THE GERONTOLOGICAL SOCIETY OF AMERICA®

Journals of Gerontology: Medical Sciences
cite as: *J Gerontol A Biol Sci Med Sci*, 2017, Vol. 72, No. 11, 1532–1537
doi:10.1093/gerona/glx037
Advance Access publication March 9, 2017

OXFORD

Research Article

Association of Accelerometer-Measured Physical Activity With Leukocyte Telomere Length Among Older Women

Aladdin H. Shadyab,[1] Michael J. LaMonte,[2] Charles Kooperberg,[3] Alexander P. Reiner,[4] Cara L. Carty,[5] Todd M. Manini,[6] Lifang Hou,[7] Chongzhi Di,[3] and Andrea Z. LaCroix[1]

[1]Division of Epidemiology, Department of Family Medicine and Public Health, University of California, San Diego School of Medicine, La Jolla. [2]Department of Epidemiology and Environmental Health, University at Buffalo, New York. [3]Division of Public Health Sciences, Fred Hutchinson Cancer Research Center, Seattle, Washington. [4]Department of Epidemiology, University of Washington, Seattle. [5]Division of Biostatistics and Study Methodology, Center for Translational Science, George Washington University and Children's National Medical Center, District of Columbia. [6]Department of Aging and Geriatric Research, Institute on Aging, University of Florida, Gainesville. [7]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois.

Address correspondence to Aladdin H. Shadyab, PhD, Division of Epidemiology, Department of Family Medicine and Public Health, University of California, San Diego, 9500 Gilman Drive #0725, La Jolla, CA 92093. E-mail: ahshadya@ucsd.edu

Received November 16, 2016; Editorial Decision Date February 21, 2017

Decision Editor: Stephen Kritchevsky, PhD

Abstract

Background: Previous studies on physical activity and telomere length have relied largely upon self-reported physical activity data, and few studies have examined older adults. The association of objectively measured physical activity with leukocyte telomere length (LTL) is currently unknown.

Methods: In this study, we examined cross-sectional associations between accelerometer-measured total, light, and moderate-to-vigorous physical activity (MVPA) and LTL, measured using Southern blot. The sample included 1,405 older (64–95 years old) white and African American women from the Women's Health Initiative. Multiple linear regression models adjusting for potential confounders were used to determine the association between accelerometer-measured physical activity and LTL.

Results: Overall, the mean (standard deviation) of total, light, and moderate-to-vigorous activity was 5.5 (1.6), 4.7 (1.3), and 0.8 (0.5) h/d, respectively. Adjusting for accelerometer wear time, age, race/ethnicity, education, marital status, smoking, alcohol, body mass index, a history of chronic diseases, and hormone therapy use, LTL was 80 (95% confidence interval: 9, 150) base pairs longer among women with ≥2.5 compared with <2.5 h/wk of MVPA. Light activity was not significantly associated with LTL. For total activity, the most physically active women had significantly longer LTL than the least active women after adjustment for demographic and lifestyle characteristics; however, findings were not significant after further adjustment for health-related factors.

Conclusions: Older women meeting current recommendations of ≥2.5 h/wk of MVPA, as assessed by accelerometer, had longer LTL. Additional studies using accelerometers in large, diverse cohorts of older women are needed to confirm and extend these findings.

Keywords: Minority aging—Biomarker—Longevity—MVPA—Postmenopausal

Engaging in regular physical activity is an important component of healthy aging. Current guidelines recommend participating in ≥2.5 h/wk of moderate-to-vigorous physical activity (MVPA) for substantial health benefits (1). However, physical inactivity is highly prevalent among older adults, particularly among those who are burdened with chronic diseases and disability (2). Physical inactivity is associated with increased risk of obesity, heart disease, diabetes, and mortality, and remaining physically active even in old age is important for improved function and longevity (3,4).

Increasingly, physical activity is being studied in relation to telomere length (5). Telomeres are tandemly repeated DNA sequences at the ends of linear chromosomes involved in protecting genomic stability. As purported markers of cellular aging, telomeres shorten at each cell division and gradually undergo attrition over time (5). Prior studies have shown associations

between short leukocyte telomere length (LTL) and risk of age-related diseases and mortality (5–8).

Associations between physical activity and LTL have been conflicting (9–14). For example, in the Nurses' Health Study, higher levels of MVPA were associated with longer LTL among middle-aged and older women (10), but in the Cardiovascular Health Study, no association between physical activity and LTL was observed among older adults (14). However, these studies were reliant on self-reported physical activity, which is often overestimated and vulnerable to misclassification bias (15,16). Limited data currently exist on the relationship between objectively measured (i.e., from accelerometer) physical activity and LTL. Self-reported physical activity is weakly correlated with accelerometer-measured activity (correlation coefficients range from 0.14 to 0.49), which may provide a more accurate estimate of time spent in activities of varying intensity (17). Although older adults spend a large amount of time in light-intensity activity (18), this type of activity is the most difficult to query by questionnaire and recall (16). Therefore, the use of accelerometry to determine physical activity patterns is important to understand the relationship between physical activity and LTL among older adults.

The objective of this cross-sectional study was to evaluate associations of accelerometer-measured total, light, and moderate-to-vigorous physical activity with LTL among older white and African American women from the Women's Health Initiative (WHI).

Methods

Study Population

The WHI is a longitudinal investigation among postmenopausal women. The study design and methods are described elsewhere (19). Briefly, during 1993–1998, a diverse cohort of 161,808 postmenopausal women aged 50–79 years old was recruited from 40 United States clinical centers. Women participated in one or more of three clinical trials, including one of two hormone therapy (HT) trials, or an observational study. In 2005, 77% of eligible women agreed to follow-up for an additional 5 years in the first Extension Study, and in 2010, 87% of women consented to follow-up through 2015 in the second Extension Study. Between March 2012 and May 2013, more than 7,800 women from the second Extension Study participated in the Long Life Study (LLS), which involved a single study visit. The present cross-sectional study was exclusive to 1,405 women who participated in two ancillary studies of the LLS with information on accelerometer-measured physical activity and LTL assessed during 2012–2013 (Supplementary Figure 1), as previously described (20,21). All participants provided written informed consent, and Institutional Review Board approval was received by all participating institutions.

Accelerometer-Measured Physical Activity

During 2012–2013, participants wore a triaxial accelerometer (ActiGraph GT3X+; Pensacola, FL) on their right hip for up to seven consecutive days during waking and sleeping hours, removing it during bathing or swimming. Participants also completed a sleep log concurrent with accelerometer wear. Movement was captured along vertical, anteroposterior, and mediolateral axes in 15-second intervals (epochs), and activity counts were provided as composite vector magnitudes (VM) of these axes. Accelerometer wear time was determined using sleep logs and a computer-automated algorithm devised for this study (21). Intervals of ≥90 minutes of consecutive zero VM counts/minute were assigned as non-wear time. Nonzero VM counts lasting up to two minutes were considered nonwear time if no VM counts were detected 30 minutes before or after that interval (22,23). Any other nonzero VM counts were considered wear time. A valid day was defined as having ≥10 hours of wear time during wake hours. The present analysis included only women with 4–7 valid days (24).

In a calibration study among 200 study participants, relevant cutpoints along the distribution of VM counts were determined for various intensity levels of activities relevant to an older woman's life (21). Light-intensity physical activity was defined as 19–518 VM counts/15 s and MVPA as ≥519 VM counts/15 s. Variables for MVPA occurring in any bout duration and that occurring in bouts of ≥10 minutes were created. Physical activity variables are presented as the average number of hours/day spent in total, light, and moderate-to-vigorous intensity activities.

Covariates

Covariates included age, race/ethnicity, education, marital status, smoking, alcohol consumption, body mass index (BMI), physical functioning status, self-rated health, HT use, blood pressure, hypertension, and chronic diseases (coronary heart disease, stroke, diabetes, and cancer) that have been previously associated both with physical activity and LTL (6–8,25–28). Additional information on covariate data collection is provided in the Supplementary Material.

LTL Measurement

During the 2012–2013 study visit, blood samples were collected. DNA extraction was performed using the 5-prime method (5 PRIME, Inc.; Gaithersburg, MD), and DNA samples were sent in batches during a 1-year period to the Center of Human Development and Aging at Rutgers University to measure LTL. Batches had samples that were randomly selected. The laboratory measuring LTL was blinded to the identity and characteristics of all participants. DNA integrity was inspected through electrophoresis of DNA on ethidium bromide-stained 1% agarose gel (200 V for 2 hours). DNA had to appear as a single compact crown-shaped band migrating in parallel with the other samples on the gel. Telomere length in kilobases was determined by using the mean length of the terminal restriction fragments from the Southern blot method, which has low measurement error compared with other methods (29) and is described in detail elsewhere (30). Samples that did not pass the integrity test were not processed for further terminal restriction fragment analysis. Samples were run in duplicate on different gels, and the average of the two LTL measurements was used in the analysis. An average inter-assay coefficient of variation of 2.0% was observed for blinded pair sets. Additional information on LTL measurement is provided in the Supplementary Material.

Statistical Analysis

Accelerometer-measured total, light, and moderate-to-vigorous activity (in hours/day) were analyzed as quartiles. MVPA was also categorized as <2.5 or ≥2.5 h/wk of MVPA occurring in any bout duration as well as in bouts of ≥10 minutes, which is equivalent to the amount of activity currently recommended for adults (1). Characteristics of participants were compared across levels of physical activity using analysis of variance and Kruskal–Wallis tests for normally and non-normally distributed continuous variables, respectively. χ^2 tests were used to compare differences for categorical variables across levels of physical activity. Age-adjusted linear models were used to compare physical activity levels and LTL by race/ethnicity.

Multiple linear regression models were used to examine associations between accelerometer-measured physical activity variables and LTL. The first model was adjusted for accelerometer wear time, and subsequent models were additionally adjusted for age, race/ethnicity, education, marital status, smoking, alcohol, BMI, a history of chronic diseases, and HT use. Multicollinearity in the multivariable models was tested using tolerance values but was not observed in the analysis. To test for linear trends, physical activity variables were included as continuous variables in multivariable models. Interaction tests were performed by including the product terms of physical activity variables and age, race/ethnicity, BMI, and physical performance score in the fully-adjusted multivariable models. *p*-values were two-tailed and $p < .05$ was considered significant. All statistical analyses were performed using SAS Version 9.3 (SAS Institute Inc., Cary, NC).

Results

This study included 818 (58.2%) white and 587 (41.8%) African American women aged on average 79.2 (standard deviation [*SD*] 6.7; range 64–95) years old. Women wore the accelerometer for an average of 6.5 (*SD* 0.8) days with an average wear time of 14.9 (*SD* 1.3) h/d. Women spent an average of 5.5 (*SD* 1.6) h/d in total activity, 4.7 (*SD* 1.3) h/d in light activity, and 0.8 (*SD* 0.5) h/d in MVPA. Overall, 1,026 (73%) women achieved physical activity guidelines of ≥2.5 h/wk of MVPA in any bout duration; 117 (8%) attained ≥2.5 h/wk of MVPA in ≥10-minute bouts.

MVPA was significantly higher in white compared with African American women (age-adjusted mean [standard error] = 0.87 [0.02] and 0.66 [0.02], respectively; $p < .001$). Light and total activity did not vary significantly by race/ethnicity. Average LTL was 6.62 (*SD* 0.60; range 4.92–8.86) kilobases and longer in African American than white women (age-adjusted mean LTL [standard error] = 6.76 [0.02] and 6.52 [0.02], respectively; $p < .001$).

Women engaging in greater amounts of MVPA were more likely to be younger, college graduates, married or living as married, and in excellent health (Supplementary Table 1). They were also more likely to have a higher physical performance score and less likely to be obese, have high blood pressure, or have a history of chronic diseases. Women with greater amounts of light activity were more likely to be younger and in excellent health, and less likely to be obese or have a history of chronic diseases (Supplementary Table 2).

Adjusting for accelerometer wear time, age, and race/ethnicity, there was a significant linear association between MVPA and LTL ($p_{trend} = .04$; Supplementary Table 3). However, linear associations were not significant in subsequent models, and findings across quartiles of MVPA were not significant in the fully-adjusted model. When categorizing MVPA according to a cutpoint of ≥2.5 h/wk, there were significant associations of MVPA with LTL across all models (Table 1). In the fully-adjusted model, LTL was on average 80 (95% confidence interval [CI]: 9, 150) base pairs longer among women with ≥2.5 compared with <2.5 h/wk of MVPA. In analyses using MVPA occurring in bouts of ≥10 minutes, findings were not significant when comparing women with ≥2.5 compared with <2.5 h/wk of MVPA (data not shown).

There was a significant linear association between light activity and LTL adjusting for wear time, age, and race/ethnicity ($p_{trend} = .04$; Table 2). After additional adjustment for other demographic, lifestyle, and health-related factors, the data were suggestive of a linear trend but no longer statistically significant ($p_{trend} = .09$ in the fully-adjusted model).

In a model adjusted for accelerometer wear time, age, race/ethnicity, education, marital status, smoking, alcohol, and BMI, LTL was 100 (95% CI: 8, 200) base pairs longer among women in the highest compared with the lowest level of total physical activity ($p_{trend} = .05$; Table 3). After additional adjustment for a history of chronic diseases and HT use, this difference was not significant. Furthermore, findings were suggestive of a linear association between total activity and LTL, but were not statistically significant in the final model ($p_{trend} = .09$).

Findings did not vary by age, race/ethnicity, BMI, or physical performance score (data not shown).

Discussion

Older white and African American women engaging in ≥2.5 h/wk of accelerometer-measured MVPA had longer LTL, after adjusting for demographic, lifestyle, and health-related characteristics. Accelerometer-measured light activity was not significantly associated with LTL. Women in the highest compared with the lowest level of total activity had longer LTL independent of demographic and lifestyle characteristics; however, after adjusting for health-related factors, this difference was not significant.

Previous studies evaluating the association of physical activity with LTL have relied upon self-reported data (9–14). In a cross-sectional study among women aged 43–70 years old, there was a positive linear association between total leisure-time physical activity and LTL (10). Although our findings were suggestive of a linear association between total and light activity and LTL, the *p* values for trend did not reach statistical significance. Larger studies of older women are needed to determine whether a linear association of this magnitude is present.

Although MVPA was not linearly associated with LTL in our study, LTL was significantly longer among women with ≥2.5 h/wk of MVPA in all multivariable models. Similarly, a study among middle-aged and older women observed that LTL was significantly longer only among those with 2 to <4 h/wk of self-reported MVPA (10). Meeting physical activity guidelines of MVPA occurring in ≥10-minute bouts, however, was not associated with LTL in our study. This may be partly explained by the low number of women performing

Table 1. Association of Accelerometer-Measured Moderate-to-Vigorous Physical Activity With Leukocyte Telomere Length (in Kilobases) Among Older Women in the Women's Health Initiative, 2012–2013

	Accelerometer-Measured Moderate-to-Vigorous Physical Activity, h/wk	
		≥2.5
	<2.5	β (95% CI)
Model 1[a]	Ref	0.22 (0.15, 0.30)
Model 2[b]	Ref	0.10 (0.03, 0.17)
Model 3[c]	Ref	0.10 (0.03, 0.17)
Model 4[d]	Ref	0.09 (0.02, 0.17)
Model 5[e]	Ref	0.08 (0.009, 0.15)

Note: β = beta estimate; CI = confidence interval; Ref = reference.

[a]Model 1: Adjusted for wear hours ($n = 1,405$). [b]Model 2: Adjusted for model 1 + age and race/ethnicity ($n = 1,405$). [c]Model 3: Adjusted for model 2 + education and baseline marital status, smoking behavior, and alcohol consumption ($n = 1,375$). [d]Model 4: Adjusted for model 3 + body mass index ($n = 1,361$). [e]Model 5: Adjusted for model 4 + history of chronic diseases and hormone therapy ($n = 1,340$).

Table 2. Association of Accelerometer-Measured Light Intensity Physical Activity With Leukocyte Telomere Length (in Kilobases) Among Older Women in the Women's Health Initiative, 2012–2013

	Accelerometer-Measured Light Activity, h/d				
		3.84–<4.67	4.67–<5.51	≥5.51	
	<3.84	β (95% CI)	β (95% CI)	β (95% CI)	*p* for Trend
Model 1[a]	Ref	0.04 (–0.05, 0.13)	0.12 (0.03, 0.21)	0.17 (0.07, 0.26)	<.001
Model 2[b]	Ref	0.03 (–0.06, 0.11)	0.04 (–0.04, 0.12)	0.08 (–0.008, 0.16)	.04
Model 3[c]	Ref	0.03 (–0.06, 0.11)	0.04 (–0.04, 0.12)	0.07 (–0.02, 0.16)	.06
Model 4[d]	Ref	0.03 (–0.06, 0.11)	0.04 (–0.04, 0.13)	0.08 (–0.01, 0.17)	.05
Model 5[e]	Ref	0.03 (–0.05, 0.11)	0.04 (–0.05, 0.12)	0.07 (–0.02, 0.16)	.09

Note: β = beta estimate; CI = confidence interval; Ref = reference.

[a]Model 1: Adjusted for wear hours (n = 1,405). [b]Model 2: Adjusted for model 1 + age and race/ethnicity (n = 1,405). [c]Model 3: Adjusted for model 2 + education and baseline marital status, smoking behavior and alcohol consumption (n = 1,375). [d]Model 4: Adjusted for model 3 + body mass index (n = 1,361). [e]Model 5: Adjusted for model 4 + history of chronic diseases and hormone therapy (n = 1,340).

Table 3. Association of Accelerometer-Measured Total Physical Activity With Leukocyte Telomere Length (in Kilobases) Among Older Women in the Women's Health Initiative, 2012–2013

	Accelerometer-Measured Total Physical Activity, h/d				
		4.41–<5.42	5.42–<6.50	≥6.50	
	<4.41	β (95% CI)	β (95% CI)	β (95% CI)	*p* for Trend
Model 1[a]	Ref	0.10 (0.01, 0.19)	0.17 (0.08, 0.27)	0.25 (0.15, 0.34)	<.001
Model 2[b]	Ref	0.06 (–0.02, 0.14)	0.06 (–0.02, 0.14)	0.10 (0.02, 0.19)	.03
Model 3[c]	Ref	0.06 (–0.02, 0.15)	0.05 (–0.03, 0.14)	0.09 (0.005, 0.18)	.06
Model 4[d]	Ref	0.06 (–0.02, 0.15)	0.06 (–0.03, 0.15)	0.10 (0.008, 0.20)	.05
Model 5[e]	Ref	0.06 (–0.02, 0.15)	0.06 (–0.03, 0.14)	0.09 (–0.005, 0.18)	.09

Note: β = beta estimate; CI = confidence interval; Ref = reference.

[a]Model 1: Adjusted for wear hours (n = 1,405). [b]Model 2: Adjusted for model 1 + age and race/ethnicity (n = 1,405). [c]Model 3: Adjusted for model 2 + education and baseline marital status, smoking behavior, and alcohol consumption (n = 1,375). [d]Model 4: Adjusted for model 3 + body mass index (n = 1,361). [e]Model 5: Adjusted for model 4 + history of chronic diseases and hormone therapy (n = 1,340).

MVPA in ≥10-minute bouts. Understanding how duration of activity bouts influences LTL later in life requires further investigation.

Prior studies measured telomere length using quantitative polymerase chain reaction (qPCR) techniques and were not exclusively focused on older adults (9,10), thus it is difficult to compare base pair differences in LTL from our study with those of other studies. The Southern blot method is considered the gold standard and provides LTL in kilobases, unlike qPCR methods that provide a ratio of telomeric DNA content (29). We observed that LTL was on average 80 base pairs longer among women meeting current physical activity recommendations of ≥2.5 h/wk of MVPA. A study among white twins found that LTL, measured using Southern blot, was on average 200 base pairs longer among the most compared with the least physically active participants. However, the study population had a wide age distribution (18–81 years), and meeting MVPA guidelines was not evaluated in relation to LTL (11). Additional studies of physical activity among older adults that measure telomere length using Southern blot are currently needed.

We adjusted for chronic diseases such as coronary heart disease and diabetes that are associated both with physical activity and LTL (6–8,25–28). Consequently, the most active women did not have significantly longer LTL than the least active women after this adjustment. It is currently unknown whether LTL shortening causes or is a consequence of chronic diseases, although recent genetic Mendelian randomization studies are supporting a potential causal role of LTL in chronic diseases such as cancer (31). Therefore, it is unclear whether chronic diseases confound or mediate the association between physical activity and LTL.

We observed that women spent an average of 48 min/d in MVPA and the majority of their time in light activity, consistent with previous findings among older populations (2,32). Average time spent per day in MVPA as assessed by accelerometer has varied substantially in previous studies, likely due to various count thresholds used to define this level of intensity (2,32–35) as well as variation in actual movement patterns and intensities among study cohorts. For example, a recent study among Women's Health Study participants aged on average 72 years old observed that the percentage of women meeting physical activity guidelines of ≥2.5 h/wk of MVPA (irrespective of bout duration) varied from 26% to 93% based on the cutpoint used for accelerometer-measured MVPA, and was substantially lower for MVPA occurring in ≥10 minute bouts (range 19%–50%) (35). Optimal accelerometer cutpoints to define physical activity intensity among older adults have not been established. We performed a calibration study to determine intensity-specific cutpoints for physical activity intensity among our older population of women, thus providing a more accurate estimate of the amount of physical activity at various intensity levels in this group.

Physical activity may induce antioxidant and anti-inflammatory responses, thus preventing telomere attrition due to oxidative stress and inflammation (36,37). It is possible that obesity may mediate

the relationship between physical activity and LTL; that is, physically inactive women may have higher BMI, which has been associated with shortened LTL (38). Chronic diseases such as diabetes and cardiovascular disease, which are associated with being physically inactive and having short LTL, may also explain the association. Nonetheless, our findings were independent of BMI and chronic diseases. Finally, a previous study showed that exercise may influence telomere dynamics by elevating the activity of telomerase, an enzyme that elongates telomeres (39). Messenger RNA expression of telomerase reverse transcriptase has been shown to be upregulated following exercise (40).

Our study was limited by a cross-sectional design and a sample that consisted only of older women. Since we only evaluated leukocytes, our findings may not be generalized to telomere length activity in other cell types, such as skeletal muscle cells. We did not examine whether muscle-strengthening resistance activity confers any benefit on LTL among older women. A diverse sample of white and African-American women, use of the Southern Blot method for telomere measurement, and adjustment for several variables that may confound the association between physical activity and telomere length are study strengths. The use of accelerometry and cutpoints specific to older women to quantify physical activity intensity is novel and also an important strength of our study.

In summary, older women participating in ≥2.5 h/wk of accelerometer-measured MVPA had longer LTL. Accelerometer-measured light and total physical activity were not associated with LTL. Given the association of LTL with aging, morbidity, and mortality, future prospective studies among larger, diverse populations of older adults are needed to determine the relationship between cumulative changes in accelerometer-measured total, light, and moderate-to-vigorous activity and LTL dynamics.

Supplementary Material

Supplementary data is available at *The Journals of Gerontology, Series A: Biological Sciences and Medical Sciences* online.

Funding

This work was supported by the National Heart, Lung, and Blood Institute (contracts HHSN268201300007C, HHSN268201100046C, HHSN268201100001C, HHSN268201100002C, HHSN268201100003C, HHSN268201100004C, and HHSN271201100004C; grant R01 HL105065; and grant R01 HL121023 to T.M.M.) and the National Institute of Arthritis and Musculoskeletal and Skin Diseases (grant T32 AR064194 to A.H.S), National Institutes of Health, Department of Health and Human Services.

Acknowledgments

Role of the Sponsor: The National Heart, Lung, and Blood Institute has representation on the WHI Steering Committee, which governed the design and conduct of the study, the interpretation of the data, and preparation and approval of manuscripts.

Conflict of Interest

None declared.

References

1. Nelson ME, Rejeski WJ, Blair SN, et al.; American College of Sports Medicine; American Heart Association. Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. *Circulation*. 2007;116:1094–1105. doi:10.1161/CIRCULATIONAHA.107.185650
2. Jefferis BJ, Sartini C, Lee IM, et al. Adherence to physical activity guidelines in older adults, using objectively measured physical activity in a population-based study. *BMC Public Health*. 2014;14:382. doi:10.1186/1471-2458-14-382
3. US Department of Health and Human Services. Physical activity and health: a report of the Surgeon General. http://www.cdc.gov/nccdphp/sgr/pdf/sgrfull.pdf. 1996. Accessed November 1, 2016.
4. Stessman J, Hammerman-Rozenberg R, Cohen A, Ein-Mor E, Jacobs JM. Physical activity, function, and longevity among the very old. *Arch Intern Med*. 2009;169:1476–1483. doi:10.1001/archinternmed.2009.248
5. Müezzinler A, Zaineddin AK, Brenner H. A systematic review of leukocyte telomere length and age in adults. *Ageing Res Rev*. 2013;12:509–519. doi:10.1016/j.arr.2013.01.003
6. Haycock PC, Heydon EE, Kaptoge S, Butterworth AS, Thompson A, Willeit P. Leucocyte telomere length and risk of cardiovascular disease: systematic review and meta-analysis. *BMJ*. 2014;349:g4227. doi:10.1136/bmj.g4227
7. Zhao J, Miao K, Wang H, Ding H, Wang DW. Association between telomere length and type 2 diabetes mellitus: a meta-analysis. *PLoS One*. 2013;8:e79993. doi:10.1371/journal.pone.0079993
8. Wentzensen IM, Mirabello L, Pfeiffer RM, Savage SA. The association of telomere length and cancer: a meta-analysis. *Cancer Epidemiol Biomarkers Prev*. 2011;20:1238–1250. doi:10.1158/1055-9965.EPI-11-0005
9. Latifovic L, Peacock SD, Massey TE, King WD. The influence of alcohol consumption, cigarette smoking, and physical activity on leukocyte telomere length. *Cancer Epidemiol Biomarkers Prev*. 2016;25:374–380. doi:10.1158/1055-9965.EPI-14-1364
10. Du M, Prescott J, Kraft P, et al. Physical activity, sedentary behavior, and leukocyte telomere length in women. *Am J Epidemiol*. 2012;175:414–422. doi:10.1093/aje/kwr330
11. Cherkas LF, Hunkin JL, Kato BS, et al. The association between physical activity in leisure time and leukocyte telomere length. *Arch Intern Med*. 2008;168:154–158. doi:10.1001/archinternmed.2007.39
12. 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;168:2163–2164. doi:10.1001/archinte.168.19.2163
13. Ludlow AT, Zimmerman JB, Witkowski S, Hearn JW, Hatfield BD, Roth SM. Relationship between physical activity level, telomere length, and telomerase activity. *Med Sci Sports Exerc*. 2008;40:1764–1771. doi:10.1249/MSS.0b013e31817c92aa
14. Soares-Miranda L, Imamura F, Siscovick D, Jenny NS, Fitzpatrick AL, Mozaffarian D. Physical activity, physical fitness, and leukocyte telomere length: the Cardiovascular Health Study. *Med Sci Sports Exerc*. 2015;47:2525–2534. doi:10.1249/MSS.0000000000000720
15. Tucker JM, Welk GJ, Beyler NK. Physical activity in U.S.: adults compliance with the physical activity guidelines for Americans. *Am J Prev Med*. 2011;40:454–461. doi:10.1016/j.amepre.2010.12.016
16. Washburn RA. Assessment of physical activity in older adults. *Res Q Exerc Sport*. 2000;71(2 suppl):S79–S88.
17. Dyrstad SM, Hansen BH, Holme IM, Anderssen SA. Comparison of self-reported versus accelerometer-measured physical activity. *Med Sci Sports Exerc*. 2014;46:99–106. doi:10.1249/MSS.0b013e3182a0595f
18. Bann D, Hire D, Manini T, et al.; LIFE Study Group. Light intensity physical activity and sedentary behavior in relation to body mass index and grip strength in older adults: cross-sectional findings from the Lifestyle Interventions and Independence for Elders (LIFE) study. *PLoS One*. 2015;10:e0116058. doi:10.1371/journal.pone.0116058
19. The Women's Health Initiative Study Group. Design of the Women's Health Initiative clinical trial and observational study. *Control Clin Trials*. 1998;19:61–109. doi:10.1016/S0197-2456(97)00078-0
20. Shadyab AH, Macera CA, Shaffer RA, et al. Associations of accelerometer-measured and self-reported sedentary time with leukocyte telomere length in older women. *Am J Epidemiol*. 2017. doi:10.1093/aje/kww196

21. LaCroix AZ, Rillamas-Sun E, Buchner D, et al. The Objective Physical Activity and Cardiovascular Disease Health in Older Women (OPACH) Study. *BMC Public Health*. 2017;17:192. doi:10.1186/s12889-017-4065-6
22. Choi L, Liu Z, Matthews CE, Buchowski MS. Validation of accelerometer wear and nonwear time classification algorithm. *Med Sci Sports Exerc*. 2011;43:357–364. doi:10.1249/MSS.0b013e3181ed61a3
23. Choi L, Ward SC, Schnelle JF, Buchowski MS. Assessment of wear/nonwear time classification algorithms for triaxial accelerometer. *Med Sci Sports Exerc*. 2012;44:2009–2016. doi:10.1249/MSS.0b013e318258cb36
24. Troiano RP, Berrigan D, Dodd KW, Mâsse LC, Tilert T, McDowell M. Physical activity in the United States measured by accelerometer. *Med Sci Sports Exerc*. 2008;40:181–188. doi:10.1249/mss.0b013e31815a51b3
25. Lee IM, Rexrode KM, Cook NR, Manson JE, Buring JE. Physical activity and coronary heart disease in women: is "no pain, no gain" passé? *JAMA*. 2001;285:1447–1454. doi:10.1001/jama.285.11.1447
26. Hu FB, Stampfer MJ, Colditz GA, et al. Physical activity and risk of stroke in women. *JAMA*. 2000;283:2961–2967. doi:10.1001/jama.283.22.2961
27. Jeon CY, Lokken RP, Hu FB, van Dam RM. Physical activity of moderate intensity and risk of type 2 diabetes: a systematic review. *Diabetes Care*. 2007;30:744–752. doi:10.2337/dc06-1842
28. Friedenreich CM, Orenstein MR. Physical activity and cancer prevention: etiologic evidence and biological mechanisms. *J Nutr*. 2002;132(11 suppl):3456S–3464S.
29. Aviv A, Hunt SC, Lin J, Cao X, Kimura M, Blackburn E. Impartial comparative analysis of measurement of leukocyte telomere length/DNA content by Southern blots and qPCR. *Nucleic Acids Res*. 2011;39:e134. doi:10.1093/nar/gkr634
30. Kimura M, Stone RC, Hunt SC, et al. Measurement of telomere length by the Southern blot analysis of terminal restriction fragment lengths. *Nat Protoc*. 2010;5:1596–1607. doi:10.1038/nprot.2010.124
31. Stone RC, Horvath K, Kark JD, Susser E, Tishkoff SA, Aviv A. Telomere length and the cancer-atherosclerosis trade-off. *PLoS Genet*. 2016;12:e1006144. doi:10.1371/journal.pgen.1006144
32. Davis MG, Fox KR, Hillsdon M, Sharp DJ, Coulson JC, Thompson JL. Objectively measured physical activity in a diverse sample of older urban UK adults. *Med Sci Sports Exerc*. 2011;43:647–654. doi:10.1249/MSS.0b013e3181f36196
33. Arnardottir NY, Koster A, Van Domelen DR, et al. Objective measurements of daily physical activity patterns and sedentary behaviour in older adults: Age, Gene/Environment Susceptibility-Reykjavik Study. *Age Ageing*. 2013;42:222–229. doi:10.1093/ageing/afs160
34. Evenson KR, Buchner DM, Morland KB. Objective measurement of physical activity and sedentary behavior among US adults aged 60 years or older. *Prev Chronic Dis*. 2012;9:E26. doi:10.5888/pcd9.110109
35. Shiroma EJ, Cook NR, Manson JE, Buring JE, Rimm EB, Lee IM. Comparison of self-reported and accelerometer-assessed physical activity in older women. *PLoS One*. 2015;10:e0145950. doi:10.1371/journal.pone.0145950
36. Kasapis C, Thompson PD. The effects of physical activity on serum C-reactive protein and inflammatory markers: a systematic review. *J Am Coll Cardiol*. 2005;45:1563–1569. doi:10.1016/j.jacc.2004.12.077
37. von Zglinicki T. Oxidative stress shortens telomeres. *Trends Biochem Sci*. 2002;27:339–344. doi:10.1016/S0968-0004(02)02110-2
38. Valdes AM, Andrew T, Gardner JP, et al. Obesity, cigarette smoking, and telomere length in women. *Lancet*. 2005;366:662–664. doi:10.1016/S0140-6736(05)66630-5
39. Werner C, Fürster T, Widmann T, et al. Physical exercise prevents cellular senescence in circulating leukocytes and in the vessel wall. *Circulation*. 2009;120:2438–2447. doi:10.1161/CIRCULATIONAHA.109.861005
40. Chilton WL, Marques FZ, West J, et al. Acute exercise leads to regulation of telomere-associated genes and microRNA expression in immune cells. *PLoS One*. 2014;9:e92088. doi:10.1371/journal.pone.0092088