

HOW CAN WE ENSURE QUALITY WITH EXTENDED LIFE EXPECTANCY?

———— Aubrey D.N.J. de Grey ————

It is often noted that life expectancy roughly doubled during the 20th century, but that statistic is an unhelpful merger of two phases. Until roughly World War II, gains were achieved mostly via a progressive lowering of mortality rates in infancy and child-birth; thereafter, by contrast, the ages at which the most progress has been made are middle-age and above. Most observers predict that these more recent gains, which have averaged roughly two years per decade, will continue for some time, subject only to appropriate public health measures to curtail the rise in obesity and its associated diseases.

This success in postponing death from age-related causes has been something of a mixed blessing. The average age until which people remain relatively free of age-related ill-health has also risen, by an amount comparable to the rise in average longevity. But when specific age-related diseases are considered individually, the picture

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is mixed: the average age of survival with cardiovascular disease has diminished, while for Alzheimer's and cancer it has risen.

The economic benefits of postponing age-related ill-health and death are also mixed. It has been estimated that progress against age-related diseases has enormously benefited the economies of the industrialized world over the past 50 years — due to an increase in the proportion of individuals who are net contributors to national wealth rather than consumers of it. However, because the age at which people retire has not remotely kept pace with rising life expectancy, the proportion of the population who are receiving pensions and related benefits has also risen, with the result that a major crisis of pension plans in both the private and public sector is looming. This problem is exacerbated in the short term by the "baby boom," the sharp (albeit temporary) rise in the birth rate in the United States and elsewhere following World War II, which is just about to start feeding through into the pension system.

Therefore, considerable challenges are facing the world's major economies in regard to maintaining elderly people's quality of life in the coming decades. How can these challenges best be addressed? Several options must be considered.

Without doubt, there will continue to be immense value in pursuing new ways to postpone the onset and progression of the major age-related diseases, especially those with a long survival time (such as Alzheimer's disease). These diseases sharply diminish the quality of life of both sufferers and their loved ones, and the financial cost of caring for sufferers impacts the quality of life of the whole of society.

In principle, any economic benefit accruing from postponing age-related ill-health could be considerably increased if such therapies did not similarly postpone death. This concept, generally

described using the term “compression of morbidity,” has been energetically championed by biogerontologists for the past 30 years. However, such an argument is decidedly dubious. First of all, there is no evidence that therapies which postpone age-related ill-health, but do not extend longevity by a comparable amount, are feasible.

It is intuitively much more likely that the period of ill-health will be

shifted to a greater age, but not shortened. Second, it is not at all clear — indeed, arguably the opposite is clear — that the public wish for a compression of morbidity. There seems to be unequivocal support for interventions that keep the frail and sick elderly alive, in fact.

However, a robust reason for optimism about the impact of increasing our lifespan exists. It arises from the impressive and ever-accelerating progress being seen in regenerative medicine, which is fast reaching a level of sophistication that will allow it to be applied to the immensely multi-faceted problem of aging. Regenerative medicine

has the crucial advantage that it actually reverses age-related decline, rather than merely retarding it. The demographic, and thus economic, impact of that feature can hardly be overstated.

To see this, we must consider the relationship between the average proportion of one’s life that is spent in ill-health at the end of life and the proportion of people in that condition at any given instant. In a world where no progress is being made in postponing either age-related ill-health or death, these proportions are clearly equal. But when progress is occurring, a sort of Doppler effect emerges, whereby the latter proportion is smaller than the former.

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And unlike the auditory Doppler effect, in this case the relationship is asymptotic: There is a finite rate of progress in postponing aging beyond which no one is in a state of age-related ill-health. That rate is, of course, one year per year — only a few times what we are achieving already.

It is, however, crucial to bear in mind that preventative therapies exhibit a lag between their onset and their beneficial consequences. Accordingly, even if we were to develop therapies that postponed aging when begun in childhood, and we improved those therapies faster than one year of postponement per year, those unfortunates who are already too old to benefit from the therapies would remain in (or would enter) age-related ill-health just as before.

Thus, the ideal therapies, in terms of both quality of life and economic benefit, are without doubt regenerative interventions that benefit those who are already experiencing, or at least approaching, the decrepitude and disease of old age. Such interventions would reduce the number of such sufferers more rapidly than any other type of treatment, and the economic impact would be correspondingly more severe and more rapid.

The sole question remaining, therefore, is this: Are such interventions feasible in the foreseeable future? In my view, they almost certainly are. Regenerative medicine is arguably the most burgeoning field in the whole of biomedicine at present, with progress on all fronts occurring by leaps and bounds. In large part, the foundations for applying it to aging are already in place or imminent. It also remains to combine those therapies (which will inevitably be piecemeal) into a sufficiently comprehensive panel to span all the pathways by which lifelong accumulating molecular and cellular damage eventually causes age-related decline. The time to start addressing these challenges in earnest is now. ☺