

Healthy aging and longevity: challenges and opportunities



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As the number and proportion of older people in the global population grows, healthcare priorities are changing. Healthy aging – and more specifically, healthy longevity – is an important aspect of this. With medical care pathways shifting from reactive to proactive and preventive care, healthy longevity is set to centre around earlier detection and better prediction of age-related diseases, and self-care. Sitting at the convergence of next-generation molecular-level diagnostics, novel geroprotective therapies, and advanced data analytics, healthy longevity is becoming a major category spanning medical and consumer health. In this whitepaper, Sagentia Innovation summarises the current healthy longevity market, suggesting that its evolution and maturation will open a new realm of clinical and commercial opportunities to ensure more people achieve healthy longevity across the life course.

Aging and healthy longevity

According to World Health Organization figures¹, population aging has become a global phenomenon affecting every country in the world. By 2050 22% of the world population (2.1 billion people) will be aged 60 and older, with 426 million of those aged 80 or over. This presents new challenges for healthcare. Helping people stay healthier for longer will be paramount, both for individuals' quality of life and to manage the demands placed on healthcare systems.

Population aging is attracting the interest of governments and intergovernmental organisations such as the United Nations (UN). The UN's Decade of Healthy Ageing (2021-2030)² encourages collaborative and concerted efforts to improve the lives of older people, their families, and the communities in which they live. Some of this is being implemented via the Healthy Ageing Collaborative³, a multi-sector, multi-stakeholder partnership supporting progress towards the UN vision of a world in which everyone can live a longer and healthier life.

Other initiatives include Singapore's Centre for Healthy Longevity⁴ which looks at optimising health and extending health span and lifespan. In England, the Chief Medical Officer's 2023 annual report focused on improving quality of life in later years.

Prof Sir Chris Whitty speaks of shifting disease 'out to the right in time'. It's about reducing how long people live with ill health through prevention and treatment strategies that delay the onset of disease:

"Contrary to the assumption by many that as the population grows older the length of time spent in ill health must inevitably rise, it is possible to compress the period of ill health if we are systematic about delaying disease. If we delay the point at which people get life-limiting disease for as long as possible, disease may occur only shortly before their eventual death, or not at all." ⁵

Aging research has experienced unprecedented advances over recent years, particularly with the discovery that the rate of aging can be, to some extent, controlled. This creates opportunities for increased alignment and synergy between the medical and consumer health sectors, with new developments encompassing everything from diagnostic technologies (including the application of multi-omics approaches for early diagnosis and pre-diagnosis of diseases) to treatment solutions (including genetic, pharmaceutical, and nutritional interventions).



What are healthy aging and healthy longevity?

The terms 'healthy aging' and 'healthy longevity' are often used interchangeably. However, discussions on healthy aging tend to encompass both societal and health-related factors, whereas the notion of healthy longevity is more centred on extending good health into older age.

It is important to acknowledge the high level of interplay between socioeconomics, cultural factors, and health. This can have an impact at a microlevel where the health needs of aging populations in deprived areas may be different to those in neighbouring affluent areas. It can also lead to differences between countries. For instance, healthy longevity priorities and requirements in Japan or Singapore will not necessarily align with those in the UK or US.

Why and how do we age?

Aging is a complex multifaceted process influenced by various factors including genetics and lifestyle. The time-dependent accumulation of cellular damage is widely considered to be the general cause of aging.^{6,7}

While population statistics focus on chronological age to reflect disease risk, scientists are more interested in estimating biological age, the rate at which a person ages physically. Although chronological age reflects disease risk, the rate of aging varies across individuals, organs, tissues, and clinical conditions. Chronological age does not capture this variation well, hence the interest in estimating biological age to predict morbidity.^{8,9}

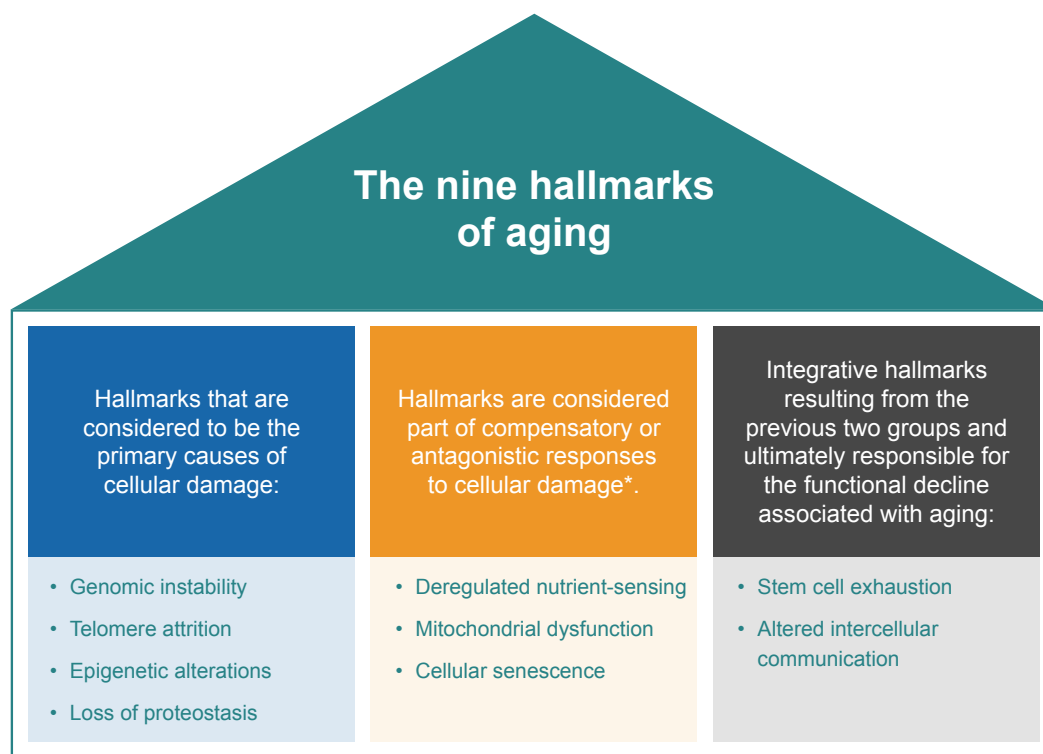
Chronological age and biological age are closely aligned during childhood and among adults who are aging typically, in the absence of any clinical indications. However, there can be a difference between chronological age and biological age, known as the 'age gap', which conveys whether aging is faster or slower than expected. It's likely that a biological age far exceeding chronological age increases a person's susceptibility to age-related health conditions. On the other hand, closing the age gap may prolong better health or delay the onset of disease.

Scientific understanding of the aging process is deepening and the discipline of epigenetics, which suggests that behaviours and environment influence how genes are expressed, is gaining more credibility. Epigenetic changes involve alterations in DNA methylation patterns, post-translational modification of histones, and chromatin remodeling.⁸ The Information Theory of Aging proposes that a decline in epigenetic information, resulting in changes in gene expression, triggers a cascade of events, including mitochondrial dysfunction, inflammation, and cellular senescence, leading to a progressive decline in cell and tissue function, manifesting as aging and age-related diseases.^{10,11}

Unlike DNA mutations, epigenetic alterations are theoretically reversible.^{12,13} This means that the rate of aging is controlled, at least to some extent, by genetic pathways and biochemical processes conserved in evolution, but we can still have a significant influence on how well we age.^{8,14}

How are aging processes measured?

Aging is characterised by a progressive loss of physiological integrity, leading to impaired physical and mental function, increased susceptibility to age-related issues, and increased vulnerability to death.⁸ At present there is a lack of consensus on how aging processes might be precisely measured and analysed for the prediction or early detection of aging-related diseases. However, in 2013, a team of biochemists and molecular biologists defined nine hallmarks of aging that contribute to the deterioration and dysfunction of cells as they age (see Figure 1).



**These responses initially mitigate damage, but eventually (if chronic or exacerbated) become deleterious themselves.*

Figure 1: The nine hallmarks of aging.⁸

Each hallmark indicates biological aspects of age-related deterioration. They influence one another and operate in a large and tightly connected network, suggesting a holistic approach to anti-aging interventions might be beneficial.¹⁵

While the original research team was interested in pharmaceutical targets, the hallmarks have become a reference point for a wide range of aging research and innovation. A better understanding of the hallmarks of aging can facilitate strategies to assess and manage associated health implications. For instance, a team of researchers has developed an 'epigenetic clock' that is claimed to accurately measure biological aging in a clinical setting, in both healthy and unhealthy tissues. Epigenetic clocks have been proposed as a 'gold standard' for estimating biological age as they can measure DNA methylation levels.¹⁶

Other approaches to derive biological age predictions gaining interest include measurement of telomere attrition and analysis of movement data (accelerometer readings) from wearable devices based on Machine Learning (ML).¹⁷

Health conditions associated with aging

It's well-known that age-related deterioration increases the risk of various diseases and conditions, including cancer, diabetes, cardiovascular disorders, neurodegenerative diseases, and arthritis.⁸

The researchers who first described the nine hallmarks of aging point out parallels in the way cancer and aging research have progressed, and the importance of hallmark categorisation to help conceptualise underlying mechanisms. As they explain, “cancer and aging can be regarded as two different manifestations of the same underlying process – namely, the accumulation of cellular damage.”

Other pathologies associated with aging, such as atherosclerosis and inflammation, involve uncontrolled cellular overgrowth and hyperactivity.¹⁸ Figure 2 suggests how certain health conditions are linked to accumulated age-related deterioration.













Factors to consider	
Metabolic health conditions <i>(including diabetes and obesity)</i> 	Aging is associated with immunosenescence and accompanied by a chronic inflammatory state which contributes to metabolic syndrome, diabetes and their cardiovascular consequences. ¹⁹
Cardiovascular health 	Aging can cause changes in the heart and blood vessels that may increase a person's risk of developing cardiovascular disease. ²⁰
Immune health 	Beginning with the sixth decade of life, the human immune system undergoes dramatic aging-related changes, which continuously progress to a state of immunosenescence. The aging immune system loses the ability to protect against infections and cancer and fails to support appropriate wound healing. ²¹
Neurodegeneration 	Aging is the primary risk factor for most neurodegenerative diseases, including Alzheimer's disease and Parkinson's disease. ²²
Mental health 	According to the Global Health Estimates (GHE) 2019, mental health conditions account for 10.6% of the total disability (in Disability Adjusted Life Years, DALYs) among older adults. The most common mental health conditions for older adults are depression and anxiety. ²³
Cognitive health <i>(including memory)</i> 	Age-related diseases accelerate the rate of neuronal dysfunction, neuronal loss, and cognitive decline, with many persons developing cognitive impairments severe enough to impair their everyday functional abilities. ²⁴
Bone, joint and muscle health <i>(mobility)</i> 	Loss of bone, degraded articular cartilage, and degenerated, narrowed intervertebral discs are primary features of an ageing skeleton, and together they contribute to pain and loss of mobility. ²⁵
Gastrointestinal health <i>(gut microbiome)</i> 	Aging affects all functions of the gastrointestinal system, including motility, gastric acidity, gastric emptying, enzyme and hormone secretion, digestion, and absorption. Dysregulation of the gut microbiome is an important trigger for chronic low-grade inflammation which is associated with aging and age-related diseases. ²⁶
Oral health 	Aging is associated with oral diseases and conditions including moderate or severe periodontitis, dry mouth, and tooth loss. Periodontal disease is increasingly associated with chronic conditions including diabetes, heart disease, and stroke. ²⁷
Cancer 	There is a bidirectional relationship between cancer and aging. Aging is a risk factor for adult cancers, and emerging evidence suggests that cancers and some cancer treatments might accelerate aging. ²⁸

Figure 2: The health impact of aging.

The current commercial landscape

People age differently, in highly complex ways, meaning there is much scope for personalised approaches to healthy longevity. The emerging healthy longevity market is largely based on this principle.

There’s also increasing evidence that lifestyle factors can have detrimental or beneficial impacts at the individual level. One recent study reported that insufficient or excessive sleep duration may be a risk factor for cognitive decline in aging.²⁹ Findings like this indicate that it is possible to influence how long people remain healthy as they age, with epigenetic re-programming offering opportunities for the design of novel anti-aging interventions.

At present, commercial activity broadly encompasses three categories:

- Diagnostics (e.g., wearable devices, test kits, apps for measuring, tracking, and quantifying biomarkers for biological age assessment/prediction)
- Formulated treatment solutions (e.g., drugs, functional supplements, nutritional support)
- Recommendations for self-care (e.g., lifestyle guidance)

Holistic healthy longevity solutions may involve interplay between these categories. For instance, a consumer-focused diagnostic service might use postal test kits, followed up with personalised supplements or lifestyle recommendations.

Several healthcare and consumer offerings with varying levels of sophistication are already on the market, as detailed in Figure 3.

Offering / categories	Description
AgeMeter agemeter.com	‘Functional age’ is calculated via testing of physiological and cognitive biomarkers that decline with age (e.g., short-term memory, reaction time). The aim is to validate the results of biological age tests. It can also be used by healthcare practices, researchers, or fitness programs to validate aging reversal or anti-aging therapies.
Longevity Biomarkers longevitybiomarkers.com	A consumer app to help track and manage biomarkers such as blood pressure, body fat, visceral fat, and reaction time. Each biomarker is plotted on a colour-coded scale running from alarming (professional help needed) to poor (strong lifestyle changes needed), unsatisfactory (mild lifestyle changes needed), healthy (with some room for improvement), and optimised for longevity.
GlycanAge glycanage.com	Consumers provide a finger prick blood sample for biological age testing via a postal kit. Once the results are ready, customers receive a one-to-one video consultation with a health span doctor to discuss areas for improvement.
InnerAge insidetracker.com	Blood tests are used to calculate biological age based on 17 biomarkers for men and 13 for women. Users also complete a detailed personal profile. Findings underpin evidence-based recommendations for lowering the biological age and optimising health span through targeted nutrition, exercise, and supplement intake.
NOVOS Age Longevity Kit novoslabs.com	The package includes a nutritional supplement and biological age testing via a postal finger prick blood test, followed by actionable longevity insights.

Figure 3: Examples of commercial offerings in the healthy longevity space*

*Examples were current at the time of writing (February 2024)

Driving progress: geroprotective intervention, biomarkers, and data analytics

While healthy longevity solutions already on the market are interesting, ongoing developments are set to break new ground. Some of these will go beyond the treatment of age-related diseases to potentially restore lost function and prevent age-related diseases.



Geroprotective interventions

Early-stage research includes the application of CRISPR/cas gene editing for diagnosis and correction of genetic abnormalities, the use of liquid and virtual biopsy, in-situ diagnostics, and advances in regenerative medicine and organ bioengineering.

Current development of geroprotective therapies includes the design of individual medicines and ‘chemical cocktails’ to selectively target the nine hallmarks of aging to repair the damage that accumulates in our bodies long before symptoms manifest.^{30,31}

Several organisations are exploring possible healthy longevity solutions in this vein. The vision of scientists at **Cambrian Biopharma**³⁰ is to develop interventions to lengthen ‘health span’ (the period of life spent in good health). Therapeutics currently under development are targeting the biological drivers of aging to slow, prevent, or even reverse diseases across multiple organs at the same time. At the time of writing, programs at the ‘Lead’ stage of discovery and preclinical development include two that are focused on addressing the loss of proteostasis. One is looking at overactive cell growth signals, and the other is focused on stiffening of the extracellular matrix.

During 2023, several studies with positive implications for healthy longevity captured the attention of scientific and mainstream media. These include findings surrounding six chemical ‘cocktails’ to induce reprogramming to reverse cellular aging published by a team of Harvard researchers. The cocktails consist of a combination of five to seven agents, some of which are already prescribed for the treatment of various physical and mental disorders. It is claimed that the cocktails “in less than a week and without compromising cellular identity, restore a youthful genome-wide transcript profile and reverse transcriptomic age.”³² This indicates that rejuvenation by age reversal could be achieved not only by genetic means but also by chemical means.

Meanwhile, a **Columbia University** study found that the amount of the semi-essential amino acid taurine in circulation decreased with age and showed that supplementation with taurine slowed some of the key markers of aging such as increased DNA damage, telomerase deficiency, impaired mitochondrial function, and cellular senescence, and improved lifespan in mice and health span in monkeys.³³ Researchers were quick to caution the public against buying taurine-rich products in response to the findings. Nevertheless, the study represents further progress in the mission to prolong good health into older age.

Biomarkers for assessment of biological age

The research for biomarkers to quantify biological aging and predict aging-related outcomes has intensified in recent years. Figure 4 illustrates the main groups of relevant biomarkers for healthy longevity solutions.^{34,35}

Wearable devices, test kits and apps are being developed to measure the rate at which a person ages physically through the examination of physiological characteristics of aging. More advanced solutions go beyond the delivery of interesting data to generate actionable insights. However, harnessing, integrating, and analysing vast quantities of biomarker data to develop and validate solutions for healthy longevity is not easy. The ability to derive biological age predictions and draw meaningful, actionable insights from biomarker data depends upon ML and Artificial Intelligence (AI).



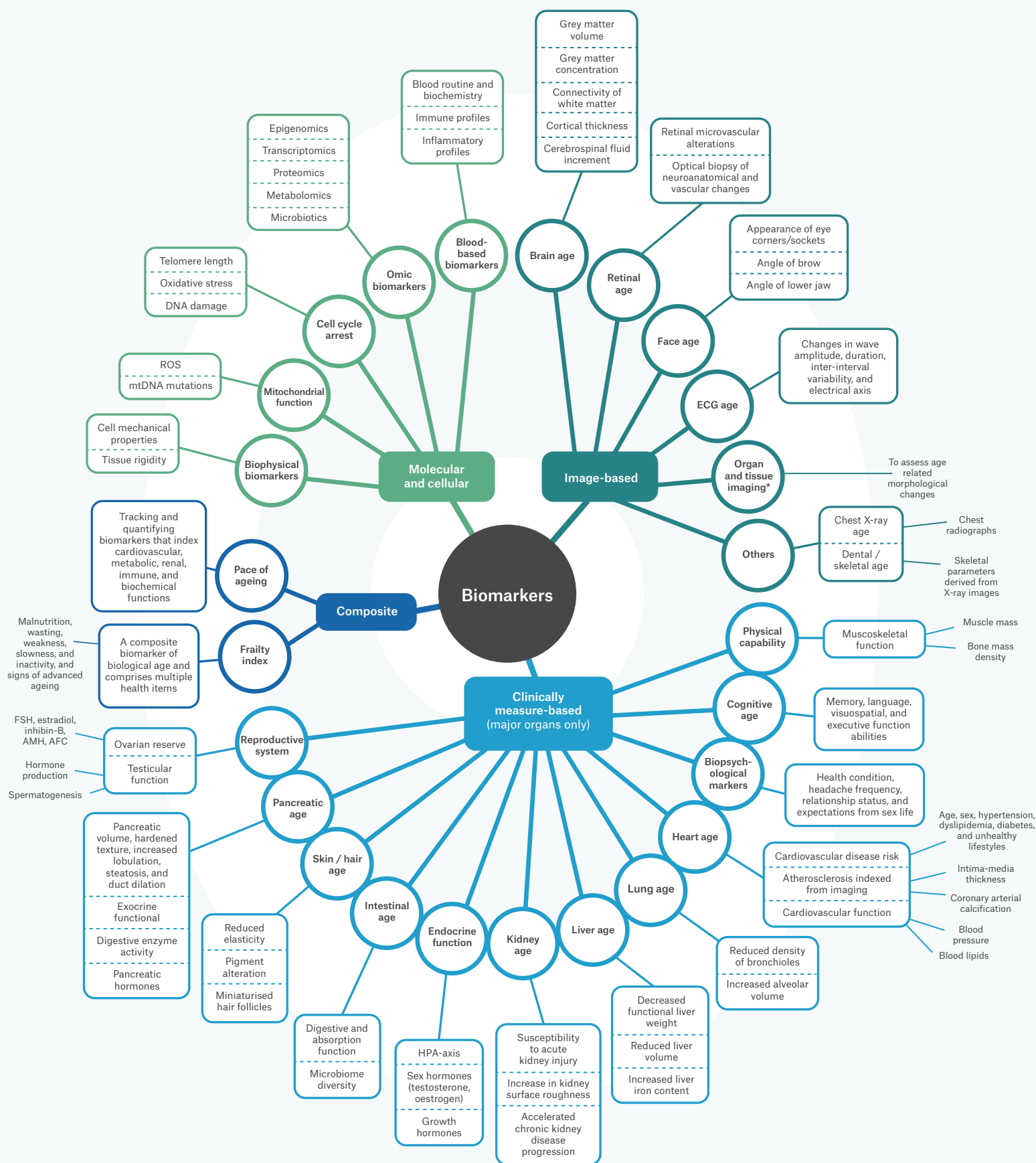


Figure 4: The main groups of biomarkers for healthy longevity solutions (representative examples; not exhaustive list).

Use of data analytics for healthy longevity

ML/AI techniques and algorithms are increasingly used in longevity research for developing reliable metrics of aging and assessing biological age and the effectiveness of geroprotective medications.³⁶ ML/AI-enabled systems can be used to regulate behaviour and psychological elements of age-related conditions and inform the most relevant treatment or self-care options for an individual based on their personal biomarkers and lifestyle preferences.

For example, chatbots (natural language processing systems) can be used to communicate curated healthcare messages for preventive care. This aids individuals in maintaining their wellbeing and forestalling the development of chronic conditions.^{37,38} One recent example is **GECA**, a chatbot that offers information, advice, and monitoring to patients undergoing home treatment. **GECA** is part of the **iCare4NextG** international platform, which provides wellness and care services; it's anticipated that initially, **GECA** will offer remote support to patients with COVID-19 and dementia.³⁸

Deep Learning (DL) can also be applied for the analysis of different types of biomarkers to establish any gaps between chronological age and biological age. For example, it has been shown that compared to other approaches, DL typically yields a better prediction of brain age.³⁹ However, its inherent black-box nature hinders the interpretability of its feature attribution for brain age estimates. Furthermore, many DL estimates of brain age lack generalisability to cohorts not encountered during DL training.⁴⁰

AI has proved effective in helping identify anti-aging drug candidates, particularly at the early stages of drug discovery. **University of Edinburgh** researchers leading an interdisciplinary team of data scientists, chemists, and biologists have developed an innovative method that employs AI to discover three senolytic chemicals (ginkgetin, periplocin and oleandrin), to target malfunctioning cells linked to aging while preserving the integrity of healthy cells. The scientists were able to build robust models (and save screening costs) by using only published data for model training.⁴¹



How to be at the forefront of healthy longevity

The healthy longevity landscape is vast, and the science is moving at pace. Preventive medicine is a critical component of this movement, facilitated by earlier detection, faster diagnosis, and better prediction of health issues to maximise healthy longevity. As governmental policies and guidance gain traction, the shift from reactive to proactive healthcare is set to accelerate, benefiting individuals and healthcare systems alike.

Organisations that leverage relevant technologies effectively to make early inroads to healthy longevity have much to gain. Focusing on aspects of health and aging that are easy to monitor (e.g. sleep quality) may be a good place to start. However, specific opportunities and priorities are likely to vary across international markets.

So, what does the near- to mid-term future hold? Continued focus on addressing innovation challenges, with R&D outcomes translated into commercial offerings, will ensure better healthy longevity equity for more people.⁴²

Five areas ripe for innovation

Conceptualising the essence of aging for a holistic approach to intervention

Knowledge of cellular and molecular aspects of aging, and their potential impact on health, is increasing. However, more work is needed to understand clinical associations and determine which factors are simply a consequence of aging and which increase susceptibility to aging-related health conditions.

The hallmarks of aging are tightly interconnected and influence one another. This opens opportunities for treatment options that don't simply target one hallmark but act on the entire network, or a large section of it.¹⁵ Further research is required to 'dissect the interconnectedness between the candidate hallmarks and their relative contribution to aging' to identify genetic, pharmacological, and nutritional intervention targets with minimal side effects.⁸



Developing criteria for biomarkers of aging and standards for collecting health data sets

ML/AI tools are a critical enabler of future progress for healthy longevity across diagnosis and treatment. Their use will help identify new reliable metrics of aging, predict the aging health trajectory (e.g., via gendered risk prediction models), and evaluate the effectiveness of preventive and curative treatments.

However, the reliability of ML/AI-enabled health solutions is limited by the quality of the available data. Collecting and validating large quantities of health data is inherently problematic, and an imprecise data source may cause an algorithm trained on one dataset to fail in other situations or to make unreliable predictions.³⁶ This highlights the need for standard criteria for biomarkers of aging and for collecting large health datasets, with market participants incentivised to exchange data.

Validating biomarkers of aging to accelerate clinical use

Varied rates of aging in humans make it difficult to translate fundamental findings into clinical practice.¹⁷ At present there is no consensus on how biomarkers of aging should be validated before they transition to the clinic. A new study, led by **Harvard University** scientists, proposes a framework for validating biomarkers of aging to help translate them into clinically actionable tools. They suggest that 'multi-omic approaches' will provide greater insights into biomarker predictive performance to ensure accurate and reliable clinical outcomes. They also emphasise the need for standardising omic data to enhance validation efforts.^{43,44}

Integrating sex and gender for innovation in healthy longevity

Including sex and gender considerations in clinical R&D is critical to healthy longevity innovation for both women and men. These considerations can have an impact on testing models, the overall patient journey, and preferences for the uptake of interventions.^{45,46}

Further research is needed to define and add gender-related indicators to current risk assessments to optimise diagnostic and management strategies. This is especially true in areas such as Alzheimer's disease, cardiovascular health, and menopause drug development.⁴⁵ As an example, cardiovascular disease risk prediction models are often designed for the general population based on risk factors that are shared by men and women. Female-specific predictors are still rarely included, which increases the failure to detect symptoms and underlying cardiovascular problems faced by midlife women.^{45,47}

Combining multidisciplinary principles and expertise to maximise healthy longevity

Effective promotion of healthy longevity requires a combination of multidisciplinary principles and expertise from various scientific domains. These range from precision diagnostics (from the molecular level to the entire organism), to in silico screening of novel geroprotective drugs using omics data and ML, and regenerative therapies based on the use of stem cells, engineered tissues, and bio-printed organs.^{48,49}

Long-term road-mapping activities should potentially incorporate an understanding of the quantum underpinning of living systems. It is now possible to begin to describe some of the functions of living cells using insights from quantum physics.⁵⁰ Continued integration of advanced findings across physical and biological disciplines promises to deepen our understanding of cell biology and the possible role of quantum effects in the manipulation of mammalian physiology and pathology for example, to contribute to innovative approaches in regenerative medicine.^{50,51}

How Sagentia Innovation can help

Sagentia Innovation leverages multidisciplinary capabilities to define actionable value propositions. We do this by identifying market opportunities and determining when, where, and how diagnostic technologies and treatment solutions can enhance offerings in the medtech, biopharma, and consumer health markets. With decades of experience in molecular diagnostics and precision genetics, we increasingly use data analytics and ML techniques to integrate genetic, microbiome, and phenotypic data for high-resolution diagnostic solutions and personalised digital and formulated interventions.

Contact info@sagentiainnovation.com if you'd like to discuss R&D strategy, front end innovation, or product development activities for healthy longevity based on validated approaches and sustainable roadmaps.

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