



**THE ALLIANCE FOR
LONGEVITY INITIATIVES**

**Policymakers Guide to the Longevity
Therapeutics Industry**

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Executive Summary

The development of therapies targeting aging will fundamentally transform society. These “longevity therapies” have the potential to prevent a multitude of diseases and disabilities associated with old age by addressing the root cause – the biological damage that accumulates during the aging process. By taking this root-cause approach, longevity therapeutics will subsequently increase individuals' healthspans – the length of time a person lives with quality health – and significantly enhance societal productivity. Countries that prioritize extending healthspan will achieve the “Longevity Dividend,” adding trillions of dollars in economic value from reduced late-life healthcare spending and increased productivity. In order to realize the immense promise of these therapies, policymakers must take action to pave the way for their introduction to society.

This guide provides an introduction to the longevity biotechnology space for policymakers. The first 2 sections offer a brief overview of the aging population crisis the world is facing, why modern medicine’s approach to aging is insufficient to deal with the stress this crisis is causing, what the longevity therapeutics industry is, the twelve hallmarks of aging and the effects of modulating them. The section also explores the history, current state, and promising companies within the longevity sector.

Various factors should motivate the government’s support of longevity therapeutics. There is a moral imperative: supporting these therapies will radically improve Americans’ health outcomes. Geopolitical considerations highlight the competitive advantage the U.S. stands to secure by establishing leadership in the field of longevity research and development. The economic rationale is compelling: having a healthier, longer-lived population would lead to significant financial savings and economic gains, known as the Longevity Dividend.

Policymakers can support the development of longevity therapies through several concrete actions. The Alliance for Longevity Initiatives (A4LI) calls on Congress to increase allocations to the National Institute of Aging – Division of Aging Biology, make geroscience and longevity therapeutics a focus of ARPA-H, create a dedicated regulatory pathway for longevity therapeutics, fund Congressional research into the longevity dividend, and initiate a national movement to increase healthy lifespan by setting an actionable, time-bound goal.

Society is on the verge of a revolution in medicine, but science alone cannot bring the country across the finish line. A4LI seeks to work with policymakers to advance this cutting-edge field, a field that will improve the lives and future of the American people.

Section 1: An Aging Population

Overview of our Aging Demography

Society is experiencing something never-before-seen in human history: an aging population. Over the last few decades, there has been a dramatic increase in the number and percentage of the older population aged 60 years and above, and at the same time, a decrease in the number and percentage of the young population aged 15 years old and below. This phenomenon can be attributed to dramatic increases in life expectancy and plummeting fertility rates.

Since 1950, global life expectancy from birth has climbed from 46.5 years to 73.33 in 2024. In the past few years, we have observed a 0.24% increase in global life expectancy, with a trajectory of reaching nearly 82 by the end of the century (Figure 1).¹ This nearly three-decade lifespan increase for humans over these last seven decades is the result of advancements in medical technology, public health initiatives and living standards. Namely, medical innovations, such as vaccines, antibiotics, and advanced surgical techniques, and public health innovations, such as improved sanitation, health education campaigns, better nutrition, safer work environments, access to healthcare services and decreases in war and violence, are the main drivers of the nearly doubling in life expectancy.

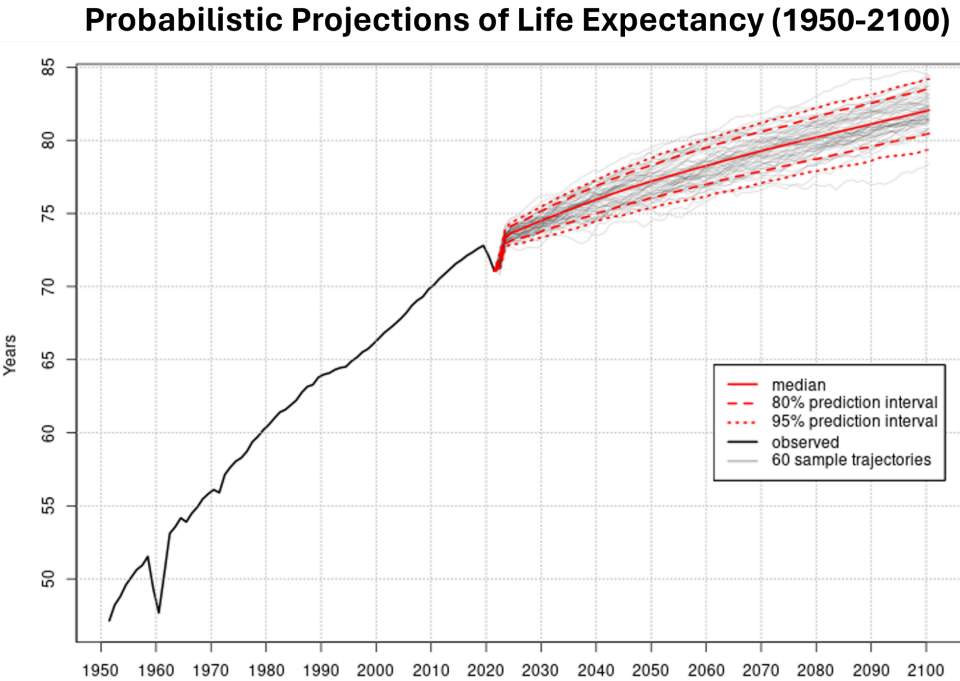


Figure 1. Projected World Human Life Expectancy through 2100

¹ 2022 United Nations, DESA, Population Division. World Population Prospects 2022. <http://population.un.org/wpp/>. Retrieved 2024-06-01.

Simultaneously, society has seen a sharp decline in fertility rates and far below replacement level across most of the developed world. In the same time frame (since 1950) cities have emerged as the supreme option for job and career opportunities. Subsequently, the cost of living has increased and having children is now seen as more of a luxury than a necessity. With the move into the cities, people have less space for kids and less of a need (when we were all living on the farms, children were a source of free labor). These factors, along with other societal shifts, like women participating in the workforce and access to contraceptives, are why we see global fertility rates in nearly every single developed country lower than replacement level – 2.1 births per woman (Figure 2).²

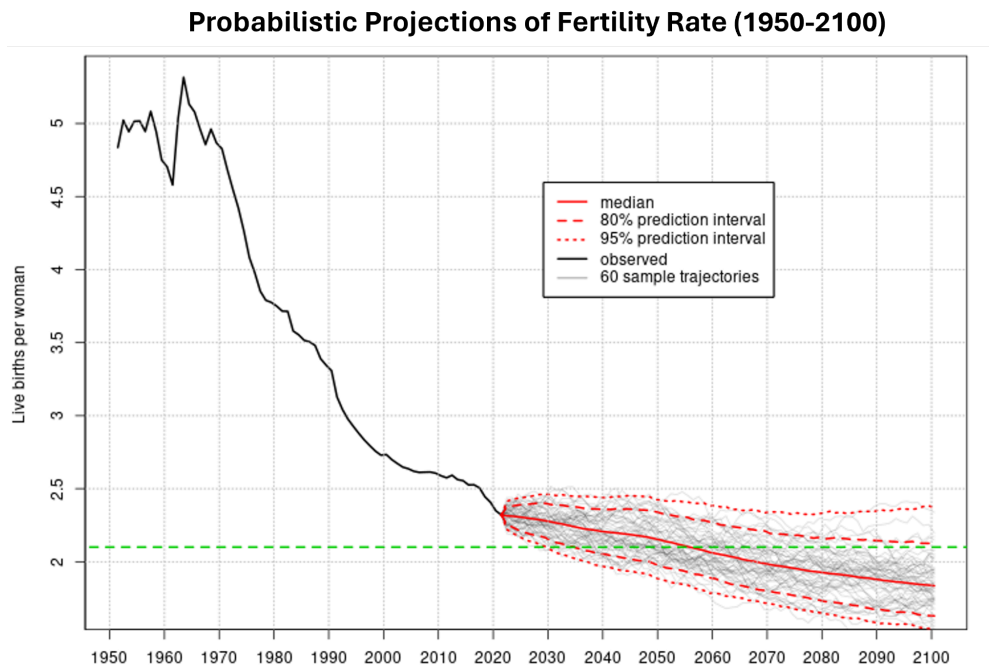


Figure 2. Projected World Fertility Rate through 2100

These trends have been baked into the cake for a long time now and show no sign of reversing course. Populations all over the advanced world, for the first time ever, stand to have more citizens over the age of 65 than citizens under the age of 15. In the United States, the percentage of 65 year olds and older have gone from 8% in 1950 to roughly 62 million adults ages 65 and older living in the U.S., accounting for 18% of the population in 2024. By 2054, 84 million adults ages 65 and older will make up an estimated 23% of the population. In the same years (1950 and 2024) mentioned above, U.S. fertility rates have dropped from over 3 births per woman to just 1.66 births per woman, reaching a historic low.³ By 2030 (less than 6 years away),

² Max Roser (2014) - "Fertility Rate" Published online at OurWorldInData.org. Retrieved from: <https://ourworldindata.org/fertility-rate> [Online Resource] on 2024-06-01

³ Hamilton BE, Martin JA, Osterman MJK. Births: provisional data for 2023. Vital Statistics Rapid Release; no 35. April 2024. DOI: <https://dx.doi.org/10.15620/cdc/151797>.

for the first time the population of 65 year olds and older in the U.S. will surpass the population of under 18 years olds. Additionally, the percentage of U.S. centenarians – those that reach over 100 years old is expected to more than triple from 2024 to 2054.⁴ These trends are more pronounced abroad, in both allied and adversarial countries to the United States. In the European Union, the percentage of people aged 65 and over is projected to rise from 20% in 2022 to 30% by 2050. In China, the number of people aged 65 and older is expected to reach 365 million by 2050, making up nearly 26% of its population.⁵ These same areas have a more pronounced drop in fertility rates. In many parts of Europe, like Italy and Spain, fertility rates are below 1.3 births per woman, far below the required 2.1 births per woman for a stable population.² In China, fertility rates have precipitously dropped unlike anywhere in the world, from 1.81 births per woman in 2017 to roughly 1.00 births per woman in 2024.²

Consequences of an Aging Population

An aging population will have devastating impacts on global economic development, governmental programs, and societal stability, if left unaddressed. The financial burden of an aging population is multifaceted. Increased demand for healthcare services, pensions, and social security leads to significant financial pressure on younger generations who are expected to support these systems through taxation. For instance, in the United States, the Old Age and Survivor Insurance Trust Fund reserves are projected to decline and become depleted by the end of 2033. In result, only 79% of the beneficiaries will be paid if no legislative action is taken.⁶ The cost of Medicare and Social Security programs will grow faster than our Gross Domestic Product (GDP) due to the rapid aging U.S. population and the persistently lower birth rates.⁶ Similarly, healthcare costs are rising as the population ages, with the Centers for Medicare & Medicaid Services (CMS) projecting that national health expenditures will grow to average rate of 5.2% per year from 2019 to 2028, reaching nearly \$7.2 trillion.⁷ Japan has been grappling with not only an aging population for decades, but a historic low fertility rate that will result in a rapid population decline has increased government spending on pensions and elder care, contributing to the country's mounting public debt, which is the highest among developed nations.⁸ This economic strain is not only a government issue but also affects individual families, as more

⁴ Katherine Schaeffer (2024) - "U.S. centenarian population is projected to quadruple over the next 30 years" Published online at Pewresearch.org. Retrieved from: <https://pewrsr.ch/47werl0> [Online Resource] on 2024-06-01

⁵ Hannah Ritchie and Max Roser (2019) - "Age Structure" Published online at OurWorldInData.org. Retrieved from: 'https://ourworldindata.org/age-structure' [Online Resource]

⁶ Status of the Social Security and Medicare Programs. Published online at ssa.gov. Retrieved from <https://www.ssa.gov/oact/trsum/> [Online Resource] on 2024-06-01

⁷ National Health Expenditure Fact Sheet (2022). Retrieved from: <https://www.cms.gov/data-research/statistics-trends-and-reports/national-health-expenditure-data/nhe-fact-sheet> [Online Resource] on 2024-06-01.

⁸ Statista (2024) Japan: National debt from 2019 to 2029 in relation to gross domestic product. Retrieved from <https://www.statista.com/statistics/267226/japans-national-debt-in-relation-to-gross-domestic-product-gdp/> [Online Resource] on 2024-06-01

people need to support elderly relatives, reducing disposable income and financial stability for younger generations. Couple that with free-falling birth rates, and we stand to experience a severe lack of workers and caregivers to support our sick and retired population.

Lifespan increases and lead to arise in age-related diseases and conditions places immense pressure on healthcare systems and resources. Older adults are more likely to suffer from chronic illnesses such as heart disease, diabetes, and dementia. For example, the Alzheimer’s Association estimates that by 2050, nearly 14 million Americans will be living with Alzheimer’s, a significant increase from the current 7 million.⁹⁻¹⁰ This surge in chronic conditions necessitates long-term care, specialized medical services, and increased hospitalizations, leading to higher healthcare costs and resource allocation challenges. In countries with aging populations like Italy, the healthcare system is strained by the high demand for geriatric care. The Italian National Health Service is facing budget constraints while trying to accommodate the growing needs of its elderly population, resulting in longer waiting times and reduced quality of care.¹¹

This shrinking working-age population leads to potential labor shortages and reduced economic productivity. As the number of retirees grows, the ratio of workers to retirees decreases, putting pressure on the remaining workforce to sustain economic growth and support social welfare programs. In Germany, the working-age population is projected to decline by 4-6 million people by 2035, more than any other G7 country, leading to significant labor market shortages in key industries such as healthcare, engineering, and information technology.¹² Considering the rapidly aging demographic issue is completely novel in human history, a new approach is needed to deal with the consequences.

Section 2: Overview of the longevity therapeutics Movement

Modern Medicine’s Insufficient Approach to Aging

As highlighted in Section 1, the world is witnessing an unprecedented demographic shift characterized by a growing percentage of older individuals and a shrinking younger population. Although advancements in medical technology and public health have significantly extended life expectancy, increasing from 45 years in 1950 to over 73 years in 2024, with projections reaching nearly 82 by the end of the century, this increased lifespan has not been matched by an increase in healthspan (healthy lifespan). From 2000 to 2019, life expectancy worldwide increased from

⁹ Alzheimer’s Association Facts and Figures (2024). Retrieved from <https://www.alz.org/alzheimers-dementia/facts-figures> [Online Resource] on 2024-06-01.

¹⁰ Centers for Disease Control and Prevention Alzheimer’s Disease and Dementia (2023).

¹¹ Longo F Locatelli F Vecchio MD Giulio PD Giordano S Odone A. Tackling the crisis of the Italian National Health Fund January 2024. DOI: [https://doi.org/10.1016/S2468-2667\(23\)00277-3](https://doi.org/10.1016/S2468-2667(23)00277-3).

¹² International Monetary Fund: Germany’s Real Challenges are Aging, Underinvestment, and Too Much Red Tape. March 2024. Retrieved from <https://www.imf.org/en/News/Articles/2024/03/27/germanys-real-challenges-are-aging-underinvestment-and-too-much-red-tape> [Online Resource] on 2024-06-01.

66.8 to 73.4 years (an increase of 6.6 years), but Health Adjusted Life Expectancy (HALE) only increased from 58.3 to 63.7 years (an increase of 5.4 years). According to the WHO, “this was due to declining mortality rather than reduced years lived with disability.”¹³ Consequently, many individuals spend their extended years managing chronic age-related diseases such as heart disease, diabetes, and dementia.

Modern medicine has made tremendous strides in treating acute illnesses and managing chronic conditions, yet it remains largely ineffective at addressing the root causes of age-related diseases, which is the aging process itself. Traditional healthcare systems focus on treating symptoms and diseases as they arise rather than proactively preventing or reversing the biological processes that lead to age-related diseases and disabilities. This reactive approach has led to an increased lifespan without a corresponding increase in healthspan – the period of life spent in good health. As a result, many individuals spend their later years battling multiple age-related diseases, diminishing their quality of life and placing a heavy burden on healthcare systems.

Moreover, the approach of treating individual diseases one at a time has significant limitations. Research from the University of Southern California (USC) has shown that even if we were to cure all forms of cancer, the increase in average life expectancy would only be about three years.¹⁴ This is because curing a single disease does not address the underlying aging processes that contribute to the development of multiple age-related conditions. For example, while treating heart disease may extend life, it does not prevent the onset of other conditions like Alzheimer's disease or diabetes. This piecemeal approach fails to extend the period of life spent in good health and leaves individuals vulnerable to a cascade of other health issues as they age.

A New Way: The Development of the “longevity therapeutics” Industry

The field of longevity therapeutics emerged from the realization that targeting the biological mechanisms of aging could simultaneously address multiple age-related diseases. This shift from a disease-centric approach to a healthspan-focused approach has paved the way for innovative research and therapeutic developments.

Before the 2010s, aging research was primarily disease-based, focusing on individual diseases without addressing aging as the root cause. Although the NIH funded aging research as early as 1940 and the NIA began sponsoring research on basic aging biology in 1974, investments in

¹³ World Health Organization: Global Health Estimates: Life expectancy and leading causes of death and disability (December 2020). Retrieved from <https://www.who.int/data/gho/data/themes/mortality-and-global-health-estimates/ghe-life-expectancy-and-healthy-life-expectancy#:~:text=Globally%2C%20life%20expectancy%20has%20increased,years%20lived%20with%20disability> [Online Resource] on 2024-03-27.

¹⁴ Wu, S. (October 2023). USC Today: Delayed aging is better investment than cancer, heart disease research. Retrieved from <https://today.usc.edu/delayed-aging-is-better-investment-than-cancer-heart-disease-research/> [Online Resource] on 2024-03-27.

medicines targeting healthspan holistically, preventatively, and systematically were limited and slow to develop.¹⁵ This period was marked by sparse private sector funding due to various regulatory and reimbursement barriers stemming from outdated 20th-century drug development and insurance models. The regulatory environment made it difficult for researchers and companies to pursue therapies targeting the aging process itself. Pharmaceutical companies were reluctant to invest heavily in longevity research without clear pathways for approval and reimbursement.

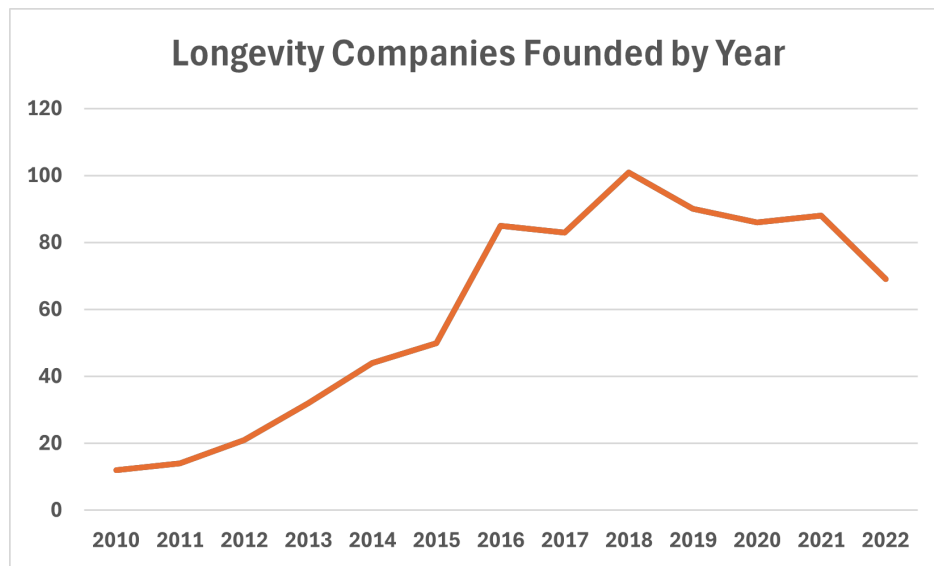


Figure 3. Number of longevity founded

Over the last decade plus, the landscape of the longevity therapeutics industry has transformed significantly. Advances in biotechnology and a growing understanding of the biological mechanisms of aging have spurred increased interest and investment in the field. The number of longevity biotech companies has grown substantially. To date, there are 1,110 active longevity companies; 71% were started in 2010 or later and most of them are in the US (**Figure 3**).¹⁶ This period has seen increased preclinical and clinical research into therapies targeting the twelve hallmarks of aging. Lifespan.io, an advocacy and research organization, is currently tracking 62 preclinical and clinical programs investigating therapies that target the hallmarks of aging.¹⁷ Of these, five have already reached Phase 3 trials, indicating a maturation of the field from basic research to more advanced stages of drug development. This rapid progress and increased investment activity underscore the potential of longevity therapeutics to revolutionize healthcare, significantly extending the healthy years of life for many individuals.

¹⁵ National Institutes of Health ExPORTER. Accessed on 2024-06-05.

¹⁶ Spann: Longevity Companies. Retrieved from <https://spannr.com/companies> [Online Resource] on 2024-06-01.

¹⁷ Lifespan.io: The Rejuvenation Roadmap. Retrieved from <https://www.lifespan.io/road-maps/the-rejuvenation-roadmap/> [Online Resource] on 2024-06-01.

Defining longevity therapeutics and The Hallmarks of Aging

longevity therapeutics aims to extend the healthy years of life by targeting the biology of aging to delay age-related diseases and improve quality of life through advances in biotechnology, pharmacology, and genetics. Aging is characterized by the gradual loss of physiological integrity during adulthood, leading to impaired function and increased vulnerability to co-morbidities and death. Geroscience (scientists studying the biology of aging) have identified and studied twelve hallmarks of aging that influence the rate of aging in non-mammalian and mammalian organisms. These hallmarks have been grouped into three categories: primary, antagonistic, and integrative, all representing the key processes and mechanisms that drive the aging process (Figure 4). Understanding and targeting these hallmarks is crucial for developing interventions that can slow down, stop, or even reverse aspects of aging. By mitigating these hallmarks, the longevity industry aims to extend healthspan, delay the onset of age-related diseases, and improve the overall quality of life.

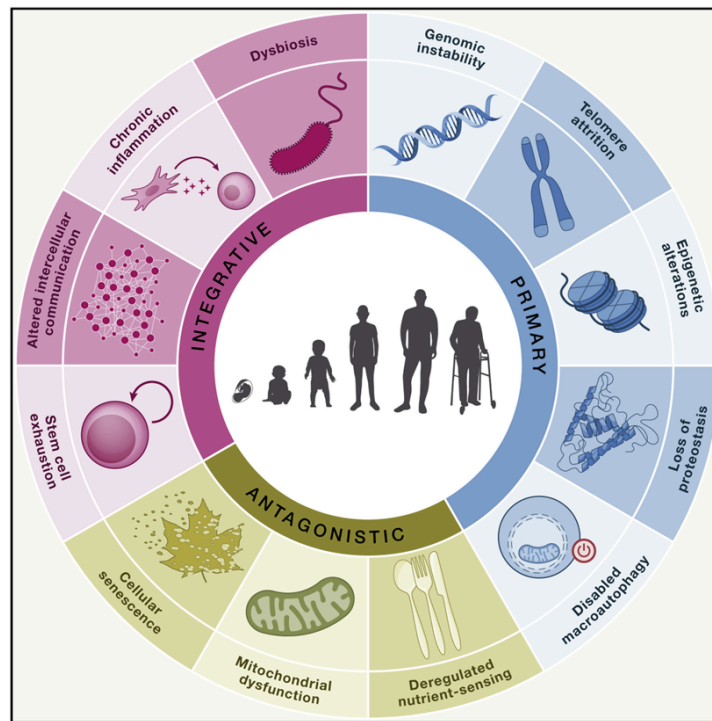


Figure 4. Hallmarks of Aging

Primary

Genomic instability refers to the accumulation of genetic damage over a lifetime due to environmental factors and replication errors. This hallmark is linked to age-related diseases such as cancer, neurodegenerative diseases, and age-related immune dysfunction.

Telomere attrition involves the shortening of telomeres, the protective caps at the ends of chromosomes, leading to cellular aging and apoptosis. Age-related diseases associated with telomere attrition include cardiovascular diseases, pulmonary fibrosis, and age-related immune dysfunction.

Epigenetic alterations encompass changes in DNA methylation, histone modification, and chromatin remodeling that alter gene expression. These alterations can lead to age-related diseases such as cancer, metabolic disorders, and neurodegenerative diseases.

Loss of proteostasis is the decline in the maintenance of protein folding, leading to the accumulation of misfolded proteins and aggregates. This hallmark is linked to age-related diseases such as Alzheimer's disease, Parkinson's disease, and cataracts.

Disabled macroautophagy is the lack of cellular digestion required to maintain optimal cellular and molecular functions. This hallmark is linked to accelerated aging, infections, cancer, cardiovascular, neurodegenerative, metabolic, musculoskeletal, ocular, and pulmonary disorders.

Antagonistic

Cellular senescence is when cells lose the ability to divide but remain metabolically active in a dysfunctional state, secreting inflammatory factors. Age-related diseases associated with cellular senescence include diabetes, osteoarthritis, cardiovascular diseases, and general inflammation.

Mitochondrial dysfunction is the decline in mitochondrial efficiency and number, leading to reduced energy production and increased oxidative stress. Age-related diseases associated with mitochondrial dysfunction include Alzheimer's disease, cardiovascular diseases, inflammation, and general age-related fatigue.

Deregulated nutrient sensing involves the impairment in pathways that sense and regulate nutrient availability, such as insulin/IGF-1 signaling. Age-related diseases associated with this hallmark include type 2 diabetes, obesity, and metabolic syndrome.

Integrative

Stem cell exhaustion refers to the depletion of stem cells, leading to decreased tissue regeneration and repair capacity. This hallmark is linked to age-related diseases such as anemia, decreased immune function, and muscle atrophy.

Altered intercellular communication involves the breakdown in the signaling pathways between cells, leading to chronic inflammation and tissue dysfunction. Age-related diseases associated with altered intercellular communication include chronic inflammation, cancer, and neurodegenerative diseases.

Chronic inflammation is a system manifestation of inflammatory markers (cytokines) and biomarkers that trigger age-related immune dysfunction, cancer, neuroinflammation, and metabolic syndrome.

Dysbiosis is the disruption of the microbiome that causes obesity, ulcerative colitis, neurological disorders, cardiovascular diseases, and cancer.

Notable Advancements in Longevity Biotechnology

This section explores notable advancements in longevity biotechnology, focusing on both repurposing FDA approved drugs for anti-aging benefits and cutting-edge developments from leading biotech companies. We'll discuss the potential of FDA approved drugs like metformin and rapamycin that are both well-studied and currently being investigated for their ability to extend healthspan, as well as highlight the significant progress made by several notable companies developing advanced therapeutics aimed at combating the biology of aging and age-related diseases.

Research on Existing Medications

Metformin, is a well-established FDA-approved drug primarily prescribed to treat type 2 diabetes for 30 years. To date, there are 1,228 published peer-reviewed studies on metformin and its implications on aging, most of them in the last decade (**Figure 5**).¹⁸ Recent published research in mammalian models have suggested that metformin may have beneficial effects on human aging and age-related diseases through attenuating the hallmarks of aging.¹⁹ This has led to the Targeting Aging with Metformin (TAME) Trial, a prominent study that will involve over 3,000 participants aged 65-79 in 14 leading research institutions across the country.²⁰ Once the TAME trial acquires the funding it needs to launch its studies, it will take 6 years to complete. The series of trials aims to determine if metformin can delay the onset of age-related chronic diseases such as heart disease, cancer, and dementia. If successful, the TAME trial could provide evidence that metformin extends healthspan by delaying the progression of age-related diseases and establish “aging” as an indication that can be treated. In addition to the TAME trial, 22 human clinical trials using metformin as an intervention to study aging have been completed and 13 are ongoing, further supporting its safety and long-term use in humans.

¹⁸ <https://pubmed.ncbi.nlm.nih.gov/>. Keyword: Metformin, Article types: Clinical Trial and Randomized Controlled Trial.

¹⁹ Kulkarni AS, Gubbi S Barzilai Nir Benefits of Metformin in Attenuating the Hallmarks of Aging July 2020. DOI: <https://doi.org/10.1016/j.cmet.2020.04.001>.

²⁰ American Federation for Aging Research: The TAME Trial. Retrived from <https://www.afar.org/tame-trial> [Online Resource] on 2024-06-05.

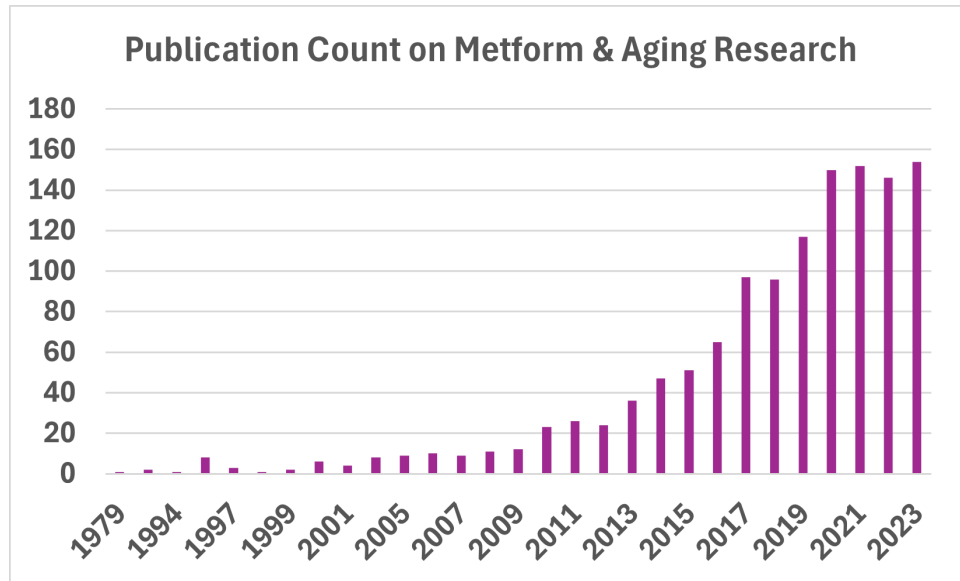


Figure 5. Publication Count on Metformin and Aging Related Research

Rapamycin/Rapamune, also known as sirolimus, was approved by the FDA in 1999 as an immunosuppressant to prevent organ transplant rejection. To date, there are 2,894 published peer-reviewed studies on rapamycin and its implications in aging (**Figure 6**). Similar to metformin, we have observed the highest publication record in the last decade. The study of rapamycin has demonstrated its efficacy in extending lifespan in mammalian aging models by inhibiting the mTOR (mechanistic target of rapamycin) pathway, a pathway crucial for cell growth and metabolism during development.²¹ This effect is conserved in yeast, worms, flies, and mice, further demonstrating its potential to delay the onset of age-related diseases.²² In humans, there have been 5 completed and 4 ongoing clinical trials using rapamycin as an intervention to study aging. More notably, The Test of Rapamycin in Aging Dogs (TRIAD) conducted by the Dog Aging Project is a large-scale double-blind, placebo-controlled clinical trial of rapamycin. This study was supported by the NIH from FY 2018-2023 but is now privately funded. It aims to evaluate whether rapamycin can extend the lifespan and healthspan of companion dogs at a large-scale, providing the world’s largest companion dog public dataset. By studying companion dogs, researchers hope to gather insights that could be applicable to human aging, given the similarities in the aging process and environmental exposure between dogs and humans. The Dog Aging Project also collects extensive health data to better understand the aging process that can be applied to humans.

²¹ <https://pubmed.ncbi.nlm.nih.gov/>. Keyword: Rapamycin, Article types: Clinical Trial and Randomized Controlled Trial.

²² Harrison DE, et al. Nature. Jul 16 2009. DOI: <https://doi.org/10.1038/nature08221>

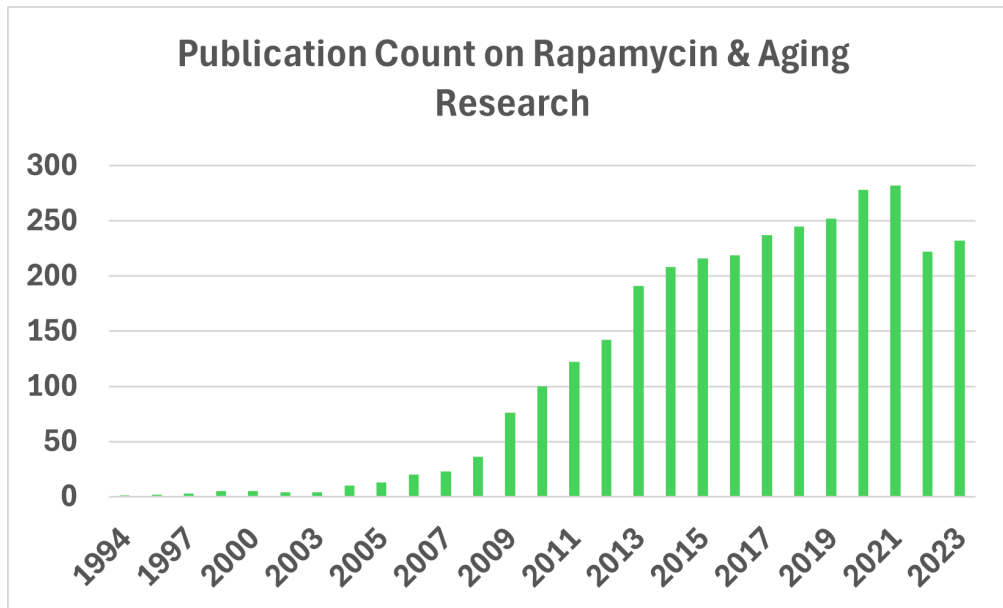


Figure 6. Publication Count on Rapamycin and Aging Related Research

Leading Biotechnology Firms in Longevity Therapeutics

BioAge Labs is a drug discovery company that targets key pathways that drive metabolic aging. The company's approach includes using machine learning and large-scale human data to discover and validate novel therapeutic targets that can extend healthspan. Its comprehensive platform integrates longitudinal omics data (genomics, proteomics, etc.) from a large and diverse cohort of older adults. One of their notable drug candidates is Azelaprag, an apelin receptor agonist that mimics the activity of the peptide apelin, which is released in response to exercise. Azelaprag has shown significant promise in preclinical and clinical studies [NCT06141889], demonstrating potential for best-in-class oral weight loss when co-administered with incretin drugs. It aims to achieve significant weight loss, improve body composition, and prevent muscle atrophy.²³

Rubedo Life Sciences is developing a new class of therapeutics aimed at eliminating senescent cells, which contribute to the aging process and age-related diseases. Their proprietary ALEMBIC™ platform identifies and targets these "zombie cells" to improve tissue function and reduce inflammation. Rubedo's lead candidate, RLS-1496, is designed for the treatment of chronic dermatological conditions such as atopic dermatitis and psoriasis. RLS-1496 has shown

²³ Business Wire: BioAge Announces Positive Topline Results for BGE-105 in Phase 1b Clinical Trial Evaluating Muscle Atrophy in Older Volunteers at Bed Rest. Retrieved from: <https://www.businesswire.com/news/home/20221205005201/en/BioAge-Announces-Positive-Topline-Results-for-BGE-105-in-Phase-1b-Clinical-Trial-Evaluating-Muscle-Atrophy-in-Older-Volunteers-at-Bed-Rest> on 2024-06-06.

significant promise in preclinical studies, effectively reducing senescence markers in skin cells. The company plans to advance this candidate into Phase 1 clinical studies.²⁴⁻²⁵

Fauna Bio leverages the biology of hibernating mammals (e.g, bears and ground squirrels) to discover novel therapeutics that target age-related chronic diseases like obesity.²⁶⁻²⁷ The company uses comparative genomics as a tool to examine highly conserved genes and pathways across species that experience disease resistance and resilience.²⁸ Fauna's platform enriches human druggable targets in multiple disease areas. Its cutting-edge research operates on the premise that studying human data is not enough to uncover new mechanisms that can be targeted in aging and age-related diseases.

Retro Biosciences is focused on developing therapies for cellular reprogramming and tissue rejuvenation. They are targeting specific hallmarks of aging like stem cell exhaustion, loss of proteostasis, and disabled macroautophagy. Using cutting-edge technology and lab automation, they are aiming to add 10 extra years of healthy human lifespan. Retro Biosciences has received significant investment to support their innovative approaches, positioning themselves as a key player in the future of longevity therapeutics.

Gordian Biotechnology uses its high-throughput screening to develop therapies that target the fundamental mechanisms of aging. Coupled with proven gene therapy delivery technology, they test a pooled library of hundreds of therapies in mouse models that closely represent patients. Their AI-powered analysis platform then examines the entire transcriptome to see how each of the therapies delivered affects cellular pathways. This efficient strategy holds significant promise for creating impactful longevity treatments.

Section 3: Arguments for Research and Development of longevity therapeutics

The development of longevity therapies likely possesses broad bipartisan support. In a January 2022 poll by the Alliance for Longevity Initiatives, 74% of Democrats and 62% of Republicans reported they would utilize longevity therapies. Additionally, the poll found that Democrats (79%) and Republicans (59%) support research into cellular aging.²⁹

²⁴ Rubedo Life Sciences. Retrieved from <https://www.rubedolife.com/science-platform/#Alembic> on 2024-06-06.

²⁵ Rubedo Life Sciences. Retrieved from <https://www.rubedolife.com/pipeline/> on 2024-06-06.

²⁶ Grabek, K.R., Cooke, T.F., Epperson, L.E. *et al.* Genetic variation drives seasonal onset of hibernation in the 13-lined ground squirrel. *Commun Biol* 2, 478 (2019). <https://doi.org/10.1038/s42003-019-0719-5>

²⁷ Ferris E Gregg C Parallel Accelerated Evolution is Distant Hibernators Reveals Candidate *Cis* Elements and Genetic Circuits Regulating Mammalian Obesity. *Cell Rep* 9, 29 (2019). <https://doi.org/10.1016/j.celrep.2019.10.102>

²⁸ Zoonomia Consortium. A comparative genomics multitool for scientific discovery and conservation. *Nature* 587, 240–245 (2020). <https://doi.org/10.1038/s41586-020-2876-6>

²⁹ The Alliance for Longevity Initiatives: Public Policy Polling (2022). Retrieved from <https://secureservercdn.net/166.62.107.20/sqj.900.myftpupload.com/wp-content/uploads/2022/08/NationalResults.pdf> [Online Resource] on 2024-06-06.

One straightforward argument in support of political action for aging therapies is predicated on the government's existing role in fighting age-related diseases such as Alzheimer's and cancer. If the government is justified in fighting these diseases, then why shouldn't it be involved in stopping aging itself? The case is made all the more salient by the fact that such efforts will likely produce clues to solving age-related diseases. However, there are several other arguments worth considering. If these arguments were well-known and understood, support for these therapies would likely be even higher. In this section, the guide discusses the moral, financial, and geopolitical arguments for political action to facilitate the development of longevity therapies. The section also addresses common arguments against developments in this field.

Moral Argument

Developing and commercializing longevity therapies is perhaps the most important thing the U.S. government can do to increase equity and stability among its citizenry. The creation of healthspan-impacting medicines will protect society's most vulnerable citizens (seniors) while decreasing disparities in healthcare outcomes between various groups in society.

Aging is the primary underlying risk factor in many of society's most tragic diseases: the risk of cancer, diabetes, heart disease, and Alzheimer's climbs rapidly as we age. As the U.S. population grows older (by 2030, the U.S. will have more elderly individuals than children), it's more important than ever to ensure Americans are able to stay healthy and vibrant as they age.³⁰

Approximately 85% of adults over the age of 65 now have at least one chronic disease such as cancer, diabetes, heart disease, stroke, or Alzheimer's disease.³¹ Even more concerning is the proportion of adults with multimorbidity, the coexistence of two or more chronic conditions. Multimorbidity often leads to exacerbated poor health outcomes and a higher risk of premature death. Half of chronically ill patients under the age of 65 were found to experience multimorbidity, compared to 62% for those aged 65-74 years and 81.5% for those 85 years and older.³² Related to morbidity, about 41% of Americans over 65 have issues performing at least one activity of daily life (ADLs) such as walking, bathing, dressing and grooming, or feeding oneself.³³ Limitations in ADLs are associated with lower quality of life as measured by the number of unhealthy days, social functioning, and emotional well-being.

³⁰ Vespa, J. (2018, March 13). The U.S. Joins Other Countries with Large Aging Populations. <https://www.census.gov/library/stories/2018/03/graying-america.html>. Accessed on 3/27/2024.

³¹ National Council on Aging. The Inequities in the Cost of Chronic Disease: Why it Matters for Older Adults. Retrieved from <https://www.ncoa.org/article/the-inequities-in-the-cost-of-chronic-disease-why-it-matters-for-older-adults> on 2024-03-27.

³² Salive ME Multimorbidity in older adults. *Epidemiol Rev.* 2013;35:75-83. doi: 10.1093/epirev/mxs009. E

³³ Na L et al, Activity Limitations Stages Are Associated with Hospitalization Risk among Medicare Beneficiaries. *PM R.* 2017 May; 9(5): 433–443. DOI: [10.1016/j.pmrj.2016.09.008](https://doi.org/10.1016/j.pmrj.2016.09.008)

The number of people ages 65 and older in the United States has increased steadily since the 1960s, but is projected to more than double from 46 million today to more than 98 million by 2060.⁴ Between 2020 and 2030 alone, the number of older persons is projected to increase by almost 18 million as the last of the large baby boomer cohorts reaches age 65. Although much smaller in total size, the number of people ages 85 and older is projected to more than triple from 6 million today to nearly 20 million by 2060.³⁴ As a group, the baby boomer generation also has higher rates of obesity and mobility-related impairments.

Furthermore, the pool of traditional family caregivers for older Americans is shrinking as marriage and fertility rates decline and divorce rates increase. More adults will reach age 65 without a spouse or adult child to rely on for care. This caregiver shortage compounds the need to ensure older adults are healthy enough to function independently. In order to accommodate the needs of an aging population and ensure older U.S. adults are able to maintain good health and functional independence as they age, it is imperative that the U.S. government do all it can to promote advances in the field. Due to high levels of comorbidity, addressing the underlying cause of these diseases – the biological hallmarks of aging – is the most feasible strategy to do so.

Longevity therapies also have the potential to address significant racial and socioeconomic disparities in the health of older adults. While these disparities exist across the spectrum of aging, they are particularly significant among the older population, and the COVID-19 pandemic has further magnified these disparities. The Hispanic population experienced the largest drop in life expectancy during the COVID-19 pandemic, falling by three years over the course of 2020 alone.³⁵ Life expectancy for the non-Hispanic black population decreased by almost as much at 2.9 years. Income also plays a significant role in life expectancy: From 2001 to 2014, the richest Americans gained approximately 3 years in longevity – an effect equivalent to the effect that curing cancer would have on life expectancy – but the poorest Americans experienced no gains. And Americans among the top 1% for household income live on average 15 years longer for men and 10 years longer for women than Americans in the bottom 1%.³⁵

The disabling effects of aging are also more likely to affect older adults of color, who are at a higher risk of having low physical capacity, poor vision, and dementia. They are also more likely to experience unmet needs related to self-care, mobility, and household activities. Additionally, older adults without a high school diploma are more likely to experience poor health outcomes and have shorter lifespans than adults with a college degree. Nearly 15% of older Americans live below the poverty threshold, putting them at increased risk of decline in mental health and the development of dementia.³⁶ And once diagnosed, low-income patients may receive lower quality

³⁴ Mather M, et al, Population Bulletin Population Reference Bureau (2015).

³⁵ Skou, S.T., Mair, F.S., Fortin, M. *et al.* Multimorbidity. *Nat Rev Dis Primers* 8, 48 (2022).
<https://doi.org/10.1038/s41572-022-00376-4>

³⁶ American Psychological Association. Fact Sheet: Age and Socioeconomic Status (2010). Retrieved from <https://www.apa.org/pi/ses/resources/publications/age> on 2022-11-12.

care: one study showed that low-income Alzheimer's patients were significantly less likely to have received specialist care within the past year.³⁷

In addition to reduced quality of life for the patients suffering from these poor outcomes, care for disabled parents can create a significant financial burden on low-income caregivers. Low-income caregivers tend to provide parental care with limited economic resources and options. This may increase their financial burden due to lost wages from reduced work hours, family leave, or early retirement. In this sense, low-income caregivers often experience a vicious cycle of increased negative outcomes. There is also a significant psychological effect: for example, low-income caregivers of dementia patients have been found to be at higher risk of depression.

Longevity therapies could help to offset the disproportionately poor health outcomes experienced by older adults of color and adults living beneath the poverty line. These therapies could treat or even prevent negative conditions such as cancer, diabetes, heart disease, stroke, or Alzheimer's disease. By addressing age-related diseases, longevity therapeutics could help to ensure people of color and those living beneath the poverty line in the U.S. age more equitably. Addressing disparities in health and health care is not only just and equitable, it's also important for improving the nation's overall health and economic prosperity. As the population becomes more diverse, with people of color projected to account for over half of the population by 2050, it is increasingly important to address disparities.

The government's responsibility to protect and advance the interests of society includes the delivery of high-quality health care. Current policies severely limit the private sector's ability to develop and deliver therapies targeting healthspan. The government must preserve its citizens' interests by implementing policies more conducive to the development of these therapies, promoting research into the underlying causes of aging, and addressing inequalities in health outcomes for the United States' aging population.

Economic Rationale

Having a healthier, longer-lived population would allow our workforce to be smarter and more productive. By implementing policies more conducive to the creation of healthspan-impacting medicines, fewer people would be chronically ill moving forward, resulting in massive savings across society. The longevity dividend economic argument states that by promoting healthy aging and making getting older a net positive on society (not net negative as it is now), we can achieve unprecedented economic growth.

By treating the underlying cause of age-related diseases and ensuring older Americans avoid the diseases associated with aging (cancer, Alzheimer's, heart disease, diabetes) and disabling

³⁷ Nikpay, S., Keohane, L.M., Cheng, A. *et al.* Utilization of Specialized Geriatric Care Among Medicare Beneficiaries with Alzheimer's Disease and Related Dementia: An Observational Analysis. *J GEN INTERN MED* 37, 469–471 (2022). <https://doi.org/10.1007/s11606-020-06460-3>

conditions of aging (weakened immune function, arthritis, loss of muscle), the United States stands to establish significant financial benefits. The government pays for more than 65% of healthcare costs for the elderly through Medicare and Medicaid spending.³⁸ This includes \$281 billion spent annually on heart disease; \$206 billion on Alzheimer’s disease; \$183 billion on cancer; and \$176 billion on diabetes.³⁹ With the average age of the population increasing, these costs could grow exponentially in coming years.

Additionally, other complications of aging – including weakened immune function, physical frailty, and physical disability – also contribute to significant medical costs covered by government programs. Declining immune function played a significant role in the disproportionate impact the COVID-19 pandemic had on older adults; this was a large driver in the approximately \$400 billion increase in national healthcare spending in the United States from 2019 to 2020.⁴⁰ And the cost of the pandemic has continued to mount in the two years since.

Physical disability also presents a significant financial burden to the United States. About 41% of Americans aged 65 or older now have issues performing at least one limitation in performing activities of daily life (ADLs) such as walking, bathing, dressing and grooming, or feeding oneself, often resulting in the need for long-term care services such as in-home nursing or assisted living facilities.⁴¹ Nursing home expenses are a significant concern for the elderly, with costs on the order of \$77,000 to \$88,000 a year. Long-term care services cost the government \$136 billion in 2020.⁴²

By addressing the underlying causes of age-related disease, the United States could see significant financial returns. The sources of these returns are multifold. The healthcare system is no longer paying to treat the symptoms of chronic disease. Families are no longer forced to pay for assisted living facilities, or give up on their own potential earnings to become full-time caregivers. The government would also experience significant savings from decreased use of assisted living facilities. Older adults would need fewer interventions to accommodate disabilities such as reduced mobility, poor vision, and poor healing. Older adults could work

³⁸ McGough M. Health System Tracker: How has U.S. spending on healthcare changed over time. (Dec 2023). Retrieved from [https://www.healthsystemtracker.org/chart-collection/u-s-spending-healthcare-changed-time/#Total%20national%20health%20expenditures.%20US%20\\$%20Billions.%201970-2022](https://www.healthsystemtracker.org/chart-collection/u-s-spending-healthcare-changed-time/#Total%20national%20health%20expenditures.%20US%20$%20Billions.%201970-2022) on 2022-11-12.

³⁹ Centers for Medicare & Medicaid Services. Diabetes Occurrence, Costs, and Access to Care among Medicare Beneficiaries Aged 65 Years and Over (2017). Retrieved from https://www.cms.gov/Research-Statistics-Data-and-Systems/Research/MCBS/Data-Briefs-Items/Diabetes_DataBrief_2017 on 2022-11-12.

⁴⁰ Centers for Medicare & Medicaid Services. National Health Spending in 2020 Increases due to Impact of COVID-19 Pandemic (Dec 2021).

⁴¹ Na L, et al, Activity Limitation Stages Are Associated With Risk of Hospitalization Among Medicare Beneficiaries. *PM R.* 2017 May;9(5):433-443. doi: 10.1016/j.pmrj.2016.09.008. Epub 2016 Sep 21. PMID: 27664405; PMCID: PMC5360539.

⁴² Who Pays for Long-Term Services and Supports? Congressional Research Service (Sept 2023). Retrieved from <https://crsreports.congress.gov/product/pdf/IF/IF10343> on 2022-11-12.

longer, improving their economic productivity. The increase in average lifespan would mean that older adults would be participating in the economy in other ways – traveling, buying groceries, seeing the movies, and such – for longer. And these savings would be further magnified as the United States is able to reinvest this money into more fruitful endeavors.

The savings add up to what is known as the Longevity Dividend. The American Federation for Aging Research estimates that by delaying or preventing chronic age-related diseases, adding just 1 year of healthy life to the average American’s lifespan, the United States could save \$38 trillion.⁴³ This is a conservative estimate. Others suggest the return could be as high as \$38 trillion for just one added year.⁴⁴

The longevity dividend relies heavily on researchers’ abilities to not only increase lifespan but healthspan as well. While the estimated value of one additional year of life for the average American is \$118,000, the value of one year of healthy life more than doubles to \$242,000.⁴⁵ This is because in order to reap the significant financial benefits of increased average productivity, workers must not only live longer but do so with the physical and mental capacity to remain productive.

The goal for policymakers, then, should be to achieve health while aging. Aging can be affected in four ways, known as forms of aging malleability: behavioral factors (such as diet and exercise), environmental factors (such as clean air and water), socioeconomic factors (addressing racial and economic disparities in health outcomes), and biological (addressing the underlying biological causes of aging). While all four forms of aging play a role, addressing the biological causes of aging is most likely to have the largest impact on increasing healthy lifespan. For example, even older adults who engaged in healthy eating and exercise habits were still at risk of increased mortality due to the COVID-19 pandemic. That is because, under the current standard of care, many of the physiological effects of aging, such as decreased immune function, are immutable. Longevity therapies, however, could offset the negative effects of aging that were once believed to be inevitable. Yet despite the potentially significant impact of addressing these biological aspects of aging, this form of age malleability receives the least attention from policymakers.⁴⁵

In 2022, the U.S. national debt exceeded \$30 trillion for the first time in the nation’s history.⁴⁶ Nearly 80% of Americans say they worry about the federal budget deficit either a great deal or a

⁴³ Goldman et al, Substantial Health and Economic Returns From Delayed Aging May Warrant a New Focus for Medical Research. *Health Affairs* 32(10) 2013. <https://doi.org/10.1377/hlthaff.2013.0052>

⁴⁴ Scott, A.J et al, The economic value of targeting aging. *Nat Aging* 1, 616–623 (2021). <https://doi.org/10.1038/s43587-021-00080-0>

⁴⁵ Scott, A.J. Achieving a three-dimensional longevity dividend. *Nat Aging* 1, 500–505 (2021). <https://doi.org/10.1038/s43587-021-00074-y>

⁴⁶ Treasury Data. Debt to the Penny. Retrieved from <https://fiscaldata.treasury.gov/datasets/debt-to-the-penny/debt-to-the-penny> [Online Resouce] on 2022-11-12.

fair amount.⁴⁷ The biggest drivers on the spending side are the aging of the population and health care costs. Those two things have caused growth in the United States' biggest programs – Medicare, and Medicaid – and they are eclipsing economic growth. Significant innovation is needed in order to cut healthcare costs. Policymakers are already beginning to recognize the significant potential that longevity therapeutics present to address this issue. In an op-ed, former Speaker of the House Newt Gingrich described aging research as key to balancing the budget. It is vital that the United States prioritize the development of therapies in order to offset healthcare costs and drive economic growth in the 21st century.⁴⁸

Geopolitical Considerations

The United States is not the only country with an aging population. Japan is, on average, the oldest country in the world: 28.7% of the population is over age 65, and by 2036, people aged 65 and older could represent one-third of the population.⁴⁹ The older population in China is also growing; while only 18.7% of China's current population is age 60 or older, that number could be 28% by 2040.⁴⁹ This trend holds true for Europe as well – the share of people aged 65 and older in the EU is expected to rise from 19% to 29% of the population, and people aged 80 and over will increase from 5% to 13% by 2070.⁵⁰

An aging population poses great risk to public policy and affairs: all else even, a lower labor participation rate results in less tax revenue for the government. On top of this, more elderly means more resources are required to fund retirement programs, healthcare, and assisted living costs. Therefore, insofar as they curtail risks posed by our nation's aging population, longevity therapies should be one of our highest priorities.

Across several metrics, the United States is the world's largest biotech hub. However, other regions – particularly China – are gaining ground. Some estimates claim that collectively, China's central, local, and provincial governments have invested over \$100 billion in life sciences research and development.⁵¹ In biomedical patents, China's annual growth rate of 16% far exceeds America's 3%, and in novel cell therapy patents China leads in both total patents and

⁴⁷ Gallup. Federal Budget Deficit. Retrieved from <https://news.gallup.com/poll/147626/federal-budget-deficit.aspx> [Online Resource] on 2022-11-12.

⁴⁸ The Alliance for Longevity Initiatives. Retrieved from <https://a4li.org/2022/02/newt-gingrich-aging-research-is-key-to-balancing-the-budget/> [Online Resource] on 2022-11-12.

⁴⁹ Sun L. South China Morning Post. China's ageing population a 'long-term reality' and its silver economy needs to catch up, State Council says (Nov 2021). Retrieved from <https://www.scmp.com/economy/china-economy/article/3157385/chinas-ageing-population-long-term-reality-and-its-silver> [Online Resource] on 2022-11-12.

⁵⁰ What an aging population in Europe means for its economic and social future (Dec 2019). ICF

⁵¹ Moore S. Brookings. China's Role in The Global Biotechnology Sector and Implications for U.S. Policy 2020. Retrieved from https://www.brookings.edu/wp-content/uploads/2020/04/FP_20200427_china_biotechnology_moore.pdf [Online Resource] on 2022-11-12.

growth rate.⁵² If the United States does not take steps now to facilitate the development of longevity therapies, it's likely the United States will lose ground to China.

In addition to direct competition, the financial benefits of longevity therapies discussed in the previous section will also benefit those countries that invest and secure supremacy in the longevity field. China's economy is already set to potentially overtake the U.S. economy by 2030.⁵³ This could be further exacerbated if China reaps the financial benefits of increased longevity while the United States does not. In order to continue to compete with countries like China in the global economy, it is vital that the United States remains dominant in this field.

longevity therapeutics will also translate into significant competitive advantages as well: longevity therapies should improve the labor force. If the average person is living longer in good health, they're also likely to participate in the workforce for longer, increasing the experience level of the average worker.

This benefit extends beyond the private sector. It also ensures U.S. service men and women are in better health, stronger, and more mentally sharp than the country's adversaries. Additionally, ensuring high-performing members of the military are in better health means benefiting from their expertise for longer. Veterans are at an increased risk for many age-related diseases, including Alzheimer's disease, Parkinson's disease, and cancer. Longevity therapies could be specifically beneficial to both active and former members of the U.S. military.⁵⁴

Debunking Myths about Longevity

Overpopulation

When discussing longevity science, the possibility of global overpopulation is often broached. The argument is that medical advances that increase lifespan by addressing the underlying biological causes of aging could contribute to an overpopulated world. The first counterargument to this is that even if overpopulation was a concern, people have a moral right to live, and it's repugnant to expect them to die simply to make room for additional people. This begs the question: is overpopulation even that much of a concern to start with?

⁵² Jaques D. Biomedical Engineering: The Patent Landscape (Feb 2023). Gill Jennings & Every LLP. Retrieved from <https://www.gje.com/resources/biomedical-engineering-the-patent-landscape/> [Online Resource] on 2024-06-07.

⁵³ China's Economy Could Overtake US Economy by 2030 (Jan 2022). VOA News. Retrieved from <https://www.voanews.com/a/chinas-economy-could-overtake-us-economy-by-2030/6380892.html> [Online Resource] on 2022-11-12.

⁵⁴ 10 Common Medical Conditions in Veterans. Unity Point Health. Retrieved from <https://www.unitypoint.org/news-and-articles/10-common-medical-conditions-in-veterans-unitypoint> [Online Resource] on 2022-11-12.

Since the 1960s, both birth rate and population growth have been gradually falling. The world population will likely level off at 10.4 billion people near the year 2100.⁵⁵ It's unlikely that the world will run out of space: if all humans lived in cities with the approximate population density of New York City, for example, 11 billion people could fit in an area the size of just three U.S. states – Louisiana, Texas, and New Mexico. Additionally, advances in agriculture have meant that world hunger continues to drop, despite recent increases in the overall population.

This suggests that the traditional concerns of overpopulation – running out of space and resources – should not be the main concern. Instead, what policymakers should be worried about is the age structure of the population. Societies need enough people of working age to produce goods and services, pay taxes, and support non-working groups – primarily children and the elderly. Right now, as the global population increases, many countries are facing the challenges of an aging population that requires more resources, including increased healthcare expenditures and more working-age people required to act as caregivers for disabled older adults.

In this case, research into longevity therapies is actually a part of the solution rather than the problem, by ensuring the elderly population is healthier for longer and reducing the resources needed to care for them.

Potential for Economic Disparities

Another concern is that novel therapies may only be accessible by the rich. However, new medical technologies typically become cheaper over time, so high costs will not be a permanent barrier. Additionally, recent breakthrough therapies with record-breaking prices – for example, Novartis's gene therapy for spinal muscular atrophy, priced at over \$2 million – are typically targeting rare diseases, so research and development costs are not shared over a large patient population. By contrast, millions of people worldwide are at risk of developing age-related diseases – meaning that the per-patient cost is expected to be much lower.

Additionally, governments are already paying exorbitant costs to support multiple health interventions for older people suffering from age-related diseases. Therefore, it is likely that governments will be able to subsidize the cost of longevity therapies while still experiencing net savings from an overall healthier population, leading to lower medical costs and increased economic productivity.

Longer Lifespans are Unnatural

Just because something is “unnatural” – in this case meaning it's made or caused by humankind – does not mean that it's a bad thing. All of modern healthcare could be described as unnatural, but that does not stop society from enjoying the benefits of vaccines, antibiotics, and surgeries.

⁵⁵ United Nations Population Division Data Portal [Online Resource] Accessed on 2024-06-07.

Outside of the healthcare realm, modern amenities such as computers, indoor plumbing, heating and air conditioning, and others could also be described as unnatural.

Furthermore, there is an argument to be made that extended lifespans are, in fact, natural. There are species in the natural world that can live over five hundred years, and some do not appear to age – meaning they show no increased risk of dying as they get older. Evolution has already created natural examples of extended lifespan.

People Should Focus on Living Better, Not Longer

If you ask a person how they would prefer to die, most will tell you they would like to go peacefully in their sleep rather than experiencing a drawn-out decline in health. Is living longer really worth it if it just means being sicker for longer?

This argument represents a misunderstanding of the core of longevity research. There isn't a natural dichotomy between living longer and remaining healthy. By targeting the underlying causes of aging, scientists will actually be able to treat age-related diseases such as Alzheimer's, diabetes, cancer, and others, and prevent the loss of muscle tone, immune function, mobility, vision, and hearing in old age. The biggest gains the longevity sector will see will be in healthspan – the part of a person's life during which they are generally in good health – not just lifespan. Simply put, this area of science will allow Americans to live both better and longer.

Pensions and Healthcare Costs will Become Unsustainable

As mentioned previously, longevity therapies would actually help to decrease healthcare expenditures. Additionally, the retirement age could potentially be raised to reflect increases in later-life productivity, and increases in economic productivity – and therefore tax revenue – could help to offset the cost of programs like Social Security. Therefore, it is likely that these therapies would actually improve the economy. The American Federation for Aging Research estimates that by delaying or preventing chronic age-related diseases, adding just 2.2 years of healthy life to the average American's lifespan, the United States could save \$7.1 trillion over the next 50 years.⁴³ This is a conservative estimate. Others suggest the return could be as high as \$38 trillion for just one added year.⁴⁴

The Future Isn't Worth Living For

Some people are concerned that the future of the world will be unpleasant for those who experience it. They may be opposed to the extension of lifespan (which is a side effect of increasing healthspan) because they are under the impression that the future isn't worth living for. However, by most objective measures, the world has been on a clear, positive trajectory. The world is experiencing lower poverty and hunger, more recreation time, less violence, improved education, improved health outcomes, faster travel and communication, and a wealth of

technological advances. And economic gains from increased longevity could be re-invested to continue these trends. Overall, one might think the future is not worth living for, but if you are a parent or a guardian who has invested in your child(s) education, you might be inclined to see that flourish for generations to come.

Living Longer Means Lower Job Turnover

As people age, they eventually retire and leave the workforce, creating job openings for the next generation. If people live longer, will that mean there are fewer job opportunities available for young people? That scenario is unlikely because of the economic gains created when the average lifespan is elongated. Living longer means an increased demand for goods and services that will fuel job creation.

Will Dictators Live Longer?

Some opponents argue longevity therapies will prolong the lives of dictators. However, addressing this problem by halting the development of therapies that could drastically improve the lives of billions of people worldwide is a net negative. No one would argue that researchers should stop developing medicines for cancer or heart disease patients because those therapies could be used to extend the lives of evil people. In addition, even if the aim is to ensure dictators die earlier due to developing age-related diseases, a positive outcome is far from assured, as in many cases another dictator will take the place of the deceased.

Additionally, there is a worldwide trend towards fewer dictators and a smaller proportion of the population living under autocratic governments. It is likely that, regardless of the development of longevity therapies, this will become less of an issue over time.

Will People Become Bored if They Live “Too Long”?

It’s unlikely that anyone will become so bored that age-related decline and eventual death is preferable. This is especially true given that better health in old age means that older Americans will be able to work longer, travel more, maintain interpersonal relationships, and pursue hobbies and recreational activities more easily. Therefore, these therapies are likely to decrease the boredom experienced by older adults. In cases where an individual feels that they are no longer receiving personal satisfaction from living longer, they would be free to discontinue treatment to prolong their lifespan.

Section 4: Roadblocks in the longevity therapeutics Field

Lack of Private and Public Funding

One of the most significant barriers to advancing the longevity therapeutics field is the lack of both private and public funding. Despite the immense potential of longevity therapies to transform healthcare and significantly improve quality of life, investments in this area remain disproportionately low compared to other medical research fields.

Public Funding (graphic)

As mentioned above, NIA was created in 1974 to lead a national scientific effort to understand the nature of aging in order to promote the health and well-being of older adults, however it is still one of the institutions within the NIH to be severely underfunded. Based on the FY 2025 NIH Proposed Budget, less than 10% of the NIH budget is allocated to research into the biology of aging.⁵⁶ This is a stark contrast to the funding allocated to research in heart disease, cancer, and Alzheimer’s disease and dementia-related research. The limited public funding constrains the scope of research that can be undertaken and delays the development of promising therapies.

Private Funding

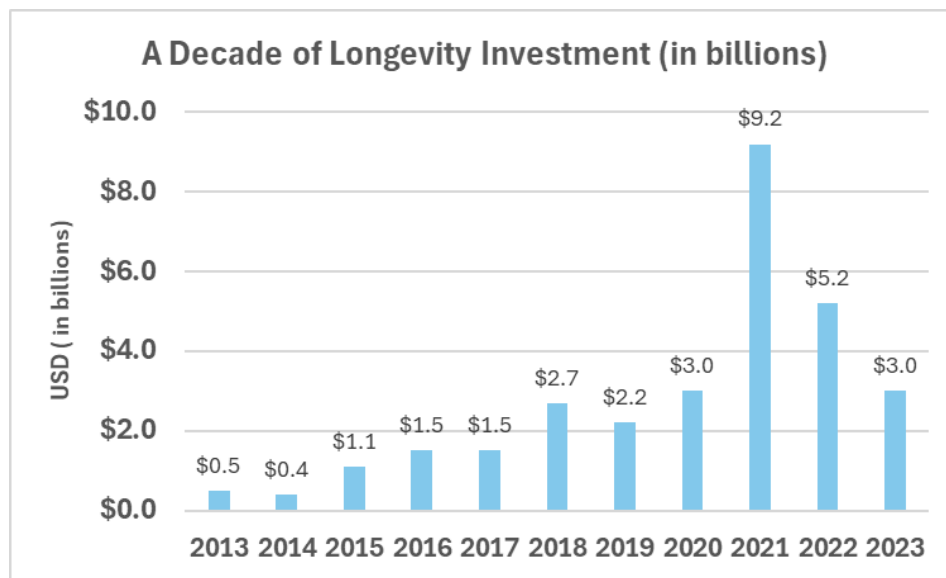


Figure 7. Total Private Investment in the Longevity Industry

Private funding into the longevity biotech industry began in 2013 with a total raise of \$0.5 billion USD. In the last decade, the industry has experienced an outpour of interest along with increased funding. In 2021, the total amount of private funding hit its peak at \$9.2 billion and has declined

⁵⁶ Overview of NIH FY 2025 Presidential Budget. Retrieved from <https://officeofbudget.od.nih.gov/pdfs/FY25/br/Overview%20of%20FY%202025%20Presidents%20Budget.pdf> [Online Resource] on 2023-06-07.

thereafter (**Figure 7**).⁵⁷ The reason for this is that many venture capitalists and biotech companies are hesitant to invest in longevity research due to the perceived high risk and long time frames associated with developing and commercializing these therapies. The complexity of the aging process and the lack of immediate financial returns further deter private investment. The funding gap stifles innovation and slows the progress of translating scientific discoveries into viable treatments, making private investment in longevity research insufficient without stronger public funding. Increasing both public and private funding is crucial for the advancement of longevity therapeutics. Policymakers and stakeholders need to recognize the immense potential of this field and allocate resources accordingly. Public-private partnerships could also be a viable solution to bridge the funding gap and accelerate the development of longevity therapies.

Lack of Standardization for Longevity Clinical Trials

Another major roadblock in the longevity therapeutics field is the lack of standardization for clinical trials. Current approved and accepted interventions to target aging in humans are restricted to diet and exercise. Additionally, advances in longevity therapeutics (pharmacological interventions) have also been investigated and shown to directly and indirectly target the hallmarks of aging, improving age-related conditions. While age remains the major risk factor for age-related diseases, regulatory agencies such as the FDA and EMA have not accepted these geroscience-guided clinical outcomes as a path to regulatory approval.

Challenges in Trial Design

Longevity therapies pose unique challenges for clinical trial design because the processes for validating specific pharmacological interventions to delay the onset and progression of multiple chronic diseases have not yet been delineated in humans. More specifically, measuring the efficacy of these therapies requires long-term studies, which are time-consuming and costly. Additionally, defining appropriate endpoints for these trials is complex. Traditional endpoints, such as disease incidence or mortality, may not be suitable for evaluating the impact of longevity therapies on healthspan. Thus, there is an urgent need to demonstrate a well-designed clinical trial that improves a cluster of age-related diseases, whether it's through repurposing existing or developing novel longevity therapies.

Regulatory Uncertainty

The lack of clear regulatory guidelines for longevity clinical trials further complicates the development of these therapies. Without standardized protocols, researchers face difficulties in designing and conducting trials that meet regulatory requirements. Without regulatory approval, insurers are not inclined to pay for such treatments, further disincentivizing pharmaceutical

⁵⁷ Annual Longevity Investment Report 2022. Longevity.Technology. Retrieved from <https://longevity.technology/investment/report/annual-longevity-investment-report/> on 2024-06.07.

companies from developing these longevity therapies without a viable business model. Thus, this uncertainty can deter investment and hinder the progress of clinical research in the longevity field. To address these issues, it is essential to develop standardized protocols for longevity clinical trials. Regulatory agencies, such as the FDA, should work closely with researchers and industry stakeholders to establish clear guidelines for trial design and endpoints. This would provide a more predictable and supportive environment for the development of longevity therapies.

Mindset Shift: Age is the Number One Risk Factor for Chronic Diseases

A significant roadblock to the advancement of longevity therapeutics is the need for a mindset shift among healthcare professionals, researchers, and the public. Traditionally, medicine has focused on treating specific chronic diseases rather than addressing the cellular deterioration that happens with age that causes these diseases. This disease-centric approach limits the potential to develop therapies that can extend healthy lifespan and improve overall well-being.

Current Medical Paradigm

The current medical paradigm prioritizes acute care and disease management. While this approach has led to significant advancements in treating individual diseases, it does not address the root cause of many age-related conditions. As a result, medical interventions often target symptoms rather than the underlying biological processes of aging.

Shift in Perspective

To advance the field of longevity therapeutics, it is crucial to shift the focus from disease-specific treatments to interventions that rejuvenate and reverse age-dependent cellular deterioration. This requires a fundamental change in how we view and approach our medical system. By adopting a geroscience perspective, which integrates the biology of aging into medical research and practice, we can develop therapies that address the root causes of multiple age-related diseases simultaneously.

Promoting this mindset shift will require education and advocacy efforts to raise awareness about healthspan versus lifespan and longevity and the impact of longevity therapies. Medical curricula should incorporate geroscience principles to train the next generation of healthcare professionals. Additionally, public health campaigns can help to inform the public about the benefits of extending healthy lifespan and encourage support for longevity research.

Lack of Public Awareness

Public awareness and understanding of longevity therapeutics remain limited. Despite the significant advancements in aging research, many people are not aware of age being the number

one risk factor for chronic diseases and the potential of therapies that will target the underlying mechanisms of these chronic diseases.

Information Gap

There is a substantial gap between scientific knowledge and public understanding of aging and healthspan. Many individuals still view aging as a natural, inevitable and untreatable process. This perception limits public support for longevity research and reduces the demand for innovative therapies.

Media Representation

The media often portrays aging research in a sensationalized or misleading manner, focusing on the idea of "immortality" rather than the practical goal of preventing age-related chronic diseases that will lead to healthy lifespan extension. This misrepresentation can create unrealistic expectations and skepticism about the feasibility of longevity therapies.

To overcome this roadblock, it is essential to increase public awareness and education about longevity therapeutics. Public engagement initiatives, such as science communication campaigns, educational programs, and community outreach, can help to bridge this information gap. Highlighting the real-world benefits of longevity therapies, such as improved quality of life and reduced healthcare costs, can also garner public support and drive demand for these innovations.

Section 5: Policymaker Action to Support the longevity therapeutics Field

For the first time in history, it appears aging is not an inevitable fate to which every human is consigned. Recent scientific advances demonstrate that the underlying causes of aging can be treated to prevent age-related diseases, ensuring Americans live longer, healthier lives. Supporting this kind of medicine is not only a morally imperative – it's a fiscally and politically sound investment. So what actions can the government take to advance the field?

The Alliance for Longevity Initiatives (A4LI) has identified five actions Congress can take:

1. Increase allocations to the National Institute of Aging – Division of Aging Biology;
2. Make geroscience and longevity therapeutics a focus of ARPA-H;
3. Create a dedicated regulatory pathway for longevity therapeutics;
4. Fund Congressional Budget Office research into the longevity dividend; and
5. Initiate a national movement to increase healthy lifespan by setting an actionable, time-bound goal.

In this section, the guide explains these legislative actions and how they will move the dial on the health of all Americans.

1. Increase Allocations to the National Institute of Aging – Division of Aging Biology

Aging research in the United States is severely underfunded. Just under 10% of the budget for the National Institutes of Health – \$4.4 billion of the nearly \$50.1 billion budget – is spent on research into aging biology.⁵⁶ In comparison, cancer receives \$7.8 billion in research funding; COVID-19 received \$4.9 billion; and heart disease receives \$2.6 billion (**Figure 8**)⁵⁸. Even the National Institute of Aging within the NIH spends just 8% of its budget on the biology of aging. Most of its funding is spent on neuroscience – in particular, research into Alzheimer’s disease and dementia.

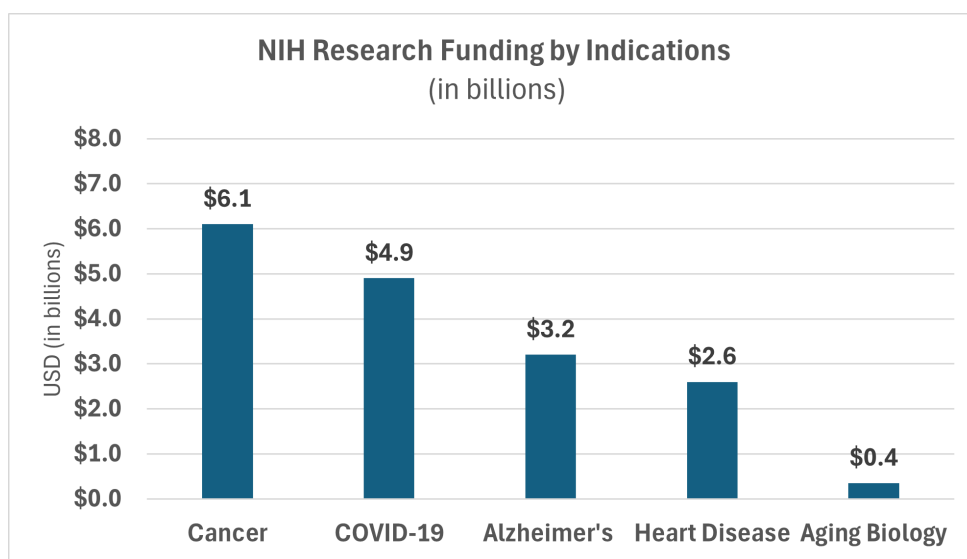


Figure 8. NIH funding for each age-related chronic diseases for fiscal year 2023

Increasing funding for aging biology research is vital, because aging is the number one risk factor for each of these diseases. Take cancer, for example. President Biden recently announced that the White House will reinvigorate Cancer Moonshot: reduce the death rate from cancer by at least 50 percent over the next 25 years, and improve the experience of people living with cancer. Funding aging research may be the most effective way to achieve these goals. Consider that, while smoking increases your risk for cancer by a factor of 15, aging increases it by 100.⁵⁹ Any comprehensive research into cancer prevention will require a better understanding of the aging biology underlying this risk factor.

⁵⁸ Estimates of Funding for Various Research, Conditions, and Disease Categories (May 2024). Retrieved from <https://report.nih.gov/funding/categorical-spending/> [Online Resource] on 2024-06-05.

⁵⁹ Age and Cancer Risk (Mar 2021). National Cancer Institute. Retrieved from <https://www.cancer.gov/about-cancer/causes-prevention/risk/age> [Online Resource] on 2024-06-05.

Furthermore, funding this research will not only develop strategies for cancer prevention. The same research will create in-roads for preventing other age-related diseases including diabetes, heart disease, and Alzheimer’s disease. That’s why every dollar spent on aging biology research is like spending a dollar for research on every single age-related disease.

Given the benefits that such research will have on health outcomes for a wide variety of diseases, it is vital that the U.S. prioritizes funding for this field. A4LI calls for Congress to treble the budget of the National Institute of Aging – Division of Aging Biology to \$1 billion by 2025.

2. Make Geroscience and longevity therapeutics a Focus of ARPA-H

To accelerate research that can improve Americans’ health, President Biden is proposing the establishment of the Advanced Research Projects Agency for Health (ARPA-H). Included in the President’s FY 2022 budget as a component of the NIH with a requested funding level of \$6.5 billion available for three years, ARPA-H will be tasked with developing high-risk, high-reward technologies to drive biomedical breakthroughs – ranging from molecular to societal – that would provide our nation’s patients with transformative solutions. The program is modeled after the extremely successful Defense Advanced Research Projects Agency (DARPA), which is responsible for technological advancements such as the computer mouse and “packet-switching” – the foundation for today’s internet.

ARPA-H would help to fund bold ideas that slip through current cracks in research and development because:

- the risk is too high;
- the cost is too large;
- the time frame is too long;
- the focus is too applied for academia;
- there is a need for complex coordination among multiple parties;
- the near-term market opportunity is too small to justify commercial investment; and/or
- the scope is so broad that no company can capture the economic benefit.

Research into longevity therapies meets several of these qualifiers. Drug development is always commercially risky. However, it is especially risky when exploring a new class of medicines predicated on novel underlying biology. Designing clinical trials to test interventions that target the aging process poses a unique set of challenges – for example, testing the effect on longevity itself may not be feasible in the time frame of a typical clinical trial – which can further increase costs and risks. Because of these aspects of aging research, it is particularly suited for ARPA-H.

A key factor in DARPA’s success is the role of program managers. They work with R&D stakeholders to establish rigorous, aggressive program goals (including detailed technical milestones) needed to manage a portfolio of sophisticated R&D projects. For ARPA-H to

succeed in its mission, program managers must have an understanding of the geroscience approach and the potential impact longevity therapeutics will have on society.

Like DARPA, ARPA-H should be solely focused on making pivotal investments in next-generation, breakthrough medical technologies. Geroscience has the ability to simultaneously treat many of the diseases Americans face in later life, and should be given high priority as ARPA-H is established. Given these parameters, A4LI supports the establishment and appropriate funding of ARPA-H, and urges policymakers to make geroscience a priority as the program moves forward.

3. Establish a Dedicated Regulatory Pathway for longevity therapeutics

In 2016, Congress passed the 21st Century Cures Act, intended to accelerate medical product development and commercialization.⁶⁰ The Cures Act established a new expedited product development program, the Regenerative Medicine Advanced Therapy (RMAT) Designation.

This designation is intended to expedite the approval of cell therapy, therapeutic tissue engineering product, human cell and tissue product, and certain human gene therapies and xenogenic cell products to treat a serious disease and have shown preliminary clinical evidence indicating the drug has the potential to address unmet medical needs.⁶¹ The benefits of the designation include increased FDA interaction and eligibility to apply for priority review for approval of the new therapy. To date, FDA states that it has received a total of 260 RMAT requests, but only 96 are publicly known to be awarded.⁶² Over the years of RMAT approvals, we have seen 37 cellular and gene therapy products and 9 biologics regenerative medicine approvals to treat sickle cell disease, fatal genetic disorders, and cancers that no longer respond to chemotherapy to name a few.⁶³⁻⁶⁴

While there are other FDA Designations that are technology agnostic – the Breakthrough and Fast Track Designations – the RMAT Designation has some advantages over those pathways. For example, while the benefits of the Breakthrough Designation and RMAT Designation are very similar, the RMAT Designation has slightly less strenuous requirements for receiving the designation. This allows the FDA to better incentivize development for this novel class of therapeutics.

⁶⁰ Public Law 114-255 114th Congress (Dec 2016).

⁶¹ Expedited Programs for Regenerative Medicine Therapies for Serious Conditions (Feb 2019).

⁶² Hildreth C. What is An RMAT? List of Publicly Announced RMAT Designation (96) (June 2024). Retrieved from <https://bioinformant.com/rmat/> [Online Resource] on 2024-06-05.

⁶³ Approved Cellular and Gene Therapy Products (Apr 2024). Retrieved from <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products> [Online Resource] on 2024-06-05.

⁶⁴ CBER Regenerative Medicine Advanced Therapy (RMAT) Approvals (Mar 2024). Retrieved from <https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/cber-regenerative-medicine-advanced-therapy-rmat-approvals> [Online Resource] on 2024-06-05.

The RMAT Designation has catapulted regenerative medicine into the mainstream. A Longevity Therapeutics Designation (LTD) could do the same for longevity therapies. While some aging therapies fall under the category of regenerative medicines, some would not. They will need to meet the stricter requirements of a Breakthrough Designation. Additionally, because aging is not currently recognized as a disease by the FDA, and because many of these therapies would be preventative in nature, it is possible that they may not qualify as intending to treat, modify, or reverse a serious or life-threatening disease or condition. Instead, sponsors would need to resort to showing that the therapy could treat one specific age-related disease, and then conduct additional trials to expand into other indications.

A4LI calls for the establishment of the Advanced Approval Pathway for longevity therapeutics (AAPLM). The proposed AAPLM aims to align economic incentives with the transformative health improvements that these breakthrough therapies can offer. The AAPLM's three core provisions, which mirror existing incentive programs established in other areas, will encourage investment in the field, increase financial incentives, and facilitate clinical development of novel drugs for diseases with significant unmet medical needs—all without imposing additional costs on taxpayers.

1. The special approval track offers a faster pathway to drug approval for longevity medicines, bringing them to patients more rapidly and accelerating profitability.
2. The priority review voucher system rewards sponsors who receive approval for a longevity therapeutics by granting expedited FDA review for a future drug, conferring a competitive advantage for the sponsor. Alternatively, vouchers can also be sold to, effectively transferring financial resources from established industry players to innovative companies focused on developing longevity therapeutics.
3. Indication-by-indication patent term extensions will be granted for each clinically approved longevity therapeutics, incentivizing companies to develop drugs not only for an initially selected disease, but also for broader approval to treat multiple chronic diseases of aging.

The AAPLM could help to create regulatory clarity for aging therapeutic companies and accelerate their development by supporting accepted companies.

4. Fund Congressional Research into the Longevity Dividend

By addressing the underlying causes of age-related disease, the United States could see significant financial returns. The government pays for more than 65% of healthcare costs for the elderly through Medicare and Medicaid spending. Age-related diseases pose the most significant financial burden on the American healthcare system. For example, Alzheimer's and other forms

of dementia cost the U.S. \$345 billion in 2023, with Medicare and Medicaid paying for roughly \$222 billion of those costs.⁶⁵ And with the average age of the American population increasing, those expenses are expected to nearly triple by 2050.

Besides offsetting the direct cost of treating age-related diseases, this field will provide significant indirect financial benefits. The savings will be further amplified when the U.S. reinvests these hundreds of billions of dollars. Additionally, older adults could work longer, improving their total economic output. Moreover, an increase in average healthspan would mean older adults participate as consumers – traveling, buying groceries, seeing movies – for longer.

As described previously, these economic benefits add up to what is known as the longevity dividend. Economists have previously evaluated the value of increasing the healthy human lifespan; estimates range from \$7.1 billion in returns for increasing the average healthy human lifespan by 2.2 years, to \$38 trillion for just one additional year of healthy life.⁴³⁻⁴⁴

It is clear that developing aging therapies has financial benefits, but the exact return depends on many factors. There is a need for objective, nonpartisan, and timely analysis of the longevity dividend to inform Congressional actions in this field of science. With many voters and politicians increasingly concerned with the national debt, it is imperative that the United States is able to fully realize the financial benefits of longevity therapies. The Congressional Budget Office is uniquely positioned to provide this analysis. A4LI urges Congress to conduct research to determine the potential impact of the longevity dividend in the U.S.

5. Initiate a National Movement to Increase Healthy Lifespan

In 2017, the United Kingdom released a white paper identifying four ‘grand challenges’ designed to tackle significant issues the country is facing. One of those was a grand challenge on aging, championed by the country’s All-Party Parliamentary Group on Longevity. Like many other countries, people over 65 are a rapidly growing proportion of the population – potentially leading to lower tax revenue as retirees exit the workforce and an increased strain on national resources. In 2018, the UK set a new goal to propel this ‘grand challenge on aging’ forward: to add five years to healthy life expectancy by 2035.⁶⁶ To help reach this goal, the UK has announced £130 million of investment to support healthcare innovation, including £69.5 million towards new treatments that allow people to lead healthier and longer lives.⁶⁷

⁶⁵ 2024 Alzheimer’s Disease Facts and Figures. *Alzheimers Dement* 2024;20(5). Alzheimer’s Association. Retrieved from <https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf> [Online Resource] on 2024-06-06.

⁶⁶ A consensus on healthy aging (Feb 2023) Office for Health Improved & Disparities. Retrieved from <https://www.gov.uk/government/publications/healthy-ageing-consensus-statement/a-consensus-on-health-y-ageing> [Online Resource] on 2024-06-05.

⁶⁷ Government to invest £130 million in NHS tech. Retrieved from <https://www.ibms.org/resources/news/government-to-invest-over-130-million-in-new-tech/> [Online Resource] on 2024-06.05.

The UK is not the first major government to take this approach to extending life expectancy: in 2008, the European Union announced a goal to increase average life expectancy by two years by 2020, a goal they achieved. This approach has been adapted for other initiatives, including health-related initiatives, in the United States: President Biden’s recent Cancer Moonshot aims to cut today’s age-adjusted death rate from cancer by at least 50 percent over the next 25 years.⁶⁸⁻⁶⁹ The Department of Health and Human Services’ Healthy People program, first established in 1979, outlines clear, measurable goals as a part of a ten-year plan to improve health outcomes in the U.S.⁷⁰

These are examples of public longevity goals that are strategic, measurable, attainable, results-oriented, and time-bound (SMART), often used in government and industry. Publicizing them encourages follow-through. To increase the average American’s healthspan, policymakers should outline clear, actionable goals that can be supported by both the legislative and executive branches. As such, A4LI encourages Congress to initiate a national movement to increase healthspan by adopting a goal to increase the average American’s healthspan by five years by 2030.

Section 6: Conclusions and Call to Action

The longevity field has reached a critical moment. We are developing therapies that target the underlying causes of aging to treat and prevent diabetes, Alzheimer’s, cancer, and age-related declines in muscle and immune functions. These therapies have the potential to radically improve health outcomes for older people in the U.S., ensuring they live longer, healthier lives and maintain their independence in their later years.

Beyond the moral imperative to support medicines that will transform citizens’ lives, aging therapies represent a sound financial and political investment. The U.S. can anticipate reduced healthcare costs and greater economic growth as more citizens remain active participants in the economy for longer. The benefits of these therapies have the potential not only to offset their development costs but to exceed them significantly. Additionally, early investment in longevity therapies positions the U.S. to establish a substantial competitive advantage over other countries. By leading in the longevity industry, the U.S. can increase its economic output, enhance the experience level of its workforce, and improve the health of its servicemen and women.

⁶⁸ Cancer Moonshot. Retrieved from <https://www.whitehouse.gov/cancermoonshot/> [Online Resource] on 2024-06-05.

⁶⁹ About the Cancer Moonshot. Retrieved from <https://www.cancer.gov/research/key-initiatives/moonshot-cancer-initiative/about> [Online Resource] on 2024-06-05.

⁷⁰ Healthy People 2030. Retrieved from <https://health.gov/healthypeople> [Online Resource] on 2024-06-05.

To fully realize and accelerate these benefits, Congress must take action to support the development of longevity therapies. There is broad bipartisan support for longevity research, making this an opportune moment for policymakers to represent the interests of all Americans by advancing this transformative field.

Specific actions include

- 1) Increase allocations to the National Institute of Aging – Division of Aging Biology;
- 2) Designate ARPA-H to become a focus of geroscience and longevity research;
- 3) Adopt the AAPLM and create a dedicated regulatory pathway for longevity therapeutics;
- 4) Fund Congressional research into the longevity dividend;
- 5) Set an actionable, time-bound goals to launch a national movement to increase Americans' healthspan.

A4LI looks forward to collaborating with policymakers to advance this innovative field. Together, we can create social and political momentum around combating age-related chronic conditions and increasing the number of healthy, disease-free years for all Americans.