Reading the evidence

What a promising result can actually tell us.



Biological-age tests, fish oil and fasting show why the measured outcome matters. Three full articles trace the distance between an interesting signal and a demonstrated benefit.

3 full articles | 25 October 2026 | Version 1.1

An editorial reading booklet, distinct from The Arising book manuscript. Educational material, not an individual treatment plan. Source qualifications remain with each article.

When your biological-age number moves, what moved?

Repeating a laboratory result is not the same as measuring a stable trait

Newsletter: October 22, 2026. Study publication: August 2026.

A biological-age test can give the same answer twice from the same blood sample and still be a shaky guide to the person who provided it. An analysis of 18 epigenetic clocks makes that distinction central. Before celebrating a younger number, it helps to ask what kind of change the test can reliably detect.

Sehgal and colleagues used the TranslAGE platform to examine DNA methylation measurements across existing datasets. Published in Aging Cell, the work was a benchmarking study, not a trial of an anti-aging treatment. It assessed both technical and biological reliability.

Two different kinds of consistency

Technical reliability asks whether a laboratory obtains similar results when it runs the same sample again. Most clocks performed well on standard replicate assays. Some were sensitive to factors such as position on a testing slide or the method used to extract DNA. Certain principal-component-based clocks remained more robust across technical conditions.

Biological reliability asks a different question: do repeated samples from the same person, taken within a short interval, produce consistent readings? The researchers examined measurements around meals, acute stress and environmental exposures, as well as samples collected over days.

Here, many clocks were less stable. A test could be technically reproducible while varying substantially within the person. The distinction matters because a technically sound laboratory measurement can still be an uncertain guide to a treatment's effect.

The intervention problem

Imagine testing before and after a new regimen and seeing an apparently younger biological age. If the samples were collected under different conditions, part of the difference might reflect those conditions rather than a durable change attributable to the regimen. That example illustrates the measurement problem; it does not establish that every favorable result is noise.

In the analysis, more reliable clocks tended to produce more stable associations with cognitive outcomes and more consistent responses in intervention datasets. Less reliable measures could yield variable or misleading effects. Technical reproducibility did not predict biological reliability.

How far the finding goes

The datasets varied in size and setting, and several biological-reliability experiments were small and short. The study did not evaluate every consumer service or identify a universal commercial winner. Nor does it show that all epigenetic research lacks value.

Its contribution is more useful than that: it identifies a condition that a meaningful progress measure must satisfy. For an individual, a small change between two tests should not automatically become evidence of rejuvenation. For researchers, stable measurement conditions and biological reliability need to be part of the design.

The aspiration remains compelling. A trustworthy measure could help reveal which interventions matter. But the ability to produce a number comes before the ability to interpret that number with confidence.

Primary source: https://pubmed.ncbi.nlm.nih.gov/42525215/

Fish oil reached the brain. The hoped-for benefit did not follow.

A two-year DHA trial separates biological activity from clinical benefit

Newsletter: October 23, 2026. Study publication: July 2026.

High-dose DHA supplementation changed a biological measure in a randomized trial of older adults at risk for dementia. Over two years, however, the researchers did not observe better cognition or brain-volume outcomes than with placebo. The distinction is central to longevity medicine: reaching a target is not the same as improving a life.

The phase IIa trial, published in EBioMedicine, enrolled 365 adults aged 55 to 80 at the University of Southern California. They did not have dementia, consumed little dietary DHA and had at least one dementia risk factor. Participants were randomly assigned to 2 grams of DHA daily or placebo for 24 months. The study was double-blind.

DHA is an omega-3 fatty acid. Nearly half the participants carried APOE ε4, a genetic variant associated with increased Alzheimer's risk. Researchers were interested in whether supplementation could change DHA availability in the central nervous system, including among carriers.

What the trial was designed to establish

The primary outcome was a change in the ratio of DHA to arachidonic acid in cerebrospinal fluid at six months. Participants willing to undergo lumbar puncture contributed to that measurement. The ratio increased with DHA compared with placebo, and the difference did not depend on APOE ε4 status.

That was evidence of biological target engagement. It showed that the intervention changed the intended biochemical measure. It did not by itself establish prevention of Alzheimer's disease.

What did not improve

Over 24 months, the researchers found no treatment differences in cognitive performance or brain volumes. Brain imaging was a secondary outcome, and cognition was exploratory. These distinctions matter: the study was built primarily to test the biochemical question rather than to deliver a definitive verdict on every possible clinical benefit.

Dropout was 38%, largely related to COVID-19. That is a substantial limitation. The trial also studied a particular population, dose and formulation. It cannot stand in for every use of omega-3 products, every dietary pattern or every stage of cognitive illness.

The absence of a detected benefit is not a demonstration that fish is useless or that a whole dietary pattern has no value. Those are different questions. Nor should the result be repackaged as proof that the supplement prevented decline simply because a blood or spinal-fluid marker changed.

The lesson for longevity

The study makes a valuable demand of future interventions: show what happens beyond the mechanism. Better biological access can be an important step, but people ultimately care about memory, independence and daily function.

The investigators suggest that future research should focus on how the brain handles DHA. For readers, the immediate implication is to distinguish the reason a supplement might work from evidence that it delivers the outcome being promised. Decisions about an existing treatment or supplement should account for its actual indication and a person's clinical circumstances.

Primary source: https://pubmed.ncbi.nlm.nih.gov/42315445/

Fasting and muscle: the unanswered part of the weight-loss story

Small short-term differences in lean mass do not settle long-term function

Newsletter: October 23, 2026. Study publication: July 2026.

A lower number on the scale can hide several different changes. Fat may fall, but so may water or lean tissue. For people in midlife and later life, preserving the ability to move and function matters alongside weight loss. A scoping review of intermittent fasting makes that unresolved question visible.

Santero and colleagues reviewed 20 randomized controlled trials involving 1,653 adults aged 45 and older. About 64% were women, and most participants had overweight or obesity. Published in Advances in Nutrition, the review mapped the evidence rather than pooling every study into a single effect estimate.

Trials had to study fasting for at least four weeks and measure body composition with validated methods. People with diseases causing muscle loss were excluded. The comparisons included a habitual diet and continuous calorie restriction - eating less overall without the same fasting schedule.

What the short trials suggest

Across the durations studied, commonly 12 weeks or less, differences between groups in total fat-free mass were generally small. Intermittent fasting produced weight, fat-mass and waist reductions comparable to continuous calorie restriction. Compared with habitual eating, reductions in weight and fat were reported more consistently with fasting.

The fasting approaches varied, including alternate-day regimens, modified fasting days and time-restricted eating. That variety is one reason the results should not become a blanket promise about a particular fasting window.

Lean mass is not the whole muscle story

Fat-free mass includes more than skeletal muscle. It also includes organs, bone and water. Most studies used DXA or bioelectrical impedance, so a finding about total lean mass cannot simply be translated into a finding about muscle strength or physical capability.

Strength, physical performance and quality of life were rarely assessed. Evidence on protein intake, insulin-related outcomes and the combination of fasting with exercise was limited and varied. Data on adults in advanced age were particularly sparse.

Those gaps matter because the question is not only what a body weighs after a few weeks. It is whether someone maintains strength, mobility and reserve over months and years. A short-term similarity between diets cannot settle that longer-term question.

What a stronger answer would require

The authors concluded that the available evidence does not permit definitive conclusions about preservation of fat-free mass, particularly over the long term in older adults. The review therefore offers context, not proof that fasting protects muscle or is safe for everyone.

Longer studies need standardized muscle and functional measurements, with clearer attention to nutrition and exercise. In practice, choosing a weight-loss approach requires attention to the whole person, including medications, nutritional needs and the capacity one hopes to preserve. The worthwhile goal is a change that supports life beyond the scale.

Primary source: https://pubmed.ncbi.nlm.nih.gov/42463249/

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