

The Healthspan Frontier

Biology, evidence and society in the science of healthy ageing.

For most of human history, the question was simply: how long can we live? That question has been substantially answered. In high-income countries, life expectancy at birth now exceeds 80 years. The question that has replaced it is harder and more interesting.

How many of those years are lived well? In good health, with full function, in meaningful social connection — rather than in managed decline. The gap between lifespan and healthspan is now the central problem of ageing science, and increasingly of social policy.

9 yrs Average gap between lifespan and healthspan in the EU	€110B Invested in longevity research globally, 2023	12 Identified hallmarks of biological ageing (López-Otín, 2023)
---	---	---

Sources: Eurostat hlth_hlye 2022; Longevity Technology / PitchBook 2023; López-Otín et al., Cell 2023

1

THE PARADIGM SHIFT

From adding years to life — to adding life to years.

The WHO's 2020 World Report on Ageing and Health formalised what researchers had been building towards for two decades: a complete reframing of what ageing interventions are for. The old model treated ageing as a process of accumulating diseases to be managed. The new model treats it as a process of maintaining functional capacity to be supported.

These are not equivalent framings with different language. They produce different research questions, different programme designs, different success metrics, and different resource allocations. The shift from disease model to capacity model is the most consequential change in ageing science in a generation.

OLD MODEL — DISEASE MANAGEMENT

- Question: what conditions does this person have?
- Goal: slow disease progression, manage symptoms
- Success: fewer hospitalisations, longer survival
- Endpoint: disease-specific mortality
- Primary setting: clinical / pharmaceutical

NEW MODEL — CAPACITY SUPPORT

- Question: what can this person do, contribute, experience?
- Goal: maintain functional ability and intrinsic capacity
- Success: years of healthy, connected, purposeful life
- Endpoint: healthspan, not just lifespan
- Primary setting: community / social / behavioural

"The most powerful determinants of how well you age are not the drugs you take or the diseases you avoid. They are the social connections you maintain, the purpose you sustain, and the environment you inhabit."

Synthesised from WHO World Report on Ageing 2020; Eurofound Social Inequalities in Ageing 2023

2

THE BIOLOGY OF AGEING

Ageing has mechanisms. Mechanisms can be studied. Some can be modified.

The 2023 update to López-Otín et al.'s landmark hallmarks of ageing framework — published in *Cell* — identifies twelve distinct biological mechanisms that drive the ageing process. These are well-characterised cellular and molecular processes with established causal roles in age-related functional decline.

Understanding these mechanisms matters for programme and policy design because it clarifies where biological, behavioural, and social interventions interact — and where the evidence for modifiability is strongest.

<p>Genomic Instability</p> <p>Accumulation of DNA damage — primary driver of cellular dysfunction and cancer risk with a...</p>	<p>Telomere Attrition</p> <p>Shortening of chromosome caps with each cell division — linked to cellular senescence.</p>	<p>Epigenetic Alterations</p> <p>Changes in gene expression with age — some are reversible, making this a key intervention targ...</p>
<p>Loss of Proteostasis</p> <p>Declining protein quality maintenance — drives neurodegenerative disease and dysfuncti...</p>	<p>Disabled Macroautophagy</p> <p>Reduced cellular recycling and waste clearance — allows damage accumulation.</p>	<p>Deregulated Nutrient Sensing</p> <p>Disruption of metabolic signalling — primary target for dietary and pharmacological interventi...</p>
<p>Mitochondrial Dysfunction</p> <p>Declining energy production — central to physical capacity loss in older age.</p>	<p>Cellular Senescence</p> <p>Accumulation of dysfunctional cells driving inflammation — major target for senolytics.</p>	<p>Stem Cell Exhaustion</p> <p>Declining regenerative capacity — limits recovery from injury and illness.</p>
<p>Altered Cell Communication</p> <p>Disruption of inter-cell signalling — drives systemic inflammation and tissue decline.</p>	<p>Chronic Inflammation</p> <p>"Inflammageing" — persistent low-grade inflammation driving cardiovascular and cognitive disea...</p>	<p>Dysbiosis</p> <p>Changes in gut microbiome with age — emerging evidence for systemic effects on immunity and cogniti...</p>

Source: López-Otín, C. et al. (2023). Hallmarks of ageing: An expanding universe. *Cell*, 186(2), 243–278.

"The significance of the hallmarks framework is not that it explains ageing completely. It is that it makes ageing tractable — a set of specific, identifiable mechanisms that can be studied, targeted, and potentially modified."

3 WHAT THE EVIDENCE SAYS WORKS

Behaviour moves the needle more than anything else currently available.

The research field distinguishes sharply between interventions with robust evidence across multiple study types and populations, and those with promising but preliminary findings. The summary below reflects the current state of evidence — not the state of popular discourse, which is significantly more optimistic about pharmacological intervention than the trial data warrants.

Physical activity · resistance and aerobic combined

The single most evidence-supported intervention for extending healthspan. Consistent positive effects on cardiovascular health, cognitive function, muscle mass retention, bone density, depression, and all-cause mortality. Effect sizes are large by clinical standards — equivalent to or exceeding most pharmacological interventions at population level. Dose matters: 150+ minutes moderate activity per week is the evidence threshold.

Strong RCT + longitudinal evidence

Social connection and purposeful engagement

The Holt-Lunstad meta-analysis (3.4 million participants) established social isolation as a mortality risk factor comparable to smoking. Purposeful engagement — civic, volunteer, caregiving roles — shows independent positive effects on cognitive reserve and longevity beyond social contact alone.

Strong longitudinal + meta-analytic evidence

Dietary patterns · Mediterranean and plant-forward

Mediterranean dietary pattern has the strongest evidence base of any dietary intervention for healthy ageing. The PREDIMED trial (Spain, n=7,447) provided RCT-level evidence for cardiovascular benefit. Caloric restriction shows robust effects in animal models; human evidence is accumulating.

Strong cohort + RCT evidence (PREDIMED)

Sleep quality and duration

7–9 hours of quality sleep is consistently associated with reduced dementia risk, better metabolic outcomes, and lower cardiovascular mortality. Sleep disruption in midlife (50–60) is an independent risk factor for late-life cognitive decline.

Good longitudinal evidence · mechanisms active

Senolytics · clearing senescent cells

Senescent cells accumulate with age and drive inflammation through the SASP. Dasatinib + quercetin combination has shown promising results in early human trials. Multiple senolytic compounds in clinical trials as of 2024. Human evidence remains early-stage.

Emerging · early human trials · watch this space

■ NAD+ restoration (NMN, NR supplementation)

NAD+ levels decline with age and are central to mitochondrial function and DNA repair. NMN and NR supplementation can raise NAD+ levels in humans. Whether this translates to meaningful healthspan outcomes remains under investigation. Animal data compelling; human outcomes pending.

Emerging · mechanism established · outcomes pending

Sources: Holt-Lunstad (2015, 2017) PLOS Medicine; PREDIMED Trial (2013) NEJM; López-Otín hallmarks; multiple Cochrane reviews; clinicaltrials.gov 2024

4 HOW SOCIETY IS RESPONDING

Policy and society are catching up — unevenly and with significant blind spots.

The scientific shift from disease management to capacity support has begun to reach policy — but the translation is partial, slow, and concentrated in higher-income member states. The following represent the most significant active societal responses to the healthspan challenge in the European context.

EU POLICY FRAMEWORK

Active and Healthy Ageing — Mission and Partnerships

The EU's Partnership on Active and Healthy Ageing (PAHA) explicitly targets extending healthy life years by 2 years across the EU by 2030. The European Innovation Partnership on Active and Healthy Ageing has engaged 1,200+ organisations across 37 countries. Funding flows primarily through Horizon Europe and the European Social Fund+.

RESEARCH INVESTMENT

The Longevity Research Surge

Global investment in longevity-focused research reached approximately €110 billion in 2023 — up from €8 billion in 2018. The CALERIE trial, TAME trial, and multiple senolytic programmes represent the leading edge of clinical translation. This is no longer fringe science — it is mainstream biomedical research with institutional backing.

WORKPLACE AND SOCIAL ARCHITECTURE

Redesigning the Environment for Longer Healthy Life

Age-friendly city initiatives (WHO Global Network, now 1,500+ cities) are redesigning urban environments through accessible transport, social infrastructure, and age-inclusive employment. Extended working life policies are increasingly mainstream across EU member states, responding to fiscal pressure while evidence accumulates on the health benefits of continued purposeful engagement.

CONSUMER AND COMMERCIAL

The Longevity Economy — Opportunity and Risk

Consumer demand for healthspan products generates a market estimated at €600 billion globally by 2025. This creates genuine opportunity — investment is flowing into wearables, diagnostics, and digital health with real clinical utility. It also creates significant risk: a consumer supplement market worth billions is significantly ahead of the clinical evidence base.

THE UNRESOLVED EQUITY QUESTION

Healthspan gains are not being distributed equally

The most consistent finding across European healthspan research is that gains in healthy life years are concentrating among higher-income, higher-education, urban populations. Eurofound's 2023 analysis shows that the healthspan gap between the top and bottom income quintiles in the EU increased between 2010 and 2020.

Sources: EC PAHA Partnership 2022; Longevity Technology Market Report 2023; WHO Age-Friendly Cities Network 2024; Eurofound Social Inequalities in Ageing 2023

5 THE RESEARCH HORIZON

Where the field is going in the next decade.

The pace of ageing science has accelerated significantly. Several developments that appeared speculative five years ago are now in clinical trials. The following represent the most significant near-term developments — not predictions, but active research programmes with institutional backing and plausible timelines.

2024–2026

TAME Trial results — Metformin as ageing intervention

The Targeting Aging with Metformin (TAME) trial — the first large RCT designed to test an intervention against ageing itself — will report primary outcomes. If positive, this would be the first regulatory-standard evidence for a pharmaceutical healthspan intervention and would reshape clinical practice guidelines globally.

2025–2027

Senolytic therapies — first conditional approvals likely

Multiple senolytic compounds are in Phase 2/3 trials for age-related conditions including pulmonary fibrosis, diabetic kidney disease, and frailty. First conditional approvals for specific indications are plausible within this window.

2026–2030

Epigenetic reprogramming — from lab to early trials

Partial epigenetic reprogramming has shown dramatic results in animal models (vision restoration, lifespan extension). Human safety trials are beginning. This is the most radical technology in the pipeline: if it translates, it could reverse rather than merely slow biological ageing.

2027–2032

Biological age clocks — from research to clinical practice

Epigenetic and proteomic clocks can now estimate biological age with high accuracy and predict mortality risk better than chronological age. As these tools become clinically validated and cost-accessible, they will transform preventive medicine.

2030+

The equity divergence — the defining policy challenge

As healthspan technologies mature, the central policy challenge will be distribution. Technologies that extend healthy life could either compress the healthspan gap between rich and poor — or dramatically widen it, if they remain exclusive to those who can afford private longevity medicine.

Sources: ClinicalTrials.gov TAME trial NCT04994736; Altos Labs / Retro Biosciences epigenetic reprogramming; Horvath epigenetic clock research; NIA-funded longevity research portfolio 2024

6

WHAT THIS MEANS FOR SOCIAL INNOVATION

The science is advancing. The social infrastructure is not keeping pace.

The most important insight from the healthspan research field for social innovation organisations is not that new drugs are coming. It is that the most powerful interventions currently available — physical activity, social connection, purposeful engagement, sleep, diet — are social and environmental, not pharmaceutical.

And the most significant structural finding is that access to these interventions is determined largely by social conditions: income, geography, housing, transport, community infrastructure. The biology of healthy ageing is becoming better understood every year. The social architecture that would distribute its benefits equitably is lagging significantly behind.

WHERE INVESTMENT IS CONCENTRATED

- Pharmaceutical and biotech longevity research
- Consumer supplement and wearables market
- Clinical interventions for high-income populations
- Urban age-friendly infrastructure

WHERE THE EVIDENCE POINTS

- Social connection infrastructure at community scale
- Purposeful engagement and civic role in older age
- Physical activity environments accessible to all incomes
- Rural and peripheral region infrastructure investment

"The science of healthy ageing is telling us clearly what matters. The challenge is not knowledge — it is the social and political will to build the conditions in which that knowledge can benefit everyone, not only those who can afford to buy it."

ABOUT THIS PIECE

This visual essay synthesises current evidence from the ageing biology literature, EU-level policy frameworks, and epidemiological research. Primary sources include: López-Otín et al. (2023) Cell hallmarks of ageing; WHO World Report on Ageing and Health 2020; EU PAHA Partnership documentation; Eurofound Social Inequalities in Ageing 2023; PREDIMED trial; Holt-Lunstad et al. meta-analyses; and active clinical trial registrations at ClinicalTrials.gov. This is an evidence synthesis, not clinical advice.

Social Innovation Centre · socialinnovation.lv · Health Programme · Ageing · 2024