

Part I

Executive Summary

Longevity Research Landscape Overview 2017



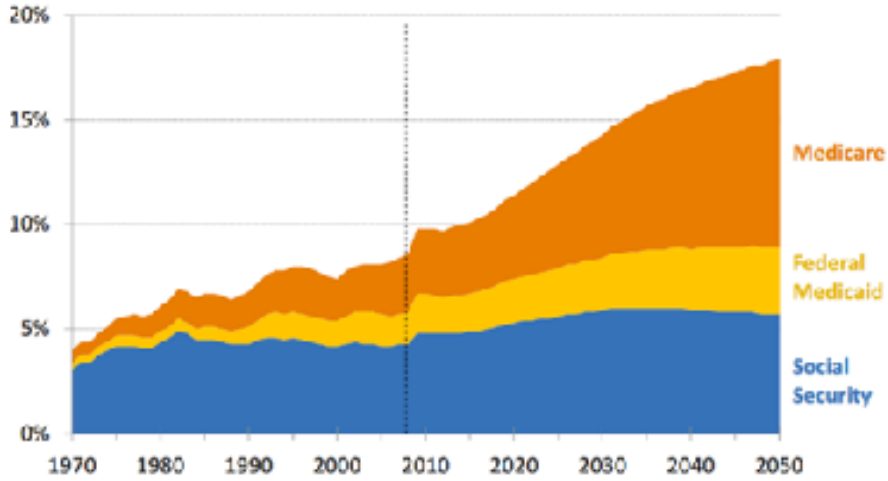
Biogerontology
Research Foundation
Prevent. Restore. Preserve.



DEEP KNOWLEDGE
LIFE SCIENCES

Medicare poses a greater financial challenge than Social Security.

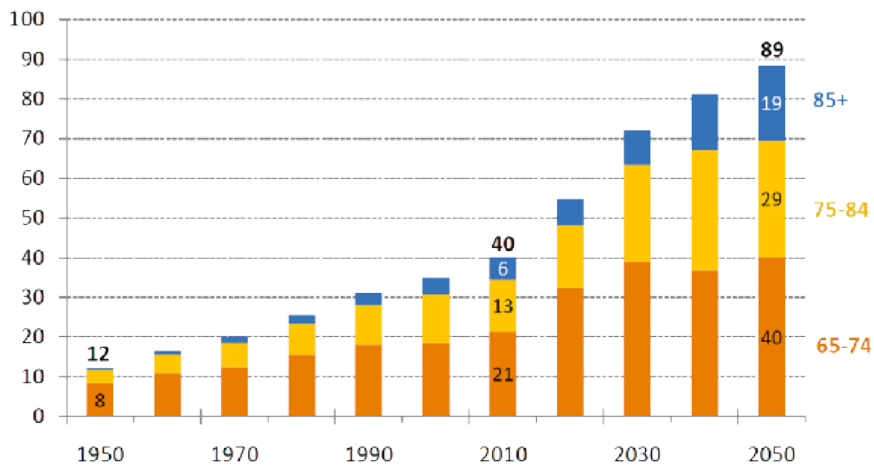
Medicare, federal Medicaid and Social Security spending as a % of GDP



Source: Congressional Budget Office, 2009, extended baseline scenario. Stanford Center on Longevity

As the boomers reach 65, then 75, then 85, the population in each age bracket will swell; the age mix of the old will shift upward.

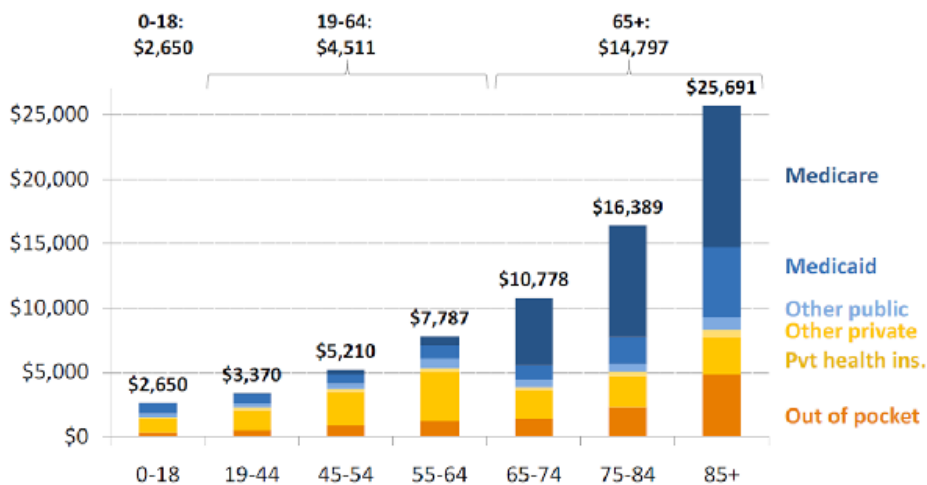
Population 65+, millions



Source: U.S. Census Bureau, 2002b and 2008d. Stanford Center on Longevity

Per capita health care spending skyrockets with age.

Per capita health care spending, by age group and source of payment, 2004



Note: Other public: e.g. workers compensation. Other private: e.g. philanthropy. Source: Centers for Medicare and Medicaid Services, 2009. Stanford Center on Longevity

Executive Summary

The list of major global hazards in the next century has grown long and familiar. It includes the proliferation of nuclear, biological, and chemical weapons, other types of high-tech terrorism, deadly superviruses, extreme climate change, the financial, economic, and political aftershocks of globalization, and the violent ethnic explosions waiting to be detonated in today's unsteady new democracies.

The greatest problem threatening global economic prosperity and social stability is demographic aging. Declining birthrates and increased lifespan are increasing population dependency ratios (working tax payers versus the elderly supported by taxes), placing a growing burden on already tenuous government budgets.

The Silver Tsunami, aptly, will hit Japan first, which already has the worst dependency ratio in the world and also the highest debt to GDP ratio of the OECD. China's workforce began shrinking in 2015, and China's 65+ population will double to 200 million by 2030.² The United States has trillions in unfunded pension and healthcare liabilities expected to expand as the Baby Boomers retire en masse over the next decade.³

“

Yet there is a less-understood challenge - the graying of the developed world's population - that may actually do more to reshape our collective future than any of the above.

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- Former US Secretary of Commerce
- Co-Founder of the Blackstone Group
- Fmr. Deputy Chairman Federal Reserve Bank of New York
- Chairman emeritus of the Council on Foreign Relations
- Author of *Gray Dawn: How the Coming Age Wave Will Transform America-and the World*

– Peter G. Peterson, in *Foreign Affairs*(1999)¹

“

I see a storm coming. [Unfunded pension and medical liabilities are] the least sustainable situation I have seen in my career.

”

– Stanley Druckenmiller, of Duquesne Capital and formerly the Quantum Fund of Soros Fund Management, to Bloomberg March 1, 2016



1. Peterson, P. (1999) *Grey Dawn: The Global Aging Crisis*. *Foreign Affairs*.
2. *UN World Population Prospects 2016*, Stanford University Center on Longevity.
3. Zhavoronkov A, Debonneuil E, Mizra, N, Artuhov, I. (2012) *Evaluating the impact of recent advances in biomedical sciences and the possible mortality decreases on the future of health care and Social Security in the United States*. *Pensions*. doi:10.1057/pm.2012.28

The current retirement age (OECD average of 64 years) was established prior to the rapid rise in life expectancy that occurred in the second half of the 20th century. Government and private sector pension schemes have not adjusted their actuarial tables to account for gains in life expectancy due to modern medicine (longevity risk).

The rate of medical advancement is accelerating. This underestimation of rising life expectancy is a mistake worth many trillions of dollars⁴. Failure to meet pension obligations would result in rising poverty among elderly, higher taxes, inflation and political instability.⁵ The post-war boom cohort is living longer but experiences an extended period of chronic disease in the years prior to death. The system of sick care is costly, particularly for diseases lacking any disease-modifying treatment, such as Alzheimer's disease. Due to the exponentially rising risk of disease as a function of age, curing any individual disease like cardiovascular disease or cancer only increases a population's healthy lifespan by 2-3 years before another age-related disease (diabetes, stroke, pulmonary disease) strikes.

The aim of geroscience and regenerative medicine is not for us to live longer in a sick, disabled state, but to prevent and delay the occurrence of age-related disease. An individual's final few years of chronic illness are their costliest to the healthcare system. The goal of the US National Institutes on Aging is the **compression of morbidity** – to extend years of healthy life. The only sustainable solution is to extend healthy lifespan (**healthspan**). This will require the use of geroprotective drugs, stem cells, and progressively complex genetic therapy to mimic the salutary mutations enjoyed by rare

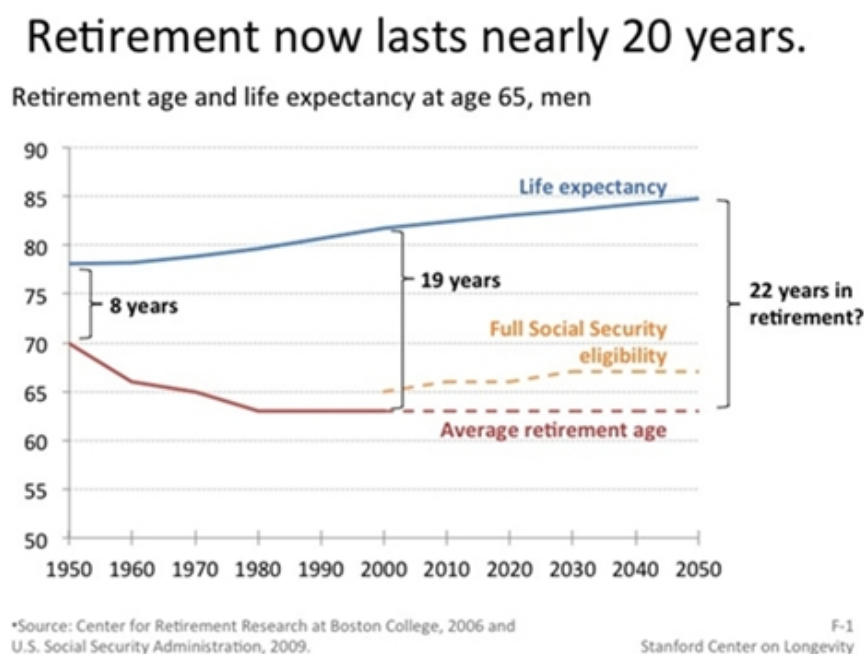
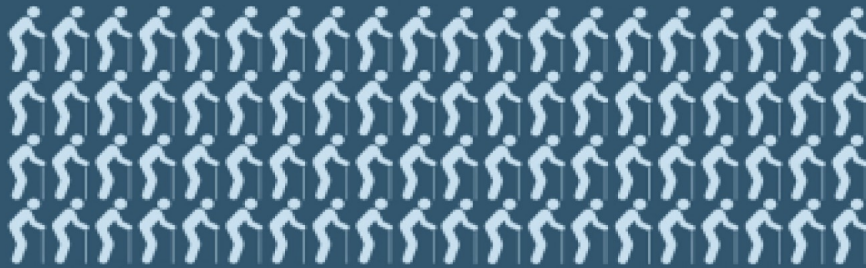


Figure 1: Working in retirement is becoming the new normal (TheMarketSurge)

4. Debonneuil E, Planchet F, Loisel S. (2015) Do actuaries believe in longevity deceleration? HAL Archives. hal-01219270
5. 2 Kotlikoff L, Burns S. (2004) The Coming Generational Storm. The MIT Press.

THE COST OF AGING TODAY

8,000 Americans turn 65 every day.



100 By 2050, the United States will be home to about 19 million people older than 85, according to U.S. Census projections.*

* and half of these people are forecasted to have Alzheimer's

These seniors will need care,



34% of seniors living alone report having at least one physical limitation.

but eldercare costs a lot.

LIVING AT HOME:

Companion care services - \$18/hr
Home Health Aide services - \$19/hr
Adult Day Health Care - \$60/day



LIVING AT A FACILITY:

Assisted Living Facility - \$3261/month
Nursing Home (semi-private room) - \$5,790/month
Nursing Home (private room) - \$6,390/month

BeClose solves the problem and helps seniors age in place

The BeClose System - Less than **\$3/day**
Annual savings with BeClose: **\$16,509**

Aging in Place, staying happy and healthy



“Compression of Morbidity” = Add life to your years, rejuvenation

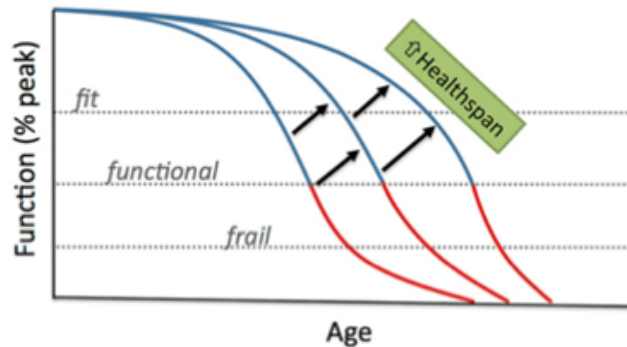


Figure 2: Medical research: Treat ageing (Luigi Fontana et al., 2016, Nature)

supercentenarians (who bear saluary mutations that delay or stop the onset of age related diseases – they are healthy past 100 years of age despite suboptimal diet and lifestyle).^{6,7}

Clearly it would be desirable to add life to our years rather than merely years to our lives. But few are aware that health span extension is becoming routine in the laboratory. Scientific breakthroughs have demonstrated up to 30% increased healthspan extension in mice,⁸ and much more in non-mammalian model organisms by various pharmacological, environmental and genetic interventions.

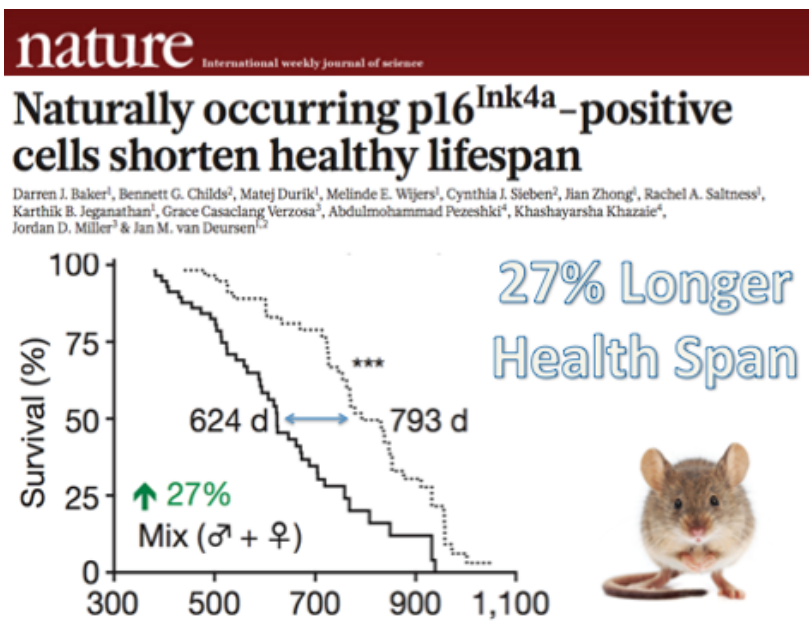


Figure 3: Naturally occurring p16 Ink4a-positive cells shorten healthy lifespan (Darren J. Baker et al., 2016, Nature)

6. Collins F. (2014) Secrets of a Supercentenarian’s Genome. NIH Director’s Blog.
7. Barzilai N, Shuldiner A. (2000) Searching for Human Longevity Genes The Future History of Gerontology in the Post-genomic Era. The Journal of Gerontology.
8. Baker D. (2016) Naturally occurring p16Ink4a-positive cells shorten healthy lifespan. Nature.

Even though it has been known for a century that caloric and dietary restriction increases healthspan in model organisms, aging was once thought too complex to be tractable by mainstream science. The field was, and remains, held back by charlatans engaged in fraud.

In recent years, scientists have elucidated the fundamental mechanisms or hallmarks of aging, opening the field of geroscience – the understanding and manipulation of the fundamental biological processes in age-related disease.

The War on Aging received reinforcements in recent years from Google's company Calico and J. Craig Venter's Human Longevity Inc., both boasting considerable intellectual and financial resources. In late 2016, Unity Biotechnology (a company developing drugs shown to slow aging by eliminating damaged, senescent cells) raised over \$116M from venture investors including Jeff Bezos, VenRock and ARCH Venture Partners.



The US National Institutes on Aging have also received budget increases as part of a new Alzheimer's Disease initiative, but of the vast majority of "aging research," less than 0.32%⁹ of the US NIH budget goes to fundamental mechanisms of aging – the knowledge necessary to slow aging itself and all of its attendant diseases. This is already possible in model organisms and translation to humans is underway but desperately underfunded relative to its importance.



The longevity industry trend is just the beginning. Combining geroscience with rapid advances in stem cell and gene therapies, the biopharmaceutical industry can expect major disruption to the current model of palliative chronic disease management as more true cures emerge.¹⁰

9. US National Institutes on Aging. Fiscal Year 2017 Budget. \$183.1M for "Aging Biology" out of \$32B NIH Budget.

10. Zhavoronkov A. (2013) The Ageless Generation: How Advances in Biomedicine Will Transform the Global Economy. St. Marten's Press.

Despite the optimistic outlook for geroscience, it is unlikely that, at the current pace of funding and awareness, meaningful health span extensions will be available in time to avert the impending crisis of demographic aging. It is critical for investors, policymakers, scientists, NGOs and influential entities to prioritize the amelioration of the geriatric world scenario and recognize aging as a critical matter of global economic security.



Figure 4: The Hallmarks of Aging (Lopez-Otin et al. 2013, Cell)

“

My lab is not concerned with diseases of aging, which are effects rather than causes; it's trying to get at the causes of aging and reverse them. And there are a fair number of precedents for this in animals, but the idea is to get it transferred to humans.

Some examples of this are if you take blood from a young mouse and exchange it with an old mouse. The small molecules, macromolecules, and cells in the blood result in a variety of biomarkers of aging being reversed. You can affect the vasculature, the blood vessels, the nerves, skeletal and cardiac muscles, and there are measures of these that indicate that it's not just prolonging a very aged state or going for longevity; you're actually reversing it.”

”



– Dr. George M. Church, Professor of Genetics at Harvard, author of *Regenesis: How Synthetic Biology Will Reinvent Nature and Ourselves*