Articulating the Case for the Longevity Dividend

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The survival of large segments of human populations to advanced ages is a crowning achievement of improvements in public health and medicine. But, in the 21st century, our continued desire to extend life brings forth a unique dilemma. The risk of death from cardiovascular diseases and many forms of cancer have declined, but even if they continue to do so in the future, the resulting health benefits and enhanced longevities are likely to diminish. It is even possible that healthy life expectancy could decline in the future as major fatal diseases wane. The reason is that the longer we live, the greater is the influence of biological aging on the expression of fatal and disabling diseases. As long as the rates of aging of our bodies continues without amelioration, the progress we make on all major disease fronts must eventually face a point of diminishing returns. Research in the scientific study of aging has already showed that the aging of our bodies is inherently modifiable, and that a therapeutic intervention that slows aging in people is a plausible target for science and public health. Given the speed with which population aging is progressing and chronic fatal and disabling conditions are challenging health care costs across the globe, the case is now being made in the scientific literature that delayed aging could be one of the most efficient and promising ways to combat disease, extend healthy life, compress morbidity, and reduce health care costs. A consortium of scientists and nonprofit organizations has devised a plan to initiate an accelerated program of scientific research to develop, test for safety and efficacy, and then disseminate a therapeutic intervention to delay aging if proven to be safe and effective; this is referred to as the Longevity Dividend Initiative Consortium (LDIC). In this review, I articulate the case for the LDIC.

The rise in human longevity and the increase in our healthy lifespan are two of humanity's greatest achievements. In the developed world, and now even among growing subgroups in developing nations, increasingly larger segments of the population have gained access to one of the most precious of all commodities—the opportunity to live life into older ages. In developed nations, ~85% of everyone born today will live to at least their 65th birthday, and >42% will live past their 85th birthday—a privilege that has been denied to most people throughout history (Human Mortality Database, www.mortality.org). However, the price to pay for common access to older ages is the opportunity to witness the aging of our bodies,

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and the fatal and disabling diseases that accompany extended survival.

The trade-off of chronic degenerative diseases for decades of life that was accomplished during the 20th century has undeniably been worth it, but humanity now faces a rather daunting health and economic dilemma. The combination of additional life extension with a forthcoming rapid upward shift in age structure (population aging) will lead to a dramatic increase in the prevalence of the diseases of old age—producing a major challenge to health care systems and age-entitlement programs. The National Institutes of Health, World Health Organization, United Nations, World Economic Forum, MacArthur Foundation, and other organizations have appropriately acknowledged that aging and life extension also offer an equal measure of opportunity (e.g., see Beard et al. 2011), but the rising prevalence of costly diseases is an inevitable by-product of our success.

The usual approach to combatting the diseases of old age has been to lower the behavioral risk factors that influence their expression, delay their appearance through earlier detection, and to use medical technology to extend survival for those whose bodies are already diseased. This approach has been successful in the past, but there is a growing body of evidence to suggest that continuing down this path will lead to diminishing gains in life extension and, more importantly, the possibility (perhaps likelihood) that the historic rise in health span may come to a halt—leaving future older cohorts the prospect of rising frailty and disability in later ages (Olshansky et al. 2006; Butler et al. 2008). The fact is, the longer we live, the more the biological aging of our bodies influences the fatal and disabling diseases that emerge (Miller 2012).

Recognizing the important linkage between the biological aging of our bodies and disease expression, an exciting line of scientific research has emerged that offers an opportunity to extend our healthy years further (Miller 2002; Sierra et al. 2009; Kirkland 2013). The health and economic benefits that would accrue to individuals and nations if this approach is successful has been documented (Goldman et al. 2013). As a result, a consortium of scientists has formed with the purpose of developing a new weapon to extend health span, combat the diseases of aging, compress mortality, morbidity, and disability, and help to ameliorate the economic challenges of an anticipated rising prevalence of late-onset diseases. Numerous experimental animal studies have now shown that interventions that ameliorate multiple fatal and disabling maladies of aging are possible, and will likely be transformative to human health if successfully brought to fruition. A large-scale, concerted, and coordinated effort is now underway to develop, test, and then push the translation of these findings into real-world clinical investigation and use—referred to as the Longevity Dividend Initiative Consortium (LDIC).

The LDIC aims at accelerating the pace of translation from the basic biology of aging into clinical interventions that will improve quality of life at all ages, but especially for people reaching older ages. The goals are ambitious because they address needs in several scientific domains; from basic biology, to genetics, preclinical and clinical research, as well as population-level modeling. This review and other literature provide the rationale behind the LDIC and begin outlining the various scientific pathways that researchers are pursuing to this end.

HEALTHY LIFE EXTENSION

The most precious of all commodities is life itself, and if there is one attribute most of us share, it is the desire to remain alive. The yearning for healthy life is equally important, perhaps more so—especially for those struggling to regain health that has been lost. One would think, therefore, that making the case for the development of new more effective methods of extending our healthy years would be universally accepted and easy to make, regardless of how it is achieved. Sadly, this is not the case.

In public health, examples of interventions that in the past had a profound influence on the length and quality of life include the development and dissemination of clean water, sanitation, indoor living and working environments, and refrigeration. During the last century, epidemiologists made the public aware of the life-

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shortening effects of smoking and other harmful risk factors, and the life-extending effects of proper diet and exercise, among others.

In the modern world of medicine and medical technology, a trip to the doctor, dentist, or other health professional is justified today as forms of primary prevention. When a health issue arises, such as a serious infection, cancer, or heart disease, it is now routine to seek out and trust modern medical treatment as the best approach to regaining one's health. In fact, a strong endorsement for the efficacy of medicine's ability to extend healthy life comes from its validation by the insurance industry.

These three pillars of healthy life extension have earned our trust, and deservedly so, but now concerns are being raised about how much more healthy life can be manufactured using these approaches. The reason is the biological aging of our bodies.

In the last half-century, a combination of public health and medicine enabled most people born in the developed world to live past age 65, and for them, a large percentage live past age 85. As appealing as this is, the problem that arises with extended survival is that a less tractable risk factor has emerged—biological aging. Public health can manufacture only so much survival time through lifestyle modification, after which medical technology has an important life-extending impact, but even these methods of life extension eventually lead the survivors to face the increased and accelerated ravages of the biological aging of our bodies.

Consider the effect of aging on the body as the same as the effect of miles on your car. Very few things go wrong with most cars during the first 3 years and 36,000 miles, and for some automobiles the warranty period has been extended to 10 years and 100,000 miles. Operate these cars beyond their warranty period, and a cluster of problems emerges. These problems are an inevitable by-product of the passage of time and the accumulation of damage that arises from operating the machine—they are not programmed to occur at a set time by the auto manufacturers. Although planned obsolescence is part of the manufacturing ethos for some manufacturers of certain products, what is meant here is that a specific "death time" is not built into a car.

The same principles hold true for human bodies. Once we operate our bodies beyond the equivalent of their biological warranty period, a large number of health issues begin to emerge and cluster tightly into later regions of the life span. Among scientists who track these events, this is known as "competing causes," which is another way of saying that a large number of lethal and disabling conditions accumulate in aging bodies. Ameliorating any one lethal condition independent of all others leaves the person with a remaining high risk from all other remaining conditions. With time (and age), the treatments devised through medicine (that tend to focus on one disease at a time) and risk factor modification, then become progressively less effective as survivors move further into older age windows, in which aging-related diseases cluster ever more tightly together. Keep in mind that, just like automobiles, our bodies are not programmed with aging or death genes that are set off at a predetermined age. Aging is best thought of as an inadvertent by-product of fixed genetic programs that evolved under the direct force of natural selection for early life developmental events—aging is a product of evolutionary neglect, not evolutionary intent.

Recognizing the fact that competing causes place a damper on the future effectiveness of medical interventions that are disease oriented, scientists in the field of aging have proposed that the next big step in public health and healthy life extension is to attack the seeds of aging rather than just its consequences as we do now. The idea is to slow the aging of our bodies such that 1 year of clock time is matched by less than 1 year of biological time. In this way, we would retain our youthful vigor for a longer time period and, if delayed aging interventions work the way we hope they do, experience a compression of the infirmities of old age into a shorter time frame at the end of life. Delaying the biological aging of our bodies is the only viable approach to addressing the increasing importance of competing causes, and the rise of aging as an ever more important risk factor for disease.

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It is at this juncture where one of the main problems occurs. The contemporary proposal to slow aging as a means to extend healthy life has historical linkages to medical deception, charlatanism, and greed (Gruman 1966). Historically, the quest for immortality was couched within a "prolongevity" message suggesting that ingesting or injecting substances with alleged "antiaging" properties could manufacture youth. One of the most famous among these is the alchemist's dream to transmute lead into gold, which was thought to confer properties of immortality to those who ingested minute quantities.

In the late 19th century, the French physiologist Charles-Édouard Brown-Séquard claimed to have discovered the secret to rejuvenation. Brown-Séquard crushed the testicles of domesticated animals, extracted "vital" substances from them, and then inoculated older people against the "aging disease." Modern versions of these ancient "antiaging" potions were described by the United States Government Accounting Office as posing the "potential for physical and economic harm" (GAO 2001).

Finally, some scientists in the field of aging have formed companies designed to attract outside investors interested in cashing in on a possible breakthrough in the field of aging (Anton 2013). Although this approach enables some aging science to occur that would not otherwise be funded, it can and has led to exaggerated claims and unproven interventions that reach the marketplace before they are fully evaluated using the tools of science. This too creates suspicion among the public who already have a difficult time distinguishing between medical fraud and genuine public health interventions.

Taken together, these historical and contemporary roadblocks to legitimacy have delayed the entrance of aging science into the realm of accepted discourse as a legitimate and, quite frankly, valuable and needed public health intervention. However, these are not the only roadblocks.

RELIGIOUS ARGUMENTS

Religious objections are sometimes posed in response to proposals to enhance public health by modulation of aging. The objection usually starts from the assertion that tampering with aging is equivalent to tampering with God's plan for us—an effort that should not be pursued. However, this argument loses its power when those proposing it admit that both they and their children have been vaccinated against lethal childhood diseases. It is hard to imagine that God's plan is to kill most children from communicable diseases before reaching the age of 10, but up until the 19th century that was humanity's fate. Most people who make this argument also admit that they would seek medical attention if they (or their loved ones) experience heart disease or cancer. Why is one form of disease prevention acceptable, whereas another is not?

POPULATION GROWTH

When delayed aging was first proposed as a public health intervention in the 1950s, rapid population growth was a concern because the growth rate (GR) in the post-World War II era was ~3%. To place this GR into perspective, at that rate it takes the population 26 years to double in size. Thus, there was reason to be concerned about the population GR during most of the last half of the 20th century—this was alarming to both demographers and environmentalists. Although the rate of population growth has attenuated considerably since 1950, the momentum for population growth will remain with us through the middle of this century. However, environmental concerns have escalated considerably. Population growth and resource depletion should be on our minds, and these are issues that are appropriate to raise when having a discussion about healthy life extension.

The thing is, those making this argument believe that delayed aging will dramatically accelerate population growth, wipe out the reductions in the GR achieved in recent decades, further challenge resource depletion, and generate a new set of population and environmental headaches. As it turns out, none of these concerns are valid.

With regard to population growth, I have estimated how the GR would change with the

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hypothetical extreme scenario of immortality (i.e., no more deaths) (Olshansky 2013). Under the extreme scenario of immortality, the GR would be ~1.5% (i.e., the GR would be defined by the birth rate because the death rate would be zero)—which is three times faster than the current GR of ~0.5%. However, longer lives tend to be accompanied by lower fertility, so I estimate a GR under conditions of hypothetical immortality of ~0.9%, still twice the current GR. Because immortality is not likely to happen any time soon, and because the longevity dividend associated with delayed aging would yield only marginal increases in life expectancy, the actual population GR would only rise slightly if the longevity dividend is achieved.

In fact, the population GR would also rise marginally with a hypothetical cure for cancer or heart disease. I have yet to hear anyone argue that cures for these diseases should not be pursued because success would be accompanied by accelerated population growth and resource depletion. The bottom line is that the Longevity Dividend Initiative will have a negligible effect on population growth and the environment, but it will have a dramatically positive impact on work, retirement, health care financing and costs, and physical and psychological well-being (Goldman et al. 2013).

DELAYED AGING MEANS INCREASED INFIRMITY

Perhaps the most common misconception and fear about aging science and the Longevity Dividend Initiative is the belief that delayed aging will extend the period of infirmity at the end of life—the fear that most people have as they approach older ages. There is an irony to this view because, although there may be disagreements among the scientists involved on exactly how to accomplish the goals we have set, the one thing we all have in common is the final and most important goal of extending the period of healthy life. An intervention that does not meet the test of extending the health and functionality of both body and mind together would not be pursued—in fact, such an intervention would be seen as harmful.

ARTICULATING THE CASE FOR THE LONGEVITY DIVIDEND

The case for the longevity dividend is compelling and in theory should be easy to make to funders, public health professionals, and the general public. Here is the line of reasoning:

1. Treating diseases worked well in the past to extend healthy life, but aging has emerged as the primary risk factor for the most common fatal and disabling diseases;
2. The longer we live, the greater the influence of aging on disease expression;
3. Aging science offers medicine and public health a new and potentially far more effective weapon for preventing disease, extending healthy life, and avoiding the infirmities associated with old age (Butler et al. 2008; Goldman et al. 2013);
4. Failing to take this new approach could leave people who reach older ages in the future, even more vulnerable to rising disability than they are now;
5. Aging science represents a new paradigm of primary prevention in public health that will lead to more effective methods of delaying most fatal and disabling diseases, extending healthy life, and reducing the prevalence of infirmities more commonly experienced at older ages (Sierra et al. 2009; Kirkland 2013; Tchkonia et al. 2013).

Language used to describe the longevity dividend must be unambiguous. Much like the introduction of antibiotics in the mid-20th century and the broad dissemination of basic measures of public health a century ago, humanity is once again fortunate enough to witness the rise of a new paradigm in human health. Aging science has successfully turned the spotlight on the origins of our aging bodies and minds and the fatal and disabling diseases that accompany us in our later years. What the scientific study of aging reveals shakes up a long-held assumption that aging is an inevitable and immutable by-product of the passage of time (Miller 2002), and these new discoveries funda-

mentally challenge the fatalist view that aging and death are nature's way of removing the old to make way for the young.

Science has now shown that aging is inherently modifiable. Furthermore, there is now reason to believe that aging science can be translated into new more effective medical and public health interventions that will be able to combat fatal and disabling diseases far more effectively than any intervention available today—yielding an extension of the period of healthy life in ways that could not even be conceived of just a few years ago.

Although people that benefit from advances in aging science will probably live longer, it is the extension of healthy life that is the primary goal along with reductions in the infirmities of old age, and increased economic value to individuals and societies, that would accrue from the extension of healthy life.

It is only a matter of time before aging science acquires the same level of prestige and confidence that medicine and public health now enjoy, and when that time comes, a new era in human health will emerge. There are an abundance of formidable obstacles standing in the way, including strongly held views of how to proceed, a history of association with dubious aging interventions, and misconceptions about the goals in mind and the impact of success on population growth and the environment. Once the air clears and aging science is translated into effective and safe interventions that can be measured and documented to extend our healthy years, the 21st century will bear witness to one of the most important new developments in the history of medicine.

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