

# Good Practices in Healthy Longevity Medicine

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## **Abstract**

Healthy Longevity medicine is an emerging field focused on delaying age-associated decline through personalized treatments, with potential to significantly improve healthcare trajectories. However, it remains hindered by the absence of clear and agreed definitions, certifications from Medical Boards and medical authorities, standardized protocols, and established regulatory frameworks. The present work is a position paper collectively created by medical professionals and senior members of the International Longevity Alliance (ILA) considering public protocols

and good practices of healthy longevity medicine, aiming to address some of the open issues. Though not final or determinative, this collective work aims to suggest current state of recommendations on how to assess and improve existing definitions and standards in this rapidly developing and crucial medical field.

Keywords: healthy longevity medicine, healthspan medicine, good practices, geroprotection, geromedicine, healthspan, clinical standards

## **1 Introduction**

There is growing recognition that degenerative aging, broadly understood as the physical (including cognitive) degeneration associated with chronological aging, represents the main challenge for global health, as pathological aging is arguably the main risk factor or underlying cause of all major chronic, disabling and life-threatening diseases.

To develop effective interventions to prevent and treat degenerative aging processes and related diseases, and to extend healthy longevity, much fundamental and clinical research is still required to establish theoretical feasibility of proposed interventions, and test them on model organisms (Jin et al. 2015; Stambler 2017). Such fundamental research has been commonly termed “geroscience” (Sierra 2016). Following fundamental research, the next step is to translate proposed interventions into effective, safe and accessible medical procedures that can prevent and ameliorate adverse aging processes and related diseases, and broadly extend healthy longevity. Such medical interventions have been initially termed as “longevity medicine” and their providers as “longevity clinics” and “longevity physicians” (Bischof et al. 2021). Many specialists and clinics now designate themselves under the heading of “longevity”, yet not much agreement exists about what does or should constitute the practice of longevity medicine. Medical boards are still not regulating the certifications of practitioners or institutions, besides that of Abu Dhabi which recently deployed clinical standards developed by Healthy Longevity Medicine Society for the practice of longevity medicine (UAE Department of Health 2024). Longevity promoting regimens vary from practitioner to practitioner, with apparently as many different “longevity medicine” regimens as there are “longevity practitioners”. The standards in such practice are still undefined. Conditions that constitute “evidence” or “good practice” for a “longevity intervention” are equally varied and ill-defined, and there is a clear need to bring more structure into this variety, to attempt to develop basic criteria and guidelines. In the absence of a theoretical justification (even in the absence of an agreed-upon theory of aging), expert opinion can be used operationally as a guiding direction considering developments of good practices, protocols and evaluation criteria in healthy longevity medicine.

This is the latest edition of a position paper exploring these topics, collectively created by medical professionals and senior members of the International Longevity Alliance (ILA), in which we present some initial discussion for such recommendations. By no means exhaustive, it is intended to establish grounds for further discussion, expansion and enhancement. Based on the expert opinions of members of the International Longevity Alliance (ILA), a global healthy-longevity promoting umbrella organization, that includes over 70 non-profit

organizations and social enterprises, working in over 70 countries, including several medical associations, research foundations and public health groups, we suggest that good practices in healthy longevity medicine should include elements outlined in this position paper.

## **2 Core requirements for healthy longevity medicine services**

### ***2.1 The mission and vision of healthy longevity medicine: the main definitive components***

Based on the present expert opinion, the aims of the healthy-longevity medicine service are to:

- Promote health, wellness, healthy longevity and disease prevention.
- Promote healthier lifestyles and habits.
- Enable early and preventive intervention in age-related diseases.
- Enhance healthspan, the period of life spent in good quality health. Optimize healthspan by effectively targeting aging processes across the lifespan, resulting in measurable improvements in health outcomes, functional capacity and overall quality of life.
- Promote and support scientific research in the field of healthy longevity medicine, including collaboration with academic institutions and research centers. Foster a partnership between clinical practice and basic research, ensuring that the latest geroscience discoveries are rapidly integrated into patient care, while also providing researchers with valuable clinical insights and access to real-world data, accelerating innovation and enabling development of first-in-class interventions.
- Support ethical, equitable, and globally-accessible delivery of geroscience-based interventions addressing the underlying processes of aging, ensuring that advancements in healthy longevity medicine are implemented with fairness and cultural sensitivity, and contribute to reducing health disparities across populations.
- Engage in development of recommendations and policy strategies that support initiatives and investments in research on longevity and healthy aging. Integrating various scientific disciplines such as medicine, biology, technology, psychology, and sociology to achieve the broadest possible approach to the challenges of longevity.
- Establish and allow external validation of standardized protocols and measurable benchmarks for assessing the safety, efficacy and quality of longevity interventions, laying the groundwork for professional certification, regulation, and evidence-based clinical guidelines in the emerging field of longevity medicine.

### ***2.2. Longevity Clinics Participants***

The participants of longevity clinics are people who sign up for longevity medicine treatments. The term “participants”, rather than “patients”, implies that a person who wants to use the services of a longevity medicine clinic can be healthy, and personally participatory in the treatment process. The person does not need to be a patient treated for a particular sickness to benefit from the longevity programs. However, patients with specific diseases can also benefit. The term “participants” also suggests more autonomy – doctors usually consult diagnostic and intervention methods and often prescribe solutions that are personalized and adjusted to lifestyle. Other terms, such as “subjects” and “clients” can be used, rather than “patient”, though the routine term “patient” can also be applied.

In addition, several methods already implemented in longevity medicine can also be used in rehabilitation centres under collaboration or partnership with experienced doctors in the field of longevity medicine.

### **2.3. Geroscience**

The main conceptual basis of longevity medicine is based on “geroscience” – a field of aging research that focuses on understanding the genetic, molecular and cellular mechanisms that make aging a key risk factor for multiple acute and chronic diseases, as well as decreased resilience and plasticity. Elucidating many of the molecular, cellular, and supracellular mechanisms underlying aging has spurred the birth of geroscience, which aims to identify the actionable hallmarks of aging (Kroemer et al. 2025).

These processes include, not only but mainly: telomere shortening, DNA damage, mitochondrial dysfunction, counterproductive inflammation, deregulated nutrient-sensing, including insulin resistance, immune system decline, hormonal changes, fibrosis and other aging processes commonly recognized as “hallmarks of aging” or “pillars of aging” (López-Otín et al. 2013; Kennedy et al. 2014; López-Otín et al. 2023; Khaltourina et al. 2020).

Geroscience takes a comprehensive approach by targeting the underlying biology of aging, rather than individual diseases, to address multiple conditions simultaneously. The field is highly interdisciplinary, bringing together experts from biology, medicine, bio-technology, epidemiology and other fields to advance knowledge and interventions.

In a recently published review, potential gerotherapeutic benefits of various interventions as parts of disease management have been reported. Gerotherapeutics have the potential to offer strategies to mitigate the molecular drivers of aging to reduce chronic diseases and geriatric syndromes. The review highlights that longevity clinics can play a significant role in introducing translational geroscience to individuals seeking care through a pragmatic approach combining both pharmacological and non-pharmacological strategies. However, the study cautions that risk-benefit assessment should be considered before suggesting any treatment plan to the individuals seeking care (Forman and Pignolo 2024).

### **2.4. Healthspan and hallmarks of health**

The primary goals of longevity medicine are to preserve life and health in old age, to extend the “healthspan” - the period of life during which a person is generally healthy and free from severe disease or disability. This encompasses the quality of life, functional independence and the ability to engage in daily activities without significant health-related limitations. The goal is more than just living longer — it is about optimizing those additional years to ensure they are healthy, active and fulfilling.

The concept of the “healthspan” can be related to the concept of the “hallmarks of health”. While the Hallmarks of Aging provide a framework to understand the biological processes driving decline (López-Otín et al. 2013; López-Otín et al. 2023), recent scholarship has emphasized the importance of complementing this with the Hallmarks of Health, which describe the positive, resilience-based capacities of living systems (López-Otín and Kroemer 2021; Kroemer et al. 2025). These include effective tissue repair and regeneration, immune robustness, metabolic flexibility, proteostasis, and neuroendocrine balance.

Integrating both frameworks allows healthy longevity medicine to pursue a dual aim: not only delaying or repairing age-associated damage but also strengthening intrinsic mechanisms of health maintenance and resilience. In this sense, healthspan is defined not only by the absence of disease but also by the preservation of these fundamental hallmarks of health.

## ***2.5 Longevity medicine – general considerations***

Longevity medicine includes personalized preventive, augmentative and curative medicine, encompassing biogerontology, geroscience, regenerative medicine, precision and functional medicine, employing advanced computational biomedicine (Bischof et al. 2021).

Longevity medicine aims to optimize health and healthspan by targeting aging processes throughout one’s lifespan. This innovative approach combines preventive and therapeutic medical practices and methods, encompassing a broad spectrum of diagnostics and interventions.

The importance of longevity medicine lies in its potential to revolutionize healthcare by shifting the focus from reactive to anticipatory care, from disease treatment to proactive health diagnostics, optimization and age-related disease prevention by applying gerodiagnostics and gerointerventions or gerotherapeutics.

Longevity medicine differs from general preventive care by its focus on aging biomarkers, geroscience interventions and therapies and methods aiming at extending healthspan and lifespan and delaying the onset of age-related diseases.

Briefly, Longevity Medicine is a personalized approach to healthcare addressing the underlying causes of aging, based on the understanding that aging is not a single process, but rather a collection of interconnected processes that can be targeted for intervention.

### **3 Diagnostics**

In addition to the well established health check-up routine, the practitioners of longevity medicine should perform gerodiagnostic tests and physical measurements to evaluate the aging processes, and detect potential health problems, in order to avoid their transition into diseases.

Longevity medicine practitioners have the option to utilize the latest innovative technologies for obtaining in-depth health data for diagnosis, such as whole-genome sequencing, polygenic risk scores, plasma proteomics and metabolomics, gut microbiome metagenomics, etc. However, their use and personalised choice of patients to whom to apply them, need a careful triage of criteria. Comprehensive diagnostic images and records could optimally be obtained, evaluating the biological age of complex biological organs and systems and other medical data.

Available data should be used to create individualised long term patients' programs, which take into account the individuals' health status, sex and age. Such data aggregation also enables creation of a digital twin which allows for in silico evaluation of the effectiveness of personalized interventions before they are implemented in real life. This approach enhances precision, reduces risk, and accelerates the optimization of longevity strategies.

Longevity medicine practitioners should create personalized recommendations and intervention programs with the support of a team of longevity medical experts in different fields of aging biology, gerontology and life sciences.

Presently, a significant gap exists in formally accepted international standards/guidelines for diagnosing or applying systematic validation of biomarkers of aging for clinical use (Herzog et al. 2025).

Diagnostic tests for longevity medicine rely on high sensitivity of assays. The diagnostic tools require accurate detection and quantification of even trace amounts of target biomolecules like hormones, metabolites, nucleic acid etc. Therefore, there is a necessity to adhere to internationally accepted medical laboratory quality and competence standards (e.g. ISO 15189 2022, or equivalent). This standard includes requirements for calibration, maintenance, accuracy, reproducibility, preventive maintenance, management responsibility, audits, document control, quality management system, etc.

Diagnostics in longevity clinics can involve an array of biochemical, molecular and genetic tests. In such instances, the molecular testing standards from the Clinical and Laboratory Standards Institute (CLSI, USA) can be helpful (Hall et al. 2011; Chen et al. 2012; Miller et al. 2018; Sheppard et al. 2020). CLSI guidelines related to workflow automation, interoperability of diagnostic data, point of care testing (POCT), remote access of data and statistical verification

tools can be helpful for diagnostic laboratories within longevity clinics. For longevity clinics in resource constrained settings it might be beneficial to refer to the World Health Organization (WHO) Laboratory Quality Stepwise Implementation (LQSI) Tool for establishing, maintaining and offering quality care in longevity clinics in such resource constrained settings (Roper 2014).

Even though longevity medicine is founded upon research of an extremely complex and in-depth nature, medical practitioners are frequently left uncertain as to the actions they can take for their patients in the present moment.

Whilst whole-body imaging and exome sequencing may seem like the ideal approach for every patient, this is often not feasible due to technical limitations (e.g. lack of specialists), interpretation bias (false positive and negative results), cost, and other patient-specific characteristics. To promote longevity and empower patients to achieve this goal themselves, a holistic approach is imperative. It is therefore recommended that the process be initiated with basic, research-based tests.

A pragmatic protocol for assessment, examination, and laboratory testing aimed at promoting longevity in primary health care should combine elements from international guidelines in geroscience, healthy ageing, and evidence-based longevity medicine (World Health Organization 2024; Department of Health – Abu Dhabi 2024; Mironov et al. 2024; Tavassoli et al. 2022; Bischof et al. 2021; Valdonė Alšauskė 2025). Assessment should be individualised and iterative, with initial baseline testing, followed by adaptation and repetition according to age, risk, and results (e.g., annual to biennial retesting). It is vital to recognise the significance of early detection and risk management in this context, as these factors are of greater importance than isolated disease screening.

### **3.1 Biomarkers of Aging**

Practitioners of longevity medicine should utilize the analysis of biomarkers of aging that have been shown to correlate with and predict aging health trajectory and mortality, and indicate the effectiveness of intervention for the improvement of health and functional capacity for the long term. In this regard, it should be emphasized that currently biomarkers of aging are not standardized, and currently there are no fully consensus-based or axiomatic biomarkers of aging. Many of the putative biomarkers of aging are still of investigatory nature. Examples under investigation include, but are not limited to:

- Molecular biomarkers, including routine blood and urine tests that can be used not only for general health assessments, but also as a part of aging diagnostics, including some biological aging tests, DNA methylation patterns (epigenetic clocks), telomere length and circulating proteins and metabolites associated with aging processes.
- Physiological biomarkers: These measure functional decline in various organ systems and include markers such as grip strength, walking speed, lung function and cognitive performance.



- Digital biomarkers: These are quantifiable physiological and behavioral data collected and measured using digital devices (such as smartphones, smartwatches, or wearables). These emerging non-invasive tools for continuous monitoring of health parameters include measures of cognitive capacity, physical activity, sleep patterns, heart rate variability and gait analysis.
- Imaging techniques, including MRI, up to skin and hair or posture analyses.
- Body composition: Body composition refers to the distribution of fat, muscle, bone and other tissues in the body. It is often expressed as the percentage of total body weight that consists of fat and/or lean body mass. Body composition offers numerous insights into health, fitness and nutritional status. Bioelectrical Impedance Analysis (BIA) is a technology that measures human body composition. Such technology quantitatively measures body composition through impedance that occurs when an electric current flows through the human body. Body composition analysis should also include the DEXA method (X-Ray densitometry) as a "golden standard" enabling the diagnosis of such age-related problems as osteoporosis and sarcopenia.

### **3.2 Biological age**

Biological age is a measure of how well or how poorly a person's body or body parts are functioning in comparison to the chronological age (Zhang 2023). Biological age scales are considered a more accurate predictor of health status and mortality risk than chronological age itself. Factors influencing biological age include genetics and epigenetics, in part due to lifestyle choices, environmental exposures and the accumulation of molecular and cellular damage over time. And as the field is evolving, there are many more experimental and commercial biological age tests becoming available, though their accuracy and reliability are still being studied.

### **3.3 Biomarkers of aging and additional evaluation criteria - general functionalities**

As virtually any biological and physiological parameter changes with age, and can potentially serve as a "biomarker of aging" there is a need to select the most informative, yet economical panels of biomarkers (Stambler 2017).

A biomarker of aging is a measurable characteristic that can be used to assess the aging process. Biomarkers of aging can be utilized to track the progress of aging, identify people who are at risk for age-related diseases and measure the effectiveness of longevity-promoting and healthspan-promoting interventions.

Yet, it should be understood that, at the present state of knowledge, designating an intervention as a longevity-promoting or healthspan-promoting intervention is difficult methodologically, as it would require long-term observations and evaluations or truly reliable methods of prediction, utilizing biomarkers of aging. Increasing the reliability of such evaluation and prediction methods is a vast task for the future.

There are many different biomarkers, currently utilized for the evaluation of the aging processes, including: Telomere length, DNA methylation, Proteome profiling, Lipidomics, Transcriptomics, Metabolomics, and many others.

The ideal biomarker of aging would be a simple, inexpensive and accurate way to measure the aging process.

- It must predict a person's physiological, cognitive and physical functions in an age-related way. In other words, it must predict the future onset of age-related conditions and diseases and do so independently of chronological age.
- It must be testable and not harmful to test subjects. For example, it could be a blood test or an imaging technique. It must also be technically simple so that most clinical laboratories could perform the test accurately and reproducibly without the need for specialized equipment or techniques.

Simply put, biomarkers should be simple and not very expensive to use. They should cause little or no pain or stress. And they must measure aging accurately.

Yet, no single biomarker of aging is perfect. Instead, a combination of biomarkers is often used to get a more complete picture of the aging process.

However, not everyone is convinced that biomarkers of aging actually exist. Some critics doubt that there is an underlying aging process at all (Peto and Doll 1997; Cohen et al. 2020; Gems et al. 2015). Therefore, there can be no marker for it. Some scientists believe that as people age, deleterious physiological processes can occur that may lead to cancer, heart disease, dementia or other diseases. These processes can overlap, but there is no single, underlying biological process driving them all. Critics also argue that aging doesn't occur at a single rate and therefore the rate of aging can't be measured (Anti-aging Guide 2009, Miller RA 2001; Nie et al. 2022). Different body functions can change at different rates over time. A person may lose muscle strength faster than their eyesight deteriorates. And there can be different reasons for the deterioration. For example, a person may lose muscle strength faster because he or she never had much strength to begin with. Despite these criticisms, the concept remains that aging takes place at a measurable overall rate. A goal for the scientific community is to find evidence-based and theory-based biomarkers and reason with the doubters.

### ***3.4 Examples of biomarkers of aging under investigation***

Studies on biomarkers of aging have looked for changes in cells, hormones, genes and even behaviors to find a predictor of the rate of aging. One target that has been studied is the central nervous system (consisting of the brain and spinal cord). Computerized tomography (CT) scans can be used to look for changes in the brain that may serve as biomarkers of aging. For example, the brain shrinks with age. This does not mean that brain cells necessarily die but rather that they become smaller in size and volume. Some research has been done to find out if

brain shrinkage in certain areas may underlie the changes in function that occur with age. So far, brain function and age have proved too complex to produce reliable biomarkers.

Age at menopause has been suggested as a possible biomarker of aging in women. One study showed that women who had early menopause (before age 44) had shorter lifespans than women who experienced menopause at ages 50 to 54 (Tom et al. 2012; Asslanaj et al. 2019). This suggests that ovarian function is related to the overall aging process but the mechanistic links for this require further study. Other possible biomarker targets include cell replication rate and immunological markers (Ferrucci et al. 2020; Yamaguchi et al. 2024; Zeng et al. 2024).

At the cellular level, a potential biomarker of aging may indicate the presence of senescence. Senescence is a condition in which old or damaged cells remain alive but cease to reproduce. This is an important tool in the body's ability to prevent cancerous tumors from developing. The older a person becomes, the more senescent cells he or she accumulates. Several markers of senescence in humans have been suggested as biomarkers of aging. On November 10, 2011, researchers at the Mayo Clinic published a study in the journal *Nature* showing that an accumulation of senescent cells may lead to age-related diseases, at least in animals. By removing most of these cells from several organs (body fat, eye and skeletal tissue) of lab mice, the investigators were able to significantly delay the onset of these diseases or stop their progression if they had already become established. This and subsequent studies of cell senescence represent potentially fruitful areas for future search of true biomarkers of aging (Carver et al. 2024; Baker et al. 2011; González-Gualda et al. 2021).

The list of examples can be greatly expanded, and it remains challenging to select the most informative, yet economic and convenient biomarkers.

### ***3.5 A focus on functional resilience biochemistry: considering biomarkers with reference to recovery capacity***

While much of longevity research has focused on static indicators of aging, there is growing recognition that how well the body bounces back from stress may be a meaningful predictor of long-term health and vitality. This exemplifies self-referential, rather than comparative evaluation criteria.

In this view, aging is not only the accumulation of biological damage but a slow erosion of the body's capacity to maintain equilibrium under pressure. This concept, often referred to as biochemical resilience, invites a shift from solely measuring degeneration to assessing adaptive performance (Ferrucci et al. 2020).

A prime example of this lies in the glutathione system. Reduced glutathione (GSH) plays a vital role in managing oxidative stress, while its oxidized form (GSSG) signals that the body is responding to such a challenge. The GSH:GSSG ratio serves as a practical measure of redox homeostasis. But beyond the ratio at rest, it is the speed and magnitude of recovery following oxidative stress that may be more revealing. In young, healthy individuals the ratio is typically

>100:1, this ratio declines with age and metabolic health, revealing compromised glutathione recycling and thus providing an early marker for impaired homeostasis (Tkaczhenko et al. 2025; Jones et al. 2000).

A healthy young individual, when exposed to acute stress—be it physical exertion or environmental toxin exposure—can often re-establish redox balance within hours. In contrast, delayed recovery times in older or metabolically compromised individuals may expose underlying vulnerability well before clinical symptoms arise. The delayed recovery of this ratio after a stressor is imposed reflects impaired glutathione recycling and loss of resilience (Wu et al. 2004) and the analysis gives us a redox recovery index (Pizzino et al. 2017).

Another central player in cellular adaptation is the  $\text{NAD}^+/\text{NADH}$  ratio.  $\text{NAD}^+$  acts as a coenzyme in energy metabolism and is essential for DNA repair and mitochondrial function. While its levels are known to decline with age, it's increasingly clear that the dynamic range of  $\text{NAD}^+$  fluctuations—how readily the body generates or recycles  $\text{NAD}^+$  in response to metabolic shifts—is a better proxy for vitality than total concentration alone (Yoshino et al. 2018).

Practically speaking, one might observe how this ratio changes during fasting, moderate exercise, or following a nutrient-dense meal. The capacity to flex between energy sources—glucose, ketones, fatty acids—while preserving redox balance offers a snapshot of one's metabolic resilience. A Metabolic Flexibility Score or MetFlex Score could be constructed from glucose, insulin, and ketone levels tracked over a fasting–refeeding cycle (Goodpaster et al. 2017). A Mitochondrial Resilience Marker might include  $\text{NAD}^+/\text{NADH}$  shifts alongside heart rate variability and lactate clearance after exertion (Thomas et al. 2004; Hoshi et al. 2017; Glancy et al. 2021).

These profiles could contribute to a dynamic picture of aging and should be practically considered for inclusion in assessment panels in healthy longevity medicine.

### ***3.6 Developing and implementing biomarkers of aging - a critical research task***

In the context of longevity medicine implementation, the main research questions are to establish that “longevity medicine works” and, even prior to that, to establish “what it means that the longevity medicine works”. By its basic premise, longevity medicine should use a variety of interventions to target the underlying causes of aging. These interventions may include: lifestyle changes, such as diet, exercise and sleep; supplementation with nutrients and other compounds; pharmacotherapy with drugs that target specific aging pathways, other interventions. The specific interventions that are used will vary depending on the individual's age, health status and goals.

Yet, in order to target causes of aging, it is necessary to be able to measure those causes. It is not possible to treat or prevent something that it is impossible to measure or diagnose. In this regard, the research of biomarkers of aging aims not only to predict aging health trajectory, but mainly to establish the degree of potential effectiveness of longevity medicine interventions.

Developing and applying personalized panels of the most informative, predictive and at the same time economically feasible and convenient biomarkers of aging is necessary for creating personalized therapeutic programs for healthy longevity, taking into considerations the particular circumstances, predispositions and risks of particular patients, individually and in combinations (Stambler 2017; Blokh et al. 2023). Yet, prior to selecting a personalized intervention, there is a need to conduct a more general assessment of potential therapeutic interventions as a type (e.g. a particular type of geroprotectors or physical therapy). For that purpose, more general evaluation criteria are needed. A primary criterion should be the proven effects of the therapy on all cause mortality. As the term “healthy longevity medicine” implies, its goal is to enable people to live both longer and healthier. Hence the value of the prolongation of life, the decreasing mortality, extending the life-expectancy and lifespan, should be explicitly acknowledged, in addition to improving the quality of life, intrinsic capacity and healthspan. Hence, reducing all cause mortality, the benefits for survival, should be considered among the primary evidence of the effectiveness of particular putative “longevity therapies”. In this context, evidence from biomarkers provides added value as an indicator and predictor of aging processes, and related diseases, frailty, disability and mortality.

The evidence for the effectiveness of longevity medicine is still emerging. However, there is a growing body of research that suggests that longevity medicine can help people live longer, healthier lives (Martinovic et al. 2024). While the evidence for the effectiveness of longevity medicine is still nascent, the early results are promising. Longevity medicine interventions have the potential to revolutionize healthcare by helping people live longer, healthier, more productive and fulfilling lives (Falshaw et al. 2024).

## **4 Interventions**

### ***4.1 Longevity interventions - general considerations***

Interventions for healthy longevity extension are just emerging. They may utilize personalised lifestyle intervention such as physical, cognitive or anti-stress exercises, red light or cryotherapy, hyperbaric oxygen chambers, hypoxic training, sauna etc., increasing health and general wellbeing, based on the best available evidence of efficacy and safety. The kinds and numbers of interventions, and their combinations, can be virtually unlimited, including nutritional supplements, social and environmental interventions (such as social prescribing, nature based healing), lifestyle modification interventions etc. These interventions may or may not be effective as a standalone intervention, but they can complement pharmacological interventions to enhance longevity.

Longevity medicine practitioners may create healthy dietary programs and other programs for hormone optimization therapies, administration of vitamins, supplements, platelets rich plasma, anti-aging pharmaceuticals, cell therapies and senolytics. However such programs should be clinically and regulatorily approved, either for treatment based on the best available evidence or, in some cases, for experimental use.

Longevity medicine practitioners must have the ability to develop and/or lead a health journey and intensive and ongoing health promotion and treatment programs, with skills in wellness and personalized lifestyle medicine, with the ability to assess, plan, intervene, monitor and measure results clearly and effectively (Kelly et al. 2023; Kelly et al. 2024).

The practitioners may consider applying advanced, scientifically based, anti-aging strategies, utilizing approved experimental and treatment protocols, that may include novel therapies such as stem cells, exosomes (Rudnitsky 2025), secretome, senescent cell removal (Saliev et al. 2025), gene-based treatments (Wang et al. 2025), platelet-rich plasma or anti-aging and other drugs (Guarente et al. 2024), supplements infusions, various geroprotective drugs (Kulkarni et al. 2022) through personalised programs.

It should be emphasized that, with the current state of knowledge, there **are no proven interventions that will guarantee with certainty the extension of longevity or healthy longevity**. Designating interventions as “longevity interventions” is methodologically difficult, given the limited evidence, especially for the long term. The interventions may only putatively assume effects on the actual lifespan or healthspan. Controversies may arise with regard to practically any intervention, either as a class or particular case applications. Therefore, collecting data and conducting additional studies is paramount, emphasizing large-scale, long-term randomized clinical trials, longitudinal observations and metaanalyses. In the cases evidence of effectiveness for the long term is limited, the practitioners should emphasize the experimental and forward-looking nature of the interventions, that are based on the best evidence available so far, enabling future research.

To practice these advanced treatments the medical specialists should be experienced, recognised and certified in these areas and have obtained the necessary legal practice permissions from the governmental authorities.

An explicit aim of longevity medicine is not only to optimally utilize the existing routine treatments, but also to inform, pave the way toward and facilitate the emergence of new advanced, evidence-based treatments that can significantly enhance the human healthspan and lifespan.

Some of the Longevity Medical Services already have a strong evidence base and are being implemented, others are only developing such an evidence base and should emphasize their research status, with appropriate informed consent. Of course, many controversies remain and further research is still needed to validate the effectiveness of particular therapies and their personalized regimens. These interventions may include several techniques that can be tailored to meet unique health needs and goals and ensure the best outcomes following accredited up-to-date medical protocols by recognized scientific associations. These may include:

- Neuromodulation
- TAS (transdermal electrical auricular stimulation (Auriculotherapy under evidence-based medical protocols e.g., NADA)

- PEMF (Pulsed Electromagnetic Field Technology)
- Photobiomodulation (Red Light Therapy)
- Medical Oxygen-Ozone Therapy for optimal application in clinical medicine following the evidence-based SIOOT protocols and recommendations
- Hyperbaric Oxygen Therapy and Hypoxic Training (the “hyperoxic hypoxic paradox”)
- CES (cranial electrical stimulation)
- tDCs Transcranial direct current stimulation (tDCS)
- rTMS (repeated transcranial Magnetic Stimulation)
- Transcranial Photobiomodulation (tPBM) Treatment (LLLT)
- Gyromagnetotherapy Diabetes medical Treatment
- Advanced Glycation End Products (AGEs) Risk Assessment and Therapeutics using AGE breakers
- Chelation therapy
- d-ROMs and PAT Test Assessment of Oxidative Stress and Oxidation-modulating supplementation
- Glutathione and NADH Testing, Analysis and Personalized Therapy
- Peptides and Peptide Bioregulators, Neuro-cognitive enhancement and rehabilitation/Neurogym Brain Training Neurogenesis
- Genetic and Epigenetic Screening and Therapeutics
- Gut Microbiome Testing, Screening, Health Dashboard Analytics and Personalized Therapeutics
- Various other putative geroprotective drugs (e.g. metformin, rapamycin/rapalogs, SGLT-2 inhibitors, acarbose, methylene blue, etc).

However, in this manuscript, **we do not advocate the use of those or other specific interventions in clinical care**, but rather provide examples that are currently proposed by researchers in the scientific literature. It should be noted, that under certain evidence-based medical protocols, Medical Oxygen-Ozone Therapy, Photobiomodulation and other means – alone or in combination – may induce Mitohormesis, a term used to define a biological response where the induction of a reduced amount of mitochondrial stress leads to an increment in health and viability within a cell, tissue or organism. For this reason, such techniques are now approved for the field of regenerative medicine (Hamblin et al. 2016; Fallahi et al. 2023; Frankowski et al. 2025; Franzini et al. 2022; Franzini et al. 2025).

The identification and description of pathways and molecules implicated in the beneficial effects of mitohormesis will help understand the complex balance between death and survival in the face of mitochondrial damage and will open new fields of therapy aimed at improving health in humans (Barcena et al. 2018).

#### ***4.2 Elements of Lifestyle Medicine***

Longevity medicine should involve not only specific biomedical interventions targeting mechanisms of aging, but should also holistically address the subjects as human beings,

including their life course, lifestyle and environment, by incorporating elements of Lifestyle Medicine (LSM).

Lifestyle Medicine (LSM) competencies for all professionals (Lianov et al. 2010; Lianov et al. 2022; Rippe et al. 2018) should include:

1. Understanding the foundations of LSM, including attitudes, knowledge and skills:

- Introductory LSM knowledge, including its role in overall health care.
- Role of practitioner's personal health, self-care and community building skills, including their importance in LSM interventions.
- Health behavior changes, knowledge, attitudes and practice.
- LSM clinical skills and processes, including emphasizing the spectrum of treatment algorithms for chronic diseases and the value of its application in various health care settings.

2. Understanding our patients' stories, and their role in lifestyle choice and interventions:

- The role of emotional and mental health, including assessment and interventions.
- The role of connection and relationships in health, including assessment and interventions.
- The significance of social determinants of health and their role in health behaviors.
- The significance of environmental health and its role in health behaviors.

3. Clinical skills and their application in individual, group and team-based patient care settings:

- Nutrition science, assessment and prescription.
- Physical activity science, assessment and prescription.
- Sleep and rest science, assessment and prescription.
- Toxic substance exposure (such as tobacco and nicotine) science, assessment and intervention.

#### ***4.3 Elements of Digital Health Technologies***

Longevity clinics should utilize and promote remote monitoring, telemedicine and the broader types of digital health technologies. Certified Wearable devices like smartwatches, fitness trackers and biosensors continuously monitor vital signs, activity levels, sleep patterns and other health metrics. If longevity clinics are involved with recommending and/or delivering wearable devices for use, then care should be taken to recommend products which are privacy compliant (like GDPR/HIPAA), follow quality and safety standards (like ISO 13485: 2016 for QMS; ISO 14971: 2019 for risk management in medical devices; IEC 60601-1: 2024 for safety and essential purposes of medical electrical equipment etc.). In the US, manufacturers must comply with FDA 21 CFR Part 820 Quality System Regulations (QSR) as a Current Good Manufacturing Practice (cGMP) guideline (US FDA 2024). In the EU, under Medical Device Regulation (EU) 2017/745, medical wearable devices require CE marking implying compliance with EU norms for safety, health and environmental protection standards (European Parliament and the Council of the European Union 2017).



Artificial intelligence algorithms can analyze large volumes of data collected from these devices to identify potential health issues or trends. Patients may have access to a user-friendly mobile app that displays their health data, offers personalized recommendations and facilitates communication with the clinics' healthcare team. Regular telemedicine consultations via video conferencing allow for discussion of the patient's progress, addressing concerns and adjusting treatment plans as needed. The clinic, where practical, should implement a "clinic at home" concept, enabling patients to perform basic diagnostic tests (e.g., blood pressure, glucose levels) using at-home devices that automatically sync data with the clinic's system.

#### **4.4 Diversity of interventions**

The number of potential interventions can be large, based on various aging biology mechanisms (e.g., inflammation, senescence, mitochondrial dysfunction, etc.), and with various levels of evidence and implementation, from *Experimental* (early-stage, unapproved, or theoretical interventions) through *Investigational* (in pilot studies or small-scale trials) through *Emerging* (with strong preclinical and early clinical evidence) to *Established* (supported by RCTs or systematic reviews, standard practice), and with various clinical use contexts (based on where the intervention is currently being used, such as mainstream clinics, wellness centers, research only, etc.).

For actual approved clinical interventions, the classification may be modified, to include: *Investigational* (with patient's consent to receive an experimental treatment within GCP-clinical trials only), *Established* (approved by the FDA, EMA or other national regulatory equivalents), *Established* for a different indication, but can be used in an off-label setting (not specifically regulatorily approved, but having a strong RCT basis for particular relevant indications).

This diversity represents an ever expanding and updating work in progress in developing healthy longevity medicine.

## **5 Administrative and regulatory requirements for longevity medicine**

### **5.1 Eligibility**

The contingent of longevity medicine may include adults capable of informed consent. In most legal frameworks, these are Individuals aged 18 years and above. However, in rare circumstances the services of the clinic may be offered to individuals below 18 years of age, in case such clinic services can benefit the individual. The consent for treatment can be sought from the underage individual verbally after explaining the pros and cons of the treatment by the clinic facility in charge. Additionally, an assent can be requested from the Legally Authorized Representative (LAR) of the underage individual to perform the necessary treatment. These rare circumstances in underage individuals can include but are not limited to genetic or congenital conditions that accelerate ageing (e.g. Hutchinson-Gilford Progeria Syndrome, Werner syndrome etc.), chronic conditions that accelerate ageing biologically (e.g. Juvenile Diabetes, Lupus etc.) and individuals with needs for cognitive enhancements. A multidisciplinary

internal committee can be formed by the longevity clinic to assess such circumstances on a case by case basis and determine the appropriateness of treatment through a consensus based approach.

Adults will be included, regardless of pre-existing health conditions, unless they are receiving palliative care or they have a severe cognitive impairment that impedes their ability to comply with safety precautions. Severe cognitive impairment is defined as a condition that substantially limits a person's capacity to understand, process or follow necessary safety protocols. A capacity to consent assessment should be conducted by a licensed psychologist or mental health services nurse with such individuals prior to further treatment considerations in the longevity clinic. In such cases such persons enter the field of palliative treatment and rehabilitative medicine methods' implementation.

Individuals must not be in situations that compromise their safety or the appropriateness of the services provided. This includes ensuring that their health condition (pregnancy, severe cardiovascular diseases, ongoing oncology treatment, other severe illnesses in the past 3 months or less) or environment, do not present risks that cannot be managed safely within the longevity program suggested. An initial patient history form should be offered to the individuals seeking treatment in the longevity clinic to capture their medical history. The facility in charge should ascertain the suitability of the individuals for the services provided by the clinic. Standard Treatment Protocols (STPs) should be formulated or adapted to assist the facility in charge to make such decisions. An internal Quality Assurance Committee (QAC) should be formed to formulate and approve these standard treatment protocols along with assuring continuous monitoring and periodic upgradation of these standards (Cánovas et al. 2009). In case of a violation of the protocol or any unforeseen circumstances, a Root Cause Analysis (RCA) should be conducted by this committee to identify the source of the unforeseen event and corrective actions should be taken to avoid future mishaps (Brook et al. 2015). Individuals seeking treatment in the longevity clinic, post-assessment of medical history, should be offered a treatment consent form which should detail about the procedure to be undertaken, potential treatment risks, privacy and confidentiality of personal data and any questions raised by the individuals in relation to the treatment should be clarified by the facility incharge. Additionally, individuals seeking treatment should be made aware of the mechanism for service feedback, grievance redressal mechanism and post-treatment counselling services.

Patients with stable chronic conditions still should be receiving preventive, restorative and longevity focused strategies as these may improve with better outcomes in addition to (not replacing) traditional/mainstream management. Individuals must not have acute illnesses or injuries requiring immediate medical attention, as these conditions necessitate urgent care beyond the scope of such longevity programs. In situations where during the process of treatment the individual faces any acute complications, the clinic should initiate an immediate emergency response system with referral pathways leading to nearby secondary/tertiary care hospitals (Sherman and Romfh 2003). The emergency response system should be formulated and approved in consultation with the internal QAC. For standalone clinics, the local

secondary/tertiary care hospitals should be communicated about such systems to ensure coordinated emergency clinical management and referral pathways.

Patients undergoing major treatment by medical specialists should be included within the agreement of the treating medical specialist.

## **5.2 Health Care Facilities**

Health Care Facilities should be accredited by nationally recognized bodies or international organizations involved with quality of care accreditation. These facilities offer healthcare services to individuals seeking care. A longevity clinic can be classified as a healthcare facility as a stand alone clinical establishment or be a sub-set service provider in existing healthcare setup. Such setups can include public, private and hybrid (Public-Private Partnership) models of care. In terms of level of care, longevity clinics can be part of primary, secondary and tertiary care facilities. While specific standards or guidelines for longevity clinics are not yet well established within existing healthcare frameworks, there are relevant accreditation standards that can be referenced to help ensure high-quality care. Joint Commission International (JCI) is a global leader in healthcare quality and patient safety accreditation. JCI accreditation is internationally recognized as a benchmark of excellence in healthcare. It offers accreditation programs for primary care, ambulatory care and hospitals, any of which may be applicable to healthcare facilities that incorporate longevity clinics (Joint Commission International n.d.).

Incorporating longevity clinics in public funded healthcare facilities has been promoted in a recent study which has potential to improve equitable access to care for all populations irrespective of socio-economic status (Bonnes et al. 2024). Moreover, publicly funded medical hospitals and institutions can promote vital cross-sectoral collaborations in longevity research by enabling the application of large clinical datasets for advanced data analytics and personalized management plans. However, barriers to implementation remain prominent with lack of specialised oversight and guidelines/standards for incorporation of longevity clinics in public funded healthcare facilities. To ensure widespread access to longevity-related treatments across both private and public healthcare services, public healthcare policies should place a greater emphasis on comprehensive health insurance coverage.

In a recent study, a comprehensive overview of different service delivery models for longevity clinics has been reported (Mironov et al. 2024). The review has presented a synthesized framework for an effective longevity clinic keeping research and development at the core of clinic operations. The framework centers around the concept of establishing an analytical center within the longevity clinic, serving as a point for advanced clinical data analysis and enabling a continuous research driven longevity clinic development. Opportunities could be explored to replicate such models of care for longevity clinics incorporated within healthcare facilities.

Health Care Facilities providing healthy longevity medicine clinic services shall adhere to the state's Laws, clinical establishment act, standards and regulations for providing healthy longevity medicine clinical services.

### **5.3 Staffing requirements**

All Health Care Practitioners should hold an active license within their scope of practice.

Healthy longevity medicine clinical service should be provided by a multidisciplinary team including, at a minimum, the following:

- *Physicians*: Physicians are required to have finished their specialty training and worked as senior physicians prior to joining the healthy longevity clinic. Physicians must have experience in a related field or have completed formal training in healthy longevity medicine, lifestyle medicine and disease prevention. Sufficient expertise and a comprehensive understanding of the underlying biological processes of aging are recommended.

- *Registered Nurses*: Registered nurses are responsible for administering treatments, providing patient education and assisting with medical procedures.

*Allied health professionals, such as:*

- *Dietitian / Nutritionist*: These provide personalized dietary plans promoting optimal nutrition for healthy longevity.

- *Physiotherapists and exercise physiologists*: These practitioners deliver tailored exercise programs to improve mobility, muscle strength and overall physical well-being.

- *Pharmacists*: These specialists assess drug-drug and drug supplement interactions. They can also assist with optimization of prescription medication regimes for medications that may be appropriate for a medical diagnosis and demonstrate additional anti-aging benefits.

- *Clinical Psychologists* to assist with cognitive, mental and emotional assessments and support.

- *Health Coaches* to assist clients/patients in their journey to encourage, troubleshoot and occasionally offer insight into how clients/patients may plan to achieve their goals.

- *Additional team members*: Each facility may have additional team members to help their clients/patients achieve their goals. These team members may include a genetic counselor to provide comprehensive pre- and post-genetic testing counseling, including risk assessment, education and guidance on test results and their implications, sports therapist to achieve specific sports goals, and more quality of care. The laboratory staff should be an appropriate skill-mix of pathologists, biochemists, phlebotomists and lab technicians. In a longevity clinic, lab technicians should receive training on assessment of aging bio-markers and complex molecular methods of diagnostic assessments like ELIZA tests, CLIA tests etc. For such purposes of personnel selection, competency requirements and necessity for continuing education, 'Clause 6.2: Personnel' in ISO 15189:2022 can be referred to by the longevity clinic.

Additionally, housekeeping and support staff play a crucial role in maintenance and upkeep of the clinic. The housekeeping staff should be trained in waste segregation, infection control and

emergency response system protocols. Orientation training must be offered to such personnel to ensure older people/vulnerable persons seeking treatment are treated with dignity. Furthermore, keeping the clinic clean and safe remains important for housekeeping staff as many individuals seeking care in longevity clinics might be immunocompromised or aged people.

#### ***5.4. Medical personnel - general considerations***

The medical personnel providing healthy longevity medicine services, should create personalized intervention programs with the support of a team of longevity medical experts with up-to-date multidisciplinary knowledge in medical technology, genetics, epigenetics, proteomics, aging biology, life sciences generally and geroscience in particular.

The medical staff must follow the discoveries and innovations in medical longevity research and practice in order to consider developing and applying these in individualised patient interventions, under appropriate approval processes, including experimental or investigational applications.

These may also include new regenerative therapies, such as stem cells, gene technologies, and plasma infusions. To practice these advanced treatments, the medical staff should be educated, experienced and have obtained the necessary legal practice permissions from the governmental authorities.

Healthcare professionals should obtain at least 10 CME (Continuing Medical Education) credits in the field of healthy longevity medicine on an annual basis, which can be obtained either virtually or in person.

Healthcare professionals should adhere to ethical principles and guidelines for all treatments and interventions, including experimental and investigational interventions, ensuring client/patient safety and obtaining informed consent.

It is recommended that healthcare professionals practicing healthy longevity medicine maintain membership in a reputable professional society related to healthy longevity. This helps promote ongoing learning and networking in the field.

#### ***5.5. Non-Medical personnel - staff specifications and general considerations***

The non-medical personnel play a crucial role in the care process by ensuring smooth care transitions and better user experience. Primarily, assuming that non-medical personnel might have limited exposure to the regular activities of the longevity clinics, an orientation program to ensure seamless integration with the clinics regular activities should be organized prior to assigning them to their respective job profile. The suggested orientation program should include sensitization on existing quality care protocols, the procedures of the clinic's emergency response system, guidelines for ensuring privacy and confidentiality of clinical data, principles of respectful and dignified engagement with care-seeking individuals, and a clear overview of the

clinic's organizational and management structures. During the initial period of employment (typically 3-4 months), a mentor can be assigned to the newly joined staff to offer hands-on learning on the regular activities and management practices of the clinic. The longevity clinic should ensure that the personnel remain up to date with the latest regulatory norms and care practices associated with the clinic through training, workshops, certification courses, personalized learning materials and, possibly, periodic seminars to enhance peer to peer learning. Annual human resources performance and competency review should be part of the standard clinical protocol to support continuous quality improvement initiatives and workforce optimization. The process should assess staff performance, training needs, role alignment and professional development goals of the personnel.

Furthermore, the non-medical staff plays a significant role in supporting the clinical services of the clinic. The suggested roles and responsibilities of non-clinical staff are outlined below:

- **Facility Incharge / Clinical Administrator:** The personnel should offer oversight on the day to day activities of clinic operation, resource optimization and human resources work schedule. The facility in charge should assist with onboarding of new staff, coordinate with vendors and suppliers for clinic's resource upkeep, monthly forecast of materials requirement of the clinic and ensure that standard protocols approved by the internal QAS are adhered to by the clinic. The compliance with regulatory standards, clinical establishment rules and accreditation with existing care norms should be part of the job profile. The personnel should have an academic background in healthcare management or related subjects with minimum 3 years of work experience in healthcare organizations.
- **Research and Documentation Specialist:** The research staff (auxiliary to the physicians conducting research) should be part of designing new therapeutic clinical trials and supporting ongoing clinical trials of the clinic. The personnel should ensure ethical compliance of the trials in alignment with the clinical trials regulations of the country. As a part of outreach activities, the research specialist should organize conferences and community health campaigns while maintaining the clinic's relationship with professional societies. The research specialist should ensure completeness and correctness of the patient history forms and consent forms submitted by the individuals seeking care. The personnel should be involved with publication of scientific papers in academic journals, developing educational content for individuals seeking care and conducting data analysis relevant to the clinic. The personnel should have work experience in a related domain and an academic background in life sciences or related topics with competency in health education and statistical analysis.
- **Client Relation/Front Desk Executives:** The role of the client relations/front desk executives should be to ensure a seamless service experience for individuals seeking treatment in the longevity clinic. The personnel should be involved with new patient registration, appointment scheduling and basic patient orientation with services of the clinic. Front desk executives should ensure confidentiality of individual information and treat individuals seeking care with dignity. The personnel should have work experience in

a similar clinical setup and an academic background in health sciences or similar domain.

- **IT & Clinical Data Manager:** The remote patient monitoring infrastructure along with design and maintenance of the mobile app based appointment booking services should be managed by the IT & Clinical Data Manager of the clinic. The personnel plays a crucial role in managing the Electronic Health Records (EHR). The personnel should ensure that patient information is collected in compliance with privacy regulations (like GDPR/HIPPA), utilizing a secured two-way data encrypted system. Data backups should be performed regularly to safeguard against data loss due to unforeseen events. Furthermore, patient information should be easily accessible to clinic staff and wider members of the health system. The IT & Clinical Data Manager should ensure seamless data interoperability between devices in the clinic and monitor that interoperability protocols are aligned with existing global standards like Fast Healthcare Interoperability Resources (FHIR®). The personnel plays a crucial role in managing Electronic Health Records (EHR). The personnel should have work experience in a similar field of work and an academic background in Information Technology (IT) or similar domain. Additionally, professional certifications in project management (like PMP® or PRINCE2) and data privacy (like CIPP, CIPM) can be advantageous for such job roles.
- **Finance Manager:** The staff manages the financial issues pertaining to the clinic. A daily log of expenses and deposits are maintained by the Finance Manager. Personnel shall play a key role in forecasting the clinic's annual budget and shall be responsible for ensuring timely renewal of clinical establishment licenses, as well as the regular submission of tax filings and related statutory compliances. Additionally, the personnel should offer transparent communication to the patients on charges related to treatment and possible payment modalities in circumstances where health insurance does not support treatments at the longevity clinic. The personnel should have work experience in a similar field of work and an academic background in financial management or similar domain.

## **5.6 Referrals**

Referrals to a Healthy Longevity Medicine Clinic may be made by primary care physicians, all medical specialists (including but not limited to geriatricians, cardiologists, endocrinologists and other medical specialists), as well as licensed allied health professionals such as dietitians, physiotherapists, occupational therapists, psychologists, etc. This ensures that patients receive comprehensive care and that referrals come from a wide range of healthcare providers who are qualified to assess the patient's health and longevity needs. Patients may also self-refer for such services.

Referrals should include the following information: identification, reason for referral and supporting information (e.g. medical history, medications, allergy, functional assessments, diagnostic test results and other relevant information).

Individuals seeking to optimize their health, improve fitness and enhance physical performance and longevity, as per the stated eligibility criteria, may directly access licensed longevity clinic facilities without requiring a referral. The referral system can be both paper based and through an interoperable privacy compliant (like GDPR/HIPAA) online interface which is accessible to medical specialists and licensed allied health professionals. To increase uptake of longevity clinics among the general population, access can be improved by expanding the number and distribution of clinics. It is also important to ensure equitable non-discriminatory care and include longevity clinic services in health insurance schemes. Implementation of such steps will aid progress in expanding Universal Health Coverage (UHC) for people seeking care (Evans et al. 2012).

### ***5.7 Patient and physician protection***

Patient protections must be ensured in longevity medicine, with regard to all patients rights, as well as their safety. We fully agree with the statement that “countries with gaps and areas of interpretive uncertainty in legislation related to stem cells, exosomes and other regenerative medicine products should develop and enforce more comprehensive regulatory structures” (Turner et al. 2023). There is thus an urgent need to improve education and clarify regulations in such countries to protect patients (Fujita et al. 2024; Asadpour 2023). Failure to do so may lead to disastrous outcomes, potential severe complications and even death (Fujita et al. 2024).

There is an urgent need to develop regulations to protect patients from serious risks associated with interventions based on little or no scientific evidence and to ensure that adverse events are reported to regulatory agencies when they occur. Nevertheless, such regulations should not impede the development of clinical research.

Under such conditions, products used under research purpose should apply to the local governmental Research Ethics Committee or equivalent in order to ensure:

- 1) Contribution to safeguarding the dignity, rights, safety and well-being of all actual or potential research participants.
- 2) Provide independent, competent and timely review of the ethical aspects of proposed studies.
- 3) Be responsible for carrying out the review of research proposals before the commencement of the research.

At the same time, longevity physicians and scientists should be protected to enable them to do their work in security and good faith. Conditions should be created that will not disincentivize them from innovation and undertaking complex study and intervention.

### ***5.8 Inclusion in longevity research***

Longevity medicine is essentially a research-based and research-coupled enterprise. Hence facilitating medical longevity research is of vital importance. Among the conditions for producing valid, widely applicable as well as personalizable results in diagnosis and treatment, wide and



diverse inclusion of research subjects must be ensured, ideally including all ages, genders, races and ethnicities, and socioeconomic statuses.

In particular, the inclusion of women in longevity research is critical. Longevity medicine cannot fulfill its promise without a deep understanding of sex-based biological differences in aging. Although women generally live longer than men, they endure more years with chronic diseases and disability in late life (Austad and Fischer 2016). Yet geroscience research and clinical trials have historically often overlooked these differences, perpetuating a gender gap in knowledge and care. Women's hormonal, immune, and metabolic systems follow distinct aging trajectories, especially around menopause. The cessation of ovarian estrogen production impacts multiple tissues—brain, bone, cardiovascular system, and metabolism—and understanding these shifts is vital to designing effective interventions for older women (Muka et al. 2016). Moreover, population studies show that early menopause ( $\leq 44$  years) is associated with reduced life expectancy and higher cardiovascular and all-cause mortality compared to menopause at 50–54 years (Asllanaj et al. 2019). This indicates that ovarian function decline marks accelerated somatic aging. To close this gap, there is a need for systematic inclusion of women in all gerodiagnostic and gerotherapeutic clinical trials; sex-disaggregation of aging biomarkers (epigenetic clocks, telomere length, proteomic profiles); priority research on female-specific mechanisms, such as ovarian senescence, female immunosenescence, post-menopausal mitochondrial resilience; development of diagnostic panels and intervention protocols tailored to female biology. Ignoring these differences undermines not only equity but also the efficacy of emerging therapies. Advancing our understanding of female aging biology is thus a prerequisite to understanding—and ultimately delaying or reversing—aging in our species.

Another critical category that must be included in longevity research is older subjects. At the national level, for over three decades, the regulatory authorities of the EU, US and Japan have struggled to obtain special consideration for older patients in the research, development and application of medical treatments, to involve elderly subjects in all clinical trials, and to establish criteria for treatment efficacy and safety specifically for older persons. Thus, in 1993, “The International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)” issued the “Harmonized Tripartite Guideline E7” (recommended for adoption in the EU, US and Japan) regarding “Studies in Support of Special Populations: Geriatrics”. This guideline posited the general principle that “Drugs should be studied in all age groups, including the elderly, for which they will have significant utility” (US FDA 2012). Still, this basic requirement has not yet become an overwhelming practice, while comprehensive criteria for the special medication needs of older patients, in particular the efficacy and safety criteria for older persons, are still deficient or even lacking in many studies. These basic requirements must be implemented in longevity medicine research and practice. As it is often difficult to show clinical benefits in older frail subjects, such subjects are frequently and unjustifiably excluded from medical research (Stambler 2017; Stambler 2025). Yet, they must be included in longevity medicine research to provide an inference of actual benefits for healthy longevity.

## **5.9 Sharing of Health Data**

Researchers and longevity medicine practitioners should strive that data of patients should be shared after anonymisation or pseudonymisation each time this is legally and technically possible and permissible. New therapies and good practices should also be shared as well as genomic data. Sharing of data can improve the interoperability, standardization and dissemination of the most evidence based, safe and effective interventions. Clinical health data of individuals are considered as sensitive information in the majority of the global privacy regulations. Health data should be shared under compliance with existing data privacy regulations like GDPR/HIPAA to ensure privacy, security and confidentiality of data (McMahon and Lee-Huber 2001). For longevity clinic laboratory specific purposes, 'Clause 4.2: Confidentiality' in ISO 15189: 2022 can be referred to by the IT/data manager. Data interoperability norms should be in lines with globally accepted standards like Fast Healthcare Interoperability Resources [FHIR®-HL7®] (Vorisek et al. 2022).

The primary goal of longevity medicine is to extend the “healthspan” - the period of life during which a person is generally healthy and free from severe disease or disability. In this context, developing health data biobanks, oriented toward geroscience applications, represents a critical strategy. Biobanks not only accelerate the development of knowledge and innovation across the longevity sector but also hold significant value for individuals. Longitudinal data collection allows for tracking subtle health changes over time and helps establish personalized baselines (“set points”). Deviations from these individual set points can serve as early warning signals, potentially identifying health deterioration before traditional risk factors or clinical symptoms emerge. This proactive approach is a cornerstone of precision and preventive medicine aimed at longevity.

## **5.10 Cultural adaptations**

Providers of longevity medicine services should be sensitive to cultural variations. “Personalization” concerns not only biological characteristics, but also social and cultural characteristics, with reference to such aspects as communication style, work ethic, decision making, and time management.

*Communication style:* People from some countries may have more direct communication styles, while others may prefer indirect language or avoid confrontation. This can impact how team members give and receive feedback, resolve conflicts and share ideas.

*Work ethic:* People from different countries may approach work and productivity differently. Some cultures may value long hours and dedication to work, while others may prioritize work-life balance and taking breaks throughout the day.

*Decision-making:* In some cultures, decisions are made by a single authority figure, while in others, decisions are made by consensus or after extensive discussion. This can impact how team members make decisions and how they approach problem-solving.

*Time management:* Cultural differences may exist in how people approach time management and deadlines. Some cultures may prioritize punctuality and meeting deadlines, while others may have a more flexible approach to time.

Between the particular cultures and milieus, the goal of healthy longevity medicine remains the same, to optimize healthspan and lifespan, prevent aging-related diseases, and ensure the highest quality of life in all ages.

## **6 The Future of Longevity Medicine**

### ***6.1 Increasing accessibility***

Continued advancements in comprehensive, non-invasive diagnostics, innovative gene therapies, stem cell therapy, 3D bioprinting of biomaterials and organs, medical nanotechnologies, biotechnological and artificial intelligence medical applications, are unavoidably accelerating the translation process of the innovative technologies to the clinic. This will position longevity medicine, with its proactive and preventive approaches, increasingly close to mainstream medicine with accessible longevity treatments for everyone (Lens-Pechakova 2021) in the future public clinics.

The field of longevity medicine seeks to redefine the concept of aging as a treatable condition, thereby shifting the healthcare paradigm from a focus on disease treatment to a more proactive stance that emphasises prevention and optimisation – where timely assessment is crucial. The objective of this approach is to extend healthspan by diagnosing early, targeting ageing mechanisms and optimizing biological age.

Citizen science and integration of translational research will engage a broader population into the research dimension, creating a strong continuum from research to clinic, and speed up innovation.

The structure of the longevity clinic should be versatile and adaptable to keep pace with rapidly developing longevity technologies.

Departments engaged in practical work with patients or clinics should be organized according to the cluster principle, allowing for changes in their functions as technologies evolve.

Longevity clinics can play a crucial role in the emerging longevity ecosystem, providing valuable data and serving as sites for clinical trials. Further research is required to establish scientific consensus, develop validated protocols and consider socioeconomic factors.

At present, the field of longevity medicine is more accessible to individuals of substantial financial means, primarily due to the high costs associated with research and development, the absence of adequate infrastructure, and the early stage of its development. However, with technological scaling, clinical validation, and public health integration, a pathway towards equitable, population-level implementation is emerging. In order to ensure that this is the case, it

is essential that health policy, regulation, and education address the socioeconomic and ethical challenges posed by the rise of personalized longevity care.

In addition, periodic Health Technology Assessments (HTAs) should be conducted for interventions related to longevity medicine to evaluate their clinical effectiveness, cost-effectiveness and equity in design (Charlton 2020). HTAs can provide policymakers with a comprehensive understanding of the value of these interventions and inform decisions on their inclusion within national health services through strategic purchasing (Honda 2014).

## **6.2 Increasing use of AI**

Artificial intelligence (AI) holds significant potential in the field of longevity (Schwarz 2025), offering advanced diagnostic and predictive capabilities. AI is poised to play an increasingly vital role in the development and operation of longevity clinics in the coming years. By leveraging machine learning algorithms and vast amounts of health data, AI can enable more precise, personalized and proactive approaches to extending healthspan and lifespan. AI, biomarkers, ageing science and longevity medicine together provide a strong foundation for extending human healthspan.

AI improves drug discovery and clinical trials through more precise and personalized clinical strategies that merge digital tools with life sciences understanding. The use of standard biomarkers alongside modern aging clocks is helping create more precision based medicines. By measuring immunosenescence, aging clocks offer a way to evaluate immunity levels and guide the development of new therapies to enhance immune function (Zhavoronkov et al. 2019a). Omics technologies supported by AI now allow researchers to explore the biology of long-lived animals such as bats, whales and naked mole rats to find aging pathways that are useful for human health (Lyu et al. 2024). Drug repurposing is a common approach in pharmaceuticals for identifying alternative innovative targets for existing drugs. AI based computational drug repurposing has been recently gaining momentum across the world. Similar modified computation based AI systems could be assistive in stem cells differentiation process to enhance longevity (Zhavoronkov et al. 2019b). AI-based systems can support evidence synthesis by providing concise evidence summaries that help professionals in the longevity field make more informed clinical decisions. However, AI has a tendency to hallucinate and it should be used responsibly to ensure the quality and reliability of findings are not compromised, thereby underpinning the ethical importance of research integrity in health. Recently, guidelines such as Responsible AI in Evidence Synthesis (RAISE) have gained traction in the evidence synthesis field and such guidelines can be adopted by professionals in the longevity sector to develop high-quality evidence summaries (Thomas et al. 2025).

As part of the increasing AI deployment, AI-powered robotics have emerged as a promising solution to support elderly individuals in their daily lives, particularly those without close family support. These technologies encompass a broad range of functionalities, from physical assistance (e.g., helping with mobility, household tasks such as cleaning and cooking, medication reminders, and fall detection) to mental and emotional support (e.g., social companionship, cognitive engagement, and mood recognition). It can be expected that AI

robotics will play an increasing role in the future in longevity medicine diagnosis, administration and surveillance.

A coordinated effort between public institutions, private industry, and civil society will be essential in transforming these promising tools into real-world solutions.

### ***6.3 Developing longevity clinics***

As a rule, the concept of the clinic is largely determined by society's needs and investors' interests. Investment in longevity continues to grow steadily in the last few decades. The economic justification and investment potential of longevity clinics are becoming increasingly evident as the global longevity market is expected to grow significantly in the coming years. This growth is driven by several factors:

Firstly, the demographic trend of an aging population is a crucial driver for investment in the longevity sector. As the global population is aging, there is a growing demand for innovative solutions to address age-related diseases and conditions.

Secondly, there is an increasing recognition of the economic and social benefits of the investment in the longevity sector. Longer lifespan and healthier lives can improve productivity, reduce healthcare costs and increase economic growth. Additionally, a growing awareness of the social challenges and ethical responsibilities in an aging population has led to a greater focus on developing solutions to improve healthspan and quality of life in later years.

Moreover, the development of medical technologies is accelerating, creating diversified and synergistic opportunities to intervene into aging processes.

Additionally, longevity clinics can serve as pivotal sites for clinical trials, facilitating groundbreaking research and the translation of scientific discoveries into practice. These multi-purpose possibilities position longevity clinics as attractive investment opportunities poised to disrupt conventional healthcare models and it has potential to enhance human lifespan. Longevity clinics can become hubs for developing health technology based interventions.

Integrating scientific research with practical considerations alongside clinical application will stimulate innovation in longevity clinics, contributing to improved healthcare practices that extend and enhance human life.

## **7. Healthy Longevity as a Human Right: Equity, Access and Public Responsibility**

### ***7.1 Reframing the Right to Health in the Age of Longevity***

As scientific progress increasingly enables us to prevent and even reverse biological aging, we must reconceptualize the human right to health. The principle of the “highest attainable standard of health,” enshrined in Article 12 of the International Covenant on Economic, Social and

Cultural Rights (ICESCR), demands more than treating disease—it requires active promotion of health, prevention of decline, and now, potentially, the extension of healthy life itself.

Longevity medicine, with its focus on preventing age-related deterioration, optimizing biological function, and expanding healthspan, offers transformative potential. However, it also introduces new obligations for governments and public health institutions: to ensure that the benefits of longevity science do not become the privilege of a wealthy few, but part of a universal, equitable health framework.

### ***7.2 A People's Longevity Charter – Principles for Fair Access***

To meet these obligations, we propose the foundation of a People's Longevity Charter—a normative framework that aligns longevity innovation with principles of justice, solidarity, and universal access. Core principles should include:

- Longevity equity: All individuals, regardless of income, geography, gender, or age, should have fair access to validated longevity diagnostics and interventions.
- State responsibility: Governments must progressively realize access to longevity technologies as part of their right-to-health obligations.
- Transparency and regulation: Ethical and scientific standards must be enforced equally across public and private providers.
- Prevention over privilege: Longevity interventions should prioritize population-level prevention strategies, not just elite optimization.
- Intergenerational solidarity: Investments in healthy longevity must consider future generations and sustainable public financing.

### ***7.3 Towards Public Integration of Longevity Medicine***

While current longevity care is largely delivered in specialized private clinics, we must envision a path toward public health integration. This includes the following components:

- Defining essential longevity services that can be included in national prevention plans (e.g., biological age testing, health risk stratification from 40+).
- Embedding longevity medicine into public reimbursement systems, based on evidence of cost-effectiveness and health impact.
- Establishing national or regional centers for longevity innovation, akin to cancer or diabetes networks
- Leveraging health technology assessment (HTA) mechanisms to evaluate longevity diagnostics and therapies for public coverage.

The landmark report 'UN Decade of Healthy Ageing: Plan of Action 2021-2030' prioritizes that functional ability and independence is core to maintaining a healthy life in old age (World Health Organization 2020). Moreover, enhancing longevity has the potential to reduce Disability Adjusted Life Years (DALYs) and enhance the Quality of Life (QoL) for people. Implications for

enhanced QoL highlights a focus towards preventative health strategies supported with possibilities for publicly funded healthcare systems and, therefore, potentially offering options to lower out of pocket (OOP) expenditure of especially older people for longevity clinic services.

Universal Health Coverage (UHC) should be a core consideration while designing population level longevity clinic services to ensure equitable non-discriminatory distribution of health resources. Long term funding for research related to longevity and clinic services is desirable to gain steady increments in population health parameters. For example, Singapore recently has focused on precision medicine for enhancing longevity in line with the nationwide Healthier SG initiative (Amalaraj et al. 2025). The European Commission (EC) has increasingly supported geroscience and age related research as a mission to enhance health and longevity (European Commission n.d.). In fact, European Innovation Partnership on Active and Healthy Ageing (EIP on AHA) is a classic example of a long term funded partnership promoting longevity and ageing research. Such initiatives position the EU as one of the leaders in longevity innovations.

Cross-border regulatory harmonization should be facilitated through frameworks such as the WHO, EMA, and European Commission initiatives. Such steps will be essential to avoid creating a “longevity divide,” where only those with sufficient wealth benefit from extended health and functionality, while others face earlier decline and exclusion.

In such circumstances this might be the time to establish Longevity medicine, as an emerging and iterative healthcare discipline.

#### ***7.4 Ethical Imperative and Societal Readiness***

Equitable longevity is not only a policy challenge—it is an ethical imperative. Just as sanitation, vaccination, and antibiotics were once seen as public goods, we must now work to establish the same status for aging-related care. Scientific progress must not outpace our social readiness and regulatory frameworks. Access to longevity interventions must not depend solely on personal choices or purchasing power. Structural determinants—education, housing, labor conditions, environmental exposures—must be addressed in tandem. Without this systemic view, longevity will remain a luxury rather than a right. Longevity medicine represents the next horizon of the human right to health. To realize its potential, we must ensure that scientific innovation is accompanied by political commitment, regulatory clarity, and inclusive health system design. The future of longevity must be collectively shaped, ethically grounded, and equitably delivered.

### **8. Conclusion**

The present work outlines some of the core elements and requirements of longevity medicine, based on the present expert consultation. The development of the foundational principles of longevity medicine and their practical implementation is a continuous work in progress, and is expected to remain work in progress for years and decades to come. These principles and implementations will continue to be elaborated via collective expert opinion, with an ever

increasing use of operational field evidence as well as rational theoretical substantiation. Not only biological and medical premises, but also societal, regulatory and cultural premises will be further elaborated. With an ever expanding and improving theoretical and practical basis, longevity medicine is expected, even relied on, to provide critical benefits for public and individual health, by implementing preventive strategies for aging-related mortality and morbidity, extending the productive and enjoyable period of life. Thus, it is expected, even relied on, to provide not just massive health benefits, but also vast societal and humanitarian benefits, in the rapidly aging societies, creating practical solutions for the challenges of aging. It is hoped that the present consultation paper will contribute to the advancement and accomplishment of these goals.

## **Compliance with ethical standards**

### **Conflict of interest**

The authors declare that they have no conflict of interest.

## **References**

Amalaraj JJP, Island L, Ong JYY, Wang L, Valderas JHM, Dunn M, Chong YS, Meij J, Maier AB (2025) Towards precision geromedicine in Singapore. *GeroScience*, 10.1007/s11357-025-01686-7. <https://doi.org/10.1007/s11357-025-01686-7>

Anti-aging guide (2009) Anti-aging Biomedicine High Tech Bio-Medical Technologies for Disease Treatment and Life Extension Experimental and Clinical Data 62: Biomarkers of aging. American Federation of Aging Research, Infoaging Guide to Biomarkers of Aging

Asadpour A, Yahaya BH, Bicknell K, Cottrell GS, Widera D (2023) Uncovering the gray zone: mapping the global landscape of direct-to-consumer businesses offering interventions based on secretomes, extracellular vesicles, and exosomes. *Stem Cell Res Ther* 14:111. <https://doi.org/10.1186/s13287-023-03335-2>

Asllanaj E, Bano A, Glisic M, Jaspers L, Ikram MA, Laven JSE, Völzke H, Muka T, Franco OH (2019) Age at natural menopause and life expectancy with and without type 2 diabetes. *Menopause*. 26(4):387-394. <https://doi.org/10.1097/GME.0000000000001246>

Austad SN, Fischer KE (2016) Sex Differences in Lifespan. *Cell Metab* 23(6):1022-1033. <https://doi.org/10.1016/j.cmet.2016.05.019>

Baker DJ, Wijshake T, Tchkonja T, LeBrasseur NK, Childs BG, van de Sluis B, Kirkland JL, van Deursen JM (2011) Clearance of p16Ink4a-positive senescent cells delays ageing-associated disorders. *Nature* 479(7372):232-6. <https://doi.org/10.1038/nature10600>



Barcena Clea, Pablo Mayoral, Pedro M Quirós (2018) Mitohormesis, an Antiaging Paradigm Int Rev Cell Mol Biol. 340:35-77. <https://doi.org/10.1016/bs.ircmb.2018.05.002>

Bischof E, Scheibye-Knudsen M, Siow R, Moskalev A (2021) Longevity medicine: upskilling the physicians of tomorrow. Lancet Healthy Longev 2(4):e187-e188. [https://doi.org/10.1016/S2666-7568\(21\)00024-6](https://doi.org/10.1016/S2666-7568(21)00024-6)

Blokh D, Gitarts J, Mizrahi EH, Kagansky N, Stambler I (2023) The utility of information theory based methods in the research of aging and longevity, In Moskalev A, Stambler I, Zhavoronkov A (eds) Artificial Intelligence for Healthy Longevity. Springer Nature, Cham, pp 245–274

Bonnes SL, Strauss T, Palmer AK, Hurt RT, Island L, Goshen A, Wang LY, Kirkland JL, Bischof E, Maier AB (2024) Establishing healthy longevity clinics in publicly funded hospitals. Geroscience 46(5):4217-4223

Brook OR, Kruskal JB, Eisenberg RL, Larson DB (2015) Root cause analysis: Learning from adverse safety events. Radiographics 35(6):1655-1667

Cánovas JJ, Hernández PJ, Botella JJ (2009) Effectiveness of internal quality assurance programmes in improving clinical practice and reducing costs. J Eval Clin Pract 15(5):813-9. <https://doi.org/10.1111/j.1365-2753.2008.01100.x>

Carver CM, Rodriguez SL, Atkinson EJ, Dosch AJ, Asmussen NC, Gomez PT, Leitschuh EA, Espindola-Netto JM, Jeganathan KB, Whaley MG, Kamenecka TM, Baker DJ, Haak AJ, LeBrasseur NK, Schafer MJ (2025) IL-23R is a senescence-linked circulating and tissue biomarker of aging. Nat Aging 5(2):291-305. <https://doi.org/10.1038/s43587-024-00752-7>

Charlton V (2020) NICE and fair? Health technology assessment policy under the UK's National Institute for Health and Care Excellence, 1999–2018. Health Care Anal 28(3):193–227.

Chen B, Dequeker E, Dong J, Emmadi R, Gordon JT, Howell RM, Killeen A, Levin JD, Murray CN, Pratt VM, Rousseau F, Stockley TL, Scheuner MT (2012) CLSI MM20-A: Quality management for molecular genetic testing; approved guideline, 1st edn. Clinical and Laboratory Standards Institute, Wayne, PA.

Cohen AA, Legault V, Fülöp T (2020) What if there's no such thing as "aging"? Mech Ageing Dev 192:111344. doi: 10.1016/j.mad.2020.111344

Department of Health – Abu Dhabi (2024) Healthy Longevity Medicine Clinic Standard. Version 1. Department of Health, Abu Dhabi. <https://www.doh.gov.ae/en/resources/standards>. Accessed 1 Aug 2025

European Commission (n.d.) Human development and ageing. [online] Research & Innovation – Health Research Area. [https://research-and-innovation.ec.europa.eu/research-area/health/human-development-and-ageing\\_en](https://research-and-innovation.ec.europa.eu/research-area/health/human-development-and-ageing_en). Accessed 1 Aug 2025

European Parliament and the Council of the European Union (2017) Regulation (EU) 2017/745 of 5 April 2017 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009, and repealing Council Directives 90/385/EEC and 93/42/EEC. <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32017R0745>. Accessed 1 Aug 2025

Evans DB, Marten R, Etienne C (2012) Universal health coverage is a development issue. The Lancet 380(9845):864-865

Fallahi F, Mostafavinia A, Sharifi Z, Mohaghegh Shalmani L, Amini A, Ahmadi H, Omid H, Hajhosseintehrani M, Bayat S, Hamblin MR, Chien S, Bayat M (2023) Effects of photobiomodulation on mitochondrial function in diabetic adipose-derived stem cells in vitro. Spectrochim Acta A Mol Biomol Spectrosc 285:121835. <https://doi.org/10.3389/fragi.2024.1417455>

Falshaw N, Sagner M and Siow RC (2024) The Longevity Med Summit: insights on healthspan from cell to society. Front. Aging 5:1417455. <https://doi.org/10.3389/fragi.2024.1417455>

Ferrucci L, Gonzalez-Freire M, Fabbri E, Simonsick E, Tanaka T, Moore Z, Salimi S, Sierra F, de Cabo R (2020) Measuring biological aging in humans: A quest. Aging Cell 19(2):e13080. <https://doi.org/10.1111/accel.13080>

Forman DE, Pignolo RJ (2024) A pragmatic approach to introducing translational geroscience into the clinic: a paradigm based on the incremental progression of aging-related clinical research. J Gerontol A Biol Sci Med Sci 79(9):glae062. <https://doi.org/10.1093/gerona/glac062>

Frankowski David W, Luigi Ferrucci, Praveen R. Arany, Dawn Bowers, Janis T. Eells, Francisco Gonzalez-Lima, Nicole L. Lohr, Brendan J. Quirk, Harry T. Whelan, Edward G. Lakatta (2025) GeroScience 47:2777-2789. <https://doi.org/10.1007/s11357-025-01505-z>

Franzini M, Valdenassi L, Pandolfi S, Tirelli U, Ricevuti G, Simonetti V, Berretta M, Vaiano F, Chirumbolo S (2022) The biological activity of medical ozone in the hormetic range and the role of full expertise professionals. Front Public Health 10:979076. <https://doi.org/10.3389/fpubh.2022.979076>

Franzini M, Vaiano F, Tirelli U, Chirumbolo S, Valdenassi L (2025) SIOOT recommendations for the optimal application of the oxygen-ozone therapy in clinical medicine. Int Immunopharmacol 145:113751. <https://doi.org/10.1016/j.intimp.2024.113751>

Fujita M, Hatta T, Ikka T, Onishi T (2024) The urgent need for clear and concise regulations on exosome-based interventions. Stem Cell Reports 19(11):1517-1519. <https://doi.org/10.1016/j.stemcr.2024.09.008>

Gems D (2015) The aging-disease false dichotomy: understanding senescence as pathology. Front Genet 6:212. <https://doi.org/10.3389/fgene.2015.00212>

Glancy B, Kane DA, Kavazis AN, Goodwin ML, Willis WT, Gladden LB (2021) Mitochondrial lactate metabolism: history and implications for exercise and disease. J Physiol 599(3):863-888. <https://doi.org/10.1113/JP278930>

González-Gualda E, Baker AG, Fruk L, Muñoz-Espín D (2021) A guide to assessing cellular senescence in vitro and in vivo. FEBS J 288(1):56-80. <https://doi.org/10.1111/febs.15570>

Goodpaster BH, Sparks LM (2017) Metabolic flexibility in health and disease. Cell Metab 25(5):1027-1036. <https://doi.org/10.1016/j.cmet.2017.04.015>

Guarente L, Sinclair DA, Kroemer G (2024) Human trials exploring anti-aging medicines. Cell Met 39(2):354-376. <https://doi.org/10.1016/j.cmet.2023.12.007>

Hall L, Wilson J, Bernard K, Carbone MP, Mubarak HSE, Hallam SE, Klein RD, Pancholi P, Schoonmaker MM, Spector EB, Vitazka P, Boonyaratankornkit j, Bryant B, Dong J, Emmadi R, Furtado MR, Lacbawan F, Martinez-Murillo F, Schutzbank TE, Selvarangan R, Shyamala V, Williams LO, Wu A (2011) CLSI MM19-A: Establishing molecular testing in clinical laboratory environments; approved guideline, 1st edn. Clinical and Laboratory Standards Institute, Wayne, PA

Hamblin MR (2016) Shining light on the head: Photobiomodulation for brain disorders. BBA Clin 6:113-124. <https://doi.org/10.1016/j.bbacli.2016.09.002>

Herzog C, Poganik JR, Barzilai N, Basisty N, Beerman I, Belsky DW, de Cabo R, Candia J, Faghri F, Horvath S, Maier AB, Perez V, Sen P, Moqri M, Gladyshev VN, Ferrucci L (2025) Biomarkers of Aging–NIA Joint Symposium 2024: New insights into aging biomarkers. Aging Cell 24(7):e70124. <https://doi.org/10.1111/accel.70124>

Honda A (2014) What is strategic purchasing for health? Other RESYST. <https://doi.org/10.17037/PUBS.02760470>

Hoshi RA, Vanderlei LCM, de Godoy MF, Bastos FDN, Netto J Jr, Pastre CM (2017) Temporal sequence of recovery-related events following maximal exercise assessed by heart rate variability and blood lactate concentration. Clin Physiol Funct Imaging 37(5):536-543. <https://doi.org/10.1111/cpf.12339>

ISO 15189 (2022) Medical laboratories-requirements for quality and competence. International Organization for Standardization, Geneva.

Jin K, Simpkins JW, Ji X, Leis M, Stambler I (2015) The critical need to promote research of aging and aging-related diseases to improve health and longevity of the elderly population. *Aging Dis* 6(1):1-5. <https://doi.org/10.14336/AD.2014.1210>

Joint Commission International (n.d.) Accreditation programs. <https://www.jointcommissioninternational.org/what-we-offer/accreditation/accreditation-programs/>. Accessed 1 Aug 2025

Jones DP, Carlson JL, Mody VC, Cai J, Lynn MJ, Sternberg P (2000) Redox state of glutathione in human plasma. *Free Radic Biol Med* 28(4):625-35. [https://doi.org/10.1016/s0891-5849\(99\)00275-0](https://doi.org/10.1016/s0891-5849(99)00275-0)

Kelly JH, Lianov L, Shurney D, Guimarães ST, Palma M, Esselstyn C, Stoll S, Patel P, Rea B, Reddy K, Guthrie G, Reiss M, Karlsen MC (2023) Lifestyle Medicine Intensivist Competencies: 2023 Expert Consensus Update. *Am J Lifestyle Med* 18(1):141-149. <https://doi.org/10.1177/15598276231192846>

Kelly JH, Lianov L, Shurney D, Guimarães ST, Palma M, Esselstyn C, Stoll S, Patel P, Rea B, Reddy K, Guthrie G, Reiss M, Karlsen MC (2024) Lifestyle medicine performance measures: An expert consensus statement defining metrics to identify remission or long-term progress following lifestyle medicine treatment. *Am J Lifestyle Med* 18(4):567-573. <https://doi.org/10.1177/15598276241230237>

Kennedy BK, Berger SL, Brunet A, Campisi J, Cuervo AM, Epel ES, Franceschi C, Lithgow GJ, Morimoto RI, Pessin JE, Rando TA, Richardson A, Schadt EE, Wyss-Coray T, Sierra F (2014) Geroscience: linking aging to chronic disease. *Cell* 159(4):709-713. <https://doi.org/10.1016/j.cell.2014.10.039>

Khaltourina D, Matveyev Y, Alekseev A, Cortese F, Ioviță A (2020) Aging fits the disease Criteria of the International Classification of Diseases. *Mech Ageing Dev* 189:111230. <https://doi.org/10.1016/j.mad.2020.111230>

Kroemer G, Maier AB, Cuervo AM, Gladyshev VN, Ferrucci L, Gorbunova V, Kennedy BK, Rando TA, Seluanov A, Sierra F, Verdun E, Lopez-Otin C (2025) From geroscience to precision geromedicine: Understanding and managing aging. *Cell* 188(8):2043-2062. <https://doi.org/10.1016/j.cell.2025.03.011>

Kulkarni AS, Aleksic S, Berger DM, Sierra F, Kuchel GA, Barzilai N (2022) Geroscience-guided repurposing of FDA-approved drugs to target aging: A proposed process and prioritization. *Aging Cell* 21(4):e13596. <https://doi.org/10.1111/accel.13596>

Lens-Pechakova LS (2021) Regional inequality in longevity and lifestyle in Europe. In: Gu D, Dupre ME (eds) Encyclopedia of Gerontology and Population Aging. Springer, Cham. [https://doi.org/10.1007/978-3-030-22009-9\\_471](https://doi.org/10.1007/978-3-030-22009-9_471)

Lianov L, Johnson M (2010) Physician competencies for prescribing lifestyle medicine. JAMA 304(2):202-203. <https://doi.org/10.1177/15598276221121580>

Lianov LS, Adamson K, Kelly JH, Matthews S, Palma M, Rea BL (2022) Lifestyle Medicine Core Competencies: 2022 Update. Am J Lifestyle Med 16(6):734-739. <https://doi.org/10.1177/15598276221121580>

López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G (2013) The hallmarks of aging. Cell 153(6):1194-217. <https://doi.org/10.1016/j.cell.2013.05.039>

López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G (2023) Hallmarks of aging: An expanding universe. Cell 186(2):243-278. <https://doi.org/10.1016/j.cell.2022.11.001>

López-Otín C, Kroemer G (2021) Hallmarks of Health. Cell 184(1):33–63. <https://doi.org/10.1016/j.cell.2020.11.034>

Lyu YX, Fu Q, Wilczok D, Ying K, King A, Antebi A, Vojta A, Stolzing A, Moskalev A, Georgievskaya A, Maier AB, Olsen A, Groth A, Simon AK, Brunet A, Jamil A, Kulaga A, Bhatti A, Yaden B, Pedersen BK, Bakula D (2024) Longevity biotechnology: bridging AI, biomarkers, geroscience and clinical applications for healthy longevity. Aging 16(20):12955–12976. <https://doi.org/10.18632/aging.206135>

Martinović A, Mantovani M, Trpchevska N, Novak E, Milev NB, Bode L, Ewald CY, Bischof E, Reichmuth T, Lapidès R, Navarini A, Saravi B, Roider E (2024) Climbing the longevity pyramid: overview of evidence-driven healthcare prevention strategies for human longevity. Front Aging 5:1495029. <https://doi.org/10.3389/fragi.2024.1495029>

McMahon EB, Lee-Huber T (2001) HIPAA privacy regulations: Practical information for physicians. Pain Physician 4(3):280-284.

Miller RA (2001) Biomarkers of aging. Sci Aging Knowl Environ 2001:pe2.

Miller SA, Dawson BD, Arbefeveille S, Babady E, Bankowski MJ, Bisht H, Day SP, Dunbar SA, Grigorenko E, Hallam SE, Hirschhorn JW (2018) CLSI MM17-A: Validation and verification of multiplex nucleic acid assays, 2nd edn. Clinical and Laboratory Standards Institute, Wayne PA.

Mironov S, Borysova O, Morgunov I, Zhou Z, Moskalev A (2024) A Framework for an Effective Healthy Longevity Clinic. Aging Dis 16(4):1971-1986. <https://doi.org/10.14336/AD.2024.0328-1>

Muka T, Oliver-Williams C, Kunutsor S, Laven JS, Fauser BC, Chowdhury R, Kavousi M, Franco OH (2016) Association of Age at Onset of Menopause and Time Since Onset of Menopause

With Cardiovascular Outcomes, Intermediate Vascular Traits, and All-Cause Mortality: A Systematic Review and Meta-analysis. *JAMA Cardiol* 1(7):767-776. <https://doi.org/10.1001/jamacardio.2016.2415>

Nie C, Li Y, Li R, Yan Y, Zhang D, Li T, Li Z, Sun Y, Zhen H, Ding J, Wan Z, Gong J, Shi Y, Huang Z, Wu Y, Cai K, Zong Y, Wang Z, Wang R, Jian M, Jin X, Wang J, Yang H, Han JJ, Zhang X, Franceschi C, Kennedy BK, Xu X (2022) Distinct biological ages of organs and systems identified from a multi-omics study. *Cell Rep* 38(10):110459. <https://doi.org/10.1016/j.celrep.2022>

Peto R, Doll R (1997) There is no such thing as aging. *BMJ* 315:1030–1032. <https://doi.org/10.1136/bmj.315.7115.1030>

Pizzino G, Irrera N, Cucinotta M, Pallio G, Mannino F, Arcoraci V, Squadrito F, Altavilla D, Bitto A (2017) Oxidative stress: harms and benefits for human health. *Oxid Med Cell Longev* 2017:8416763. <https://doi.org/10.1155/2017/8416763>

Rippe JM (2018) Lifestyle medicine: The health promoting power of daily habits and practices. *Am J Lifestyle Med* 12(6):499-512. <https://doi.org/10.1177/1559827618785554>

Roper K (2014) LQSI: a tool to enhance quality in your laboratory. GABRIEL Network: Global Approach to Biological Research, Infectious diseases and Epidemics in Low-income countries, (16):1-2. <https://www.gabriel-network.org/>. Accessed 1 Aug 2025

Rudnitsky E, Braiman A, Wolfson M, Muradian KK, Gorbunova V, Turgeman G, Fraifeld VE (2025) Mesenchymal stem cells and their derivatives as potential longevity-promoting tools. *Biogerontology* 26(3):96. <https://doi.org/10.1007/s10522-025-10240-z>

Saliev T, Singh PB (2025) Targeting senescence: a review of senolytics and senomorphics in anti-aging interventions. *Biomolecules* 15(6):860. <https://doi.org/10.3390/biom15060860>

Schwarz ER, Bruce JL, Kiev LC (2025) Algorithms to Ageless: AI in Anti-Aging Medicine. *J Clin Cardiol Cardiovasc Interv* 8(5):462. <https://doi.org/10.31579/2641-0419/462>

Sheppard E, Madej RM, Alfaro MP, Anderson N, Bijwaard KE, Chen SCA, Cheng YW, Compton CC, Dollins C, Gargis AS, Ghosh S, Herajata P, Jackson CL, Leon A, Maghakian D, Schutzbank TE, Sepehri S, Sundin T, Todd HN, Tusneem NA, Vernovsky K, Zheng G (2020) CLSI MM13-A: Collection, transport, preparation, and storage of specimens for molecular methods; approved guideline, 2nd edn. Clinical and Laboratory Standards Institute, Wayne, PA.

Sherman M, Romfh P (2003) Improving clinical emergency response in an outpatient setting. *AAACN Viewpoint* 25(5):1.

Sierra F (2016) The Emergence of Geroscience as an interdisciplinary approach to the enhancement of health span and life span. *Cold Spring Harb Perspect Med* 6(4):a025163. <https://doi.org/10.1101/cshperspect.a025163>

Stambler I (2017) Recognizing degenerative aging as a treatable medical condition: methodology and policy. *Aging Dis* 8(5):583-589. <https://doi.org/10.14336/AD.2017.0130>

Stambler I (2025) The politics of the Longevity Dividend. How much is healthy longevity worth us? In: Umbrello S, Hughes J, Cali C (eds) *The Biopolitics of Human Enhancement*. De Gruyter, Berlin, pp 137-160. <https://doi.org/10.1515/9783111242651-009>

Tavassoli N, de Souto Barreto P, Gillette-Guyonnet S, Rolland Y, Vellas B (2022) Implementation of the WHO integrated care for older people (ICOPE) programme in clinical practice: a prospective study. *Lancet Healthy Longev* 3(6):e394–e404. [https://doi.org/10.1016/S2666-7568\(22\)00097-6](https://doi.org/10.1016/S2666-7568(22)00097-6)

Thomas C, Sirvent P, Perrey S, Raynaud E, Mercier J (2004) Relationships between maximal muscle oxidative capacity and blood lactate removal after supramaximal exercise and fatigue indexes in humans. *J Appl Physiol* 97(6):2132-2138. <https://doi.org/10.1152/japplphysiol.00387.2004>

Thomas J, Flemyng E, Noel-Storr A et al. (2025) Responsible AI in Evidence Synthesis (RAISE): guidance and recommendations (version 2; updated 3 June 2025). In: *Open Science Framework*, Washington DC: Center for Open Science. <http://OSF.IO/FWAUD>. Accessed 1 Aug 2025

Tkaczenko H, Kurhaluk N (2025) Antioxidant-rich functional foods and exercise: unlocking metabolic health through Nrf2 and related pathways. *Int J Mol Sci* 26(3):1098. <https://doi.org/10.3390/ijms26031098>

Tom SE, Cooper R, Wallace RB, Guralnik JM (2012) Type and timing of menopause and later life mortality among women in the Iowa Established Populations for the Epidemiological Study of the Elderly (EPESE) cohort. *J Womens Health (Larchmt)* 21(1):10-16. <https://doi.org/10.1089/jwh.2011.2745>

Turner L, Martinez JR Jr, Najjar S, Rajapaksha Arachchilage T, Wang JC (2023) Businesses marketing purported stem cell treatments and exosome therapies for COVID-19: An analysis of direct-to-consumer online advertising claims. *Stem Cell Reports* 18(11):2010-2015. <https://doi.org/10.1016/j.stemcr.2023.09.015>

UAE Department of Health (2024) Abu Dhabi sets standards for the world's first healthy longevity medicine centers. <https://www.doh.gov.ae/en/news/abu-dhabi-sets-standards-for-the-world-first-healthy-longevity-medicine-centres>. Accessed 1 Aug 2025

US FDA (2012) Guidance for industry. E7 studies in support of special populations: Geriatrics. Questions and answers. US Department of Health and Human Services. Food and Drug Administration (FDA) Silver Spring, Maryland. <http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm189544.pdf>. Accessed 1 Aug 2025

US FDA (2024) Title 21 CFR Part 820 Subchapter H: Medical Devices – Quality System Regulation. Electronic Code of Federal Regulations. U.S. Food and Drug Administration (US FDA), USA. <https://www.ecfr.gov/current/title-21/chapter-I/subchapter-H/part-820>. Accessed 1 Aug 2025

Valdonė Alšauskė S (2025) A Simpler Start to Longevity Medicine in Primary Care. Longevity for All. <https://www.longevityforall.org/a-simpler-start-to-longevity-medicine-in-primary-care/>. Accessed 1 Aug 2025

Vorisek CN, Lehne M, Klopfenstein SAI, Mayer PJ, Bartschke A, Haese T, Thun S (2022) Fast healthcare interoperability resources (FHIR) for interoperability in health research: Systematic review. JMIIR Med Inform 10(7):e35724. <https://doi.org/10.2196/35724>

Wang D, Stevens G, Flotte RT (2025) Gene therapy then and now: A look back at changes in the field over the past 25 years. Mol Ther 33(5):1889-1902. <https://doi.org/10.1016/j.ymthe.2025.02.040>

World Health Organization (2020) UN Decade of Healthy Ageing: Plan of Action 2021-2030. World Health Organization, Geneva. <https://www.who.int/initiatives/decade-of-healthy-ageing>. Accessed 1 Aug 2025

World Health Organization (2024) Integrated care for older people (ICOPE): guidance for person-centred assessment and pathways in primary care, 2nd ed. World Health Organization, Geneva. <https://www.who.int/publications/i/item/9789240103726>. Accessed 1 Aug 2025

Wu G, Fang YZ, Yang S, Lupton JR, Turner ND (2004) Glutathione metabolism and its implications for health. J Nutr. 2004 Mar;134(3):489-92. <https://doi.org/10.1093/jn/134.3.489>

Yamaguchi H, Hsu JM, Sun L, Wang SC, Hung MC. Advances and prospects of biomarkers for immune checkpoint inhibitors. Cell Rep Med. 2024 Jul 16;5(7):101621. <https://doi.org/10.1016/j.xcrm.2024.101621>

Yoshino J, Baur JA, Imai SI (2018) NAD<sup>+</sup> Intermediates: The Biology and Therapeutic Potential of NMN and NR. Cell Metab 6;27(3):513-528. <https://doi.org/10.1016/j.cmet.2017.11.002>

Zeng Z, Zhu Q (2024) Progress and prospects of biomarker-based targeted therapy and immune checkpoint inhibitors in advanced gastric cancer. Front Oncol 14:1382183. <https://doi.org/10.3389/fonc.2024.1382183>



Zhang Q (2023) An interpretable biological age. *Lancet Healthy Longev* 4(12):e662-e663. [https://doi.org/10.1016/S2666-7568\(23\)00213-1](https://doi.org/10.1016/S2666-7568(23)00213-1)

Zhavoronkov A, Mamoshina P (2019a) Deep aging clocks: the emergence of AI-based biomarkers of aging and longevity. *Trends Pharmacol Sci* 40(8):546–549. <https://doi.org/10.1016/j.tips.2019.06.004>

Zhavoronkov A, Mamoshina P, Vanhaelen Q, Scheibye-Knudsen M, Moskalev A, Aliper A (2019b) Artificial intelligence for aging and longevity research: recent advances and perspectives. *Ageing Res Rev* 49:49–66. <https://doi.org/10.1016/j.arr.2018.11.003>