TRUAGE BY TRUDIAGNOSTIC

Telomere Length

This report explores telomere length and its relation to biological age and accelerated biological aging by examining associated methylation patterns at various locations of your DNA.

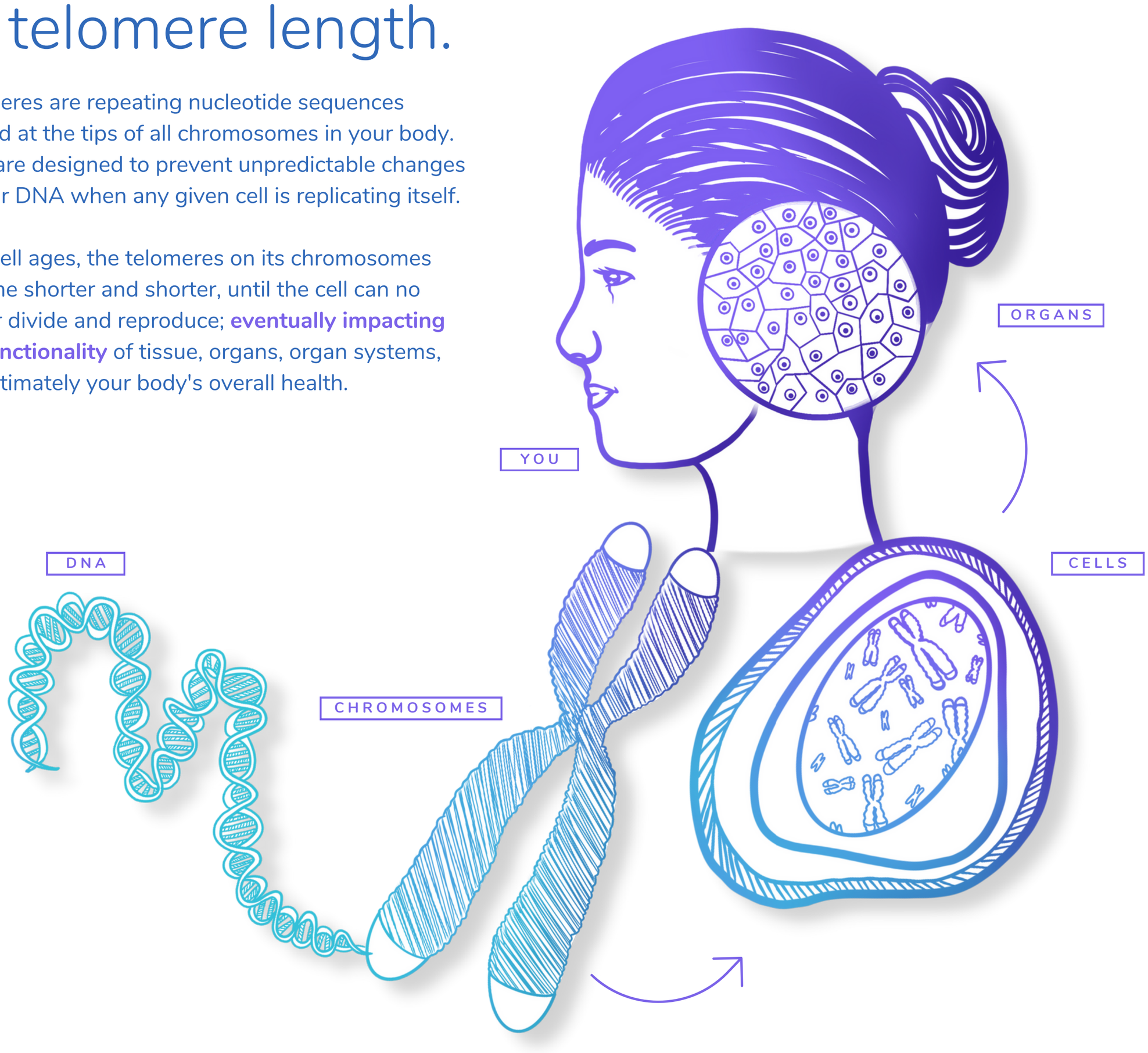
Developed By TruDiagnostic's Bioinformatics & Research Department

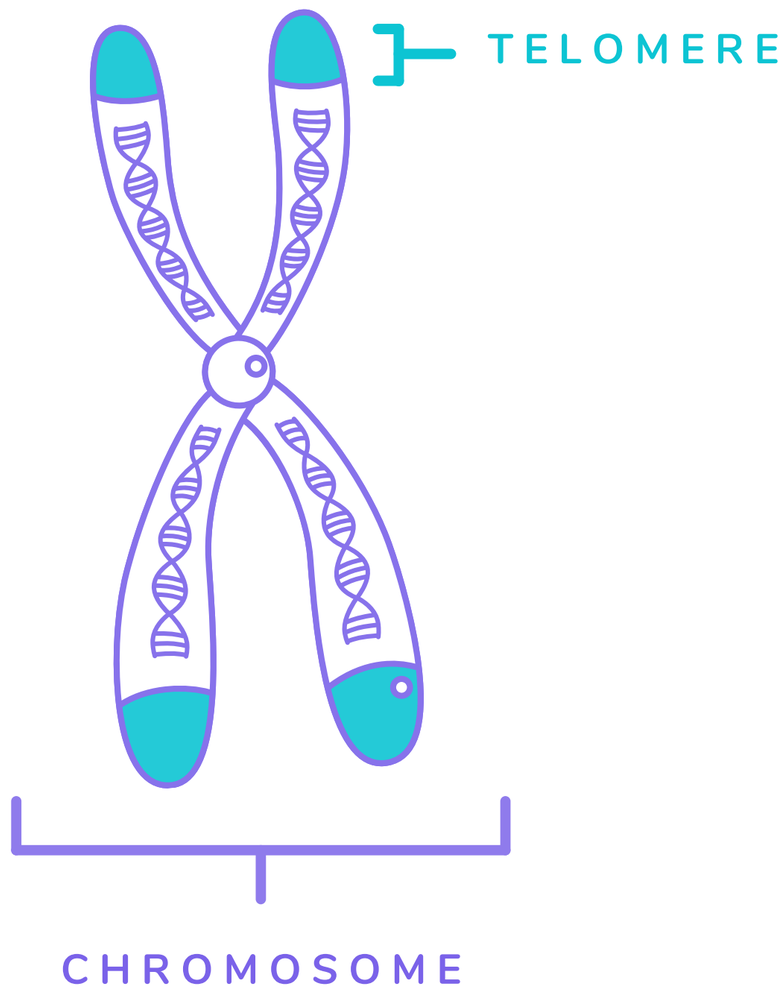
UNDERSTANDING

The importance of telomere length.

Telomeres are repeating nucleotide sequences located at the tips of all chromosomes in your body. They are designed to prevent unpredictable changes to your DNA when any given cell is replicating itself.

As a cell ages, the telomeres on its chromosomes become shorter and shorter, until the cell can no longer divide and reproduce; **eventually impacting the functionality** of tissue, organs, organ systems, and ultimately your body's overall health.





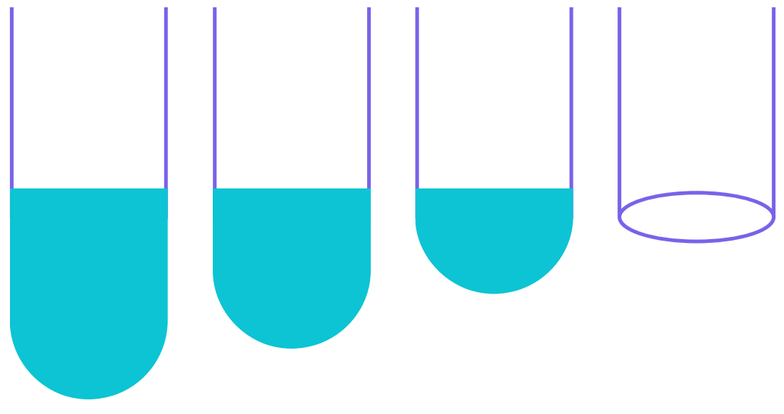
A telomere's primary function is to prevent chromosomal “fraying” when a cell replicates, much like the plastic tips on the end of shoelaces [5]. As a cell ages, its telomeres become shorter.

This shortening is thought to be one of several factors that causes cells to age. In actively dividing cells, such as those in the bone marrow, the stem cells of the embryo, and germ cells in the adult, telomere length (TL) is kept constant by the enzyme telomerase.

As humans age, this enzyme becomes less active over time. This leads to a slow decrease in telomere length, **until a point is reached at which the cell is no longer capable of replication** (replicative senescence).

A cell can no longer divide when telomeres are too short—once they reach a critical point, the cell becomes inactive (or senescent), slowly accumulating damage that it can’t repair, or it dies [6].

Telomere length is **affected by both genetic and epigenetic contributions**. A new study found that DNA methylation is closely linked to TL. The study by researchers at the University of California Los Angeles shows a very significant linkage between two different markers that indicate aging [2].



AS CELLS DIVIDE OVER TIME, TELOMERES SHORTEN UNTIL CELL DIVISION STOPS.

WHY TELOMERE

Length is important.

Telomeres are an essential part of human cells that affect how our cells age [1]. Telomere length has emerged as an important determinant of replicative senescence and cell fate - **an important indicator of the aging process** and a wide range of disease states, including cancers, cardiovascular disease, and age-related disorders.

Shorter telomeres are not only associated with age but with disease too. In fact, shorter telomere length and low telomerase activity are associated with several chronic preventable diseases. These include hypertension, cardiovascular disease, insulin resistance, type 2 diabetes, depression, osteoporosis, and obesity.

Shorter telomeres have also been implicated in genomic instability and oncogenesis. **Older people with shorter telomeres have three and eight times increased risk to die from heart and infectious diseases**, respectively [4]. The rate of telomere shortening and telomere length is therefore critical to an individual's health and pace of aging.

JANE,

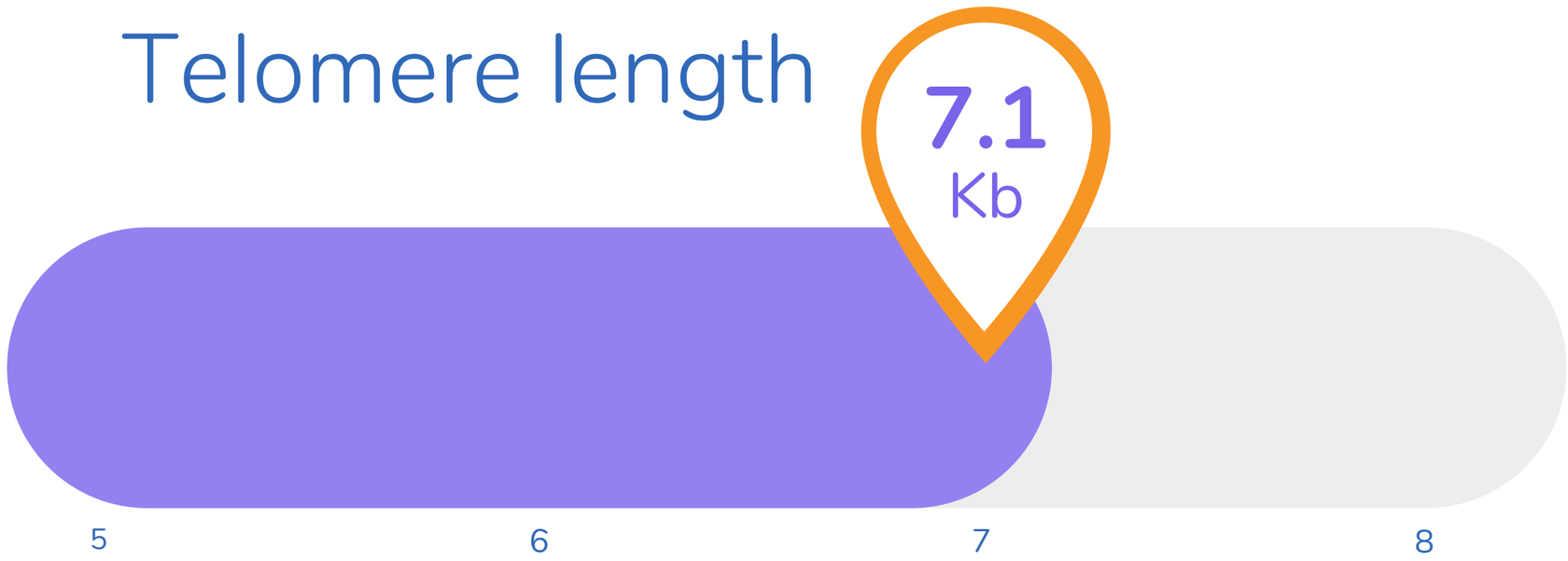
at your chronological age of 61, your telomeres are

LONGER THAN 90%

of people who share the same chronological age as you.

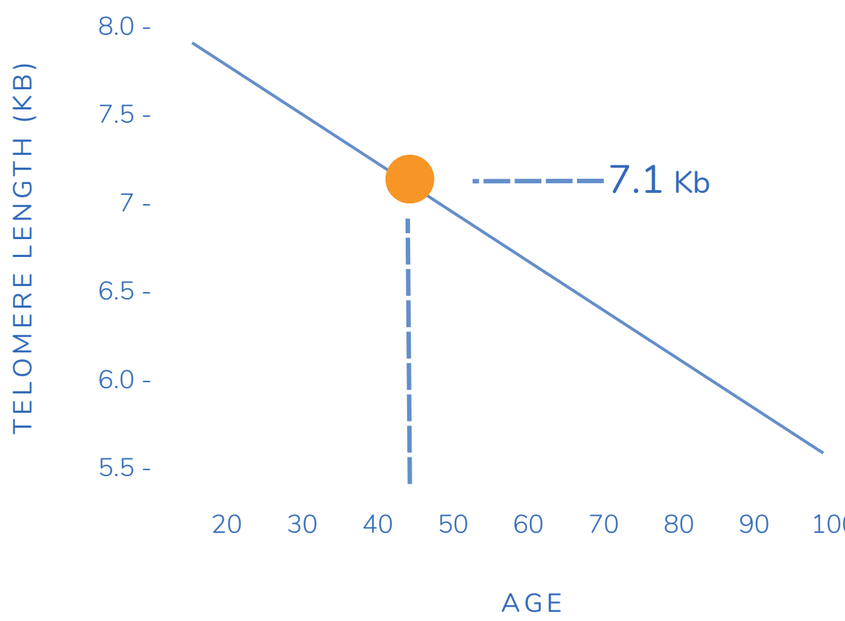
YOUR AVERAGE

Telomere length



If we were to estimate your biological age **strictly from your telomere measurement**, we would anticipate your age to be:

At your chronological age of 50, you would be in the **90th** percentile of telomere length compared to others of your same chronological age.



This means that your telomeres are longer than **90**% of people who share the same chronological age as you. Simply put, longer telomeres equal healthier telomeres and cells.

EDUCATIONAL CONTENT

FAQs

TOP QUESTIONS

Can Telomere length be increased with therapies or behaviors?

It is important to note that the research in this field is still evolving, and the effects of different interventions on telomere length are not yet fully understood.

1. Lifestyle and Behavioral Factors:
Telomeres are the protective caps at the ends of chromosomes that shorten with each cell division. Telomere length has been associated with aging and various age-related diseases. While telomere shortening is a natural part of the aging process, there has been considerable interest in finding ways to potentially increase telomere length through therapies or behaviors.

It is important to note that the research in this field is still evolving, and the effects of different interventions on telomere length are not yet fully understood. As a result, no definitive method to elongate telomeres current exists in somatic cells. However, there is some information which alludes to helpful intervention.

Several studies have explored the relationship between lifestyle factors and telomere length. While no definitive causative links have been established, certain behaviors have been associated with longer telomeres:

a. Physical Exercise: Regular physical exercise has been linked to longer telomeres. A study by Ludlow et al. (2008) found that individuals who engaged in moderate or vigorous physical activity had longer telomeres compared to those who were sedentary.

b. Diet: Some research suggests that a healthy diet, rich in fruits, vegetables, whole grains, and lean proteins, may be associated with longer telomeres. Conversely, diets high in refined sugars and unhealthy fats may be linked to shorter telomeres. However, more research is needed to establish definitive conclusions in this area.

c. Stress Reduction: Chronic psychological stress has been associated with telomere shortening. Stress reduction techniques such as mindfulness meditation and stress management programs may have potential benefits for telomere maintenance. One study by Epel et al. (2004) showed that caregivers of chronically ill children who practiced mindfulness meditation had increased telomerase activity, an enzyme that helps maintain telomere length.

2. Pharmacological Interventions:
Several studies have explored the potential of pharmacological interventions to influence telomere length. It is important to note that these interventions are still at an experimental stage and require further research before being established as effective or safe for widespread use. Here are a few examples:

a. Telomerase Activators: Telomerase is an enzyme that can elongate telomeres. Certain compounds, such as small-molecule telomerase activators, have been investigated for their potential to increase telomerase activity and lengthen telomeres. One such compound is TA-65, which has shown promising results in preclinical studies and early human trials. However, more research is needed to determine its mechanism.

b. Lifestyle Modification + Pharmacological Intervention: A study by Ornish et al. (2013) investigated the effects of comprehensive lifestyle changes, including a plant-based diet, exercise, stress reduction, and social support, in combination with a telomerase activator. The intervention group showed significant increases in telomere length over a five-year period compared to the control group.

It is essential to consult with medical professionals and researchers for the most up-to-date information regarding telomere lengthening therapies, as the field is continually advancing and new research may have emerged since this report has been created.

What factors have been shown to modify epigenetic predictors of telomere length?

In the original DNAm Telomere length algorithm created by Dr. Steve Horvath from UCLA, they saw several associations between lifestyle factors and DNAm Telomere length. They found omega-3 supplement intake was correlated to longer age-adjusted DNAmTL. The effect of omega-3 supplementation was more pronounced in males than in females. In fact, omega-3 intake is associated with longer DNAmTLadjAge even after adjusting for sex, BMI, educational levels, and smoking pack year. In addition, this study showed that smoking was associated with shorter telomere lengths. Other studies have shown that traumatic stress and PTSD also show an association between telomere length and epigenetic clocks.

How much does telomere length compare to Epigenetic aging clocks?

Both epigenetic aging clocks and telomere length are used to measure aging. However, they approach this by measuring different hallmarks of aging. DNA methylation-based clocks generally tend to be superior at capturing aging. We know this because of their ability to predict negative outcomes associated with aging. Although telomere length has been a long-used biomarker of aging, they tend to not be very predictive. This is summarized well in a 2017 review paper on biological aging where the authors said, “Briefly, telomere length is extensively validated but has low predictive power.”

This is backed up by other analyses from the generation Scotland cohort. Evidence that TL and epigenetic clock estimates are independent predictors of chronological age and mortality risk was obtained in the study by Marioni et al. (2018) performed in two Scottish cohorts aged from 70 to 90 years. In both cohorts studied, combined whole-blood TL and DNAm age explained more variance in age than each of them individually. In combined cohort analysis, TL and DNAm age explained 2.8 and 28.5% of the variance in age, respectively, and jointly they explained 29.5%. This large difference was present using even only 1st generation chronologically trained clocks which are not as effective in predicting risk as the 2nd and 3rd generation clocks available today.

How does DNAm Telomere relate to regular telomere length measures?

Leukocyte DNAmTL outperforms regular LTL (done via qPCR) in predicting

- Time-to-death
- Time-to-coronary heart disease
- Time-to-congestive heart failure
- Association with smoking history

It also has double the correlation to age than traditional telomere length.

EDUCATIONAL CONTENT

Report references.

Jaskelioff, M., Muller, F. L., Paik, J.-H., Thomas, E., Jiang, S., Adams, A. C., Sahin, E., Kost-Alimova, M., Protopopov, A., Cadiñanos, J., Horner, J. W., Maratos-Flier, E., & DePinho, R. A. (2011). Telomerase reactivation reverses tissue degeneration in aged telomerase-deficient mice. Nature, 469(7328), 102–106. https://www.researchgate.net/publication/49640982_Telomerase_reactivation_reverses_tissue_degeneration_in_aged_telomerase-deficient_mice

Lee, Y., Sun, D., Ori, A. P. S., Lu, A. T., Seeboth, A., Harris, S. E., Deary, I. J., Marioni, R. E., Soerensen, M., Mengel-From, J., Hjelmborg, J., Christensen, K., Wilson, J. G., Levy, D., Reiner, A. P., Chen, W., Li, S., Harris, J. R., Magnus, P., … Horvath, S. (2019). Epigenome-wide association study of leukocyte telomere length. Aging, 11(16), 5876–5894. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6738430/

Lu, A. T., Seeboth, A., Tsai, P.-C., Sun, D., Quach, A., Reiner, A. P., Kooperberg, C., Ferrucci, L., Hou, L., Baccarelli, A. A., Li, Y., Harris, S. E., Corley, J., Taylor, A., Deary, I. J., Stewart, J. D., Whitsel, E. A., Assimes, T. L., Chen, W., … Horvath, S. (2019). DNA methylation-based estimator of telomere length. Aging, 11(16), 5895–5923. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6738410/

Shammas M. A. (2011). Telomeres, lifestyle, cancer, and aging. Current opinion in clinical nutrition and metabolic care, 14(1), 28–34. https://doi.org/10.1097/MCO.0b013e32834121b1

Songyang, Z. (2017). Introduction to Telomeres and Telomerase. Methods in Molecular Biology (Clifton, N.J.), 1587, 1–13. https://pubmed.ncbi.nlm.nih.gov/21461806/

Zvereva, M., Shcherbakova, D., & Dontsova, O. (2010). Telomerase: Structure, functions, and activity regulation. Biochemistry (00062979), 75(13), 1563–1583. https://www.researchgate.net/publication/50591672_Telomerase_Structure_functions_and_activity_regulation

Reference: Ludlow, A. T., Zimmerman, J. B., Witkowski, S., & Hearn, J. W. (2008). Exercise alters leukocyte telomere length: a pilot study. Medicine and Science in Sports and Exercise, 40(5), 728-733.

Reference: Epel, E. S., Blackburn, E. H., Lin, J., Dhabhar, F. S., Adler, N. E., Morrow, J. D., & Cawthon, R. M. (2004). Accelerated telomere shortening in response to life stress. Proceedings of the National Academy of Sciences, 101(49), 17312-17315.

Reference: Harley, C. B., Liu, W., Blasco, M., Vera, E., & Andrews, W. H. (2011). A natural product telomerase activator as part of a health maintenance program. Rejuvenation Research, 14(1), 45-56.

Reference: Ornish, D., Lin, J., Daubenmier, J., Weidner, G., Epel, E., Kemp, C., … & Blackburn, E. (2013). Increased telomerase activity and comprehensive lifestyle changes: a pilot study. The Lancet Oncology, 14(11), 1112-1120.

Lu AT, Seeboth A, Tsai PC, Sun D, Quach A, Reiner AP, Kooperberg C, Ferrucci L, Hou L, Baccarelli AA, Li Y, Harris SE, Corley J, Taylor A, Deary IJ, Stewart JD, Whitsel EA, Assimes TL, Chen W, Li S, Mangino M, Bell JT, Wilson JG, Aviv A, Marioni RE, Raj K, Horvath S. DNA methylation-based estimator of telomere length. Aging (Albany NY). 2019 Aug 18;11(16):5895-5923. doi: 10.18632/aging.102173. Epub 2019 Aug 18. PMID: 31422385; PMCID: PMC6738410. What outcomes are associated with lower predicted DNAm telomere length?

Boks MP, van Mierlo HC, Rutten BP, Radstake TR, De Witte L, Geuze E, Horvath S, Schalkwyk LC, Vinkers CH, Broen JC, Vermetten E. Longitudinal changes of telomere length and epigenetic age related to traumatic stress and post-traumatic stress disorder. Psychoneuroendocrinology. 2015 Jan;51:506-12. doi: 10.1016/j.psyneuen.2014.07.011. Epub 2014 Jul 23. PMID: 25129579.

Marioni RE, Harris SE, Shah S, McRae AF, von Zglinicki T, Martin-Ruiz C, Wray NR, Visscher PM, Deary IJ. The epigenetic clock and telomere length are independently associated with chronological age and mortality. Int J Epidemiol. 2018 Feb;45(2):424-432. doi: 10.1093/ije/dyw041. Epub 2016 Apr 13. Erratum in: Int J Epidemiol. 2018 Feb 1;47(1):356. PMID: 27075770; PMCID: PMC4864882.

u AT, Seeboth A, Tsai PC, Sun D, Quach A, Reiner AP, Kooperberg C, Ferrucci L, Hou L, Baccarelli AA, Li Y, Harris SE, Corley J, Taylor A, Deary IJ, Stewart JD, Whitsel EA, Assimes TL, Chen W, Li S, Mangino M, Bell JT, Wilson JG, Aviv A, Marioni RE, Raj K, Horvath S. DNA methylation-based estimator of telomere length. Aging (Albany NY). 2019 Aug 18;11(16):5895-5923. doi: 10.18632/aging.102173. Epub 2019 Aug 18. PMID: 31422385; PMCID: PMC6738410.