

The Immortality Update: Extending Functional Healthspan

The past week's longevity news highlight efforts to **extend healthy life** – not just lifespan. A recent report stresses that Americans spend ~12.4 years in poor health at life's end, and urges a shift toward **healthspan** (years lived well) rather than merely longer life ¹. Even modest gains in healthy life have huge value – e.g. one extra year of healthy life is estimated to be worth ~\$38 trillion to society ². In this week's update, we focus on interventions that improve function and vitality, with evidence from multiple credible sources in the past 7 days.

Key Findings

- **Exercise-mimetic molecule (betaine):** A Chinese consortium (CAS/Xuanwu Hospital) reported that the kidney-derived metabolite *betaine* reproduces many benefits of exercise. In a human exercise trial (n=13 men), sustained running raised blood betaine, which when given to aged mice **boosted immunity and strength and reduced age-related inflammation** ³ ⁴. Betaine inhibited the pro-aging kinase TBK1, silencing “inflammaging” and improving metabolism, kidney function, coordination, cognition and even skin appearance in lab tests ³ ⁴. Importantly, the study noted *betaine's safety and efficacy*, suggesting it could benefit people who cannot exercise ⁵.
- **Rapamycin vs. calorie restriction:** A major meta-analysis (167 studies, 8 vertebrate species) found that the drug rapamycin **extends lifespan almost as effectively as dietary restriction**, whereas metformin showed no clear benefit ⁶ ⁷. This reinforces interest in rapamycin-like interventions: it matched the life-extending effects of fasting in animals ⁶. Human trials of rapamycin analogs are underway, but their functional benefits in people remain to be proven. (Notably, rapamycin has known immune-suppressing side effects ⁸, so safety will be a key focus.)
- **Emerging multi-omics biomarkers:** In tandem with interventions, researchers continue developing tools to **measure biological age**. (See next section.) These include blood-protein “healthspan scores” and imaging-based clocks. For example, a Duke-led team used brain MRI scans to predict each person's *pace of aging*, identifying MRI features (cortical thickness, grey-matter volume) that correlated with cognitive decline ⁹. Such biomarkers will help test new therapies by tracking functional biology in real time.

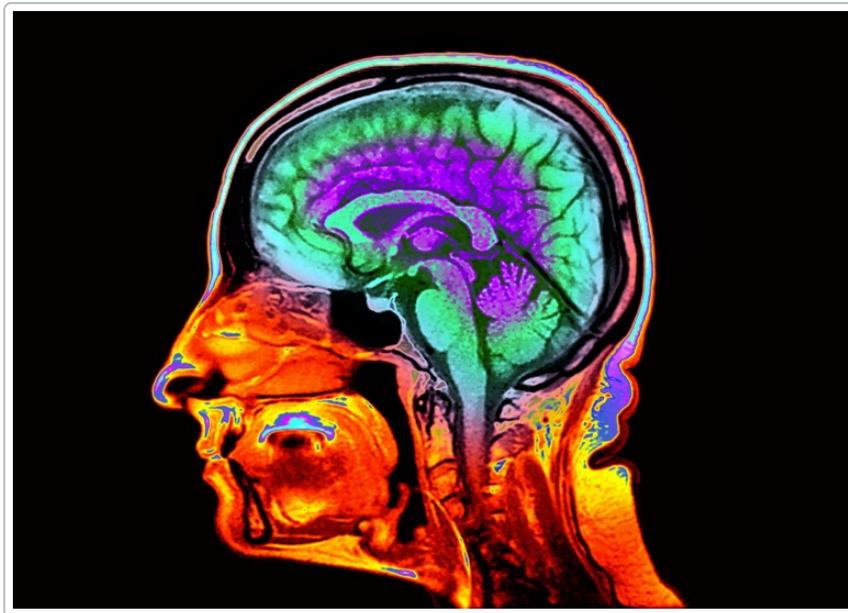
Early-Stage Research vs. Clinical Trials

Most cutting-edge longevity insights are **preclinical** or exploratory. The betaine finding, for instance, stems from laboratory and mouse work following a small human exercise study ³ ¹⁰. Likewise, the rapamycin result is based on animal meta-analysis ⁶ ⁷. These early-stage discoveries illuminate new targets (e.g. betaine/TBK1) and justify human trials.

By contrast, **clinical trial results with functional benefits** are still scarce. Large-scale human trials of geroprotective drugs (like TAME metformin or PEARL rapamycin) are ongoing, but results on improving health markers are not yet reported. One exception (outside this week's news window) was a Werner syndrome trial: high-dose NAD precursors (nicotinamide riboside) in patients improved heart, skin and kidney function ¹¹ ¹². Such studies hint that metabolic regulators can *rejuvenate function*, but they remain limited to rare conditions or small cohorts. Thus, the field is transitioning: lab findings (molecular pathways, senescence targets, reprogramming strategies) are steadily moving toward first-in-human tests of healthspan outcomes.

Technological Tools

Researchers also unveiled new **tools and platforms** to study aging biology:



Brain imaging clocks: Artificial-intelligence analyses of routine MRI scans can now reveal a person's biological aging rate ⁹. In one study of ~50,000 scans, machine-learning features (e.g. thinning cortex, grey-matter volume) predicted cognitive decline and frailty risk ⁹. Such non-invasive "brain age" biomarkers complement blood-based clocks and may detect drug effects on neural health.

- **Multi-omics profiling:** The betaine study itself exemplifies new platforms: scientists tracked single-cell transcriptomes, proteomes, metabolomes and the microbiome in humans before and after exercise ¹⁰. Integrating these **multi-omics datasets** pinpointed the kidney as exercise's control center and identified betaine as a key metabolite ¹⁰. Future efforts will similarly combine genomics, proteomics and AI to screen drugs and biomarkers for geroprotection.
- **Blood-borne scores:** (Related work announced last week) A team developed a 86-protein "Healthspan Proteomic Score" from UK Biobank data, which strongly predicts mortality and age-related disease risk ¹³ ¹⁴. Although published slightly earlier, it highlights a trend: researchers are building *healthspan clocks* from blood tests. These scores could eventually stratify individuals by aging rate or guide preventive therapies.

Together, these technological advances — *imaging, omics, AI analysis* — are sharpening our ability to **measure aging**. They enable smaller, faster trials of interventions by focusing on functional endpoints, and they provide new drug targets (e.g. proteins identified in multi-omics screens).

Ethical and Practical Considerations

The excitement over “age-slowng” therapies brings real-world challenges:

- **Safety:** Any intervention that broadly alters aging pathways must be proven safe. For example, rapamycin is immunosuppressive, raising concerns about infection risk ⁸. In contrast, candidates like betaine appear well-tolerated, and early signals suggest broad benefits ¹⁵. Rigorous monitoring for side effects (metabolic, immune, cancer risk, etc.) will be essential in trials.
- **Accessibility and Equity:** Many proposed therapies (cell or gene therapies, novel drugs) could be extremely expensive. Ensuring **fair access** is an ethical priority. Unlike inexpensive lifestyle measures, cutting-edge treatments may widen health disparities unless carefully managed. Policymakers and funders must consider how to make life-extension interventions available beyond well-funded subsets of the population.
- **Ethical Implications:** Extending healthy life raises deep questions. How will society cope with dramatically more older adults who remain vigorous? There are debates over resource allocation and consent for “interventions in aging”. Experts argue we must **reframe aging** as a modifiable process and focus on reducing disability and dependency ¹⁶ ². For instance, shifting public health policy from treating disease toward **preventing frailty** could yield enormous societal benefit (even one extra healthy year of life can translate to a ~\$38 trillion value ²). Longevity researchers are engaging bioethicists and stakeholders early to guide responsible development.
- **Regulatory Hurdles:** No drug is currently approved specifically to slow aging. Trials typically target age-related diseases or conditions (frailty, Alzheimer’s, sarcopenia) to gain approval. There is growing consensus that *functional outcomes* (mobility, cognition, intrinsic capacity) should be the goal, but regulatory frameworks must adapt. Clear biomarkers of aging (see above) may help by serving as surrogate endpoints, but authorities will demand proof of actual functional improvement and safety before approving any “geroprotector” for broad use.

Future Directions

Looking ahead, we expect rapid progress on several fronts:

1. **Human trials of promising agents.** The exercise-mimetic betaine will likely enter early-phase trials in older adults to test for improved physical or immune function. Rapamycin analogs and metformin remain under study in aging-focused trials (e.g. TAME). New candidates — from senolytics to partial reprogramming factors — are also poised for first-in-human studies in the next few years. Combining therapies (e.g. metabolic regulators plus senolytics) may be explored to maximize functional gain.

2. **Integration of AI and personalized data.** AI-driven platforms (like those that predicted brain aging ⁹) will accelerate drug screening and trial design. Coupled with wearable sensors and digital biomarkers, they will enable *N-of-1* approaches to personalize longevity interventions. Large population datasets (UK Biobank, national health systems) will feed machine learning models to identify new drug targets and at-risk groups for early intervention.
3. **Enhanced biomarkers for healthspan.** We anticipate more FDA-qualified *biological age* markers. For example, proteomic or epigenetic clocks will be refined to predict who will benefit most from an intervention. Non-invasive imaging (brain or retinal scans) may become routine aging diagnostics. These tools will make it possible to **track functional aging in real time**, enabling shorter, cheaper trials that focus on health outcomes rather than wait for disease onset.
4. **Focus on functional outcomes.** As a result of this research, upcoming clinical trials will emphasize **quality of life and physical function**. Endpoints like frailty index, gait speed, muscle strength and cognitive battery performance will be central. The field is coalescing around the idea that extending “healthspan” (years without disability) is the true goal ¹⁶. Future work will likely test multi-domain interventions (exercise, nutrition, plus targeted drugs) as combined anti-aging regimens.
5. **Societal adaptation.** Policymakers and practitioners are starting to plan for healthier aging populations. The recent call for a “Public Health 4.0” emphasizes prevention and vitality throughout life ¹⁶. If interventions can add even a year of healthy living, the economic and social benefits will be vast ². We expect more interdisciplinary collaborations (geroscientists with public health experts, ethicists, economists) to ensure longevity gains translate into **compressed morbidity** – fewer years of disability – in a fair and sustainable way.

In summary, this week’s longevity news points to **metabolic modulators and advanced diagnostics** as frontiers in extending functional life. Early studies (like the betaine exercise-mimetic) highlight novel targets, while meta-analyses reinforce the promise of known interventions (rapamycin). Tools such as AI-driven imaging biomarkers are maturing to evaluate therapies. As trials progress, maintaining safety and broad access will be paramount. The coming months should see a wave of human data on healthspan, bringing us closer to turning the dream of longer, healthier lives into reality ² ⁵.

Sources: Recent publications and news releases (June–July 2025) from peer-reviewed journals and reputable institutions ⁴ ³ ⁶ ⁷ ⁹ ². These highlight the latest validated findings and expert analyses in longevity research.

¹ ² ¹⁶ New Report Calls for Urgent Shift from Lifespan to Healthspan | Columbia University Mailman School of Public Health

<https://www.publichealth.columbia.edu/news/new-report-calls-urgent-shift-lifespan-healthspan>

³ Can a pill replace exercise? Swigging this molecule gives mice benefits of working out

https://www.nature.com/articles/d41586-025-01994-0?error=cookies_not_supported&code=36c77d9e-b66b-422c-a1bc-6e52e1ec4ce8

⁴ ⁵ ¹⁰ ¹⁵ Unlocking exercise’s anti-aging key: Betaine as first oral mimetic | EurekAlert!

<https://www.eurekalert.org/news-releases/1089007>

6 8 **This Anti-Aging Drug Rivals Calorie Cutting for Longer Life, Study Finds**

<https://scitechdaily.com/this-anti-aging-drug-rivals-calorie-cutting-for-longer-life-study-finds/>

7 **Longevity: Can rapamycin extend lifespan? What latest research says**

<https://www.medicalnewstoday.com/articles/rapamycin-may-extend-lifespan-as-effectively-as-dietary-restrictions>

9 **How fast are you ageing? Ordinary brain scans reveal the pace**

https://www.nature.com/articles/d41586-025-02086-9?error=cookies_not_supported&code=b3029e12-c41c-497c-bc77-5256a5368d10

11 **New Hope for Patients with Werner Syndrome | Chiba University**

https://www.chiba-u.ac.jp/e/news/research/new_hope_for_patients_with_werner_syndrome.html

12 **Nicotinamide riboside shows promise in treating Werner syndrome symptoms**

<https://www.news-medical.net/news/20250605/Nicotinamide-ribose-shows-promise-in-treating-Werner-syndrome-symptoms.aspx>

13 14 **Scientists Develop New Blood-Based Proteomic Score to Predict Healthspan and Disease Risk - UConn Today**

<https://today.uconn.edu/2025/06/scientists-develop-new-blood-based-proteomic-score-to-predict-healthspan-and-disease-risk/>