Sun Q, et al. Telomere length in blood and skeletal muscle in relation to measures of glycaemia and insulinaemia. *Diabet Med*. 2012;29:e377–81.
2. Aviv H, Khan MY, Skurnick J, et al. Age dependent aneuploidy and telomere length of the human vascular endothelium. *Atherosclerosis*. 2001;159:281–7.
3. Bendix L, Thinggaard M, Fenger M, et al. Longitudinal changes in leukocyte telomere length and mortality in humans. *J Gerontol A Biol Sci Med Sci*. 2014;69:231–9.
4. Benetos A, Gardner JP, Zureik M, et al. Short telomeres are associated with increased carotid atherosclerosis in hypertensive subjects. *Hypertension*. 2004;43:182–5.
5. Blackburn EH. Telomere states and cell fates. *Nature*. 2000;408:53–6.
6. Brouilette SW, Moore JS, McMahon AD, et al. Telomere length, risk of coronary heart disease, and statin treatment in the West of Scotland Primary Prevention Study: a nested case–control study. *Lancet*. 2007;369:107–14.
7. Cawthon RM, Smith KR, O'Brien E, Sivatchenko A, Kerber RA. Association between telomere length in blood and mortality in people aged 60 years or older. *Lancet*. 2003;361:393–5.
8. Cherkas LF, Hunkin JL, Kato BS, et al. The association between physical activity in leisure time and leukocyte telomere length. *Arch Intern Med*. 2008;168:154–8.
9. Collins M, Renault V, Grobler LA, et al. Athletes with exercise-associated fatigue have abnormally short muscle DNA telomeres. *Med Sci Sports Exerc*. 2003;35(9):1524–8.
10. Correia-Melo C, Hewitt G, Passos JF. Telomeres, oxidative stress and inflammatory factors: partners in cellular senescence? *Longev Healthspan*. 2014;3:1.
11. Cui Y, Cai Q, Qu S, et al. Association of leukocyte telomere length with colorectal cancer risk: nested case–control findings from the Shanghai Women's Health Study. *Cancer Epidemiol Biomarkers Prev*. 2012;21:1807–13.
12. Daniali L, Benetos A, Susser E, et al. Telomeres shorten at equivalent rates in somatic tissues of adults. *Nat Commun*. 2013;4:1597.
13. Demissie S, Levy D, Benjamin EJ, et al. Insulin resistance, oxidative stress, hypertension, and leukocyte telomere length in men from the Framingham Heart Study. *Aging Cell*. 2006;5:325–30.
14. Du M, Prescott J, Kraft P, et al. Physical activity, sedentary behavior, and leukocyte telomere length in women. *Am J Epidemiol*. 2012;175:414–22.
15. Elks CE, Scott RA. The long and short of telomere length and diabetes. *Diabetes*. 2014;63:65–7.
16. Falus A, Marton I, Borbenyi E, et al. The 2009 Nobel Prize in Medicine and its surprising message: lifestyle is associated with telomerase activity [in Hungarian]. *Orv Hetil*. 2010;151:965–70.

17. Falus A, Marton I, Borbenyi E, et al. A challenging epigenetic message: telomerase activity is associated with complex changes in lifestyle. *Cell Biol Int*. 2011;35:1079–83.
18. Fitzpatrick AL, Kronmal RA, Gardner JP, et al. Leukocyte telomere length and cardiovascular disease in the cardiovascular health study. *Am J Epidemiol*. 2007;165:14–21.
19. Fitzpatrick AL, Kronmal RA, Kimura M, et al. Leukocyte telomere length and mortality in the Cardiovascular Health Study. *J Gerontol A Biol Sci Med Sci*. 2011;66:421–9.
20. Garland SN, Johnson B, Palmer C, et al. Physical activity and telomere length in early stage breast cancer survivors. *Breast Cancer Res*. 2014;16:413.
21. Jeanclos E, Schork NJ, Kyvik KO, Kimura M, Skurnick JH, Aviv A. Telomere length inversely correlates with pulse pressure and is highly familial. *Hypertension*. 2000;36:195–200.
22. Kadi F, Ponsot E, Piehl-Aulin K, et al. The effects of regular strength training on telomere length in human skeletal muscle. *Med Sci Sports Exerc*. 2008;40(1):82–7.
23. Kim JH, Ko JH, Lee DC, Lim I, Bang H. Habitual physical exercise has beneficial effects on telomere length in postmenopausal women. *Menopause*. 2012;19:1109–15.
24. Krauss J, Farzaneh-Far R, Puterman E, et al. Physical fitness and telomere length in patients with coronary heart disease: findings from the Heart and Soul Study. *PLoS One*. 2011;6:e26983.
25. LaRocca TJ, Seals DR, Pierce GL. Leukocyte telomere length is preserved with aging in endurance exercise-trained adults and related to maximal aerobic capacity. *Mech Ageing Dev*. 2010;131:165–7.
26. Lin J, Epel E, Blackburn E. Telomeres and lifestyle factors: roles in cellular aging. *Mutat Res*. 2012;730:85–9.
27. Lopez-Otin C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. *Cell*. 2013;153:1194–217.
28. Loprinzi PD, Smit E, Mahoney S. Physical activity and dietary behavior in US adults and their combined influence on health. *Mayo Clin Proc*. 2014;89:190–8.
29. Ludlow AT, Ludlow LW, Roth SM. Do telomeres adapt to physiological stress? Exploring the effect of exercise on telomere length and telomere-related proteins. *Biomed Res Int*. 2013;2013:601368.
30. Ludlow AT, Roth SM. Physical activity and telomere biology: exploring the link with aging-related disease prevention. *J Aging Res*. 2011;2011:790378.
31. Ludlow AT, Zimmerman JB, Witkowski S, et al. Relationship between physical activity level, telomere length, and telomerase activity. *Med Sci Sports Exerc*. 2008;40(10):1764–71.
32. Mason C, Risques RA, Xiao L, et al. Independent and combined effects of dietary weight loss and exercise on leukocyte telomere length in postmenopausal women. *Obesity (Silver Spring)*. 2013;21:E549–54.
33. Mathur S, Ardestani A, Parker B, Cappizzi J, Polk D, Thompson PD. Telomere length and cardiorespiratory fitness in marathon runners. *J Investig Med*. 2013;61:613–5.
34. Mirabello L, Huang WY, Wong JY, et al. The association between leukocyte telomere length and cigarette smoking, dietary and physical variables, and risk of prostate cancer. *Aging Cell*. 2009;8:405–13.
35. Needham BL, Adler N, Gregorich S, et al. Socioeconomic status, health behavior, and leukocyte telomere length in the National Health and Nutrition Examination Survey, 1999–2002. *Soc Sci Med*. 2013;85:1–8.
36. Ornish D, Lin J, Chan JM, et al. Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study. *Lancet Oncol*. 2013;14:1112–20.
37. Østhus IB, Sgura A, Berardinelli F, et al. Telomere length and long-term endurance exercise: does exercise training affect biological age? A pilot study. *PLoS One*. 2012;7:e52769.
38. Ponsot E, Lexell J, Kadi F. Skeletal muscle telomere length is not impaired in healthy physically active old women and men. *Muscle Nerve*. 2008;37:467–72.
39. Puterman E, Lin J, Blackburn E, O'Donovan A, Adler N, Epel E. The power of exercise: buffering the effect of chronic stress on telomere length. *PLoS One*. 2010;5:e10837.
40. Rae DE, Vignaud A, Butler-Browne GS, et al. Skeletal muscle telomere length in healthy, experienced, endurance runners. *Eur J Appl Physiol*. 2010;109:323–30.
41. Sagner M, Katz D, Egger G, et al. Lifestyle medicine potential for reversing a world of chronic disease epidemics: from cell to community. *Int J Clin Pract*. 2014;68:1289–92.
42. Sanchis-Gomar F, Lucia A. Acute myocardial infarction: 'telomerasing' for cardioprotection. *Trends Mol Med*. 2015;21:203–5.
43. Savela S, Saijonmaa O, Strandberg TE, et al. Physical activity in midlife and telomere length measured in old age. *Exp Gerontol*. 2013;48:81–4.
44. Simpson RJ, Cosgrove C, Chee MM, et al. Senescent phenotypes and telomere lengths of peripheral blood T-cells mobilized by acute exercise in humans. *Exerc Immunol Rev*. 2010;16:40–55.
45. Song Z, von Figura G, Liu Y, et al. Lifestyle impacts on the aging-associated expression of biomarkers of DNA damage and telomere dysfunction in human blood. *Aging Cell*. 2010;9:607–15.
46. Terai M, Izumiyama-Shimomura N, Aida J, et al. Association of telomere shortening in myocardium with heart weight gain and cause of death. *Sci Rep*. 2013;3:2401.
47. Vasan RS, Demissie S, Kimura M, et al. Association of leukocyte telomere length with echocardiographic left ventricular mass: the Framingham heart study. *Circulation*. 2009;120:1195–202.
48. Weischer M, Bojesen SE, Nordestgaard BG. Telomere shortening unrelated to smoking, body weight, physical activity, and alcohol intake: 4,576 general population individuals with repeat measurements 10 years apart. *PLoS Genet*. 2014;10:e1004191.
49. Werner C, Furster T, Widmann T, et al. Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall. *Circulation*. 2009;120:2438–47.
50. Werner C, Hanhoun M, Widmann T, et al. Effects of physical exercise on myocardial telomere-regulating proteins, survival pathways, and apoptosis. *J Am Coll Cardiol*. 2008;52:470–82.
51. Wolkowitz OM, Mellon SH, Epel ES, et al. Leukocyte telomere length in major depression: correlations with chronicity, inflammation and oxidative stress–preliminary findings. *PLoS One*. 2011;6:e17837.
52. Woo J, Tang N, Leung J. No association between physical activity and telomere length in an elderly Chinese population 65 years and older. *Arch Intern Med*. 2008;168:2163–4.
53. Ye S, Shaffer JA, Kang MS, et al. Relation between leukocyte telomere length and incident coronary heart disease events (from the 1995 Canadian Nova Scotia Health Survey). *Am J Cardiol*. 2013;111:962–7.