VIEWPOINT

SCIENTIFIC DISCOVERY AND THE FUTURE OF MEDICINE

From Lifespan to Healthspan

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Viewpoint

At the turn of the 20th century, life expectancy at birth in most of today's developed nations ranged between 45 and 50 years, with women routinely outliving men. About 22% of all individuals born in 1900 in the United States died before reaching the age of 10 years, mostly from infectious diseases.[1] Among those who survived into older ages in 1900, the common diseases of aging known today were present but less common.

When public health emerged in the late 19th century, including developments such as sanitation and clean water, early mortality swiftly declined. A rapid shift in the distribution of death from younger to older people occurred during the first half of the 20th century, and since then declining death rates at middle and older ages have led to survival into increasingly older ages. As a result, about 96% of infants born in developed nations today will live to age 50 years or older, more than 84% will survive to age 65 years or older, and 75% to 77% of all deaths will predictably occur between age 65 and 95 years.[2]

With declining early-age mortality and a shift in the age distribution of death, the population of the United States, and much of humanity in general, achieved exactly what was desired: the first longevity revolution. The 30-year increase in life expectancy at birth in the past 100 years is one of humanity's greatest achievements.

Lifespan Limits and Decelerating Improvements in Life Expectancy

Over the past century, the relatively easy gains in life expectancy have been achieved by reducing mortality of younger people; more recently, scientists have focused on how much higher life expectancy can increase and what the maximum lifespan is for humans. The former is a population-based metric that involves national vital statistics for groups of people; the latter is the world record for longevity held by 1 person.

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Regarding maximum lifespan, only a small proportion of all humans are capable of living to 115 years of age, with a small number of statistical outliers capable of approaching the world record of 122 years.[3] Some experts suggest that if death rates plateau at older ages, lifespans may continue to increase. This latter view has been challenged because an unrealistically high number of people (estimated at 262 200) would have to survive to age 105 years for just 1 person to exceed the world record for longevity by 1 year to 123 years.[4] As such, the probability of any substantial increase in maximum lifespan in this century is remote.

Regarding life expectancy, one view developed in 1990 suggested that the increase in life expectancy would soon decelerate because the easy gains had already been achieved.[5] Any substantive future increases require improvements in mortality at older ages, although components of the human body (eg, brain, heart, knees) are not designed for long-term use. Others suggested that historical trends in the increase in life expectancy will continue indefinitely into the future due to yet-to-be-developed medical advances and improved lifestyles.

Not one of the anticipated high-life-expectancy scenarios is remotely plausible today. In fact, a new trend in the opposite direction has emerged in much of the developed world, indicating that death rates for many major causes of death have either leveled off, experienced declining improvement, or increased since 2008.

Biological Aging and Diminishing Returns on Life Expectancy

Reductions in childhood diseases can occur only once for a population; once such gains are achieved, the only outlets for further gains in life expectancy must come from extending the lives of older people. Given that multiple fatal conditions accrue in older people because of biological aging (eg, a fundamental and inevitable risk that occurs independent of conventional behavioral risk factors for diseases), once survival past age 65 years becomes common in a country, life expectancy gains will decelerate, even with medical advances and improved lifestyles. Because the point of diminishing returns on life expectancy (approximately 85 years for men and women combined) and the longevity limit (which has never been exceeded) for the species has been approached in many parts of the world, there is good reason to conclude that the goal of life extension has largely been achieved.

There is a dilemma. Modern medicine continues its relentless pursuit of life extension without considering either the consequences of success or the best way to pursue it. The current focus of most of modern medicine is on chronic fatal age-related diseases, in much the same way infectious diseases were confronted more than a century ago (ie, one at a time as if independent of each other). Even though there have been some successes, further life extension in an aging world will expose the saved population to an elevated risk for all other aging-related diseases.

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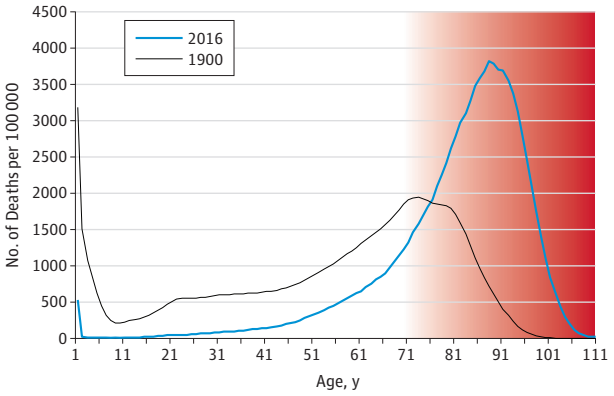
Figure. Age Distribution of Life Table Deaths for Women in the United States, per 100 000 People, 1900 and 2016



The red zone represents a period in life when the risk of frailty and disability begins to increase rapidly. The goal of aging science is to delay and compress the red zone, which may extend healthy life. Sources: 1900 data from Bell and Miller[1]; 2016 data from Human Mortality Database.[2]

The longer people live, the more important aging biology becomes as a primary risk factor in determining both length and quality of life. In long-lived populations, a substantial part of life, and certainly most deaths, now occur in a period in the lifespan when the risk for frailty and disability increases exponentially.[6] In this period, which could be called the *red zone*, it becomes increasingly more difficult to intervene using conventional disease-oriented approaches; the further into this period that humans venture, the more resistant diseases become (**Figure**).

Because the biological processes of aging force human bodies to become ever more susceptible to fatal and disabling conditions, unwanted health conditions emerge in the red zone not so much because of how life has been lived (although harmful lifestyles can accelerate their emergence and progression) but because of how long life has already been lived. Time becomes the greatest challenge.

With death inevitable, the modern attempt to counteract aging-related diseases reveals a phenomenon known as *competing risks*. When the risk of death from a disease decreases, the risk of death from other diseases increases or becomes more apparent. With advancing age, the period between the emergence of competing diseases shortens. The hazard in old age is not so much that one disease displaces another but that the new diseases are often much more debilitating. For example, finding a cure for cancer may cause an unintended increase in the prevalence of Alzheimer disease.

The inescapable conclusion from these observations is that life extension should no longer be the primary goal of medicine when applied to people older than 65 years of age. The principal outcome and most important metric of success should be the extension of healthspan.

The First Health Revolution

The conventional approaches used to counteract the diseases of older age have been to improve behavioral risk factors, find ways to detect them earlier, and use medical technology to extend survival for those who already have diseases. The more important goal of public health, medicine, biotechnology, and the health sciences should now shift toward delaying and compressing the period of the lifespan when frailty and disability increase substantially. Referred to as the *first health revolution*,[7] this new approach for public health (which is to target aging) is seen as a highly effective method of primary prevention.

A consortium of scientists as well as public health experts and organizations has formed with the purpose of developing this new approach to extend healthspan, address the diseases of aging, and help to ameliorate the economic challenges of an anticipated rising prevalence of late-onset diseases. This effort is called the Longevity Dividend Initiative[8] or geroscience.[9] Clinical trials designed to target aging have been approved by the US Food and Drug Administration, with the first trial set to begin in 2019. Large investments in aging biology have already begun through Google Calico and Human Longevity Inc. The National Institute on Aging has established the Interventions Testing Program to rigorously and quickly test prospective aging interventions for free. The National Institutes of Health has reduced the barriers between its disease-oriented research silos, and the American Federation for Aging Research is spearheading a global effort to secure funds to launch the Longevity Dividend Initiative in 2019.[10]

Conclusion

The time has come to recognize the achievement of life extension. Efforts should be focused on achieving the goals of extending and improving the healthspan.

ARTICLE INFORMATION

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