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Living a 140-year long and healthy life

Cracking the "longevity code" and what this means for life sciences and health care

Contents

Introduction

From the dawn of civilization, humankind has been enamored with the idea of "eternal life." Though once considered a distant fantasy, restorative health is on its way to becoming a reality. Breakthroughs in the study of longevity—why humans age, how they age, and interventions to slow the aging process—are fueling the possibility that humans may surpass existing life expectancies and live into their 140s. We are beginning to see a paradigm shift from disease-focused treatments to those that address the underlying mechanisms of aging, biological systems, and wellness. In fact, a growing community of scientific researchers believe they have the tools to extend healthy human life, transforming health care as we know it today.

In the past 100 years, we have achieved groundbreaking milestones in the diagnosis and treatment of disease, which in turn have extended healthy life span. But success has been uneven. Despite exponential gains early on, the extension of life span has largely leveled off in the last thirty years. A deeper dive into different disease areas uncovers why: Current systems, which don't consider aging as a disease,[1] aren't set up to target aging as its own endpoint.

With a growing cadre of scientists focused on understanding the process of aging itself, and entrepreneurs, investors, and biotech leaders launching innovative companies, we are at the cusp of a new multi-billion-dollar longevity industry—an industry that will compete head-on with incumbent life sciences and health care organizations.

While increasing human health and life spans will have a profound impact on all aspects of society, this paper will concentrate on the implications for life sciences and health care organizations. In this report, we'll provide a brief introduction to the field of longevity science and then look at how life sciences and health care organizations can facilitate and adapt to a future where humans live longer and healthier lives.

Bottom line

The longevity industry, though still in its infancy, is seeing an influx of funding from investors, academic institutions, and governments. This **longevity ecosystem** represents a growing set of players who are shifting away from the traditional disease-focused paradigm, instead **addressing the root causes of aging** and focusing on keeping patients well.

Companies that develop a long-term longevity strategy will be in the best position to influence how this new paradigm evolves. Whether they pursue M&A to gain key knowhow, partner with startups and academic institutions, or leverage their own core competencies, **these companies will be better able to compete in a future where humans live longer, healthier lives than ever before.**

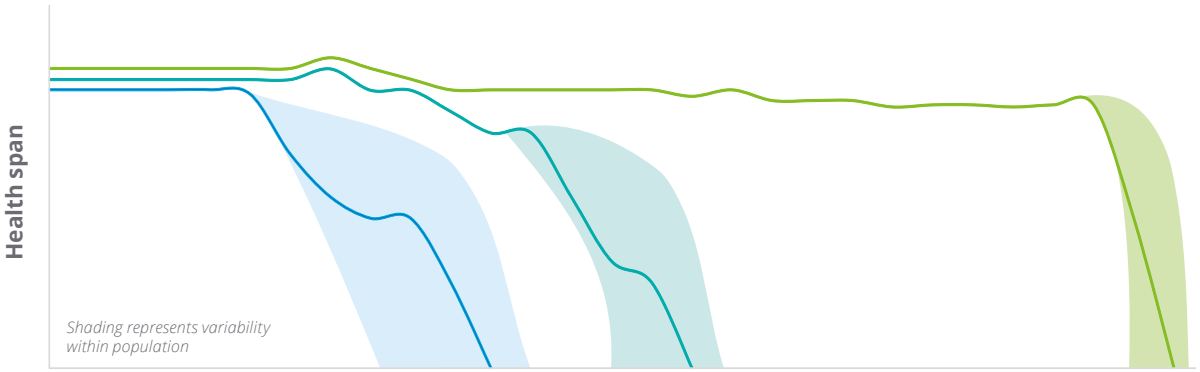
Health and life span over time—where are we today?

The goal of longevity science is not just to prolong life (life span), but also to prolong healthy years of life (health span). In the past 100 years, improvements in lifestyle, as well as disease interventions, have positively impacted both dimensions. That said, life span has only improved marginally in the last three decades (with the average American living to 75 in 1991 versus 79 today).[2] Similarly, health span (the years of life without disability or ill-health) has only experienced incremental improvement over the past decades[3] due to a multitude of factors, including the rising prevalence of chronic disease, worsening diets, and an aging population (figure 1).

Advancements in traditional therapeutic and diagnostic methods will continue to generate marginal health and life span improvements. However, we believe these approaches are unlikely to move the needle at a population level. Rather, we predict that breakthroughs in our understanding of aging and well-being will unlock the potential to radically improve existing approaches to care. Decoding the relationship between aging cells and physiological decline, or mapping the linkage between diet, the microbiome, and disease development, will allow us to substantially increase both health and life span. [4] While these are not new concepts, this longevity-focused approach to health care is increasingly gaining mainstream attention.

It is time for incumbent organizations to ask themselves what role they will play in enabling radical shifts in population health and life span.

Figure 1. Illustrative change in health and life span over time



	100 years ago	Today	Future
Life span[1]	54 years	79 years	140 years?
Health span[2]	Health decline starting mid-life	Health decline starting during retirement	Health decline delayed until near end of life

Notes: (1) Based on US mortality data in 1920 and 2020 respectively. (2) Based on Years of Life with Disability (YLD) data and anecdotal evidence.

Source: Deloitte analysis and Zhavoronkov et al. (2019)[5]

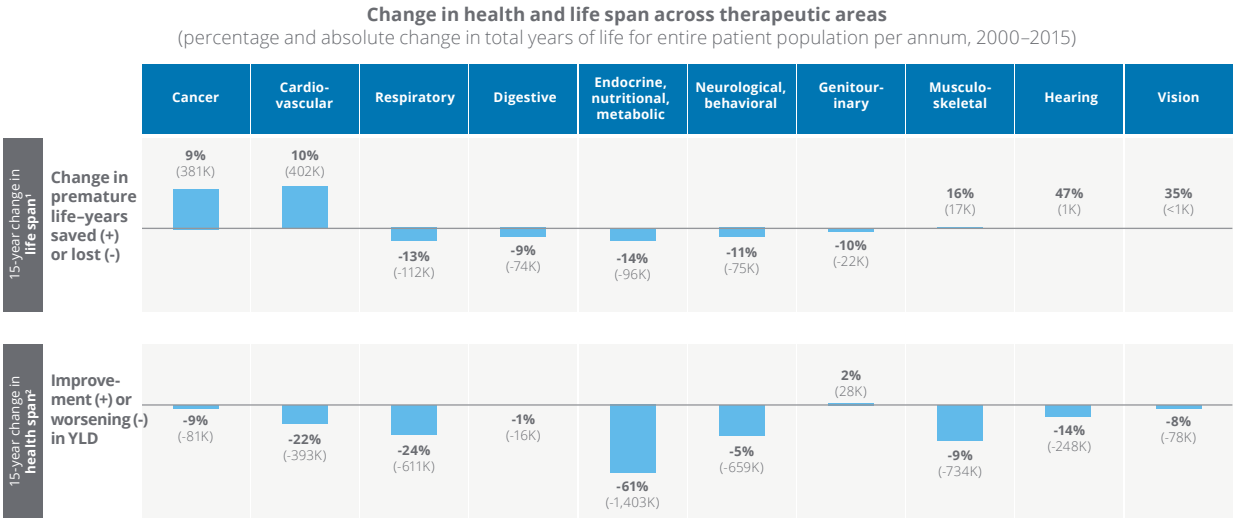
Health and life span—where have we succeeded and fallen short?

The achievements and challenges of companies in extending life and health span can be evaluated using two recognized mortality metrics: Premature Years of Life Lost (PYLL or "life span") and Years of Life with Disability (YLD or "health span").[7]

1. **Life span – Total PYLL per disease category:** Estimates the total magnitude of premature deaths (i.e., death at the age of 69 due to heart attack would be considered 10 years of premature life lost due to a cardiovascular disorder).
2. **Health span – Total YLD per disease category:** Estimates the total magnitude of disability years resulting from disease (i.e., the total number of years a patient lives with a disability or ill-health resulting from the underlying disease).

As explored in figure 2, therapeutic areas have experienced different levels of success in impacting PYLL and YLD over the past 15 years. Treatment advances for cancer and cardiovascular disease have been the primary contributors to life span improvement. Conversely, respiratory, neurological, musculoskeletal, and endocrine, nutritional, and metabolic (ENM) diseases have led to worsening life span outlooks—even making headlines as leading causes for decreasing life expectancy in the United States.[8]

Figure 2. Analysis of total PYLL and YLD in the US from 2000 to 2015

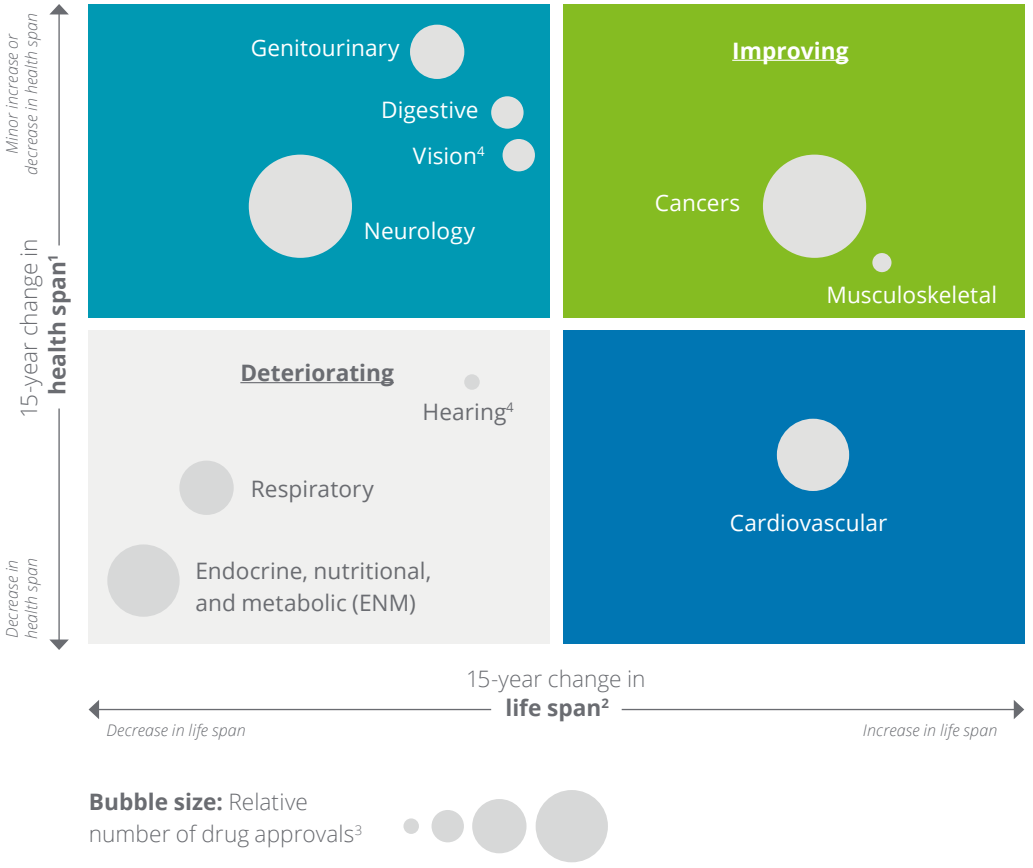


Notes: (1) PYLL analysis uses a 3-year moving average to mitigate impact of data outliers. (2) Based on US PYLL data, normalized for population growth. (3) Based on US YLD data, normalized for population growth.

Source: Deloitte analysis of WHO mortality and YLD data for the United States.[6]

This begs the question—why do we see significant gains in certain therapeutic areas, while we face major challenges in others? Can longevity-focused concepts help improve the current status quo? Figure 3 presents an analysis that aims to explain the discrepancy across 10 therapeutic areas. The analysis uncovers two extreme scenarios—disease areas that are deteriorating and those that are improving.

Figure 3. Longevity disease matrix



Analysis explained

Health and life span

- Chart illustrates the difference of a patient with a disease in 2000 vs. 2015 and whether they experience a better health or life span in the latter.
- For example, the average cancer patient experienced a materially longer health and life span in 2015 (vs. 2010).

Drug approvals

- Number of drug approvals was used as an analogue for the life sciences industry's concentration on a given therapy area.
- No statistical correlation exists between disease area concentration and improvement in health and life spans.

Notes: (1) Based on YLD data, normalized for population growth. (2) Based on PYLL data, normalized for population growth and estimated with 3-year rolling average. (3) Based on total FDA drug approvals from 2000–2015. (4) Life span data was adjusted due to data limitations and based on expert advice.

Source: Deloitte analysis of WHO mortality and YLD data for the United States,[9] FDA new drug approvals from 2000–2015[10]

Deteriorating

Deteriorating therapeutic areas saw a reduction in both health and life spans, meaning more years of life with a disability as well as premature death. This is largely driven by worsening lifestyle behavior (e.g., increasing body mass index [BMI] and type 2 diabetes) and the growing elderly population (aging is the leading risk factor for neurological and musculoskeletal disorders).

ENM diseases: Across therapeutic areas, ENM diseases saw the sharpest reduction in both health and life spans. The United States is experiencing an ENM disease epidemic, driven largely by the sharp increase in the prevalence of diabetes. Despite the multitude of available pharmacological options,[11] premature deaths from type 2 diabetes tripled between 2000 and 2015 (a 143% increase in PYLL). This negative trend can be explained by an aging, increasingly sedentary and overweight population.

Efforts by organizations to manage chronic ENM conditions, such as "whole person care" programs or advanced continuous glucose monitoring devices, continue to be offset by the rising incidence rate of ENM diseases. Individual lifestyle choices, including poor nutrition and lack of exercise, exacerbate the ENM epidemic and, unfortunately, undermine therapeutic advances. Until the industry overall migrates its focus from therapeutics to upstream well-being (including "keep-me-well" platforms) and preventative detection methods, ENM patients will continue to see limited improvements. But more to the point, a twofold longevity-focused approach that targets both individual well-being and the underlying biological mechanisms of ENM disease could dramatically improve health and life span outcomes for these patients.

Improving

Improving therapeutic areas saw the largest improvement in both life and health spans in the past 15 years, primarily due to progress in prevention and treatment.

Oncology diseases: Cancer (or oncology) saw the largest improvements because of the immense cross-industry, multi-stakeholder, and financial investment over the past few decades. Early detection has been a huge contributor to improving cancer life span and survival rates. For example, the five-year survival rate for women diagnosed with metastatic ovarian cancer increases from 30% to more than 90% if diagnosed early.[12] Additionally, significant efforts and advancements have been made in cancer pharmacological interventions. In 2015, cancer was the single largest therapeutic area for new drug approvals.[13] Clearly, focused effort and investment yields success.

> "Rapid advances in systems biology, and our understanding of the fundamental biology of aging, will transform progress in longevity."
>
> **—Anirvan Ghosh, UNITY Biotechnology CEO**

Cancer serves as a useful case study for what is required to create major impact within existing systems. Its success illustrates the level of effort, stakeholder commitment, and infusion of capital required to effect material change. Longevity-focused companies recognize this. As UNITY Biotechnology CEO Anirvan Ghosh explains: "I think of longevity the way people thought about cancer 30 to 40 years ago. People started to understand the fundamental biology of cancer. That led to thinking about how to identify cancer cells, change pathways,and ultimately to drug creation. The field is now rich with treatment options and lots of creativity and innovation. Rapid advances in systems biology, and our understanding of the fundamental biology of aging, will transform progress in longevity." Realizing the promise of transformative longevity to drastically improve health span and life span will require interdisciplinary commitment, effort, and funding.

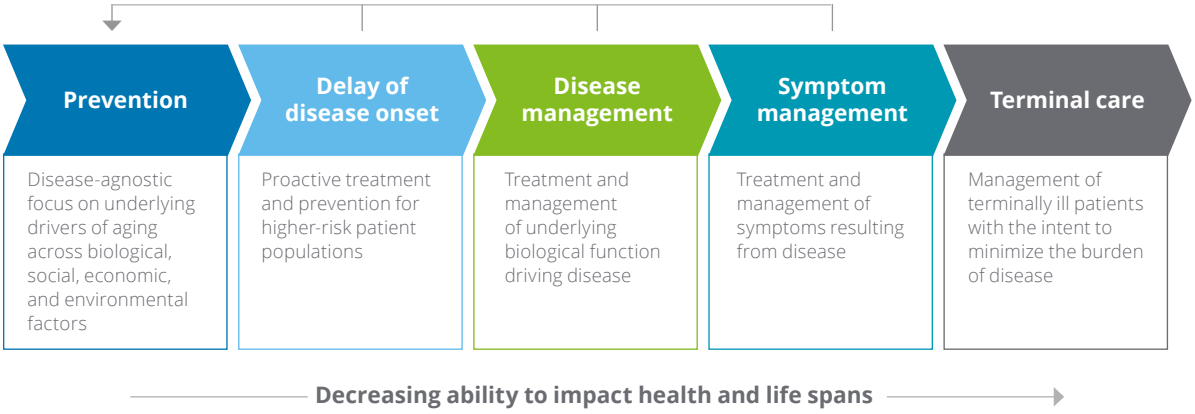
The longevity paradigm shift—were we wrong for focusing on disease?

To date, we have had varying levels of success understanding and addressing the impact of disease on life and health spans. While progress within ENM is an uphill battle, cancer continues to experience sweeping improvements due to widespread industry collaboration and investment. We believe that advances made by organizations will continue to have limited health and life span impact if organizations do not employ a multifaceted, multi-stakeholder approach—one that looks beyond a single intervention or disease.

To drive material change, organizations need to shift away from the current, disease-focused paradigm and instead address the root causes of health deterioration with preventative action. **Aging as a disease, systems biology, and wellness are examples of promising research fields that embody this preventative, holistic, and potentially regenerative approach to care.** Promising early-stage research in these fields has already uncovered potential avenues to prolong disease-free years and intervene before age-related diseases manifest irreversible symptoms.

As depicted in figure 4, the shift from individual disease and symptom management to disease-agnostic preventative care is a critical component of the *longevity* approach. Instead of single-disease treatments, companies need to focus on addressing a variety of diseases that stem from common hallmarks of aging (see Appendix 1), biological systems (see Appendix 2), or lifestyle behaviors. For example, we now know that loss of proteostasis is implicated in the development of neurodegenerative diseases like Alzheimer's and Parkinson's.[14] We also know that metabolic activity plays a role in neurodegenerative progression.[15] An approach that combines pharmacological inventions targeting biological mechanisms (i.e., proteostasis) with nutritional interventions (i.e., caloric restriction) may offer outsized potential to prevent and/or slow the progression of neurological disease. Increasingly, such approaches will have the potential to positively impact life and health spans.

Figure 4. Spectrum of treatment and care options



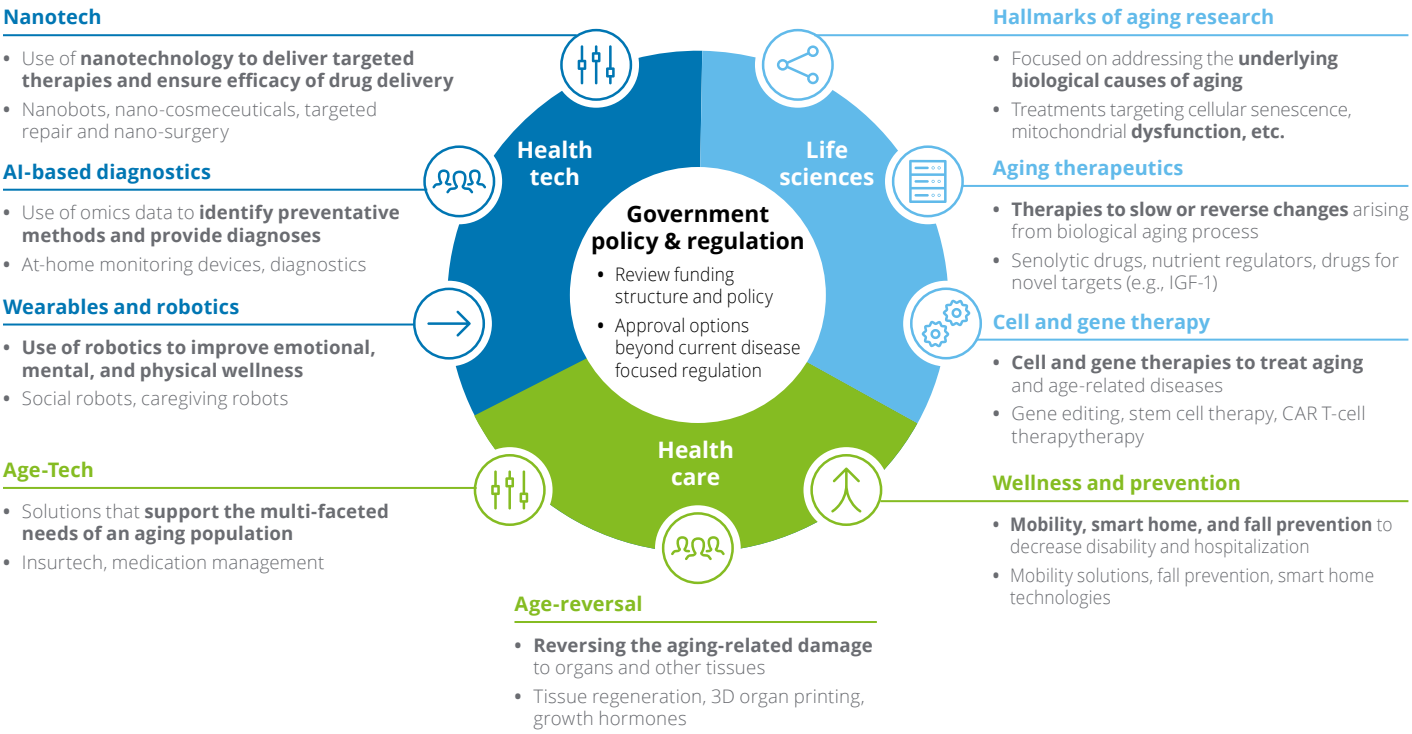
Source: Deloitte

The emerging longevity ecosystem and implications for today's players

The longevity paradigm shift has led to the development of an interdisciplinary ecosystem that looks different from traditional health care models. It comprises a growing community of life sciences and health care and health tech companies focused on solutions that address underlying drivers of disease and aging.

Though still in its infancy, the longevity ecosystem is already attracting an influx of funding from investors, academic institutions, and governments. Our analysis shows that the top 50 longevity-focused companies raised over $1 billion in venture funding as of 2020[16]—a sizable amount that continues to rise due to the growing conviction that the longevity market could outstrip the existing health care market in the long run. In fact, we also expect to see a shift within existing health care spend away from "sick care" toward wellness and well-being. This will in turn strengthen the longevity ecosystem, presenting a unique opportunity for companies to collaborate and innovate across industries and move to the forefront of aging-related therapeutics, services, and technology (figure 5).

Figure 5. Longevity ecosystem



Source: Deloitte analysis

Incumbent organizations are well positioned to evolve their business models and capitalize on the anticipated disruption of today's therapeutics and services market. Whether it be concentrating on a specific hallmark of aging or developing a new solution capable of addressing a broad scope of conditions, it is time for organizations to place their bets.

Life sciences

While companies today have greatly improved our ability to intervene and treat diseases, they remain limited by traditional therapeutic approaches. But longevity research is poised to revolutionize the therapeutics space. Life sciences companies that opt to embrace a forward-thinking longevity mindset recognize that the future of health is one where therapeutics enable prevention and well-being, as opposed to treatment-based reactionary care.

It is critical that life sciences companies examine their core technical competencies and understand how they can leverage them for longevity research. They will need to broaden their scope to focus on underlying causes of cell damage such as the hallmarks of aging. By concentrating on critical biomarkers and biological pathways, life sciences companies can move toward disease-agnostic interventions. This will allow physicians and health care providers to anticipate cellular changes and prevent diseases before they even occur.

Life sciences companies must also look externally and consider investments, partnerships, or acquisitions that will enable them to participate in cutting-edge longevity research. External interest in this space continues to grow, as evidenced by large financial investments. For example, two players focused on epigenetic alteration and stem cell exhaustion, respectively, together raised more than $800 million.[17] Partnerships are another mechanism pursued for research in the longevity field, such as a $2.5 billion program to address neurodegeneration and immuno-oncology.[18]

Health care providers and payers

Given the long-term financial and social implications, it is critical that health care providers and payers adopt a longevity mindset and support a fundamentally different ecosystem of companies. Health care providers will need to prioritize patient wellness and create hyper-personalized preventative solutions. Personalized medicine has gained traction as the future of health care because it enables a patient-centric approach to well-being and care delivery that both improves outcomes and reduces costs.

Emerging players are capitalizing on the shift to well-being and personalized medicine, making headlines with large investment rounds and valuations. For example, a prominent weight-loss app raised $540 million at a $3.7 billion valuation to expand into broader lifestyle conditions.[19] Two mental health startups—a meditation platform and a mental health platform—announced a $3 billion merger to expand access to comprehensive mental health care.[20] It is paramount that incumbent providers understand how longevity-focused concepts can improve care delivery to patients and plan for the future accordingly. Whether it be introducing new well-being offerings or providing preventative screening measures based on hereditary characteristics, providers will play a critical role in helping patients achieve longevity.

The longevity ecosystem will also create ripple effects in sectors like health insurance. Payers will need to define what life and health coverage policies look like if the average life expectancy increases by 20 years. Public health insurance, namely Medicare, stands to be severely impacted by a burgeoning elderly population. In 2019, just over 97% of the eligible US population was enrolled in Medicare for health insurance, accounting for $799 billion in costs.[21] Public and private insurance payers will need to reexamine their offerings and create services and products that support populations with longer, healthier life spans.

Health tech

Health tech companies are the newest addition to the ecosystem, driving the movement toward technology-guided medicine. From digital therapeutics to drug development and screening, the role of health tech is rapidly growing. By leveraging real-world evidence and data collected during longitudinal studies, health tech companies can make data-driven decisions for rapid diagnosis, treatment selection, and delivery. Perhaps most notably, the marriage of consumer technology with clinically validated health monitoring capabilities exemplifies the convergence of technology and the life sciences and health care industries. To advance the longevity ecosystem, incumbents and disruptors must continue to explore and integrate technology into their health offerings.

Technology also impacts longevity by helping individuals, particularly the aging population, live healthy and fulfilling lives. Health tech for the elderly has expanded over the years to include technology that supports physical activity, fall-detection sensors, and devices that support social connectivity. The benefit of these technologies on the aging population should not be underestimated. Social devices have been shown to increase personal engagement and reduce feelings of isolation and depression in the elderly.[22]

Government policy and regulation

As the elderly population continues to grow and longevity-focused technology becomes more prominent, the government must reexamine existing policy and funding structures. Programs will need to evaluate whether their current infrastructure can sustainably support a large elderly population, much of which depends on Social Security and public pensions. Given the fact that public funding infrastructures are already under strain, discussing future impact is paramount. A larger, healthier, and older population may also exacerbate the risk of greater income inequality. As a result, governments will need to redesign programs and drug approval mechanisms in the long run—shifting benefit rules and disease-focused approvals.

An exclusive interview with UNITY Biotechnology's Chief Executive Officer (CEO) **Anirvan Ghosh** and Chief Scientific Advisor (CSA) **Mike Sapieha** about the future of longevity

UNITY is at the frontier of biotechnology and medicine, developing transformative medicines to slow, halt, or reverse diseases of aging

How is interest in longevity changing?
A rapidly growing older population, and its increasing burden on the US health care system, has brought aging to the forefront of societal concerns.

"The ***threats that aging*** *and aging-associated disease pose,* ***combined with the possibility of doing something impactful****, has galvanized people."*

The work of scientists like David Sinclair, and companies like UNITY, has also spurred interest in longevity. UNITY believes that the health care industry is ready for new, innovative solutions.

"Increased interest in this space is a catalyst to future success. ***You need a significant number of committed companies, investors, and government agencies to create such life-altering products. The ecosystem is ready for it.****"*

Why cellular senescence?
Targeting cellular senescence—the deterioration of cellular function—shows early promise in altering the trajectory of aging and aging-associated diseases.

"Pre-clinical data indicates that selectively eliminating senescent cells enables us to maintain a healthy state for tissues and ***alter the trajectory of disease pathology****."*

Cellular senescence and the hallmarks of aging are exciting to UNITY because there is **evidence that these rich, interlinked mechanisms have impact across multiple organ systems**, thereby offering the potential to transform care delivery as we know it today.

"Our understanding of biological mechanisms will have a life-altering impact on the new classes of therapeutics that are expected to emerge in the next 10–20 years."
—Anirvan Ghosh, CEO

"Research and influence on tractable mechanisms like cellular senescence have the potential to ***extend and restore healthy life span in late-stage disease****."*

"We are living in the golden age of biological research. Today we have a myriad of tools that allow us to understand the mechanisms by which cells, tissues, and organisms age, at a resolution that we never had before."

—Mike Sapieha, CSA

How do we bring the concepts of longevity and health span into the clinic?
Gathering pre-clinical evidence that can easily translate into the clinic is paramount. UNITY is developing products, rigorously tested in controlled clinical studies, with a clear path to regulatory approval for defined diseases.

"To change the trajectory of health span, you need ***to demonstrate a real benefit against accepted clinical standards—this is what will garner interest and investment****."*

Establishing credibility with patients, providers, regulators, and other stakeholders is also critical.

"Our focus on ophthalmology was driven by its population impact, but also because ***we knew we would be able to demonstrate impact through quantifiable and well-understood metrics****."*

How should companies view longevity?
UNITY emphasizes that the success of therapeutic approaches enhancing longevity and health span hinges on a process that prioritizes early intervention.

"From a fundamental biology standpoint, ***early intervention to change the age-related disease trajectory is pivotal****."*

Longevity also requires a paradigm shift from focusing on specific diseases to addressing the underlying mechanisms of aging. The latter, from UNITY's perspective, is the future of longevity success.

"Instead of thinking about one disease at a time, ***can we target a fundamental biology that cuts across indications?*** *That's what we're excited about."*

What this means for organizations and beyond

Targeting the root causes of aging and disease has the potential to revolutionize the world of health care as we know it, with many implications for incumbents. From startups, to multibillion-dollar pharmaceutical organizations, to regulatory agencies, a rich ecosystem of new and emerging stakeholders is defining the future of longevity.

Traditional innovation and care models will not cease to exist, but rather they will have less influence on how we think about and deploy health care in the future. To be sure, we may never be able to prevent all diseases, nor will we be able to detect all diseases early. However, as companies shift their mindsets and pick up the pace of innovation, we will be better at learning about and responding to human conditions and diseases of the future. This in turn will help extend healthy life span across populations.

Companies that develop a long-term longevity strategy will be in the best position to influence and shift the existing paradigm. Whether they pursue M&A to gain key knowhow, partner with startups and academic institutions, or leverage their own core competencies, these companies will be better able to compete as they help bring about a future of aging and health in which humans live healthier and longer lives than ever before.

Implications for the future

There will be a long-term decrease in "sick-care" due to a delayed onset of chronic and lifestyle diseases. This will have a direct impact on life sciences and health care companies.

Profit pools will shift from treatments that intervene after disease onset to preventative treatments.

Convergence between technology and life sciences and health care industries will continue, contributing to the ecosystem and supporting structures required for longevity to thrive.

Existing industry players will reexamine their capabilities, adjusting and expanding them to address a broader set of problems, including using the know-how from other industries (e.g., pharma, medical devices, etc.).

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APPENDIX 1

Hallmarks of aging as an approach to improving health and life spans

Though often characterized by the onset of wrinkles or graying of hair, aging occurs at a much deeper level than what meets the eye. Aging, at its core, is the physiological and functional decline of biological integrity.[23] Scientists have been examining the causal impact of these various processes in enabling age-related disease for more than 20 years, but it was only in 2013 that Carlos López-Otín and his team officially grouped and categorized these disparate processes, naming them the hallmarks of aging.[24]

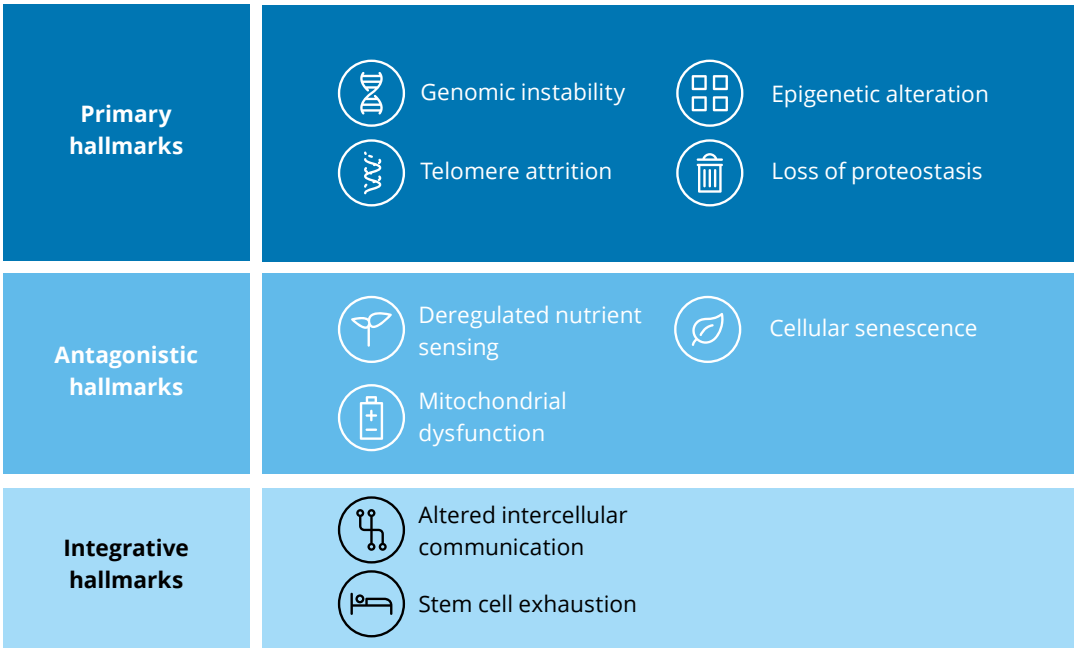
At the highest level, the hallmarks of aging reflect different mechanisms of inducing cell damage. Research is already underway, and recent developments highlight the numerous mechanisms these offer for extending health and life spans (figure 6):

1. **Epigenetic alteration**: Epigenetic alteration is the change in gene expression that harms the fundamental function of the cell. Aging impacts the efficacy of the nicotinamide adenine dinucleotide (NAD+) coenzyme that supports critical processes like tissue differentiation and metabolism. To combat declining enzyme levels and prolong the cell's healthy life cycle, longevity companies are developing NAD+ and nicotinamide mononucleotide (NMN) supplements that could materially extend life.[25]

2. **Deregulated nutrient sensing**: Deregulated nutrient sensing is the deterioration of the cell's nutrient-level response, which causes impairments to energy production, cell growth, and other essential functions. In a recent clinical trial, dehydroepiandrosterone (DHEA) and metformin showed promise in removing 2.5 years from subjects' biological age in a small human trial of men ages 51 to 65.[26]

3. **Mitochondrial dysfunction**: Mitochondrial dysfunction is the mitochondrial DNA damage that results in reduced energy production and oxidative stress. A recent clinical trial illustrated the potential of mitochondrial-targeted peptides in reversing cardiac dysfunction in mice.[27]

Figure 6. Hallmarks of aging



Source: Carlos López-Otín,[28] and Life span.io[29]

APPENDIX 2

Systems biology and wellness as an approach to improving health and life spans

When treating age-related disease, one typically thinks of a regimen of medications commonly prescribed as first-line interventions. Historically, researchers have assumed that information about individual, biochemical parts was sufficient to explain the whole. However, a growing amount of data indicates that aging is multifactorial, involving both environmental factors and multiple genes. For example, in a 2006 study, researchers found evidence of common age regulation for six genetic pathways, in three different tissues (kidney, brain, and muscle). The comparison of transcriptional networks among different tissues and at the genetic pathway level, rather than single-gene level, reveals the polygenic nature of aging and age-related disorders.[30]

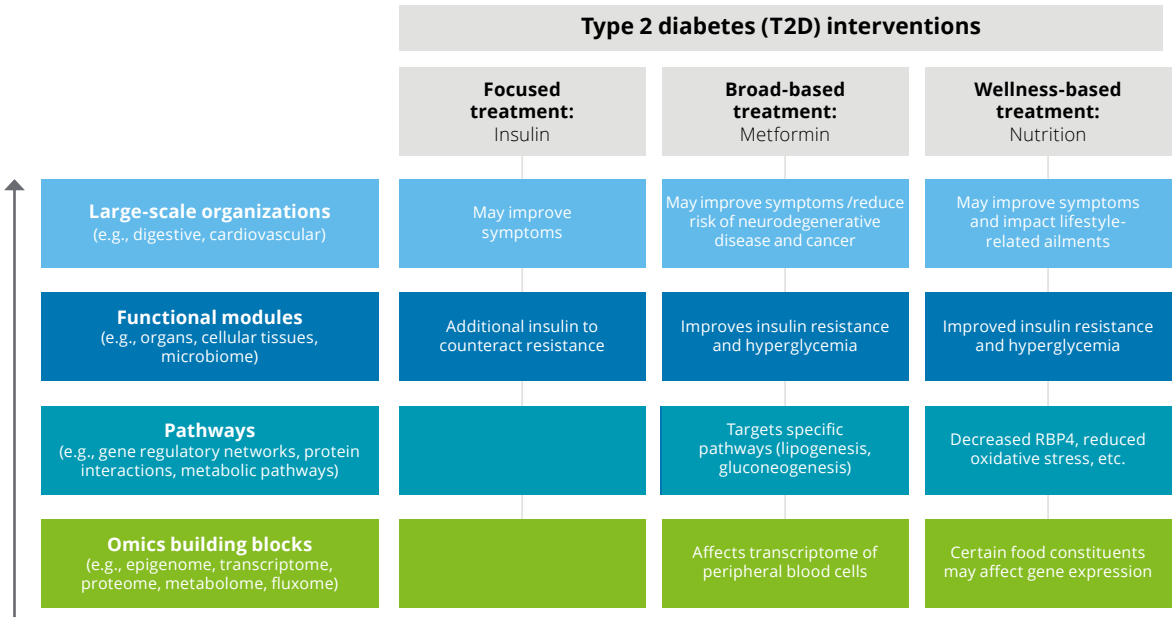
Recent advances in omics allow us to study large-scale snapshots of disease-causing processes across multiple cells, tissues, and organs.[31] As a result, there has been a shift away from trying to understand how single molecular processes function to studying how larger systems of gene expression and molecular pathways work together, also known as systems biology.[32]

Through the evaluation of broad and wellness-based treatments used in type 2 diabetes (T2D), we highlight the holistic approach these treatments take compared with more focused interventions (figure 7):

1. **Broad-based treatment**: There is emerging evidence that metformin, a commonly used anti-diabetic medication, has favorable effects on health beyond those associated with improvement in glycemia.[33] Research shows that metformin has the potential to prevent other cross-system, age-related ailments such as cognitive impairment, in which diabetes-related insulin resistance plays a direct role, as well as certain cancers.[34]

2. **Wellness-based treatment**: Wellness-based treatments are focused on nutrition and well-being, and it has long been noted that nutrition can impact T2D progression. In patients who maintain an antioxidant-rich diet that prevents obesity, retinol-binding protein 4 (RBP4) levels and oxidative stress have been seen to decrease. This may lead to increased insulin sensitivity and improvement of lifestyle-related ailments.[35]

Figure 7. Systemic and wellness-based treatment and prevention of type 2 diabetes (T2D)



Source: Deloitte research and analysis based on multiple sources[36]

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