General Session 3: Theories on Aging

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Papers Presented:

Entropy Explains Aging, Genetic Determinism Explains Longevity, and Undefined Terminology Explains Misunderstanding Both
Leonard Hayflick, PhD

Is There a Limit to the Compression of Mortality?
Jean-Marie Robine
Siu Lan K. Cheung
Shiro Horiuchi
A. Roger Thatcher

Entropy, Compression, and Decompression: Trends in Human Aging and Death

Introduction

On the third day of this conference two papers were presented related to human aging and trends in death statistics. The first paper, "Entropy Explains Aging, Genetic Determinism Explains Longevity, and Undefined Terminology Explains Misunderstanding Both," was written and presented by Leonard Hayflick. The second paper, "Is There a Limit to the Compression of Mortality?" was written by Jean-Marie Robine, Siu Lan K. Cheung, Shiro Horiuchi and A. Roger Thatcher, and was presented by Siu Lan K. Cheung. This brief paper provides some observations and comments on these papers and their findings.

Each of these papers presents provocative observations and challenges. Hayflick suggests that the predominant emphasis of research on diseases rather than the aging process itself is misguided. The Robine et al. paper explores trends in the age distribution of adult deaths, and suggests that compression of this distribution may be approaching a limit. Both papers imply a sense that mortality improvement is at least decelerating, if not limited.

In this analysis there is an attempt to inter-relate the implications of these two papers, but more important, to contrast these implications with the assumptions and projections currently being made by actuaries in the United States, Canada and the United Kingdom. These projections, in fact, suggest the prospect of a future decompression of mortality and an increasing observed maximum age at death that exceeds even the increase in the median age at death or the age to which 10 percent of births survive.

Aging, Longevity, Disease and Death

In his paper, Hayflick describes the process of ***aging*** as the gradual deterioration of molecules vital to sustaining life. Through entropy molecules lose their ability to function as required, and begin to malfunction or become inactive. Genetics, Hayflick suggests, provide the blueprint for body mechanisms to repair and maintain deteriorating molecules, and thus control our potential ***longevity***.

Disease is a constant threat to life systems, and susceptibility increases with aging, because aging brings increased deterioration of molecular function and the ability to repair damage. The natural selection for the best genetics, Hayflick argues, operates up through the ages of reproduction where a large surplus of ability to maintain and repair body systems exists. It is after this age, roughly 40 to 50, where longevity reflects largely the surplus that has been selected for through the reproductive ages, but continually diminishes through the process of aging and the diminishing capacity to repair the effects of aging. With the diminished capacity to repair, disease has increasingly negative effects with ever increasing probability of ***death***.

Hayflick does not suggest a hard limit to human lifespan, as we have the ability to alter our environment and mitigate the effects of disease, reducing the probability that exposure to disease will be fatal. But Hayflick does state that "human life expectancy has NOT increased as a result of interventions in: 1. Longevity determining processes. 2. Aging processes. 3. The use of cover-ups (hair dye, cosmetic surgery, etc.)." He further notes that "Human life expectancy has only been increased by presenting, resolving or delaying the manifestations of disease …."

This is an important observation. If, in fact, study of the aging process and the genetic determinants have not and cannot be expected to allow us to extend potential life expectancy, then it will be difficult to generate substantial interest in the study of this process in our results-oriented society. Thus, while study of the aging process and the genetic determinants of our cellular mechanisms for repairing deterioration are of interest, they may be expected to continue to take a secondary role in research behind efforts to develop specific disease interventions and healthy lifestyle strategies.

I find it hard to be this pessimistic about the prospects for extension of potential life expectancy. While it seems implausible to expect extension of life indefinitely, given the seemingly inevitable cumulative deterioration that Hayflick describes as aging, it is equally difficult to set a specific age beyond which we would believe life is not possible. This discussion leads easily to the second paper presented in this session.

Mortality Compression versus Changing Symmetry

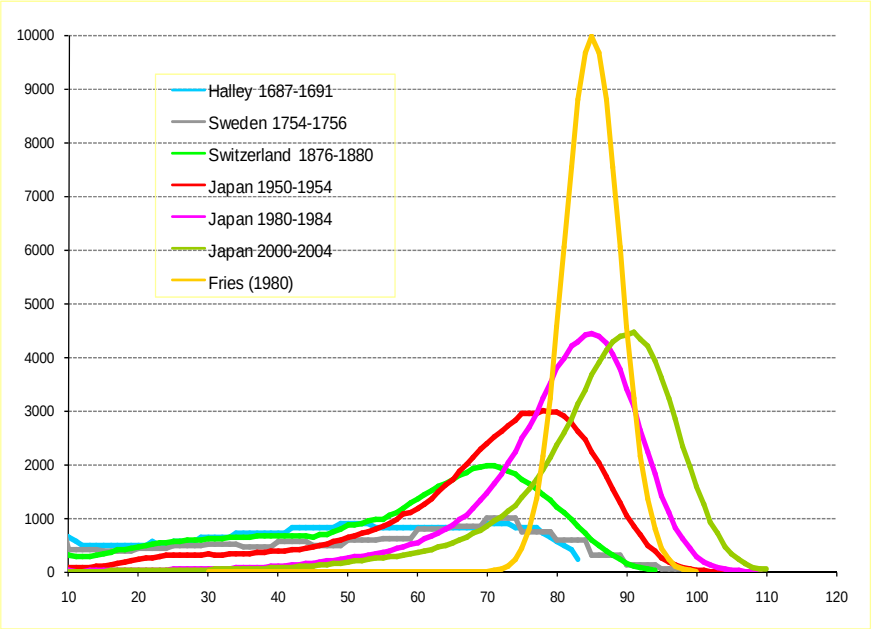
In their paper, Robine, Cheung, Horiuchi and Thatcher question whether there is a limit on the extent to which mortality can be compressed. Mortality compression here refers to the shrinking of the distribution of deaths by age among adults. The ultimate compression would be for all individuals who reach adulthood to die at the same age.

The authors studied the mortality experience of nine economically advanced countries and found that over the past 100 years the modal age at death has increased substantially and variation among countries has diminished. In 1901, the modes fell within the range of 70 to 80 years. By 2001, the modes fell largely within the range 85 to 90 years.

The authors' case for mortality compression, however, is based on a limited analysis of the distribution of deaths by age *above* the modal age. They found a decrease in the standard deviation of age at death among those who survived beyond the modal age from roughly 8.5 years in 1901, to roughly 7 years by 2001, on average. As with the modes themselves, the range of standard deviations of variation above the mode among the nine nations diminished from 1901 to 2001.

The authors' calculation of standard deviation assumed a normal distribution using observations only above the mode, thus effectively implying that mortality compression has only to do with the distribution above the median. However, while the observation of compression of the distribution of age at death above the mode is valid, it appears to miss an important additional observation. The distribution of adult deaths by age *below* the mode was expanding as the distribution above the mode was compressing. This means that the *symmetry* of the distribution of adult deaths by age around the modal age has been changing, substantially. Rather than moving toward a symmetric, normal distribution as hypothesized by Fries, the distribution of adult deaths by age has become increasingly asymmetric, with the mode advancing more than the practical "maximum age" or omega. A better test of whether there has been compression of adult mortality might be to compute the standard deviation of age at death around the mode or the mean, using all observations of death above the age of 40. It appears that this standard deviation

would reduce far less over the last century, if at all.



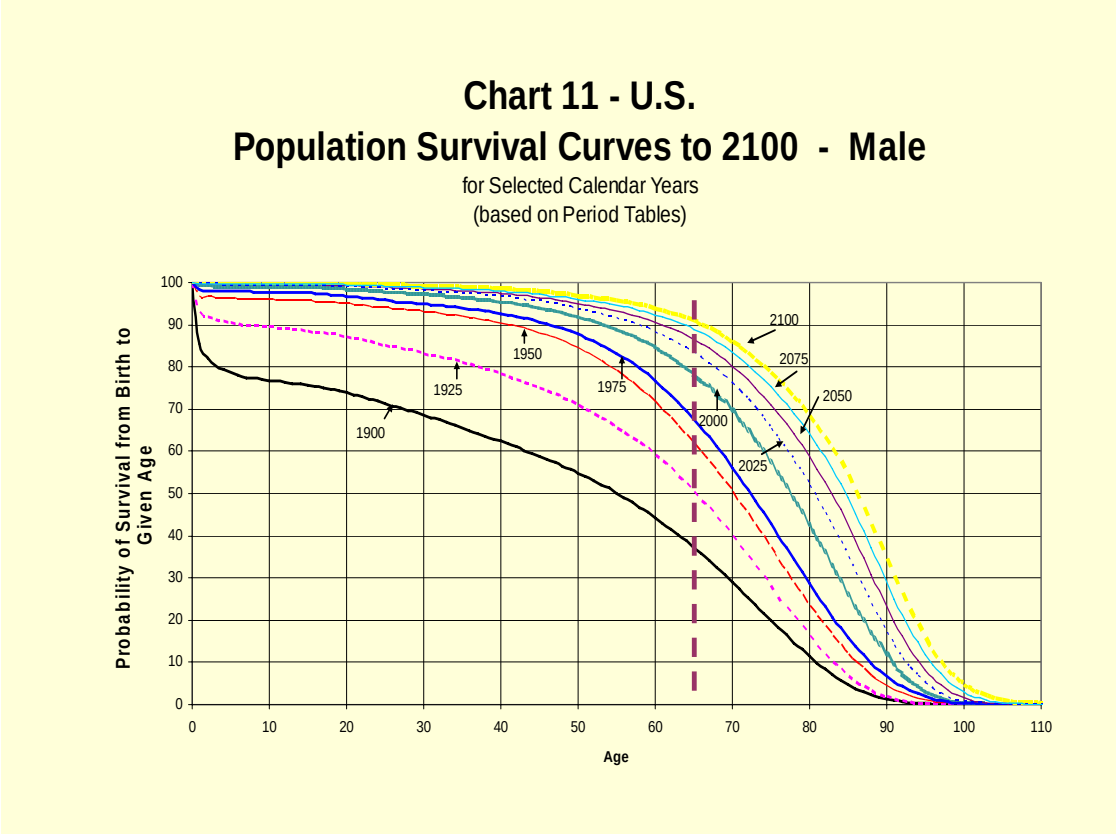
The figure above, reproduced from the paper by Robine, et al., demonstrates the non-normal symmetry of the distribution of deaths for actual records versus that hypothesized by Fries. The illustration is particularly interesting for the change in Japanese mortality between 1982 and 2002, when the mode and the distribution above shifted to the right, but the distribution below the mode effectively stretched rather than shifted. Robine et al. observed that for the United States, the standard deviation above the mode has been “roughly constant” over longer periods, unlike most other countries. In fact this observed behavior for the United States, once thought to be an aberration, may have been a predictor for Japan since 1982 and for other countries in the future. Thus, the United States for some time, and now Japan since 1982, seem to be demonstrating resistance to further mortality compression above the modal age at death.

Given the clear fact that the distribution by age at death is not normal and is apparently not moving in that direction, additional measures are worth study. It would be useful in this analysis to consider changes in the mean and the mode simultaneously. If

the two measures are changing at significantly different rates, then a change in symmetry is indicated. If the mean and mode in fact rise at about the same rate, then there are two possibilities for the changing distribution of age at death. The first is complete linear shift to the right (higher age) of the mean, mode and effective omega. The second is a stretching of the distribution to the right, where the effective omega would actually be increasing faster than other measures. Of course, as seen in the United States and Japan, a combination of these effects is possible, one above and one below the mode.

U.S. Experience and Projections

Data for the United States since 1900 provides another perspective on the analysis of deaths by age. Simple survival curves based on period life tables illustrate the degree to which the curve is being “squared” through compression of the age at death, versus a progression to higher ages for the entire distribution. Charts 11 and 12 were produced by the Office of the Actuary at the U.S. Social Security Administration using data from the National Center for Health Statistics, the Census Bureau and from Medicare and Social Security program experience.



The progression of survival curves for men and women in the United States shows substantial compression of mortality across all ages from 1900 to 1950. In this period, the probability of survival to age 40 rose from around 60 percent to over 90 percent. The probability of survival to ages 40 through almost 60 rose by about the same number of percentage points, 30. Between 1950 and 2000, the age at maximum gain in the survival rate (about 20 percentage points) was about 70 for men and 80 for women.

A better sense of the progression of survival in the United States can be seen by observing the ages to which a given percentage of the population survives. Between 1900 and 1950, this age increased by 50 years of age at the 80 percent survival rate, about 15 years at the 50 percent survival rate, and about 8 years at the 20 percent survival rate. This indicates substantial compression of mortality across all ages. However, between 1950 and 2000, increases of 5 to 10 years of age were experienced for survival rates of 80, 50 and 20 percent. Thus, the survival curve, and the distribution of deaths, is seen to have largely shifted to the right for the United States in this period, with relatively little

further compression or change in symmetry. Projections for survival and the distribution of deaths by age from 2000 to 2100 produced by the Social Security Administration's Office of the Chief Actuary for the Social Security and Medicare Trustees show a continued shift to the right with relatively little further compression or change in symmetry.

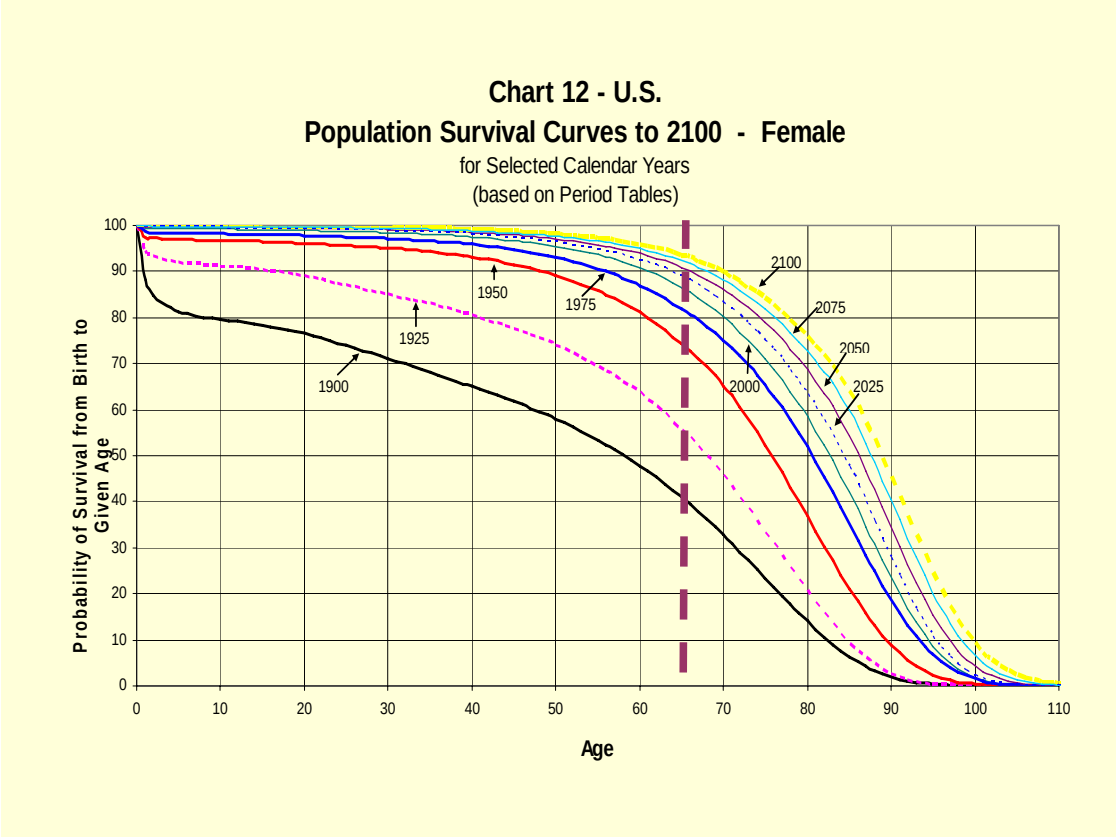
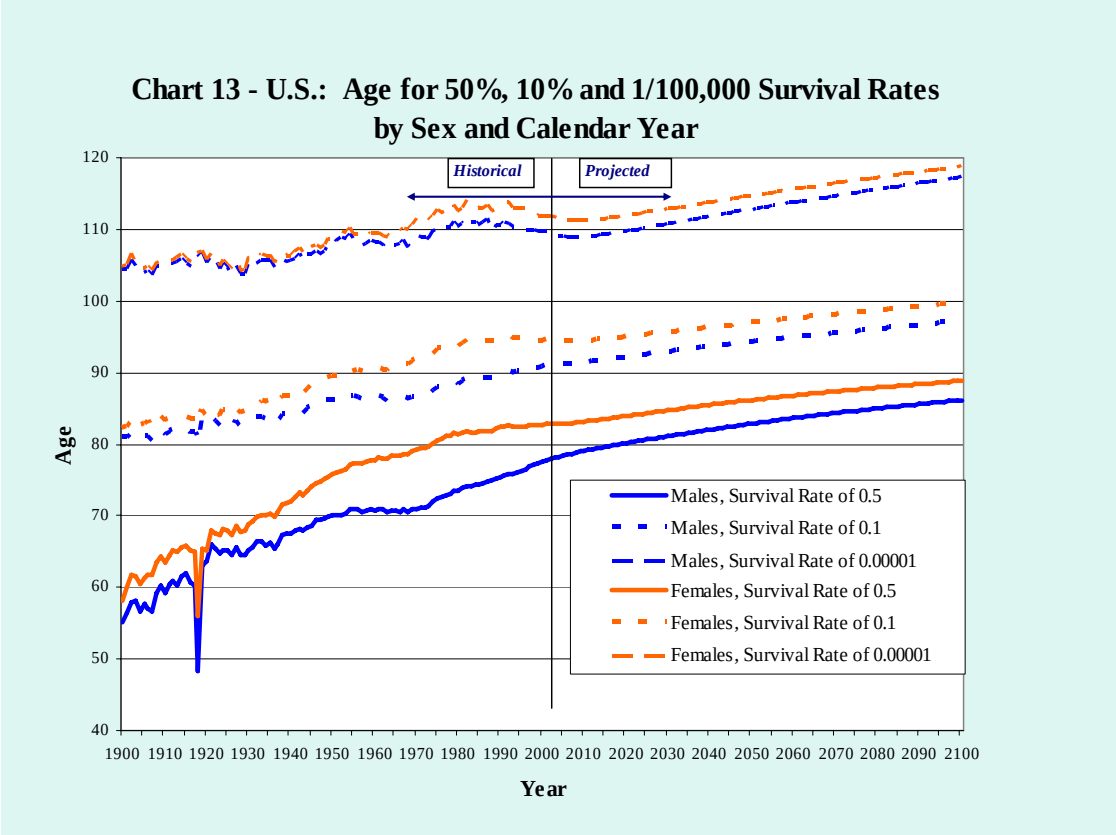


Chart 13 provides an additional graphic illustration of the progression of survival in the United States historically and as projected. Shown here are the ages for survival rates of 50 percent, 10 percent and 0.001 percent (1 in 100,000 births). The last of these represents a reasonable definition of a "practical omega" for the purpose of analysis. Because it is difficult to state the age to which survival is possible, and where survival to one year beyond that age is impossible, a true theoretical omega is a philosophical debating point. A practical omega as defined here seems to obviate the need for this debate and allows a meaningful discussion of survival.

Chart 13 clearly illustrates the fact that the median age of survival rose far faster between 1900 and 1950 than did the ages for 10 percent and 0.001 percent survival. But between 1950 and 2000, the ages for median survival and the practical omega rose at more nearly the same rate, particularly for women.



For the projections developed for the U.S. Trustees Reports, the practical omega in fact rises somewhat more between 2000 and 2100, than the ages at median and 10 percent survival. As suggested earlier, this is consistent with the prospect of going beyond a shifting of the survival curve to the right (as roughly occurred between 1950 and 2000) to a scenario in which the distribution of deaths by age will actually stretch to the right, with omega rising faster than the median or 10 percent survival ages. Contrary to experience of the last century where a compression of the distribution of deaths by age generally occurred, this projection suggests that the distribution will decompress and expand in the future. Whether this in fact will occur can only be a point of speculation at this time.

Projections for Canada, the United Kingdom, and the United States

The table below summarizes data and projections presented at this conference by participants from the Government actuary's offices of these three countries. In each case, the ratio of the projected rate of improvement (reduction) in death rates above age 85 to the rate of improvement rates at lower ages is assumed to be higher than in the past. Where the average annual rate of improvement at ages 85 and over was only about one-half the rate of improvement at ages 65-84 for all three countries over the past 60 to 100 years, this ratio is assumed to be much higher in the future. The ratio for improvement at 85 and over to improvement at 65-84 ranges from 71 percent by the Canadian Government actuary to 100 percent by the U.K. Government actuary, with the U.S. Government actuary at about 86 percent.

The implication of faster relative rates of improvement in mortality at extreme high ages is clear. If this occurs, as assumed by the actuaries in Canada, the United Kingdom and the United States, then the high death rates at these very advanced ages will diminish at much faster relative rates than in the past, and a substantial decompression of the distribution of deaths by age will result.

Historical and Projected Annual Reductions in Death Rates: Canada, UK and US

	Historical Ave % Reduction			Ultimate Assumed % Reduction		
Age	Canada	UK	US	Canada	UK	US
	last 60yrs	last 93yrs	last 103yrs			
0-14	4.0	3.6	3.2	0.7	1.0	1.5
15-64	2.0	1.5	1.4	0.7	1.0	0.8
65-84	1.5	1.0	0.8	0.7	1.0	0.7
85+	0.7	0.6	0.4	0.5	1.0	0.6
Total		1.2	1.0		1.0	0.7
Ratio 85+/65-84	0.47	0.60	0.50	0.71	1.00	0.86

Note: Ultimate is for the period roughly 2030-2080

Will this bold projection occur? Only time will tell. But it is clear that the actuarial projections of these three countries suggest unanimity of conviction that a relative acceleration of mortality improvement above age 85 is in prospect. That this conviction stands in such contrast to the theory suggested by Hayflick presents a particular challenge to the Government actuaries of these three countries.

Conclusion

Hayflick suggests that human longevity is effectively limited by our physiology and genetic control over the mechanisms that allow us to maintain and repair the ever-present deterioration (entropy) of our cellular/molecular systems. This deterioration, and our diminishing capacity to combat it after the age of reproduction, result in aging and a diminishing ability to resist disease and ultimately death.

Robine et al. demonstrate that historical data are generally consistent with a compression of the age distribution of deaths above the modal age, even if not a general compression of the distribution. However, the tendency to compress the age distribution of deaths at the highest ages suggests a concurrence with the Hayflick contention that biological limitations will limit the effective omega more than the age to which 50 percent or 10 percent of births survive. That is, the Hayflick theory and the Robine et al. observations suggest an historical and likely continued future “squaring” of the survival curve.

In fairly stark contrast to these observations and this theory stand the projections of the Government actuary offices of the United States, Canada, and the United Kingdom. In each case, the assumed future rates of reduction in mortality at ages 85 and over are substantially higher relative to the rates of reduction at ages 65-84 than observed in the past. This assumption has the effect of ceasing the compression of the age-distribution of deaths, as has already been observed in the United States and in Japan. Moreover, these assumptions go further and project a decompression of the age

distribution of deaths in the future. The projections effectively suggest that the practical omega for these populations will increase faster than the age to which 50 or 10 percent of births survive.

Demographers have debated and disputed the concept of omega as long as population statistics have been collected. While the notion of a fixed omega for human beings is generally not held currently, the extent to which it will increase in the future is certainly in doubt. Without artificial constraints on the maximum age for life, the assumptions of Government actuaries in these three countries result in an increasing and possible acceleration of increase in omega. Whether this is possible is questioned by Hayflick. Whether research on preventive medicine and life style, medical interventions for disease and even possible manipulation of the human genome will allow our species to achieve such life extension is debatable. But understanding the aging process, as Hayflick suggests, should help actuaries improve and better justify assumptions in the future.