

chapter

The Methuselah Complex

one

*Man has no dominion over the breath of life,
neither to retain that flicker of life nor the
power to determine the day of death.*

— Ecclesiastes 8:8

Do you know when you want to die?

If you could, would you choose the date?

“Never” is not an option; the death rate is one per person. “When?” is the profound and bedeviling enigma. Ending one’s own life raises great issues in moral relativism, as great as does ending the life of another. Prolonging life also raises issues in moral relativism. Should we go to lengths to prolong all life, or just life we deem sufficiently high in quality? Hence, “When?” is pregnant with, “How goes the journey?”

These are questions for the ages. The authors of the Old Testament weighed in: foreknowledge of the time of one’s death would be a heavy burden, not a blessing. Furthermore, if a world without death becomes a world without birth, the specter is bleak and joyless. Rather, death is viewed as inevitable and the imponderability of its imperative assuaged with notions of afterlife. Longevity is treated as a sign of purposefulness if not holiness. The Old Testament offers up Abraham, Moses, and that statistical outlier for the ages, Methuselah, the grandfather of Noah, whose age at death is usually translated as 969 years. Some scholars choose a different Sumerian dialect for translation or convert to lunar years and come up closer to eighty-five — exceptional, not too shabby for the time of the Great Flood, and not fatuous as is 969. Are we, the residents of the modern resource-advantaged world, likely to live to be eighty-five? Can we aspire to be purposeful for eighty-five years? Are highly functioning octogenarians still statistical outliers?

Daily, we are offered the image of the baby-boom generation going on forever, making impossible demands on successive generations to provide pensions, health care, and community. That, too, is fatuous. However, more of us are living longer than did our parents. Clearly, the likelihood that we will enjoy life as an octogenarian has increased over the course of the twentieth century. Far less clear is whether the likelihood of becoming a nonagenarian has increased similarly. It has certainly not done so at anything like the same rate as the likelihood of being an octogenarian. The effect is so striking that it has caused many of us to wonder if there is not a fixed longevity for our species, set around eighty-five years of age. Some have likened this to a warranty: you are off warranty at eighty-five, beyond is a bonus, and well beyond is a statistical oddity. This projected demographic is consistent with current population trends. With one caveat, these hard facts seem unlikely to change. It is possible that molecular biology can alter the fixed longevity of our species. But don't hold your breath. None of us will live to see that — and maybe no one ever will.

Eighty-five (\pm a little bit) appears to be the programmed life expectancy for our species. I grant that the science is imperfect. But eighty-five is a linchpin of my personal philosophy of life. I, for one, do not care how many diseases I harbor on my eighty-fifth birthday, though I prefer not to know that they are creeping up on me. I, for one, do not care which of these diseases carries me off as long as the leaving is gentle and the legacy meaningful. Perhaps the best we can reasonably hope for is eighty-five years of life free of morbidities that overwhelm our wherewithal to cope, then to die in our sleep on our eighty-fifth birthday.

Unfortunately, not all of us will arrive at our eighty-fifth birthday with tranquility or, having done so, have a peaceful passing. Fortunate, indeed, are the octogenarians of today who have the wits and faculties to contend with life's demands. But time soon whittles away even their higher level of functional capacity. Month by month they face days when they do not perform as usual and even feel the need to take to bed. Inexorably, activities of daily living, activities they always took for granted, become an insurmountable challenge. They will come to take their place among the frail elderly. They will lean on canes by the graveside of their friends. They do not merit a disease label, such as "Alzheimer's"; they merit awe, compassion, and community.

The hope is faint that contemporary medical science will shepherd more of the high-functioning octogenarians into the very meager ranks of the high-functioning nonagenarians. It is, however, possible to provide comfort and support for these octogenarians through the transition toward decrepitude and in

their final passage. Friendship, community, and love are defensible as prescriptions, clinical interventions, and targets for public policy and expenditure. To advocate otherwise, including measures purporting to increase the lifespan beyond eighty-five, is to harbor delusions of immortality. Heroic efforts on behalf of the highly functioning octogenarians will accomplish little of substance. We can, perhaps, alter the proximate cause of death—that is, the diagnosis on the death certificate—but I am aware of no data to support the premise that we can alter the date of death. This is not to advocate therapeutic nihilism. It is the invoking of the age-old ethic of medicine to contend with the reality of our aging and our mortality. When the high-functioning octogenarian declines, it is because her or his time is nearing. When death supervenes, it is because it is her or his time. That is the real proximate cause of death. It does not matter how many diseases are vying for *coupe de grâce*. It only matters that the journey was as gratifying as possible.

One might be tempted to ascribe the increasing longevity in North America to past medical programs that promote health and to ongoing medical care. Science tempers any such hubris (we return to this realization in chapter 14). Health-adverse behaviors and cardiovascular risk factors may relate to the proximate cause of death, but they account for less than 25 percent of the hazard to longevity. This might explain why multiple assaults on health-adverse behaviors and cardiovascular risk factors have uncertain effects on all-cause mortality. They might change the proximate cause of death, but they do not alter its timing.

While the best clinical management of frailty in octogenarians may be only support, comfort, and community, I welcome aggressive efforts to increase the likelihood that more members of future birth cohorts will close the story of their lives as highly functional octogenarians. Many people in the resource-advantaged world still lag behind. Who die before their time? Who live to a ripe old age?

Understanding the good fortune of vibrant octogenarians requires understanding the hazards to well-being that lurk in the course of living. These life-course hazards are aspects of our interactive and integrative worlds, our ecosystems, that can powerfully influence our biology and, thereby, our fate. Much of this is captured by measures of socioeconomic status (SES). There is an incontrovertible relationship between SES and longevity. But do not be misled into assuming SES is simply a measure of income status. Longevity is more dependent on how poor you are relative to those who are advantaged in your ecosystem. For example, the greater the gap in income between the rich and the poor (the

“Robin Hood effect”) across states in the United States, the sooner the poor die. This relationship between income gap and longevity holds across the advanced world. Also, do not be misled into assuming SES is a measure of health-care expenditures; it isn't, not in North America or elsewhere. SES is a measure of the salutary nature of the neighborhood in which you live and the context in which you pursue gainful employment.

A handmaiden of SES is educational status. For example, people born between the world wars who managed to average twelve years of education are likely to live some seven years longer than the low-SES strata of their birth cohort. For the advantaged octogenarians, the transitions to doldrums, decrepitude, and demise are telescoped into the last year or so of life. The disadvantaged in their birth cohort commence these transitions earlier in life and suffer through their painstaking unfolding. They labor in jobs that are less rewarding, satisfying, or secure (see chapter 12). They live under clouds of persistent pain and pervasive work incapacity. Their life is shorter and less sweet.

The octogenarian and great German pathologist Rudolf Virchow (1821–1902) developed a notion of “natural” as opposed to “artificial” diseases and epidemics. He considered typhus, scurvy, tuberculosis, and mental disease to be “artificial” because they were primarily due to social conditions: “The artificial epidemics are attributes of society, products of a false culture that is not distributed to all classes. They point toward deficiencies produced by the structure of the state or society, and strike therefore primarily those classes which do not enjoy the advantages of the culture.”

The stratum of society that dies before its time falls victim to an “artificial epidemic.” “Artificial epidemics” account for 75 percent of mortal hazard. They will not respond to pharmaceuticals nor can they be surgically excised. They play out well beyond the walls of the clinic and the hospital. They are not considered the proper target of the “Health Promotion, Disease Prevention” initiatives of contemporary medicine. Rather, contemporary medicine nibbles at the frays of the other 25 percent of mortal hazard. These are the health-adverse behaviors and other biological “risk factors” that we hear so much about. Any agenda that ignores the other 75 percent does little to serve the “Public Health.” For most people who are enjoying an SES they perceive as adequate, even advantaged, there is little to do to increase their longevity since they are already likely to approach the magical eighty-five when their time is near. For the disadvantaged, those who perceive their SES as lacking, adjusting cholesterol and screening for cancer is little match for the mortal hazard of their situation in life.

Evidence-Based Medicine

These and other topics have occupied the careers of thousands of clinical investigators. The literature they have produced is enormous and varied. The quality of the science ranges from the overtly flawed through the anecdotal to the elegant. The intent of the science is less heterogeneous. Throughout history, clinical investigators have sought the evidence that would ground their treatments. In times past, astute observation of reproducible health effects was the only scientific method. It served well to identify such breakthroughs as colchicine for gout 2,000 years ago, vitamin B12 for pernicious anemia eighty years ago, and streptomycin for tuberculosis sixty years ago.

The observational method also left a paper trail and legacy of false starts, false inferences, and adverse effects of medical treatment (iatrogenicity). Tonsillectomy, for the prevention of childhood pharyngitis, is an example many older readers will recall. We learned the hard way that most children outgrow recurrent pharyngitis with or without tonsillectomy. Recently, we have learned the same lesson for “ear infections” in childhood. The triumph of the last fifty years is the development of methodologies to test whether clinical inferences are valid before they are unleashed on the ill. These methodologies try to ensure that an association drawn between a stated health effect and any drug, surgical procedure, dietary change, or other intervention is genuine. Their success derives from the design of the clinical trials and the statistical methods to handle the data. Some academic disciplines are devoted to pushing back the frontier of this methodological triumph, and certain licensing agencies, beginning with the Food and Drug Administration (FDA) in the 1960s, now demand evidence of safety and efficacy before pharmaceuticals can be marketed (see chapter 9).

The ethic, the methodology, and the regulations have converged to create the modern clinical trials enterprise. It is an enormous enterprise, spewing forth trials in the thousands and data points in the millions each year. Its output threatened to overwhelm comprehensibility and effectiveness. The result is the spawning of yet another discipline devoted to making sense of all this output — “evidence-based medicine,” or EBM. Around the world, groups of investigators are sifting through all the evidence to sort the wheat from the chaff. Yes, there is chaff. Some trials were designed less well than others because nuances that improve design were unappreciated or ignored, or because of execution or even faults in data analysis. Yet it’s not rational, or feasible, simply to rely on the most adequate trials for diagnosis and treatment. Having contended with debates as to which trial is best, one is often faced with results that pertain to particular pa-

tient groups and still are likely to be inconsistent. So the investigators revisit the “more acceptable” trials and attempt to decide, or even mathematically model, which are the least flawed and, therefore, which conclusions are least likely to be spurious. I am not belittling this effort. It is spearheaded by the Cochrane Collaboration, a ten-year-old multinational undertaking supported by various federal coffers. (No pharmaceutical industry monies are involved — yet. There are pressures in that regard.) The collaboration has 10,000 participants divided into work groups according to clinical topics. It has a registry of some 500,000 studies and has already produced some 4,000 evidentiary reviews, with nearly as many in the pipeline and plans for 7,000 beyond that.

Reviews from the Cochrane Collaboration pertain to nearly every topic covered in this book, and I have taken advantage of all of them. I also discuss their limitations in many chapters and in the relevant section of the annotated readings. The collaboration, like other EBM investigators, is committed to methodological excellence. The working groups try to discern whether there *is* evidence. For the clinician and the well person faced with a decision, however, that is only the first issue. If there is evidence for some health effect, the next point is whether the evidence is likely to be reliable or whether the next clinical trial will discount it. If it is likely to be reliable, is the effect meaningful and, therefore, worthwhile? Or is the effect too trivial to bother with or not worth the tradeoff in risk? This was the point of the hypothetical trial I put forward in the introduction. Without this frame of reference, our values will be uninformed and our decisions naïve. I intend to provide a frame of reference for decisions that relate to mortality and to symptoms (morbidity) and other aspects of the quality of life. As we will see, it is more difficult to make rational decisions about quality of life, given the vagaries of health effects in this area.

The supplementary readings for the introduction and this chapter include an expanded discussion on life-course epidemiology, the construct that underlies all of my longevity arguments. No one should be as concerned about the proximate cause of their demise as they are about the likelihood their course in life will be satisfying. It matters little what carries one off, as long as it was her or his time and the journey was gratifying.