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LIVE LONG—AND PROSPER?

Glenn Harlan Reynolds^{*}

COPING WITH METHUSELAH: THE IMPACT OF MOLECULAR BIOLOGY ON MEDICINE AND SOCIETY

Henry J. Aaron & William B. Schwartz, editors Brookings Institution Press, 2004 264 pages, \$48.95 ISBN: 0815700407

THE FOUNTAIN OF YOUTH: CULTURAL, SCIENTIFIC, AND ETHICAL PERSPECTIVES ON A BIOMEDICAL GOAL

Stephen G. Post & Robert H. Binstock, editors Oxford University Press, 2004 463 pages, \$59.95 ISBN: 0195170083

THE ESCAPE FROM HUNGER AND PREMATURE DEATH, 1700–2100: EUROPE, AMERICA, AND THE THIRD WORLD

Robert William Fogel Cambridge University Press, 2004 216 pages, \$23.99 ISBN: 0521004888

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A few years ago, promised cures for baldness, impotence, and old age shared a common image as fraudulent and vaguely pathetic or as illusory straws grasped at by the desperate and gullible. Now, with Rogaine and Viagra offering relief to the hairless and the limp, it is beginning to look as if treatments for aging may offer hope to the wrinkled in the not-too-distant future. That prospect has produced both excitement and, from some, unhappiness.

It has also produced a great deal of attention in the bioethics community. The President's Council on Bioethics devoted a chapter to the subject in its report, *Beyond Therapy: Biotechnology and the Pursuit of Happiness.*¹ The chapter, entitled "Ageless Bodies,"² takes a somewhat negative view of the desirability of longer human lives but a fairly positive view of the likelihood that such life extension may prove feasible, observing:

Using rapidly growing new knowledge about how and why we age, scientists have achieved some success in prolonging lifespans in several animal species. To be sure, there is at present no medical intervention that slows, stops, or reverses human aging, and for *none* of the currently marketed agents said to increase human longevity is there any hard scientific evidence to support the hyped-up claims. Yet the prospect of possible future success along these lines raises high hopes, as well as profound and complicated questions.³

Addressing those questions, in different ways, are three new books. Henry Aaron and William Schwartz have edited *Coping with Methuselah: The Impact* of Molecular Biology on Medicine and Society,⁴ a collection of essays published by the Brookings Institution Press. A related volume, *The Fountain of Youth: Cultural, Scientific, and Ethical Perspectives on a Biomedical Goal*,⁵ was published almost simultaneously by Oxford. And Robert Fogel's *The Escape from Hunger and Premature Death*,⁶ published by Cambridge, turns out to go well with the other two volumes.

It seems that we have arrived at some sort of "harmonic convergence" of scholarship on the subject of longevity and life extension—so much so that the journal *Gerontology* published an entire symposium issue on the subject as this

^{1.} PRESIDENT'S COUNCIL ON BIOETHICS, BEYOND THERAPY: BIOTECHNOLOGY AND THE PURSUIT OF HAPPINESS (2003), *available at* http://www.bioethics.gov/reports/beyondtherapy/beyond_therapy_final_webcorrected.pdf (last visited Apr. 11, 2005).

^{2.} Id. ch. 4.

^{3.} Id. at 159-60 (footnote omitted).

^{4.} COPING WITH METHUSELAH: THE IMPACT OF MOLECULAR BIOLOGY ON MEDICINE AND SOCIETY (Henry J. Aaron & William B. Schwartz eds., 2004) [hereinafter COPING WITH METHUSELAH].

^{5.} THE FOUNTAIN OF YOUTH: CULTURAL, SCIENTIFIC, AND ETHICAL PERSPECTIVES ON A BIOMEDICAL GOAL (Stephen G. Post & Robert H. Binstock eds., 2004) [hereinafter FOUNTAIN OF YOUTH].

^{6.} ROBERT WILLIAM FOGEL, THE ESCAPE FROM HUNGER AND PREMATURE DEATH, 1700–2100: EUROPE, AMERICA, AND THE THIRD WORLD (2004).

Essay was in progress.⁷ That being the case, it is worth taking some time to look at longevity and life extension and to think about where we might be heading.

Three chief questions must be asked regarding the notion of extending human life: (1) Is it possible? (2) What are the consequences? and (3) Are those consequences desirable? There is, surprisingly, more agreement on the first of these questions than on the latter two.

I. LIFE EXTENSION: WHAT, WHETHER, AND HOW

People have wanted to live longer, healthier lives for all of recorded history. Getting there, however, has posed more of a challenge. People now live longer on average—achieving higher life expectancies on a societal basis. But maximum lifespan, the longest time that any humans live, has not advanced much if one discounts Biblical stories of people living for several centuries.

There is now some reason to think that lifespans may become considerably longer in the not-too-distant future. Experiments with rats, fruit flies, and worms have demonstrated that relatively simple modifications ranging from caloric restriction to changes in single genes can produce dramatic increases in lifespan. So far, these have not been demonstrated in human beings (whose long lifespans make us harder to work with than fruit flies, for whom a doubling only lengthens the experiment by a few days), but many researchers believe that such improvements are feasible.

At the moment, there are two approaches—both of which work: "In the past two decades, biogerontologists have established that the pace of aging can be decelerated routinely in mammals by dietary or genetic means.... There is now ... incontrovertible evidence, from many fronts that aging in mammals can be decelerated, and that it is not too hard to do this."⁸

Caloric restriction (CR) is probably the better-established of the two approaches. Animals fed diets that contain all necessary nutrients, but that provide substantially fewer calories than normal diets (and I mean *substantially*, as in 40–60% fewer) seem to lead longer and healthier lives:

[C]aloric restriction prolongs the lifespan by several different, but interrelated, mechanisms that attenuate oxidative stress

... The fundamental observation is that dietary restriction reduces damage to cellular macromolecules such as proteins, lipids, and nucleic acids. ... Caloric restriction leads to reduction in cellular oxidants such as hydrogen peroxide and increases the activity of endogenous antioxidant enzymes.⁹

^{7.} Symposium, Anti-Aging Medicine: The Hype and the Reality—Part I, 59A JOURNALS GERONTOLOGY: BIOLOGICAL SCI. 513 (2004).

^{8.} Richard A. Miller, *Extending Life: Scientific Prospects and Political Obstacles, in* FOUNTAIN OF YOUTH, *supra* note 5, at 228, 228–29.

^{9.} Gemma Casadesus et al., Eat Less, Eat Better, and Live Longer: Does It Work and Is It Worth It? The Role of Diet in Aging and Disease, in FOUNTAIN OF YOUTH, supra note 5, at 201, 203–04 (internal citations omitted).

In fact, animals on reduced-calorie diets are healthier, not simply longer-lived:

Importantly, the CR diet does not merely postpone diseases and death; it seems to decelerate aging per se and in so doing retards age-related changes in (nearly) every system and cell type examined....

 \dots Calorie-restricted rodents remain healthy and active at ages at which control littermates have long since all died. \dots Autopsy studies of CR animals at the end of their life span typically show very low levels of arthritic, neoplastic, and degenerative change, and in functional tests of immunity, memory, muscle strength, and the like, they typically resemble much younger animals of the control group.¹⁰

No struldbrugs, these.¹¹ Some humans are experimenting with caloric restriction, but it does not seem likely to appeal to most people, as it may promise a long life—but a hungry one. Still, it is promising for two reasons. Most obviously it indicates that the aging process—often regarded with almost supernatural awe—is susceptible to change through rather simple and crude interventions. Additionally, it seems likely that many of the processes affected by caloric restriction can be artificially induced by other means.¹²

Genetics also seem to offer hope—some species are notably longer-lived than others, and it turns out that they tend to have a lot of genetic characteristics in common. While one might, via a sufficiently long-term breeding program, produce long-lived humans without any high technology interventions, doing so would take many generations. And inserting new or modified genes in human beings, though likely possible in time, is difficult and poses political problems.

Scientists are, however, already researching drugs that activate or deactivate genes in order to retard aging:

Once these two longevity extension mechanisms were identified, many scientists independently tried to develop pharmaceutical interventions by feeding various drugs suspected of regulating these two processes to their laboratory animals. Six of these experiments have shown various signs of success. Although these independent experimenters used different intervention strategies and administered different molecules to their laboratory animals, they each recorded significant increases in the animals' health span and/or a significant extension of the animals' functional abilities....

The pharmaceutical extension of longevity via a delayed onset of senescence has been proved in principle by these six experiments despite their individual limitations.... The basic research has defined at least two robust anti-aging mechanisms and has shown that pharmaceutical interventions are conceptually possible and technically feasible. Just like the Wright Brothers in

^{10.} Miller, supra note 8, at 233-35.

^{11.} Jonathan Swift's "struldbrugs" lived a very long time but aged all the while, with deeply unfortunate results. See JONATHAN SWIFT, GULLIVER'S TRAVELS 199–206 (Paul Turner ed., 1998).

^{12.} See Robert Arking, Extending Human Longevity: A Biological Probability, in FOUNTAIN OF YOUTH, supra note 5, at 177, 191–92.

1900, we know an awful lot about our subject but not quite enough to fly under our own power yet. $^{\rm 13}$

Beyond these two approaches, other biogerontologists like Cambridge University's Aubrey de Grey are looking at far more dramatic interventions that would not merely slow the aging process, but stop or even reverse it, through eliminating DNA damage, replacing senescent cells with new ones, and so on.¹⁴

To paraphrase Dr. McCoy, I'm a lawyer, dammit, and not a doctor, and so I need express no opinion on which of these approaches is likely to work out. (I suspect, however, that the answer may turn out to be "both," along with other approaches that have not been thought of.) Most readers of this journal, however, are likely to be more interested in the ramifications than in the methodologies of life extension.

II. CONSEQUENCES

What would a life-extended world look like? To some degree, of course, that depends on how, and how much, lives are extended. The past century has seen life expectancies go up, but the increasing number of older Americans has also led to increasing health-care costs as the medical system responds to increasing numbers of the infirm. I once saw Jay Leno deriding the benefits of diet and exercise. What they don't tell you, he said, is that all that will get you is added years in your 80s, when what you really want are added years in your 20s.

That's not strictly true for diet and exercise, of course—they tend to get you not only more years but better years. It is likely to be far less true with anti-aging treatments. Treated with anti-aging therapies, eighty-year-olds may not look like twenty-year-olds, but they won't turn into modern day versions of Swift's struldbrugs, either, who lived longer but only in increasingly decrepit condition.

The decrepitude of age, after all, exists as the result of, well, aging. Indeed, contemporary medicine, which keeps people alive longer but which cannot address the aging process itself, is far more likely to produce such a state of affairs—though today's elderly are by no means all decrepit.

Alexander Capron looks at some of these issues in an essay entitled, *Ethical* Aspects of Major Increases in Life Span and Life Expectancy.¹⁵ As Capron notes:

[d]espite recent increases in average life expectancy in much of the world[,] *healthy* life expectancy—that is, the period of life that is free from disease—has remained the same The question, then, is whether extensions in life expectancy will raise or lower the time span spent in illness or debility.¹⁶

^{13.} Id. at 192-93 (internal citation omitted).

^{14.} See Aubrey D.N.J. de Grey, An Engineer's Approach to Developing Real Anti-Aging Medicine, in FOUNTAIN OF YOUTH, supra note 5, at 249.

^{15.} Alexander M. Capron, Ethical Aspects of Major Increases in Life Span and Life Expectancy, in COPING WITH METHUSALEH, supra note 4, at 198.

^{16.} Id. at 208 (quotation marks omitted).

Anti-aging technologies, however, might change that. This graph¹⁷ illustrates different changes.





Ideally, of course, the period of healthy life—what some scholars call the "health span"—would be extended, perhaps dramatically, while the period of debility at the end would remain the same, or even be shortened. Some writers think that outcome is likely:

Effective anti-aging interventions—those that mimic the known results of CR [calorie restriction] or the genes that produce fox terriers and miniature schnauzers—would be expected to produce 112-year-old people with the same highly variable set of abilities and disabilities seen in today's 78-year-olds. We can infer that CR, or something like it that worked in people, would not produce 112-year-olds that resemble today's supercentenarians in their precarious states of mental and physical health, because 3 1/4 -year-old CR mice, our current best guides to what we'd expect to see in a 112-year-old CR-facsimile person, are still fairly vigorous and admirably free of degenerative changes. Interventions that slow down aging—at least the ones we know about so far—do not prolong the period of late-life suffering, but instead delay its appearance by increasing the length of healthy adult life.¹⁸

^{17.} COPING WITH METHUSELAH, supra note 4, at 209. Reprinted with permission from Brookings Institution Press.

^{18.} Miller, supra note 8, at 238.

Such outcomes are likely for another reason: They are what people want. It seems probable that government programs, and pharmaceutical company researchers, will aim at producing treatments that produce healthy and vigorous oldsters, not struldbrugs. It seems even more likely that people will be willing to pay for, and undergo, the former but not the latter. While incremental, disease-at-a-time medical research may lead to (and to a degree has led to) old people who are still alive simply because their ailments can be cured, aging research is likely to produce a different outcome. If it can produce treatments or medications that let people enjoy a longer health span---more youth, or at least more middle age, by several decades---then those treatments will sell. If not, then there will not likely be much of a market for treatments that extend old age.

Thus, if we can expect anything, we can expect treatments that give us more of the good part of our lives—anywhere from a couple of extra decades to, at the most optimistic end, several extra centuries. And who could be against that?

Leon Kass, for one. Kass, Chair of the White House Bioethics Council, writes:

Is it really true that longer life for individuals is an unqualified good?... If the human life span were increased even by only twenty years, would the pleasures of life increase proportionately? Would professional tennis players really enjoy playing 25 percent more games of tennis? Would the Don Juans of our world feel better for having seduced 1250 women rather than 1000? Having experienced the joys and tribulations of raising a family until the last had left for college, how many parents would like to extend the experience by another ten years?¹⁹

To me, it seems obvious that the answer to all these questions is "yes." To Kass, the answer is obviously "no." But as it happens, we've conducted an experiment along these lines already, and the outcome is not in Kass's favor.

Lifespans, after all, have been getting steadily longer since the turn of the twentieth century. According to the Centers for Disease Control, "since 1900, the average lifespan of persons in the United States has lengthened by greater than 30 years."²⁰ That is an average, of course, and it is made more striking by reductions in death among juveniles. Nonetheless, there are a lot more old people than there used to be, and they are working longer. As *Discover* magazine recently observed, "A century ago, most Americans lived to be about 50. Today people over 100 make up the fastest-growing segment of the population."²¹ You can argue about the details, but it is clear that typical adults are living longer than at any time in human history.

^{19.} Leon Kass, L'Chaim and Its Limits: Why Not Immortality?, in FOUNTAIN OF YOUTH, supra note 5, at 304, 309, 312.

^{20.} Ctrs. for Disease Control & Prevention, U.S. Dep't of Health & Human Servs., *Ten Great Public Health Achievements—United States, 1900–1999,* 48 MORBIDITY & MORTALITY WKLY. REP. 241, 241 (1999), *available at* http://www.cdc.gov/mmwr/PDF/wk/mm4182.pdf (visited Apr. 11, 2005).

^{21.} Karen Wright, Staying Alive, DISCOVER, Nov. 2003, at 64, 64.

Indeed, that is the theme of Robert Fogel's new book, *The Escape from Hunger and Premature Death*, 1700–2100. In a slim yet information-dense volume, Fogel charts the truly impressive changes in health and life expectancy over the past centuries:

[T]he life expectancy of the [British] lower classes increased from 41 years at birth in 1875 to about 74 years today, while the life expectancy of the elite increased from 58 years at birth to about 78 years. That is a remarkable improvement. Indeed, there was more than twice as much increase in life expectancies during the past century as there was during the previous 200,000 years. If anything sets the twentieth century apart form the past, it is this huge increase in the longevity of the lower classes.

One factor arguing in support of the optimists' [lifespan] projections is the increasing span of years that individuals have free of chronic conditions. For those who reached age 65 during the first decade of the twentieth century, the average age of onset of chronic disabilities was about 51. By the 1990s, however, the average age of onset of chronic conditions was more than 10 years later. Moreover, these disabilities are now generally milder, and many effective interventions to reduce the impact of chronic conditions are available.²²

So we've already tested out an extra 20 years of healthy life, more or less. And yet people—far from being bored, as Kass suggests they should be—seem quite eager to live longer, play more tennis, have more sex, and so on. The market is proof of that: Although it possesses little in the way of actual scientific basis at the moment, so-called "anti-aging medicine" is a rapidly growing field—rapidly growing enough, in fact, that biogerontologists fear it will give *real* research in the field a bad name.²³ Nor does one hear of many otherwise healthy people who are anxious to die, even at advanced ages, out of sheer boredom. Instead, they seem eager to improve their lives—and perhaps even have more sex, as the booming sales of drugs like Viagra and Cialis indicate. Apparently, those purchasers love life more than does Leon Kass.

One might argue—and in fact bioethicist Daniel Callahan does argue—that these desires are selfish and will be satisfied at the expense of society as a whole.²⁴ All of those perpetually young oldsters, after all, will refuse to retire, and society will stagnate.²⁵

^{22.} FOGEL, supra note 6, at 40, 111.

^{23.} S. Jay Olshansky et al., Anti-Aging Medicine: The Hype and the Reality—Part I, 59A JOURNALS GERONTOLOGY: BIOLOGICAL SCI. 513 (2004).

^{24.} See Gregory Stock & Daniel Callahan, Point-Counterpoint: Would Doubling the Human Life Span Be a Net Positive or Negative for Us Either as Individuals or as a Society?, 59A JOURNALS GERONTOLOGY: BIOLOGICAL SCI. 554, 558 (2004) ("[T]o run a society, you have to both say no to people and to require people to do what they don't want to do. There are some higher goods than what we personally want.").

^{25.} See id. at 557 ("[W]e could get a pretty good sense of likely possibilities based on our present experience. For instance, I've become interested in universities: What happens now in universities that don't have mandatory retirement? First of all, some people stay beyond age 70,

That sounds plausible. At the same time that lives have been lengthening, however, the past hundred years have also been the most creative and dynamic period in human history. And it certainly does not appear that our institutions are controlled by a rigid gerontocracy. (In fact, one finds rigid gerontocracies mostly in communist countries—the former Soviet Union, the current People's Republic of China—and not in capitalist democracies. So if fear of gerontocracy is behind opposition to longer lives, it might be better expressed in terms of opposition to communism than opposition to aging research.)

At any rate, looking at how things have worked out in American society, I am not too worried. The tendency in America seems to be toward more turnover, not less, in major institutions, even as lifespans grow. CEOs do not last nearly as long as they did a few decades ago. University presidents (as my own institution can attest) also seem to have much shorter tenures. Second and third careers (often following voluntary or involuntary early retirements) are common now. As a professor, I see an increasing number of older students entering law school for a variety of reasons, and despite the alleged permanence of faculty jobs, more than half of my law faculty has turned over, in the absence of mandatory retirement, in the 15 years that I have been teaching. We have seen all of this in spite of longer lives and in spite of the abolition of mandatory retirement ages by statute over a decade ago.²⁶ It's more dynamism, not less.

To his credit, Callahan says that he doesn't want to ban life extension research or treatment:

I would not want to prohibit the research. I want to stigmatize it. I want to make it look like you are being an utterly irresponsible citizen if you would sort of dump this radical life extension on the rest of us, as if you expect your friends and neighbors to pay for your social security at age 125, your Medicare at 145.²⁷

He is wise not to suggest a ban. It seems likely that such a ban on life extension research or treatments would be unconstitutional, in light of the rights to privacy, medical treatment, and free speech established in a number of Supreme Court opinions. Such a discussion is beyond the scope of this essay, however, and I will leave it—as the old mathematics textbooks used to say—as an exercise for the reader.

It seems even more likely, however, that such a ban would be unpopular (and surely even the most hardened supporter of Social Security and Medicare would blanch at the claim that those programs create an obligation on the part of their recipients to die). Nor does it seem likely that—if life were extended to such lengths—people would be retiring and collecting Medicare.

between 5% and 10% in the universities I've looked at. . . . Most importantly, they block the entry of young people onto the faculty.").

^{26.} On the abolition of mandatory retirement, both within and without the academic world, see Pamela Perun, *Phased Retirement Programs for the Twenty-First Century Workplace*, 35 JOHN MARSHALL L. REV. 633 (2002).

^{27.} Stock & Callahan, supra note 24, at 559.

Today's notion of "retirement age" is a fairly recent one. Otto von Bismarck is often credited with craftily setting the retirement age at 65 because most people would not live that long—though in fact, Bismarck set it at 70, and it was not lowered to 65 until later.²⁸ But the justification for retirement has always been that by retirement-age people were nearly used up and deserved a bit of fun and then a comfortable and dignified decline until death. Get rid of the decline and death, and you have given up the justification for living—as Social Security recipients, at least, do—off other people's efforts on what amounts to a form of welfare. Logically, retirement should be put off until people are medically old (or perhaps just replaced entirely with disability insurance) and those who are able to work should do so, while those desirous of not working should save up as for a long vacation. Alan Greenspan—the very model of combined productivity and longevity—has argued repeatedly for extending retirement ages in tandem with increasing life expectancies, and it is possible that in some non-election year his advice may be followed.²⁹

In this regard, increased longevity, with (at the very least) much higher retirement ages, could be the salvation of many nations' pension systems, which to varying degrees are facing an actuarial disaster already as the result of longer lifespans and lower retirement ages, coupled with lowered birthrates.³⁰

Indeed, although many people worry that longer lifespans will lead to overpopulation, the world is now facing what Phillip Longman, writing in *Foreign Affairs*, calls a "global baby bust."³¹ Longer lives and later retirements will help offset at least some of the consequences of falling birthrates. And, at least conceivably, people who expect to live much longer will be more willing to take time out early to bear and raise children, without feeling that it is such a career sacrifice to do so.

As Robert Fogel notes, the twentieth century produced "unprecedented improvements in the conditions of life experienced by ordinary people."³² The extension of lifespans that took place during the twentieth century was, essentially, a byproduct of those improvements: better sanitation and diet produced healthier people who lived longer and healthier lives. The twenty-first

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^{28.} Douglas Clement, *Why 65?*, FEDGAZETTE, Mar. 2004, *available at* http://minneapolisfed. org/pubs/fedgaz/04-03/65.cfm (last visited Apr. 11, 2005).

^{29.} See, e.g., Nell Henderson, Greenspan: U.S. Must Pare Retirement Benefit Promises, WASH. POST, Feb. 29, 2004, at A3 ("Greenspan again recommended gradually raising the eligibility age for both Medicare and Social Security, to keep pace with the population's rising longevity.").

^{30.} See Sebastian Moffett, For Ailing Japan, Longevity Begins to Take Its Toll, WALL ST. J., Feb. 11, 2003, at A1; see also Phillip Longman, The Global Baby Bust, FOREIGN AFFAIRS, May/June 2004, at 64.

^{31.} Longman, supra note 30, at 64.

^{32.} FOGEL, supra note 6, at 19.

century may produce more of the same, but it's likely to produce something that goes much farther.

How much farther? When I interviewed Aubrey de Grey recently, he made the following prediction about the next 20 to 30 years:

I think we have a 50/50 chance of effectively completely curing aging by then. I should explain that I mean something precise by the suspiciously vaguesounding term "effectively completely." I define an effectively complete cure for aging as the attainment of "escape velocity" in the postponement of aging, which is the point when we're postponing aging for middle-aged people faster than time is passing.³³

De Grey is a respected figure, though it is fair to say that he is one of the more optimistic figures in the field. Nonetheless, the prospects of substantially slowing—and perhaps eliminating—the aging process look promising enough to justify the increased attention that they are getting. These three books form an excellent point of entry for those interested in joining the conversation.

^{33.} Glenn Harlan Reynolds, *Death Be Not Proud*, Tech Central Station (June 23, 2004), *at* http://www.techcentralstation.com/062304D.html (last visited Apr. 11, 2005). De Grey continued:

This is a slightly tricky concept, so I'll explain it in more detail. At the moment, a 50-year-old has roughly a 10% greater chance of dying within the next year than a 49-year-old, and a 51-year-old has a 10% greater chance than a 50-year-old, and so on up to at least 85 to 90 (after which more complicated things happen). But medical progress means that those actual probabilities are coming down with time. So, since we're 50 only a year after being 49, and so on, each of us has less than a 10% greater chance of dying at 50 than at 49—it's 10% minus the amount that medical progress has achieved for 50-year-olds in the year that we were 49. Thus, if we get to the point where we're bringing down the risk of death at each age faster than 10% per year, people will be enjoying a progressively diminishing risk of death in the next year (or, equivalently, a progressively increasing remaining life expectancy) as time passes. That's what I call "escape velocity," and I think it's fair to call it the point where aging is effectively cured.