



TeloYears™ Bibliography

Abstracts and Citations

The impact of telomere length on human health has been studied for more than 20 years, with clinical findings published in numerous peer-reviewed scientific publications.

Average Telomere Length (ATL) using white blood cells (leukocytes) offers insights into overall health as well as associations with several chronic or age-related diseases, including Cardiovascular Disease, Diabetes (Type 2), Obesity and Mood disorders.

Furthermore, the rate of telomere length shortening may be slowed or average telomere length increased when sustained changes to lifestyle are made.

Select studies are cited and summarized below.

Telomere Length and Mortality

Association between telomere length in blood and mortality in people aged 60 years or older. *Cawthon RM, et al. Lancet. 2003 Feb 1;361(9355):393-5.*

This study assessed the association between blood leukocyte average telomere length (ATL) and mortality in 143 normal unrelated individuals over the age of 60 years. Individuals with shorter telomeres had poorer survival, attributable in part to a 3.18-fold higher mortality rate from heart disease (95% CI 1.36-7.45, $p=0.0079$), and an 8.54-fold higher mortality rate from infectious disease (1.52-47.9, $p=0.015$). These results support the hypothesis that telomere shortening in human beings contributes to mortality in many age-related diseases.

Leukocyte Telomere Length and Mortality in the National Health and Nutrition Examination Survey, 1999–2002. *Needham BL, et al, Epidemiology. 2015 July;26(4): 528–535.*

This study examined the association between leukocyte telomere length and mortality in US adults aged 50–84. ($n=3,091$). A decrease of 1 kilobase pair in telomere length at baseline was marginally associated with a 10% increased hazard of all-cause mortality (HR: 1.1, 95% CI: 0.9, 1.4) and a 30% increased hazard of death due to diseases other than cardiovascular disease or cancer (HR: 1.3, 95% CI: 0.9, 1.9).

Association between telomere length, specific causes of death, and years of healthy life in health, aging, and body composition, a population-based cohort study. Njajou OT, et al, *Health ABC study. J Gerontol A Biol Sci Med Sci.* 2009 Aug;64(8):860-4.

Health ABC study, a community-based cohort of 3,075 healthy, well-functioning men and women aged 70–79 years. Average Telomere Length, as measured by qPCR, was assessed to see if those with the shortest ATL have poorer survival, shorter life span, and fewer years of healthy life (YHL).

Longer telomere length was associated with more years of healthy living. Longer ATL was positively associated with longer years of healthy life ($p = .03$). Findings suggest that ATL may be an informative biomarker of healthy aging.

Telomere Length and Cardiovascular Disease

Leucocyte telomere length and risk of cardiovascular disease: systematic review and meta-analysis. Philip C Haycock, et al, *British Medical Journal.* 2014;349: g4227.

In a meta-analysis of twenty-four studies involving 43,725 participants and 8400 patients with cardiovascular disease (5566 with coronary heart disease and 2834 with cerebrovascular disease), in a comparison of the shortest versus longest third of leucocyte telomere length, the pooled relative risk for coronary heart disease was 1.54. Available observational data show an inverse association between leucocyte telomere length and risk of coronary heart disease independent of vascular risk factors.

Cellular aging reflected by leukocyte telomere length predicts advanced atherosclerosis and cardiovascular disease risk. Willeit P, et al. *Arterioscler Thromb Vasc Biol.* 2010 Aug;30(8):1649-56.

ATL was measured by q-PCR in 800 women and men aged 45 to 84 years. The manifestation of cardiovascular disease (CVD) in ten years and the progression of atherosclerosis in five were carefully assessed in this study cohort. Participants with CVD events during follow-up ($n=88$) had significantly shorter telomeres ($P<0.001$). In multivariable Cox models, baseline ATL emerged as a significant and independent risk predictor for the composite CVD endpoint and its individual components (myocardial infarction and stroke); however, this was not the case for de novo stable angina and intermittent claudication. The top and bottom ATL quarters of ATL lengths when compared to their peers of the same chronological age differed in their CVD risk by a factor of 2.72, which is the risk ratio attributable to a 13.9-year difference in chronological age.

Telomeres and atherosclerosis. Khan S1, et al, *Cardiovasc J Afr.* 2012 Nov;23(10):563-71.

A retrospective registry analysis of 383 patients (203 cases, 180 controls) showed that patients with premature myocardial infarction had significantly shorter mean telomere lengths. In this study, the difference in telomere length between cases and chronologically age-matched controls demonstrated a biological age gap in excess of 11 years.

Compared with subjects in the highest quartile for telomere length, the risk of myocardial infarction was increased between 2.8- and 3.2-fold in subjects with shorter-than-average telomeres. In Cawthon, et al, *Lancet*, 2003 showed that subjects with shorter telomeres had poorer survival, with a 3.18-fold higher mortality rate from heart disease ($n = 143$ normal blood donors over the age of 60 years).

Telomere Length and Diabetes

Association between telomere length and type 2 diabetes mellitus: a meta-analysis. Zhao J, et al. *PLOS ONE* 2013, November 2013 | Volume 8 | Issue 11 | e79993.

In meta-Analysis of 5759 cases and 6518 controls in nine cohorts, shortened telomere length was significantly associated with type two diabetes mellitus (OR: 1.291; P:0.001) with heterogeneity (I² = 71.6%). When three cohorts responsible for the heterogeneity were excluded, the pooled OR for the remaining cohorts indicated a significant association remained (OR: 1.117; P = 0.045).

Telomere Length and Obesity

Inverse association between adiposity and telomere length: The Fels Longitudinal Study. Lee M, et al. *Am J Hum Biol.* 2011 Jan-Feb;23(1):100-6.

In a cross-sectional sample of 309 non-Hispanic white participants aged 8 to 80 yr (52% female), average telomere length was negatively correlated with age ($r = -0.32$, $P < 0.0001$) and had numerous significant correlations with established cardiovascular disease risk factors including waist circumference ($r = -0.33$), apolipoprotein B ($r = -0.26$), systolic blood pressure ($r = -0.28$), and fasting serum glucose ($r = -0.15$); all $P < 0.0025$. In backward selection linear regression models of telomere length, adiposity measures were consistently retained in the best models; BMI, waist circumference, hip circumference, total body fat, and visceral adipose tissue volume were all inversely associated with average telomere length at the nominal $P < 0.05$ level or lower, independent of age, sex, systolic blood pressure, and fasting serum lipid, lipoprotein, and glucose concentrations. Individuals with higher total and abdominal adiposity have lower average telomere length, a marker of cellular senescence, suggesting obesity may hasten the aging process.

Telomere Length and Alzheimer's Disease

Telomere shortening in T cells correlates with Alzheimer's disease status. Panossian LA, et al. *Neurobiol Aging.* 2003 Jan-Feb;24(1):77-84.

Our data show a significant telomere shortening in PBMC from AD versus controls ($P=0.04$). Telomere length of T cells, correlated with AD disease status, measured by Mini Mental Status Exam (MMSE) scores ($P=0.025$). T cell telomere length also inversely correlated with serum levels of the proinflammatory cytokine TNFalpha (a clinical marker of disease status), with the proportion of CD8+ T cells lacking expression of the CD28 costimulatory molecule, and with apoptosis. These findings suggest an immune involvement in AD pathogenesis.

Telomere Length and Mood Disorders

Telomere shortening and mood disorders: preliminary support for a chronic stress model of accelerated aging. Simon NM1, et al. *Biol Psychiatry.* 2006 Sep 1;60(5):432-5.

Accelerated telomere shortening may reflect stress-related oxidative damage to cells and accelerated aging, and severe psychosocial stress has been linked to telomere shortening. Telomere length was measured by Southern Analysis in 44 individuals with chronic mood disorders and 44 non-psychiatrically ill age-matched control subjects. Telomere length was significantly shorter in those with mood disorders, representing as much as 10 years of accelerated aging. These results provide preliminary evidence that mood disorders are associated with accelerated aging and may suggest a novel mechanism for mood disorder-associated morbidity and mortality.

Depression and telomere length: A meta-analysis. Ridout KK1, et al. *J Affect Disord.* 2016 Feb;191:237-47.

In thirty-eight studies (n=34,347), Depression severity significantly associated with telomere length (p=0.03). The association remained highly significant after accounting for publication bias. Subgroup analysis revealed depression assessment tools, telomere measurement techniques, source tissue and comorbid medical conditions significantly affected the relationship.

Depression, anxiety, and telomere length in young adults: Evidence from the National Health and Nutrition Examination Survey. Belinda Needham, et al., *Mol Psychiatry.* 2015 April ; 20(4): 520–528.

Past year major depression (MD), generalized anxiety disorder (GAD) and panic disorder (PD), as well as depressed affect and anxious affect, were assessed using the Composite International Diagnostic Inventory (N=1,290). Among women, those with GAD or PD had shorter telomeres than those with no anxious affect (β : -0.07, p.05). Among respondents currently taking an antidepressant, those with MD had shorter telomeres than those without (β : -.26, p.05). Neither depressive nor anxiety disorders were directly associated with telomere length in young adults. There was suggestive evidence that pharmacologically treated MD is associated with shorter telomere length, likely reflecting the more severe nature of MD that has come to clinical attention.

Lifestyle Changes to Increase Telomere Length

The rate of telomere length shortening may be slowed or average telomere length increased when sustained changes to lifestyle are made. Select summaries and citations follow below.

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. Ornish D, et al. *Lancet Oncol.* 2013 Oct;14(11):1112-20.

After previously finding an association between 3 months of comprehensive lifestyle changes and increased telomerase activity in human immune-system cells, the authors followed up participants to investigate long-term effects (10 men and 25 external controls with biopsy-proven, low-risk prostate cancer who chose to undergo active surveillance). Men in the intervention group followed a program of comprehensive lifestyle changes (diet, activity, stress management, and social support); men in the control group underwent active surveillance alone. Relative telomere length increased from baseline by a median of 0.06 telomere to single-copy gene ratio (T/S) units (IQR -0.05 to 0.11) in the lifestyle intervention group, but decreased in the control group (-0.03 T/S units, -0.05 to 0.03, difference p=0.03). When data from the two groups were combined, adherence to lifestyle changes was significantly associated with relative telomere length after adjustment for age and length of follow-up (for each percentage point increase in lifestyle adherence score, T/S units increased by 0.07, p=0.005).

The Association Between Physical Activity in Leisure Time and Leukocyte Telomere Length. Cherkas LN, et al. *Arch Int Med,* 2008.

The authors tested the hypothesis that physical activity level in leisure time (over past 12 months) is associated with leukocyte telomere length (LTL) in 2401 white twin volunteers. Leukocyte telomere length was positively associated with increasing physical activity level in leisure time (P<.001);

this association remained significant after adjustment for age, sex, body mass index, smoking, socioeconomic status, and physical activity at work. The LTLs of the most active subjects were 200 nucleotides longer than those of the least active subjects (7.1 and 6.9 kilobases, respectively; $P=.006$). This finding was confirmed in a small group of twin pairs discordant for physical activity (on average, the LTL of more active twins was 88 nucleotides longer than that of less active twins; $P=.03$). Conclusions: A sedentary lifestyle (in addition to smoking, high BMI, and low socioeconomic status) has an effect on LTL and may accelerate the aging process. This provides a powerful message that could be used by clinicians to promote the potentially antiaging effect of regular exercise.

Mediterranean diet and telomere length in Nurses' Health Study: population based cohort study. Crous-Bou M, et al. *BMJ* 2014;349:g6674

The study examined whether adherence to the Mediterranean diet was associated with longer telomere length. N= 4676 disease-free women from nested case-control studies within the Nurses' Health Study with telomere length measured who also completed food frequency questionnaires. Greater adherence to the Mediterranean diet was associated with longer telomeres after adjustment for potential confounders. Least squares mean telomere length z scores were -0.038 (SE 0.035) for the lowest Mediterranean diet score groups and 0.072 (0.030) for the highest group (P for trend= 0.004). In this large study, greater adherence to the Mediterranean diet was associated with longer telomeres. These results further support the benefits of adherence to the Mediterranean diet for promoting health and longevity.

For information on TeloYears™, a simple genetic test that reveals your cellular age based on telomere length, visit www.teloyears.com

The TeloYears test is not intended for screening, diagnosing, treating or preventing diseases or medical conditions. The test is available for individuals between the ages of 20 to 80 within the United States, except for the state of New York.

The information provided by the TeloYears test should not be used to replace medically appropriate screening tests recommended based upon actual age or other risk factors, nor should the information be used to make decisions about diagnosis or treatment of diseases or medical conditions. The Telomere Diagnostics lab is regulated under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical testing. The performance characteristics of this test were determined by Telomere Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration.

Test reports are kept absolutely private according to our Privacy Policy and are available only in a fashion that maintains compliance with the HIPAA security rule, which regulates privacy and security of health information.