

Editorial

Healthy Aging in the Precision Medicine Era: Why Integrated Biomarkers Matter.

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Abstract

Healthy aging is increasingly defined by the preservation of function, resilience, and independence rather than by survival alone. This shift has accelerated interest in non-invasive biomarkers that reflect biological aging more meaningfully than chronological age while remaining feasible for clinical and public-health use. The strongest near-term candidates are handgrip strength, brief cognitive assessment supported by neurotrophic biology such as brain-derived neurotrophic factor (BDNF), structured skin-aging assessment, and stress biology captured through cortisol-related dysregulation and allostatic load. These measures can be extended by wearable devices and digital phenotyping, while epigenetic and proteomic clocks add higher-resolution estimates of biological age. The central translational message is that no single biomarker is likely to capture the complexity of aging. Instead, the most useful framework is layered: inexpensive functional measures for broad implementation, digital tools for longitudinal monitoring, and molecular clocks for enrichment and intervention tracking. As summarized in Figure 1 and Figure 2, successful implementation depends on analytical validity, clinical validity, longitudinal responsiveness, clearly defined context of use, and staged qualification before routine adoption. This condensed editorial argues that integrated biomarker panels, rather than isolated measurements, offer the most pragmatic route to precision healthy aging.

Keywords:

Healthy Aging, Biological Aging, Biomarkers, Precision Medicine, Handgrip Strength, Digital Health

Introduction

Healthy aging is now understood less as the absence of disease and more as the maintenance of functional ability across later life. That distinction matters clinically. It shifts attention away from late-stage diagnosis and toward earlier identification of declining reserve in muscle, brain, metabolism, skin, and stress-response systems [1]. At the same time, geroscience has made clear that chronological age is an incomplete surrogate for biological aging. People of the same age can differ sharply in strength, cognition, resilience, multimorbidity burden, and response to intervention, which is why biomarker development has become central to precision aging medicine [1,2].

An ideal biomarker of healthy aging should be biologically plausible, reproducible, minimally invasive, responsive to change over time, and interpretable within a defined clinical context [2]. Increasingly, however, the field is moving away from the search for a single “best” biomarker. Aging is multidimensional, and the more realistic aim is to combine complementary signals that capture distinct but interacting domains of physiological reserve [2]. This is also the logic behind the translational frameworks shown in Figure 1 and Figure 2, which place discovery, validation, intervention responsiveness, and implementation within one continuous pathway rather than separate silos.

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From Single Biomarkers to Integrated Healthy Aging Assessment

Among currently available non-invasive markers, handgrip strength is the most clinic-ready. It is inexpensive, portable, rapid, and reproducible, yet it reflects much more than muscle force alone. Grip strength functions as an integrative readout of muscle quality, neuromuscular integrity, nutrition, inflammatory burden, and overall physiological reserve. In large multinational cohort data, lower grip strength predicts disability, cardiovascular disease, and all-cause mortality, supporting its use as a functional vital sign of aging [3]. For this reason, handgrip dynamometry is one of the few aging biomarkers already ready for broad implementation in outpatient medicine and community screening [3].

Cognitive aging is equally important, but less reducible to a single measure. Brief cognitive testing remains the clinical anchor, while BDNF is better understood as a mechanistic adjunct than a stand-alone screening tool. BDNF supports synaptic plasticity, learning, and memory, and its regulation links exercise, sleep, inflammation, and stress to cognitive resilience [4]. In practice, this means that brain aging is best assessed through a combination of performance-based measures and biology rather than through one laboratory analyte alone [4].

The skin deserves more attention in healthy-aging frameworks. It is the most visible and accessible organ for repeated non-invasive assessment, and it records both intrinsic aging and the cumulative effects of ultraviolet exposure, pollution, smoking, and other environmental insults. The SCINEXA framework remains useful because it standardizes visible aging into clinically interpretable components [5]. Although more advanced imaging approaches are emerging, the near-term translational value of skin aging lies in structured scoring, standardized photography, and repeated observation over time [5].

No domain unifies these markers more clearly than stress biology. Chronic psychosocial stress becomes biologically embedded through repeated activation of neuroendocrine and inflammatory pathways. The classical allostatic-load model remains highly relevant because it explains why impaired strength, poor sleep, metabolic dysfunction, cognitive decline, and visible tissue aging often cluster in the same person [6,7]. In aging research, stress should not be treated as a background covariate. It is part of the mechanism.

Finally, metabolic aging deepens the integrated view. Aging reshapes adipose distribution, insulin sensitivity, substrate use, and muscle quality, meaning that obesity and metabolic dysfunction should be interpreted not simply as comorbidities but as accelerants of functional decline [8].

Digital Technologies Are Reshaping Healthy Aging

Digital medicine has changed the tempo of biomarker measurement. Traditional visits provide snapshots; smartphones, wearables, and connected sensors provide trajectories. Activity, gait, sleep timing, heart-rate dynamics, and repeated task performance can now be measured continuously or near-continuously in daily life rather than only during clinic encounters [9]. This is especially valuable in aging, where subtle functional decline often appears gradually and intermittently.

The practical value of digital biomarkers is not novelty for its own sake. It is repeated measurement with low participant burden. For healthy aging, that means digital tools can complement brief clinical

tests by showing whether physical activity is contracting, sleep is fragmenting, or mobility patterns are deteriorating over time [10]. In cognitive aging, the same logic supports remote task repetition and ecologically valid monitoring rather than occasional, one-time assessment.

That promise, however, depends on rigor. Digital biomarker development must still pass through verification, analytical validation, and clinical validation before a technology is considered fit for purpose. This principle is central to precision healthy aging: digital tools should enhance reach and frequency, but they cannot bypass the evidentiary standards required of any clinical biomarker [11].

From Biomarker Discovery to Clinical Translation

The most valuable aspect of the two proposed figures is that they frame aging biomarkers as a translational pipeline, not just a collection of promising measurements. Figure 1 emphasizes movement from discovery and human phenotyping through analytical and clinical validation to longitudinal/interventional evaluation and population-level implementation. Figure 2 presents the same logic as a qualification pathway: discovery, assay standardization, replication, prognostic testing, intervention responsiveness, context-of-use specification, regulatory qualification, and monitoring after implementation. Together, the figures capture the editorial's main argument that aging biomarkers should be judged by intended use, not by technological sophistication alone.

This translational lens immediately separates biomarkers that are ready now from those that remain primarily research tools. Handgrip strength, brief cognitive assessment, stress screening, and structured skin examination already have clear bedside or community applications [12,13]. By contrast, molecular clocks are highly promising but should currently be used mainly for risk stratification, cohort enrichment, and intervention monitoring until broader validation, calibration, and standardization are achieved [12-15].

Epigenetic and proteomic clocks have nonetheless advanced the field in an important way: they measure biological aging more directly than chronological age and may detect change over time at higher resolution than single functional tests [16, 17]. DunedinPACE is especially notable because it was designed to quantify the pace of aging rather than simply predict age [18]. Proteomic profiling likewise suggests that circulating protein patterns can track aging-related physiological shifts across the life course [17]. These tools are likely to be most useful when interpreted alongside, not instead of, functional and clinical measures [16-18].

Clinical Implications and Future Directions

The immediate clinical implication is straightforward: healthy-aging medicine should implement mature, low-cost tools now while continuing to validate more complex technologies. Handgrip strength can be added to routine adult and geriatric assessment. Brief cognitive testing, structured sleep and mood review, central adiposity or body-composition phenotyping, and simple skin-aging documentation can also be standardized in outpatient care with minimal burden [4-6].

The next step is integration. A realistic healthy-aging index for clinical use will probably combine one functional measure, one cognitive measure, one stress or sleep measure, and one metabolic marker, with digital follow-up layered on top when feasible. Molecular clocks may then serve as adjuncts in research-rich environments or intervention trials, particularly where the goal is to

capture pace-of-aging or monitor response to gerotherapeutic strategies [2,19].

Context of use remains crucial. A biomarker intended for community screening should not be judged by the same standards as one intended for drug development or regulatory decision-making. This is why the

staged pathway in Figure 2 is so useful: it reminds investigators to define the intended population, setting, and clinical decision before calling a biomarker “ready”. Equally important is equity. Biomarkers that work only in highly resourced settings or narrowly sampled populations will not solve the broader challenge of healthy aging.

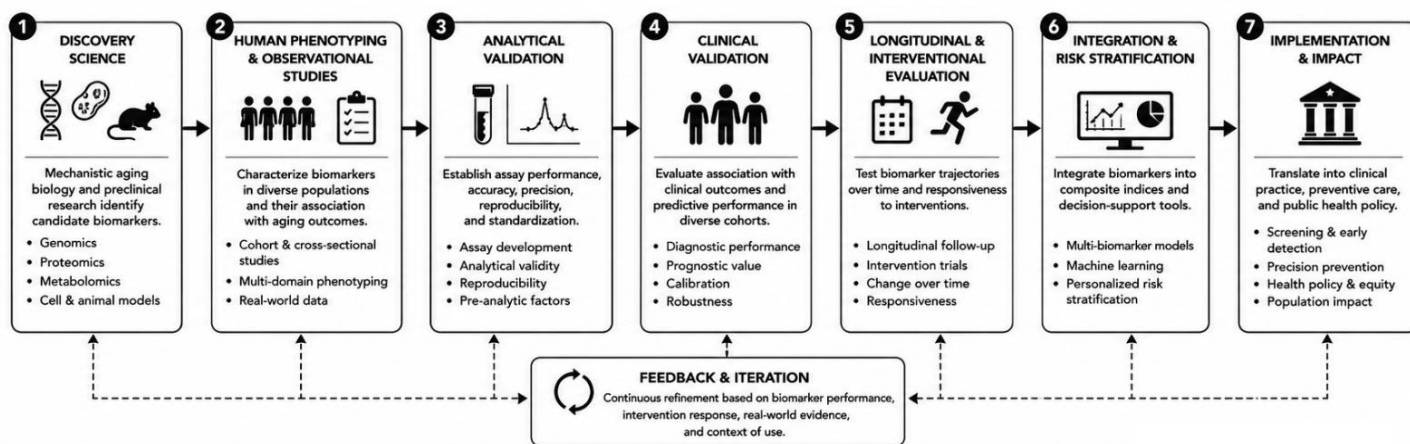


Figure 1: Translational framework for the development and implementation of non-invasive biomarkers of healthy aging. Candidate biomarkers progress from mechanistic aging research and human phenotyping through analytical and clinical validation, longitudinal and interventional evaluation, and integration into clinical risk stratification and public health practice. Continuous feedback across all stages enables refinement of biomarker performance, intervention responsiveness, and context of use, facilitating the translation of biological aging measures into precision medicine strategies for healthy aging and healthspan promotion.

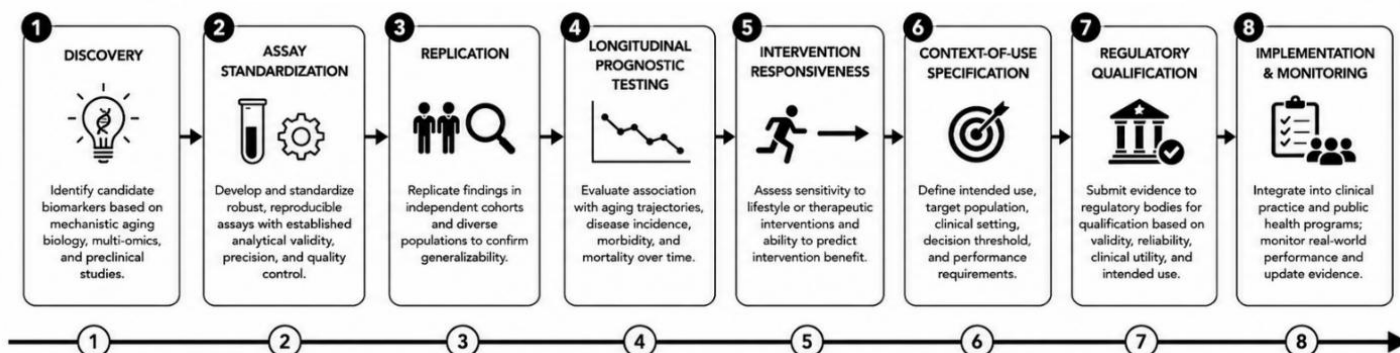


Figure 2: Staged development pathway for healthy aging biomarkers from discovery to qualification and implementation. Candidate biomarkers progress through analytical standardization, independent replication, longitudinal validation, assessment of intervention responsiveness, context-of-use definition, regulatory qualification, and clinical implementation. Each stage contributes evidence supporting validity, reproducibility, clinical utility, and intended use, ensuring that biomarkers are robust, reliable, and suitable for precision healthy aging applications.

Conclusion

Healthy aging will not be advanced by a search for one universal biomarker. The stronger strategy is integration: combine function, cognition, visible tissue aging, stress biology, metabolic health, and where appropriate, digital and molecular clocks into layered, context-specific assessment frameworks. In that hierarchy, handgrip strength is the clearest immediate winner because it is inexpensive, scalable, and prognostically robust. Brief cognitive assessment, structured skin evaluation, and stress-informed clinical interpretation should join it in broader practice now. Digital biomarkers and omics clocks are not replacements for bedside physiology; they are amplifiers of it. Their

value lies in longitudinal tracking, earlier detection of decline, and improved intervention monitoring. The translational agenda, reflected in Figure 1 and Figure 2, is therefore clear: standardize, validate, define context of use, qualify, and then implement. If that pathway is followed rigorously, precision healthy aging can move from an aspirational concept to a practical model of care.

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