Lifespan limits

We live in an age of vast technological optimism. Many believe we're on the verge of understanding the human brain, creating true artificial intelligence and organizing serious ventures to establish human colonies on Mars. As medicine advances, we hope to soon find cures for most diseases and to increase human lifespan dramatically. The optimism is understandable given the relentless pace of scientific advance.

Even so, we will almost certainly encounter problems that are far more stubborn than we expect. Today, for example, doctors and activists in many developed nations believe that, with enough focused effort, we can soon rid the world of cancer, which afflicts more than 10 million new people each year. A laudable goal, obviously, yet is cancer really something we might eradicate? And what would such an achievement mean for human longevity?

Remarkably, it's possible to get some insight into possible answers with basic statistics, at least according to physicists Peter Richmond and Bertrand Roehner (preprint at https://arxiv.org/abs/1609.08285; 2016). They argue on empirical grounds — using the statistics of human mortality and disease incidence over the human lifespan — that in many important ways cancer resembles a degenerative disease similar to dementia. Most importantly, it appears mathematically to be one of a spectrum of diseases apparently linked to physical and biological wearing out. One consequence is that, even if we do one day eradicate cancer, this probably won't make a big difference to human lifespan, as those escaping cancer will soon succumb instead to any of a variety of other illnesses. This isn't pessimism, just realism.

The analysis by Richmond and Roehner draws inspiration from the study of technology, where it is understood that devices over their lifetimes proceed through well-known stages of failure conforming to a so-called bathtub curve. At inception, the failure rate starts out high, but quickly decreases during the 'burn-in' stage, as items with fundamental defects fail and are removed from the population. This is generally followed by an interval of relatively constant failure rate; think of this as the period of normal operation. Finally, the failure rate again increases during the 'wear-out' phase, as key components begin to reach their design limits.

A perfect cure for cancer would have little influence on the extent of human life unless we also cured many other diseases.

As it happens, a similar pattern appears to hold for many organisms, including humans. Data on human mortality, the authors point out, shows essentially three distinct regimes in the region from 0 to 90 years of age. Before about 8 years of age, we too have a burn-in phase, during which mortality — the chance of death per year — decreases. In this phase, as infants with catastrophic defects die, the number of such defects in the remaining population is reduced. Unlike technologies, humans do not seem to have a considerable normal phase; ours, for reasons unknown, only spans the interval roughly from 8–12 years. Following this, we then have a long wear-out phase extending roughly from 12 years out to 90.

Taking these phases of the lifespan into account, Richmond and Roehner note that diseases can be classified by whether they afflict individuals primarily in the burn-in or wear-our stages, or instead fall across both. Using data from the incidence of diseases at different ages, they show that diseases clustering strongly in the burn-in phase include all diseases due to congenital malformations or chromosomal abnormalities. Likewise, the data for diseases occurring only in the wear-out phase of life are the degenerative diseases, including Alzheimer's disease and other forms of dementia. Finally, among the diseases that occur in both the burn-in and wear-out phases are those caused by external pathogens.

Where is cancer? This too turns out to be distributed across the two phases of life, and its death rate curves look qualitatively quite like those for pathogens such as bacteria or viruses. To look more closely, the authors tried to characterize all diseases by placing them in an abstract two-dimensional plane. They plot, on the horizontal axis, the exponent reflecting the speed of the decaying death rate for a disease prior to the 8–12 year interval, and, on the vertical, a similar exponent for the growing death rate later in life. As Richmond and Roehner note, this analysis suggests that cancer is much more strongly associated with degenerative diseases than anything else, as it appears clustered together with such diseases high in the leftmost region of the plot. Somewhat puzzling is that deaths by infection also lie in this zone, but this may well just reflect another bodily degeneration with ageing — in this case of the immune system, which copes with infectious agents. This doesn't tell us much about whether cancer is ultimately curable or not, yet it does cast some doubt on how much we might expect a cure for cancer to increase the human lifespan.

After all, this suggests that a perfect cure for cancer would have little influence on the extent of human life unless we also cured many other diseases at the same time. Every disease we cure will bring into view another that is harder to cure. So we may well find that efforts to extend human lifespan succeed only in the face of increasingly difficult obstacles. Indeed, as the authors note, studies show that the volume of grey matter (that is, the external layer of the brain) decreases steadily after the age of 10. While the volume of white matter decreases more slowly, brain function requires both, and ageing seems to imply a loss of capabilities, unless one could arrest the ageing process entirely.

"Death before the age of 120," Richmond and Roehner conclude, "seems firmly written in our genetic code and the best we shall be able to do is to help people cope with the inevitability of death as and when it arises."

Of course, there are always caveats. Some organisms — such as *Hydra* — actually show no ageing at all, as their mortality remains constant in time within experimental limits. Can we learn some of their tricks and use them ourselves? Moreover, with modern methods of biotechnology, we may be able to change our genomic function, pulling free of the constraints reflected in historical data. So the pessimism is not complete.

But it should check rampant speculation that, within a few decades, our lifespans may be radically boosted — it's not likely. ❐

MARK BUCHANAN