The Julian A. Jarman, MD Research Foundation Framework for Evaluating Aging Research

Executive Summary

The Julian A. Jarman, MD Research Foundation supports aging research that is biologically plausible, scientifically reproducible, and capable of improving measurable aspects of human health.

Aging is not simply the passage of time or the accumulation of disease. **It is best understood as the progressive decline in biological resilience: the body's capacity to maintain function, repair damage, adapt to stress, and resist disease.**

The Foundation's priority is healthspan: the preservation of physical, cognitive, metabolic, immune, and functional health for as much of life as possible. Increased lifespan, when it occurs, should be the natural consequence of preserving biological function and delaying disease.

Before supporting any aging intervention, the Foundation asks:

- What is the proposed biological mechanism?
- How strong and reproducible is the evidence?
- How closely does the evidence apply to humans?
- What measurable health outcomes improve?
- What remains unknown?
- What are the risks?

The Foundation's position is simple: aging research deserves support, but it must be evaluated with the same rigor applied to any serious medical science.

Introduction

The Foundation does not support aging interventions because they are popular on social media, fashionable across the internet, widely promoted in books, or aggressively marketed. We support research grounded in sound biology, reproducible scientific evidence, and measurable improvements in human health.

Aging matters because it is the greatest risk factor for most chronic diseases. Heart disease, cancer, dementia, diabetes, osteoporosis, frailty, and many other conditions become dramatically more common with advancing age. If we can better understand the biology of aging, we may be

able to delay the onset of many diseases simultaneously rather than treating each one individually after it develops.

Before we can study how to slow aging, we must first answer two basic questions:

What is aging?

And how would we recognize success if an intervention actually slowed it?

Aging cannot yet be measured by a single definitive test. Instead, we infer aging from changes in biological systems over time. If an intervention helps preserve cardiovascular fitness, muscle strength, immune function, cognitive performance, metabolic health, and freedom from disease better than expected for age, then it may provide evidence that aspects of biological aging have been slowed.

Health measures the body's current biological performance.

Aging measures the rate at which that performance changes over time.

The Foundation's goal is therefore not simply to chase longevity claims, but to evaluate whether biological function is being preserved.

The Foundation believes that preserving health is presently the most measurable and scientifically defensible approach to slowing biological aging because no single drug, supplement, or other intervention has yet been proven to slow or reverse human aging.

Step 1. Define Aging

Everyone knows what aging looks like. Hair turns gray. Skin changes. Muscles weaken. Reaction time slows. Diseases become more common.

But none of those observations alone defines aging.

Aging is not simply the passage of time. Nor is aging merely the accumulation of disease.

Aging is best understood as the progressive decline in biological resilience: the body's capacity to maintain function, repair damage, adapt to stress, and resist disease.

This distinction matters. Aging increases the likelihood of disease, but aging and disease are not the same thing. Diabetes, cancer, dementia, cardiovascular disease, and frailty become more common with age because the body's protective and repair systems gradually become less effective.

Step 2. Understand What May Drive Aging

Although scientists generally agree that aging reflects a progressive loss of biological function and resilience, there is still no single proven cause of aging.

Instead, current evidence suggests that aging results from the gradual accumulation of damage and dysfunction across multiple interacting biological systems.

Research has identified several processes that likely contribute, including:

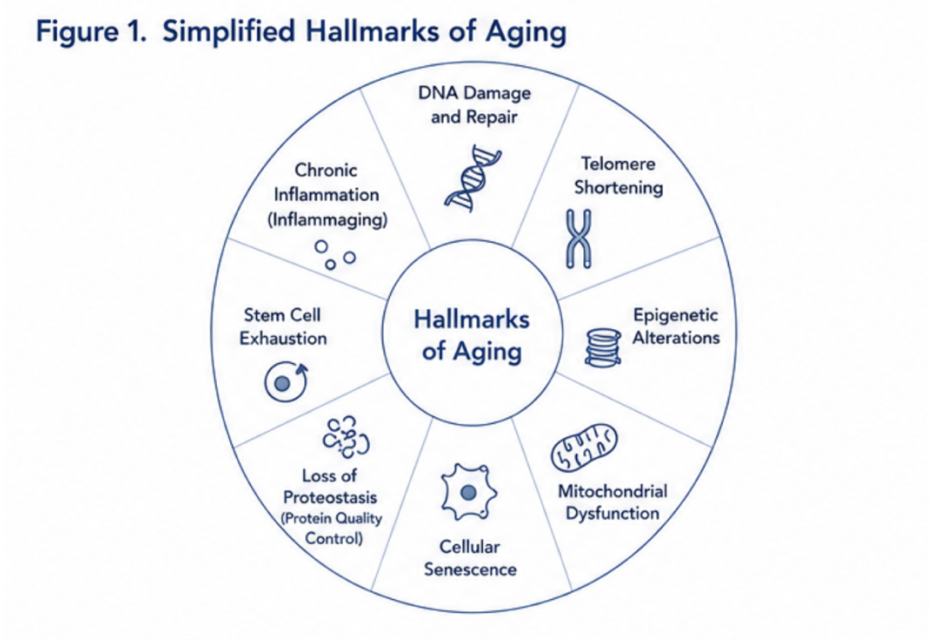
- DNA damage and imperfect DNA repair
- telomere shortening
- epigenetic alterations
- mitochondrial dysfunction
- cellular senescence
- loss of protein quality control, known as proteostasis
- stem-cell exhaustion
- chronic low-grade inflammation, sometimes called “inflammaging”
- altered nutrient-sensing pathways, including mTOR, AMPK, and insulin/IGF-1 signaling

These mechanisms should not be viewed as competing explanations of aging. Rather, they likely represent interconnected biological processes that together contribute to the progressive loss of resilience that characterizes aging.

Each of these mechanisms has scientific support. None has yet been proven to be the single primary cause of aging.

One influential framework, known as the Hallmarks of Aging, organizes many of these biological processes into a common model. This framework has helped advance the field, but it remains a scientific model rather than a final explanation of aging itself.

For this reason, the Foundation does not assume that aging has one cause or that one intervention will reverse it. Instead, we evaluate whether a therapy influences one or more plausible biological pathways and, more importantly, whether it improves measurable aspects of human healthspan and biological function.



Step 3. Ask the Fundamental Scientific Question

If aging is more than disease, then the central question becomes:

Can we slow the underlying biological processes that make many diseases more likely, rather than simply treating those diseases after they appear?

This is very different from asking whether we can treat diabetes, hypertension, cancer, or heart disease. Medicine already treats those conditions.

Aging research asks whether we can delay the biological changes that increase the risk of many age-related diseases at once.

That is the promise of serious longevity science.

Step 4. Define the Goal of Aging Research

The Foundation makes an important distinction between lifespan and healthspan.

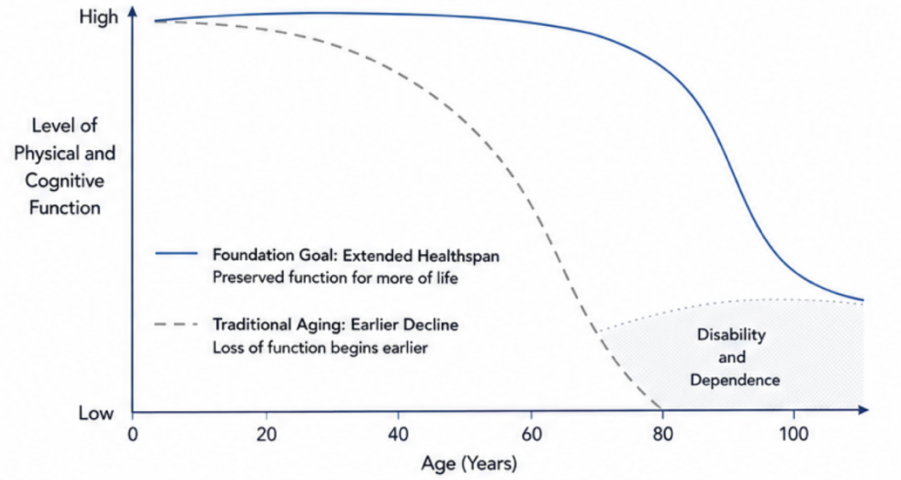
Lifespan is how long we live.

Healthspan is how long we remain physically, mentally, and functionally healthy.

Simply extending lifespan is not the Foundation's objective. Living longer while accumulating years of disability, frailty, or cognitive decline is not the outcome we seek.

The Foundation seeks to extend healthspan first. Increased lifespan, when it occurs, should be the natural consequence of preserving biological function and delaying disease.

Figure 2. Healthspan vs. Lifespan



Step 5. Decide What Evidence Matters

The Foundation assigns greater weight—and greater scientific confidence—to evidence as it moves closer to human biology and meaningful human outcomes.

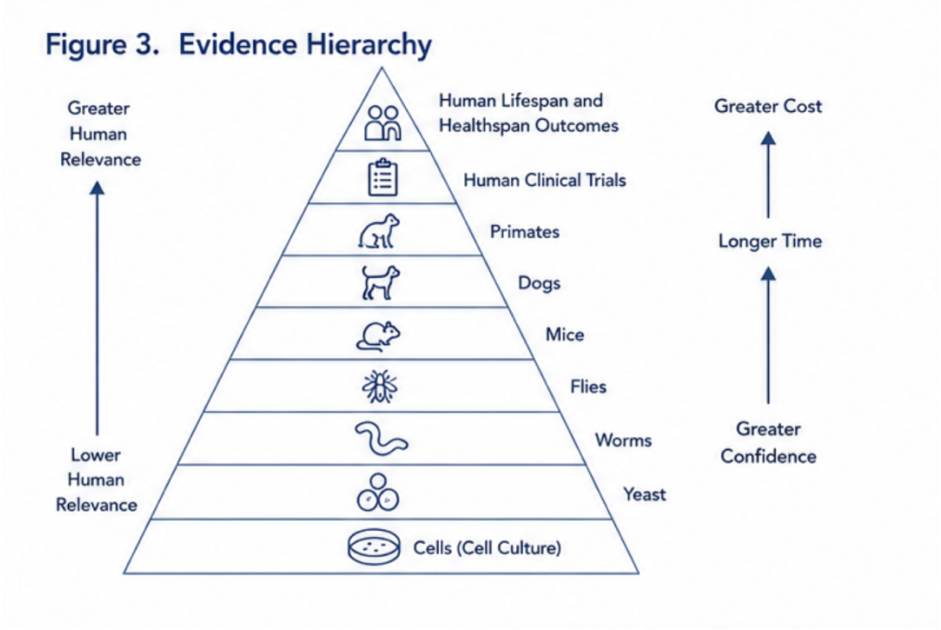
Many interventions can extend lifespan in yeast or worms. Fewer work in flies. Fewer still work in mice. Very few have convincing evidence in primates. Almost none have proven that they extend healthy human lifespan.

A useful evidence hierarchy is:

Cells → Yeast → Worms → Flies → Mice → Dogs → Primates → Human clinical trials → Human lifespan and healthspan outcomes

As evidence moves upward, biological relevance generally increases. But so do cost, time, and complexity.

Each step increases confidence, but no step automatically proves the next.



Step 6. Decide What Should Be Measured

Because we cannot wait 80 years to determine whether an intervention extends human lifespan, aging research must rely on measurable indicators that plausibly reflect preserved biological function.

Examples include:

- cardiovascular fitness
- muscle mass and strength
- VO_2max
- walking speed
- frailty
- cognitive performance
- immune function
- inflammatory biomarkers
- metabolic health
- epigenetic aging measures
- incidence of chronic disease
- quality of life
- disability-free survival

The Foundation believes that although these measures are not definitive proof that human aging has been slowed, they currently provide the strongest available evidence that an intervention may be influencing the aging process.

Step 7. Evaluate Potential Interventions

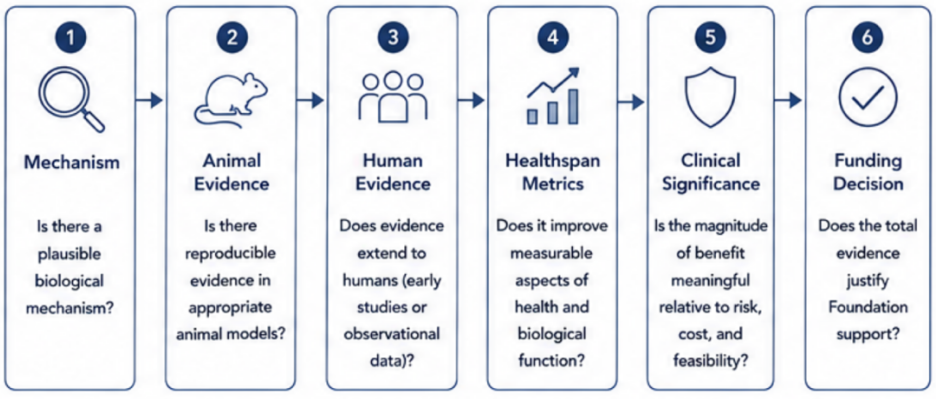
Only after defining aging, understanding plausible mechanisms, deciding what evidence matters, and determining what should be measured should specific interventions be evaluated.

Examples of interventions currently of scientific interest include:

- rapamycin and other mTOR-targeting drugs
- metformin
- acarbose and other glucose/metabolic pathway interventions
- SGLT2 inhibitors
- taurine
- glycine and GlyNAC-related approaches
- senolytics and senomorphics
- NAD+ pathway interventions
- 17-alpha estradiol and other hormone-pathway interventions
- caloric restriction and caloric-restriction mimetics
- exercise
- protein optimization
- sleep optimization
- partial epigenetic reprogramming
- stem-cell and regenerative approaches

Each intervention should be judged by the same standards: mechanism, reproducibility, human relevance, measurable outcomes, safety, and uncertainty.

Figure 4. Foundation Evaluation Pathway



Step 8. Apply Scientific Skepticism

The Foundation does not ask:

Does this sound exciting?

The Foundation asks:

- Is there a plausible biological mechanism?
- Has the finding been reproduced?
- Does the evidence extend beyond laboratory models?
- Does it improve meaningful measures of health?
- Does it improve healthspan, lifespan, or both?
- What are the risks?
- What remains unknown?

This approach separates evidence-based aging research from commercial longevity claims.

The Foundation’s position is simple: aging research deserves support, but it must be evaluated with the same rigor we would apply to any serious medical science.

As scientific knowledge continues to evolve, the Foundation's commitment will remain the same: to follow the best available evidence wherever it leads.