TRUAGE BY TRUDIAGNOSTIC

DunedinPACE

This report is able to tell you how many biological years you are aging per year at the precise moment. This algorithm was created by Duke and Columbia via a longitudinal study.

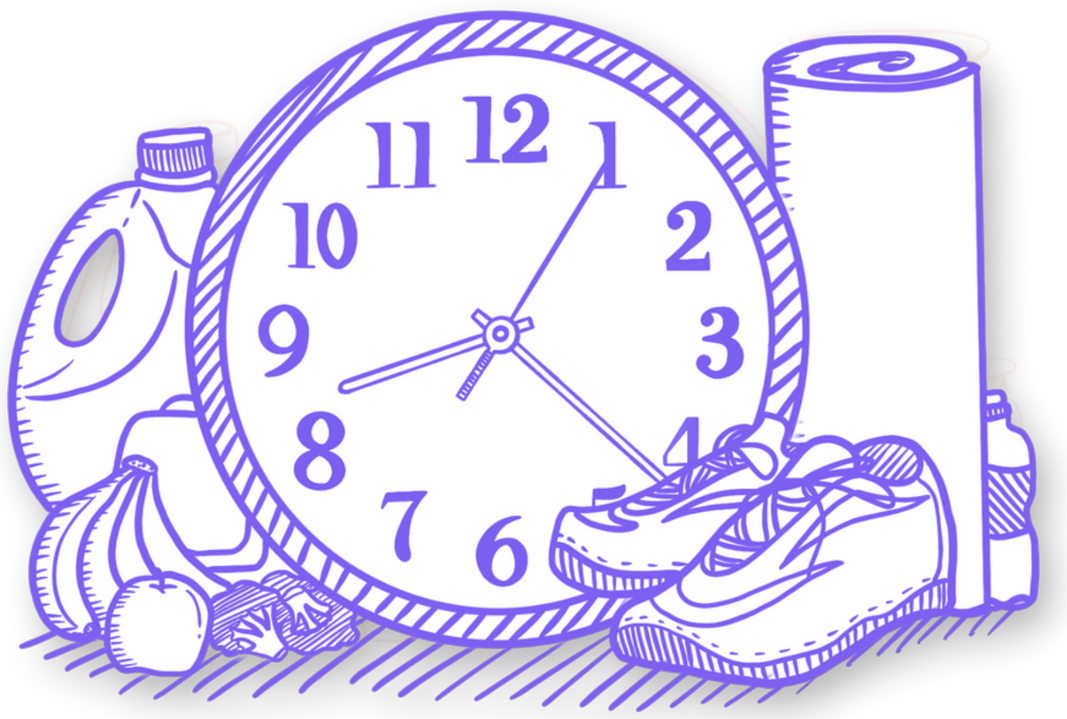
Developed By TruDiagnostic's Bioinformatics & Research Department

UNDERSTANDING

your pace of biological aging.

Methylation-based biological aging clocks changed the way we look at aging and preventive medicine!

Aging is the number one risk factor for most chronic diseases. Unfortunately, traditional determinants of age (the number of years since birth) don't always match up with how each individual ages. Some people in their 70s look and feel like they are 50, and then there are some 70-year-olds that look like they could be 90. **This is called phenotypic variation, and as a result, people have been searching for objective markers to measure the aging process.** Thankfully, a highly accurate one was created by measuring epigenetic biomarkers.



Having an objective biological age measurement has massive implications for preventative health and future investigations. However, if we can combine this with an instantaneous rate of aging, we can learn even more about our aging process, our individual aging biology, and the interventions for better preventative health when we combine these two metrics.

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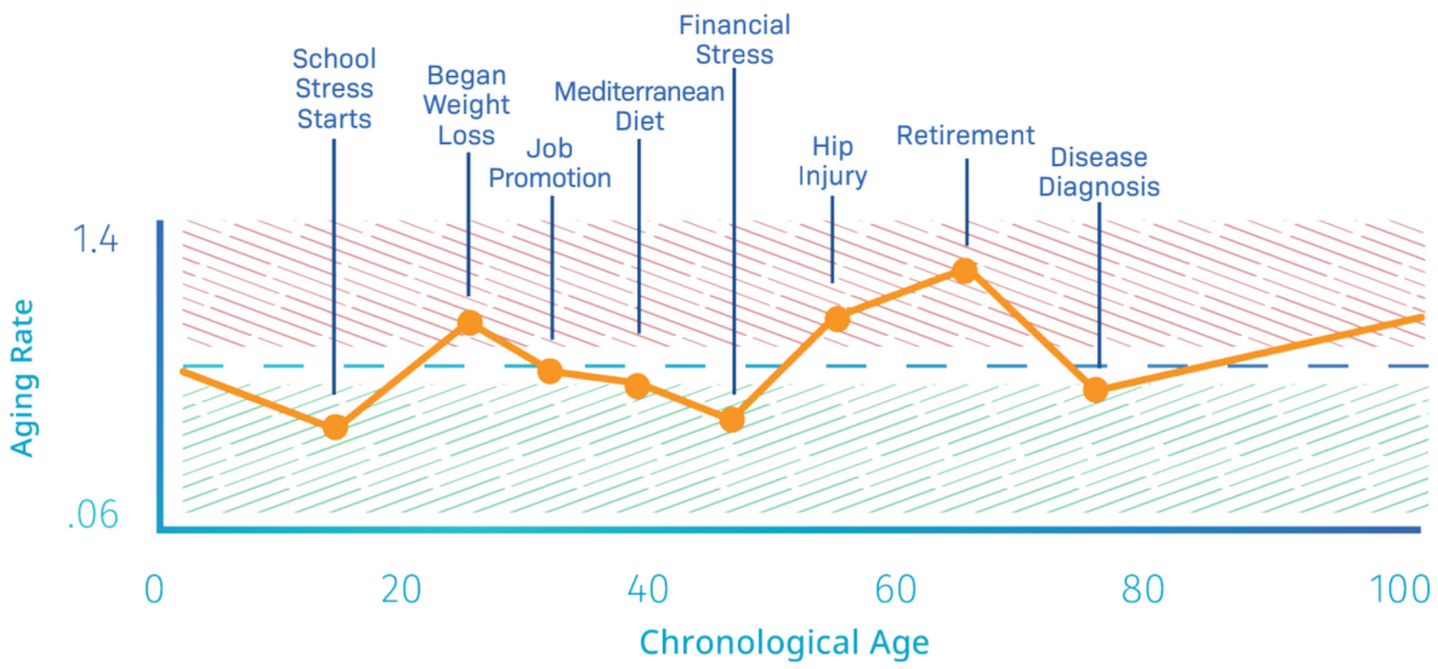
COLLECTED: 06/01/2020 | REPORTED: 07/01/2020

Your rate of aging versus your body's biological age.

Quantifying one's rate of aging versus biological age is like having a speedometer of aging instead of determining age at a fixed moment in time. Biological age is a great metric, but it doesn't compare past history from current influences on the methylome.



There are many external factors that influence one's pace of aging. The above image is a graphical representation of potential influences on your pace of aging.

There are several cases where knowing both of these metrics can be useful. The best example to illustrate this might be the theoretical case of two identical twins; Twin 1 and Twin 2.

Twin 1 (40 years old chronologically) has lived a very healthy life by implementing proper nutrition, exercise, medications, and lifestyle patterns. On the other hand, Twin B (40 years old chronologically) hasn't lived a life full of similar, healthy habits. For instance, Twin B had a very stressful life in their twenties and early thirties and recently turned their life around. Now, both twins have the exact same lifestyle, nutrition, and exercise regimens along with having the same baseline DNA sequence.

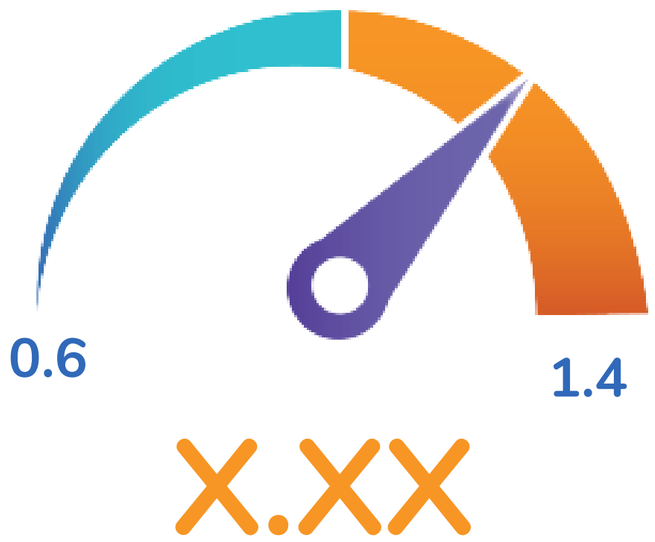
If we only looked at their biological age, we would most likely see that Twin A has a lower biological age due to their consistent history of healthy habits. The same logic would lead us to expect that Twin B might have a worse biological age due to their health history. This might lead us to believe that Twin B is currently doing things in their life to lead to faster aging when in fact the lifestyles of each individual are exactly the same.

However, if we had a way to look at the instantaneous aging rate, we would be able to distinguish advanced aging, which occurred in the past, from the current rate of aging, which is regulated by ongoing lifestyle factors. Distinguishing these two points can also help us decide which lifestyle traits we should keep and which we should change.

Thankfully, due to researchers from Duke and Columbia, an algorithm that measures the pace of aging is already available for us to use.

Your Results.

DunedinPACE Value



What Does Your Rate of Aging Mean?

You want your rate of aging to be below one; this means you would have a slowed pace of aging. An average pace of aging would be a rate of 1 biological year for every chronological year aged.

DunedinPACE is associated with chronic disease morbidity and mortality. **Within 7 years from testing those with a faster pace of aging are at a 56% increased risk of death and a 54% increased risk for diagnosis of a chronic disease.**

Population

Changes Over Time

ALGORITHM	PATIENT DATA	MORBIDITY AND MORTALITY ASSOCIATIONS	RISK STATEMENT
DunedinPACE	X.XX Biological years per year	**All-Cause Mortality** (Beslsky et al., 2020)	If you are aging above a rate of 1.00, you would increase risk of death by 56% over the next 7 years.
		Chronic Disease (Beslsky et al., 2020)	If you are aging above a rate of 1.00, you would increase risk of chronic disease diagnosis by 54% over the next 7 years.

Mortality

Those with faster DunedinPACE levels, which indicates faster aging, at baseline were at increased risk of death having a hazard ratio of 1.29. The hazard ratio represents an instantaneous risk, it is the relationship between the instantaneous hazards between accelerated DunedinPACE and mortality.

Morbidity

Those with a faster DunedinPACE baseline were at an increased risk for a new chronic disease, putting them at a hazard ratio of 1.19. Individuals with faster DunedinPACE experienced higher levels of chronic disease morbidity, which was measured as the count of diagnosed diseases (hypertension, type-2 diabetes, cardiovascular disease, chronic obstructive pulmonary disease, chronic kidney disease, and cancer).

Accelerated Aging Influences

The pace of aging typically increases across much of the adult lifespan. A faster DunedinPACE is the result of a lifetime of accumulated stress to the methylome. Childhood exposure to poverty and victimization is associated with faster DunedinPACE. Adolescents who grew up in families of lower socioeconomic status and adolescents with exposure to multiple types of victimization exhibited faster DunedinPACE.

The study behind the algorithm.

A team of researchers from Duke and Columbia were able to help create a test that could use blood samples to measure the pace of aging. This test is called the DunedinPACE and it can predict which people are at an increased risk of poor health, chronic disease, and more immediate death.

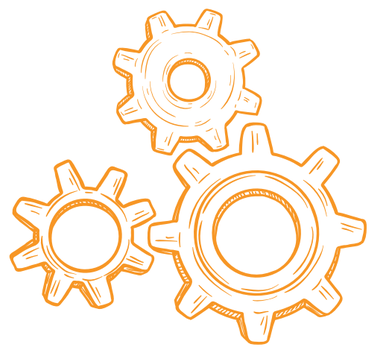
In order to develop this test, data on chemical changes to an individual's DNA, called DNA methylation, was collected from white blood cell samples from approximately 1,000 participants in a long-term health study known as "The Dunedin Study". Using the data obtained from this cohort the team developed an algorithm named "DunedinPACE". DundinPACE identified people with accelerated or slowed pace of aging based on a single blood test.

The researchers used a machine-learning technique called elastic-net regression to sort through data on more than 400,000 different DNA methylation marks to find the ones that related to the physiological changes that were captured in their Pace of Aging measure. The analysis pulled out a set of 173 methylation marks that, together, measured the pace of aging for individuals at one point in time.

Understanding Society

Analysis of chronological and biological age

PoAM Algorithm

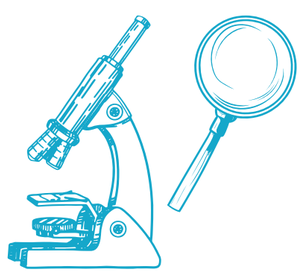


Calerie

Analysis of intervention to slow biological aging

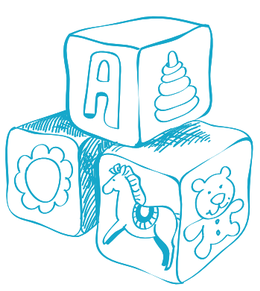
Dunedin Study

Analysis of age-45 functional decline



E-Risk Study

Analysis of early-life adversity



Normative Aging Study

Analysis of disease and mortality

These 173 methylation marks are combined together in an algorithm the researchers named “DunedinPACE” for Dunedin (P)ace (o)f (A)ging in (m)ethylation. The average person has a DunedinPACE value of 1, which indicates a single year of biological aging per chronological year. Among Dunedin Study participants, the range of values extends from just above 0.6 (indicating an aging rate nearly 40 percent slower than the norm) to nearly 1.4 (indicating an aging rate 40 percent faster than the norm).

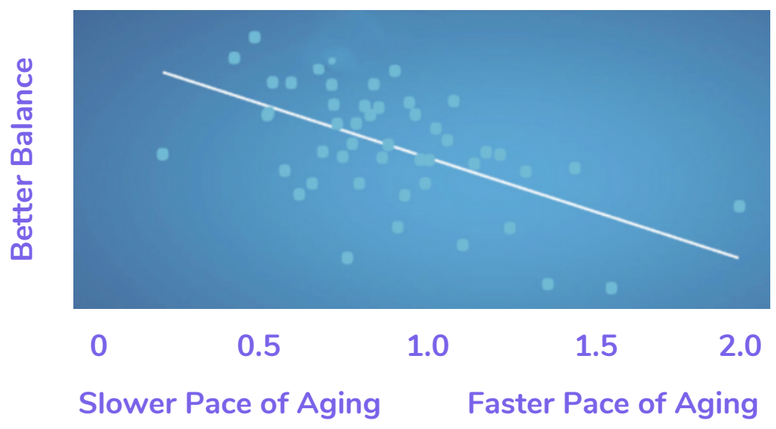
In order to validate the algorithm, the researchers used samples from participants in three other long-term studies. This analysis verified that the individuals whom the algorithm identified as aging faster; had a greater risk of poor health, developing chronic disease, or dying earlier. Similarly, those identified as aging more slowly performed better on tests of balance, strength, walking speed, and mental ability, and additionally, they appeared physically younger than trained raters for physical signs of aging.

Additionally, the DunedinPACE researchers used the test on participants in a randomized trial testing whether restricting calories had the potential to extend a healthy lifespan. The results suggested that the calorie restriction could counter the effects of an accelerated pace of aging.

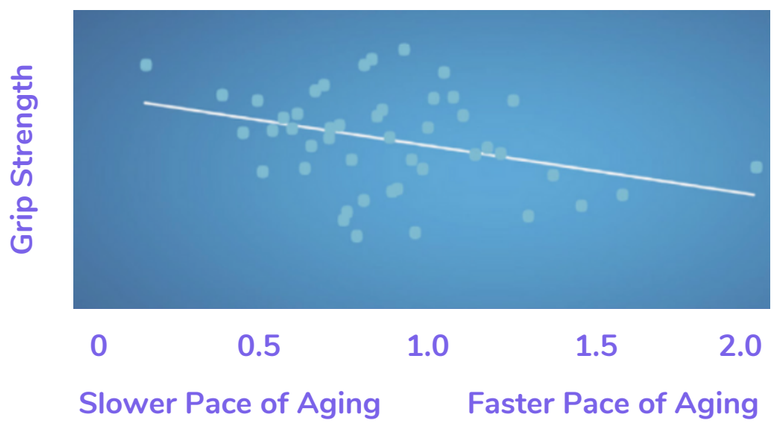
Thanks to this study's promising findings, the test developed by the Dunedin Study team will provide an alternate way of measuring whether age-slowing treatments work. This algorithm has the potential to allow faster testing of therapies able to extend the healthy lifespan of humans.

The following graphs are NOT your personal data. These graphs show how the increased rate of aging affects performance from the Dunedin cohort.

One-Leg Balance Test

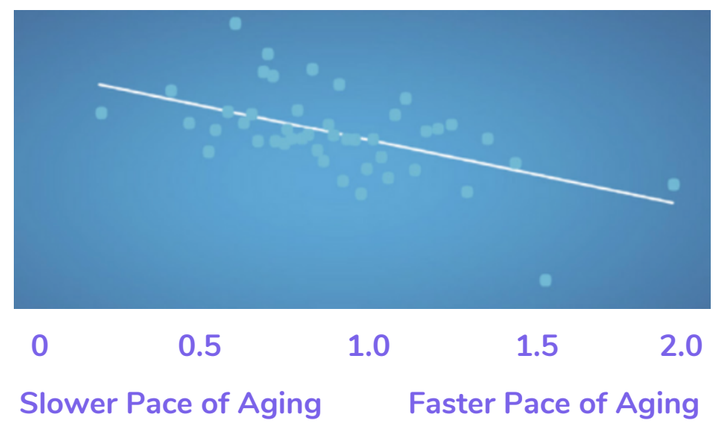


Grip Strength



Cognitive Decline

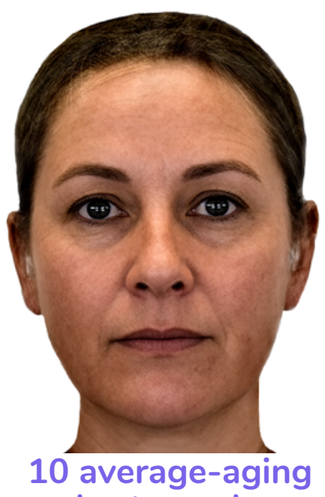
(IQ Change from Childhood to Age 45)



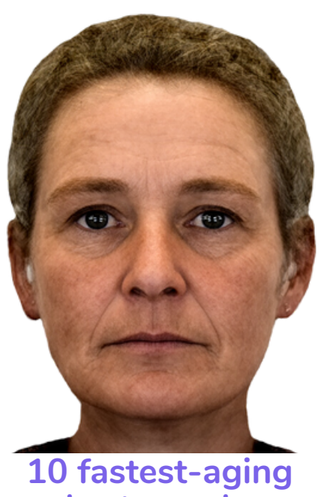
Significant Variation in Facial Aging

Female:

10 slowest-aging cohort members



10 average-aging cohort members



10 fastest-aging cohort members

Male:

10 slowest-aging cohort members

10 average-aging cohort members

10 fastest-aging cohort members

UNDERSTANDING

The value and algorithm.

How Is This Algorithm Game-Changing?

This is a report about an individual's rate of aging. Most epigenetic tests take a snapshot of biological age at the moment in time when the test was taken, but because DunedinPACE determines the pace of aging, it is able to differentiate prior biological age factors and the rate of aging at that given time. The pace of aging in a methylation algorithm outperforms a number of other methylation-based biological clock algorithms because its data is unmatched, making DunedinPACE one of the best predictors of health outcomes.

The algorithm is noteworthy because it considers the details of one’s life and by doing so it interprets your epigenetic alterations to determine the best reading of how you age. Other biological age clock outcomes are dampened by the influences across one’s lifetime and will compound the negative outcomes instead of predicting how fast a person is aging at the time of testing. DunedinPACE can interpret small adjustments to your lifestyle while still taking into consideration methylation patterns from earlier years to produce a robust measurement of how one biologically ages.

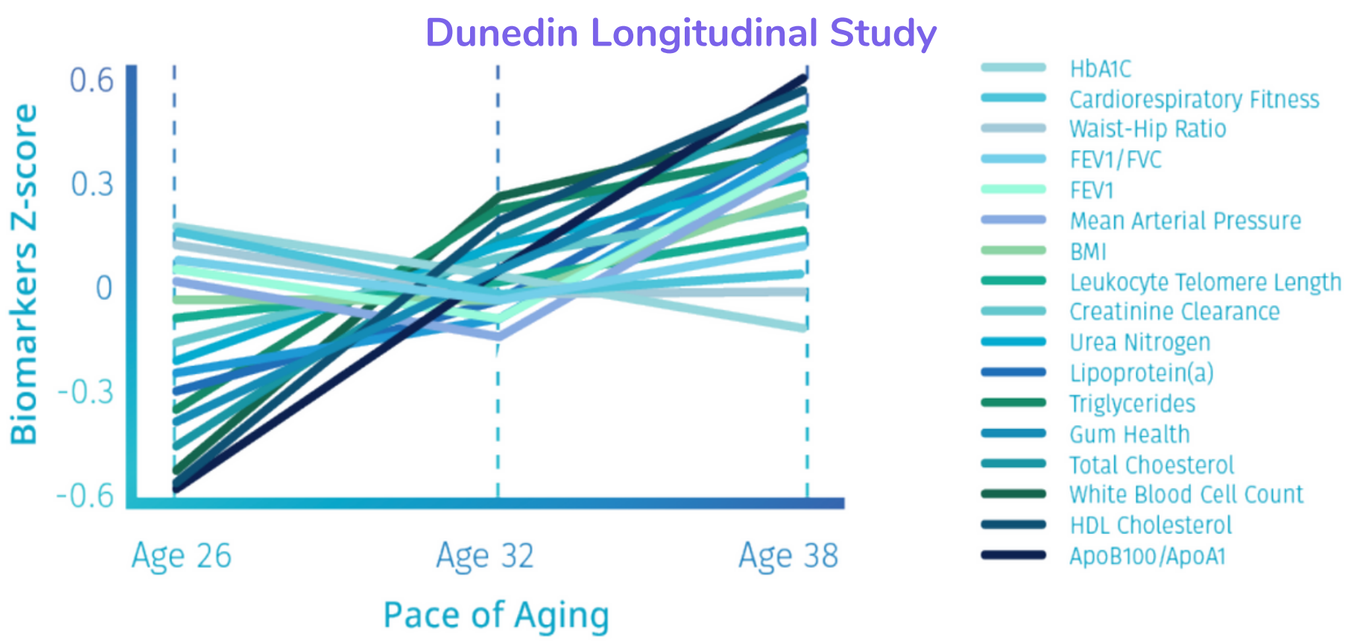
The algorithm was developed from data collected from the Dunedin study group. The significance of this study was minimizing variables. The Dunedin cohort stands out by having its subjects all born within the same year. All current methylation clock algorithms have been developed to identify the methylation patterns that characterize individuals of different chronological ages. The limitation of these other algorithms is that the study group consists of individuals born in different years who also grew up in different historical conditions.

People the algorithm identified as having a faster pace of aging had a greater risk of poor health, chronic disease, and premature death. Other methylation-clock algorithms have been developed to identify methylation patterns that characterize individuals of different chronological ages which imposes a series of limitations on the outcomes being provided by. These other methylation-clock algorithms display their outcomes as an unwavering point instead of where your aging is currently.

How It Compares Against Other Methylation Clocks

Unlike any other biological test out there, the DunedinPACE Algorithm doesn't let us see your biological age, but instead, it looks at how fast you are aging. There are a number of benefits of knowing your pace of aging versus your age at a set point in time. By 2050, the world population aged 80 years old and above will more than triple, approaching more than 400 million individuals. This useful measure is non-invasive, inexpensive, reliable, and highly sensitive to biological change; making it an easy tool for health professionals to use to combat the challenges we will soon face with the growing aging population based on real-time measurements of interventions.

The Dunedin researchers tested if higher DunedinPACE levels, which indicate faster aging, were correlated with older chronological age. Mortality rates increase with advancing chronological age, although there may be some slowing at older ages. This suggests the hypothesis that the rate of aging increases across much of the adult lifespan. Consistent with this hypothesis, understanding society participants with older chronological age tended to have faster DunedinPACE value.



The above chart shows the Dunedin Longitudinal Study. Dunedin researchers collected a blood panel of 19 markers (shown above) and organ-system-function biomarkers at four successive waves of the Dunedin Study. By using repeated measures of data the study members were aged 26, 32, 38, and 45 years old.

They calculated the rate of change in each biomarker and how each individual's rate of change differed from the cohort's norm. Then they combined the individual's 18 personal rates of change across the panel of biomarkers to compute a composite for each study member, which is how they determine the pace of aging.

The Dunedin Study

The Dunedin cohort is one of the most remarkable resources for studying human biology. This is not the biggest nor the longest longitudinal study conducted, but it is special because it has a very high retention rate of participants. With 95% of the original cohort remaining in the study since its launch, the Dunedin cohort is the most closely examined group on earth. To put in perspective a good retention rate for longitudinal studies is between 60 to 80 percent of the original cohort population. [11]

Previous studies have attempted to measure the pace of aging by analyzing DNA methylation differences between people of different chronological ages. However, the "limitation of this approach is that individuals born in different years have grown up under different historical conditions, with a possibility of more exposure to childhood diseases, tobacco smoke, airborne lead, and less exposure to antibiotics and other medications, as well as lower quality nutrition -- all of which affect DNA methylation. An alternative approach is to study individuals who were all born the same year, and find methylation patterns that differentiate those who have been aging biologically faster or slower than their same-age peers." [3] The Dunedin study focuses on a one-year age cohort makes it more effective at tracking its participants, which contributes to the low number of extraneous variability in the results.

Following the one-year birth cohort, the repeated measures of data were collected via blood when the study members were 26, 32, 38, and 45 years old to quantify their rates of biological aging. The gathered data represents a personal rate of multi-organ system decline over a dozen years which determines the algorithm for pace of aging.

Report references.

About Us: The Dunedin Study - Dunedin Multidisciplinary Health & Development Research Unit. The Dunedin Study - DMHDRU. https://dunedinstudy.otago.ac.nz/about-us.

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