

Updated Information About Telomeres and Health in People

In light of a recent New York Times article <u>https://www.nytimes.com/.../long-telomeres-age-longevity...</u>, which had a misleading title and subtitle, we feel that clarification of the realities of telomeres in humans is necessary to prevent misinformation and confusion.

To cut to the chase: the many population-based studies on this topic overwhelmingly show that long telomeres predict longer life, and none show that long telomeres shorten life. Below, we summarize the relevant extensive scientific evidence about the roles and impacts of telomeres in humans:

It has long been known that short telomeres limit cell division and predict some degenerative diseases of aging whereas long telomeres permit, and predict, cell replication and thus lead to higher risk of some cancers. As might be expected from this, multiple studies find increased disease risks at either end of the telomere length spectrum in normal human populations. See, for example, <u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544094/</u>.

Telomere length is determined by a combination of both genetic and non-genetic factors.

In humans, normal small genetic variations that cause telomeres to be shorter than average increase the risks of immune system problems, heart and lung disease and a variety of degenerative diseases including Alzheimer's. And the normal small genetic variations that instead make telomeres longer than average increase risks for several kinds of cancers. These common genetic determinants of telomere maintenance in populations (genes affecting telomerase or telomeres) impose essentially equal health burdens of longer telomeres (for cancers) vs. shorter telomeres (for other diseases of aging)

<u>https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7544094/</u>. Humans thus have evolved a genetic trade-off, with the health and mortality burdens imposed by cancer versus non-cancer partially balancing each other out. Yet, as it turns out, the net result of this trade-off is that, overall, shorter telomeres caused by normal genetic variation predict lower life expectancy <u>https://pubmed.ncbi.nlm.nih.gov/34611362/</u>.

(We speculate that this genetic trade-off for telomere maintenance might help explain the long-puzzling "cancer paradox", in which older people with dementias are protected from cancers, and vice versa. <u>https://alzres.biomedcentral.com/.../s13195-022-01090-9</u>)

Importantly, as well as the genetic influence, telomere length is also determined nongenetically. Several healthful behaviors are linked to longer telomeres. An important example of this is exercise. Across multiple studies, the major preponderance of evidence (coming from both observational and intervention studies) links longer telomeres with more exercise. While the biological mechanisms connecting the two are likely to be complex, it is important to be aware that exercise has NEVER been found to increase cancer risks – in fact, the opposite is true. As the National Cancer Institute states : "There is strong evidence that higher levels of physical activity are linked to lower risk of several types of cancer."

More information from the National Cancer Institute about the protective effect of exercise against cancer can be found on their website <u>https://www.cancer.gov/.../physical-activity-fact-sheet</u>.

Elizabeth Blackburn, PhD Elissa Epel, PhD Jue Lin, PhD