Biodemographic Trajectories of Longevity

James W. Vaupel,* James R. Carey, Kaare Christensen, Thomas E. Johnson, Anatoli I. Yashin, Niels V. Holm, Ivan A. Iachine, Väinö Kannisto, Aziz A. Khazaeli, Pablo Liedo, Valter D. Longo, Yi Zeng, Kenneth G. Manton, James W. Curtsinger

Old-age survival has increased substantially since 1950. Death rates decelerate with age for insects, worms, and yeast, as well as humans. This evidence of extended postreproductive survival is puzzling. Three biodemographic insights—concerning the correlation of death rates across age, individual differences in survival chances, and induced alterations in age patterns of fertility and mortality—offer clues and suggest research on the failure of complicated systems, on new demographic equations for evolutionary theory, and on fertility-longevity interactions. Nongenetic changes account for increases in human life-spans to date. Explication of these causes and the genetic license for extended survival, as well as discovery of genes and other survival attributes affecting longevity, will lead to even longer lives.

Humanity is aging. The social, economic, and health-care consequences of the new demography (Table 1) will drive public policy worldwide in coming decades (*1*). Growth of the older population is fueled by three factors. Baby-boom generations are growing older. The chance of surviving to old age is increasing. And the elderly are living longer—because of remarkable, largely unexplained reductions in mortality at older ages since 1950 (*2*–*4*). Biodemography, the mating of biology and demography, is, we argue, spawning insights into the enigma of lengthening longevity (*5*).

Increases in Old-Age Survival

For Sweden, accurate statistics on mortality are available going back for more than a century. Female death rates at older ages have fallen since 1950, with large absolute reductions at advanced ages (Fig. 1). The pattern is similar for males, although from conception to old age males suffer higher death rates than females, and progress in reducing male mortality has generally been slower than for females. Consequently, most older people in Sweden—and nearly all other countries—are women.

For other developed countries, trends in mortality since 1900 have been roughly similar to those in Sweden. For example, old-age survival has also increased since 1950 for female octogenarians in England, France, Iceland, Japan, and the United States (Fig. 2). If there were an impending limit to further declines in death rates at older ages, countries with low levels of mortality would tend to show slow rates of reduction. There is, however, no correlation between levels of mortality and rates of reduction (*2*). In most developed countries the rate of reduction has accelerated, especially since 1970 (*2*, *4*). Japan, which en-

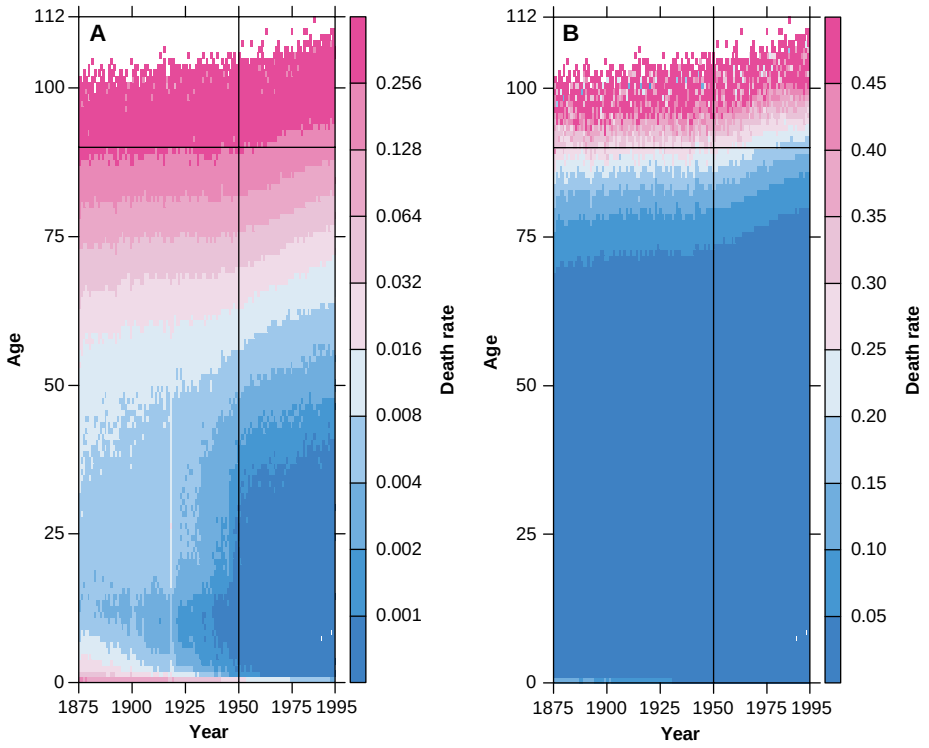

Fig. 1. Shaded contour maps (*47*) of death rates (*48*) for Swedish females from age 0 to 112 and years 1875 to 1995 (*49*), with contours on a ratio scale of mortality doublings (**A**) and on an arithmetic scale (**B**). The color of each small rectangle denotes the level of the death rate at that age and year. White rectangles indicate ages and years when no female deaths were recorded. Dark red rectangles at the highest ages mark the deaths of the last survivor of a cohort. The vertical black line marks the year 1950, when increases in old-age survival accelerated. The horizontal black line is at age 85. The large relative reductions in mortality at younger ages, especially before 1950, are apparent when a ratio scale is used to set contours (A). The vertical light line at 1919 in (A) is a consequence of deaths from the Spanish flu epidemic. The low level of mortality at ages below age 70 and the large absolute reductions in mortality at advanced ages are highlighted when an arithmetic scale is used (B).

J. W. Vaupel is at the Max Planck Institute for Demographic Research, D-18057 Rostock, Germany; Odense University Medical School, DK-5000 Odense C, Denmark; the Center for Demographic Studies, Duke University, Durham, NC 27706, USA; and Andrus Gerontology Center, the University of Southern California, Los Angeles, CA 90089–0191, USA. J. R. Carey is in the Department of Entomology, University of California at Davis, Davis, CA 95616–8584, USA. K. Christensen, N. V. Holm, I. A. Iachine, and V. Kannisto are at Odense University Medical School, DK-5000 Odense C, Denmark. T. E. Johnson is at the Institute for Behavioral Genetics, University of Colorado at Boulder, Boulder, CO 80309–0447, USA. A. I. Yashin is at the Max Planck Institute for Demographic Research, D-18057 Rostock, Germany, and the Center for Demographic Studies, Duke University, Durham, NC 27706, USA. A. A. Khazaeli and J. W. Curtsinger are in the Department of Ecology, Evolution, and Behavior, University of Minnesota, St. Paul, MN 55108, USA. P. Liedo is with El Colegio de la Frontera Sur, Tapachula 30700, Mexico. V. D. Longo is at the Andrus Gerontology Center at the University of Southern California, Los Angeles, CA 90089–0191, USA. Y. Zeng is at the Max Planck Institute for Demographic Research, D-18057 Rostock, Germany, and the Institute of Population Research, Peking University, Beijing 100871, China. K. G. Manton is at the Center for Demographic Studies at Duke University, Durham, NC 27706, USA.

*To whom correspondence should be addressed at the Max Planck Institute for Demographic Research, Doberaner Strasse 114, D-18057 Rostock, Germany. E-mail: jwv@demogr.mpg.de

joys the world's longest life expectancy and lowest levels of mortality at older ages, has been a leader in the quickening pace of increase in old-age survival (Fig. 2). Since the early 1970s female death rates in Japan have declined at annual rates of about 3% for octogenarians and 2% for nonagenarians. Mortality among octogenarians and nonagenarians has been low in the United States (Fig. 2). The reasons for the U.S. advantage and the recent loss of this advantage to Japan and France are not well understood (*4*, 6).

The reduction in death rates at older ages has increased the size of the elderly population considerably (*2*, *4*, *7*). In developed countries in 1990 there were about twice as many nonagenarians and four to five times as many centenarians as there would have been if mortality after age 80 had stayed at 1960 levels. Reliable data for various developed countries indicate that the population of centenarians has doubled every decade since 1960, mostly as a result of increases in survival after age 80 (*7*).

The decline in old-age mortality is perplexing. What biological charter permits us (or any other species) to live long postreproductive lives (*8*)? A canonical gerontological belief posits genetically determined maximum life-spans. Most sexually reproducing species show signs of senescence with age (9), and evolutionary biologists have developed theories to account for this (*10*). The postreproductive span of life should be short because there is no selection against mutations that are not expressed until reproductive activity has ceased (*11*–*13*).

The logic of this theory and the absence of compelling countertheories (*14*) have led many to discount the evidence of substantial declines in old-age mortality. Often it is assumed that the reductions are anomalous and that progress will stagnate (*15*). Only time can silence claims about the future. And empirical observations are not fully acceptable until they are explicable. We have therefore focused on testing hypotheses and developing new concepts.

Table 1. Estimated population, proportion of population, and growth of population above age 60 for the world and for selected countries in 1970 and 1997 and projected for 2025. Countries are ranked by percentage 60+ in 1997. Data are from (*46*).

Country	Millions 60+			Percent 60+			Growth	
	1970	1997	2025	1970	1997	2025	1997/1970	2025/1997
World	300.0	530.0	1200.0	8	9	15	1.8	2.3
Italy	9.0	13.0	18.0	16	23	33	1.4	1.4
Sweden	1.6	2.0	2.7	20	22	29	1.3	1.4
Germany	15.0	18.0	28.0	20	21	32	1.2	1.6
Japan	11.0	27.0	40.0	11	21	33	2.5	1.5
U.S.A.	29.0	44.0	83.0	14	17	25	1.5	1.9
China	57.0	118.0	290.0	7	10	20	2.1	2.5
India	29.0	64.0	165.0	6	7	12	2.2	2.6
Mexico	3.0	6.5	18.0	6	7	13	2.2	2.7

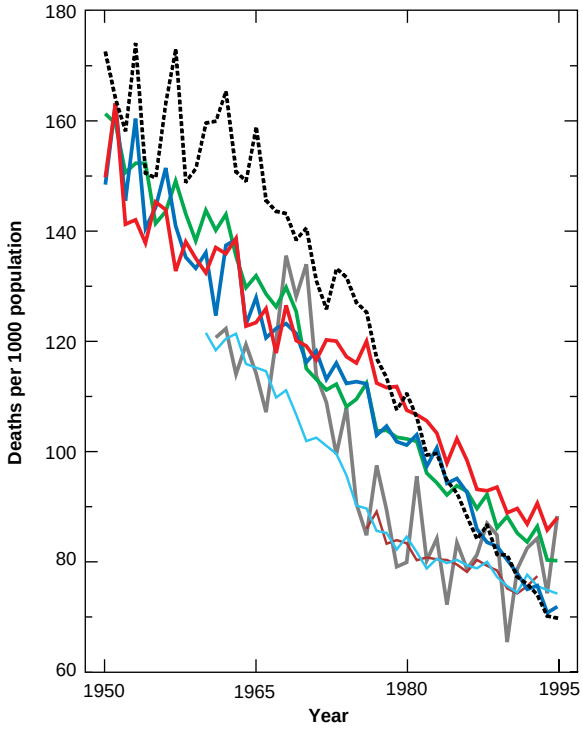

Fig. 2. Deaths per 1000 women at ages 80 to 89 from 1950 to 1995 for Japan (dashed black line), France (blue line), Sweden (green line), England and Wales (red line), Iceland (gray line), the United States (light blue line), and U.S. whites (brown line). The U.S. data (light blue line) may be unreliable, especially in the 1960s. Source: (*49*, *50*).

Mortality Deceleration

A key testable hypothesis is that mortality accelerates with age as reproduction declines. We estimated age trajectories of death rates (Fig. 3) for *Homo sapiens*, *Ceratitis capitata* (the Mediterranean fruit fly), *Anastrepha ludens*, *Anastrepha obliqua*, and *Anastrepha serpentina* (three other species of true fruit fly), *Diachasmimorpha longiacaudtis* (a parasitoid wasp), *Drosophila melanogaster*, *Caenorhabditis elegans* (a nematode worm), and *Saccharomyces cerevisiae* (baker's yeast). To peer into the remote realms of exceptional longevity we studied very large cohorts.

For humans (Fig. 3A), death rates increase at a slowing rate after age 80. A logistic curve that fits the data well from age 80 to 105 indicates that death rates may reach a plateau (*16*). A quadratic curve fit to the data at ages 105+ suggests a decline in mortality after age 110.

For four species of true fruit flies in two genera and for a parasitoid wasp (Fig. 3, B and C), death rates rise and then fall. The data on medflies (Fig. 3B) generated considerable controversy when published because it was generally believed that for almost all species mortality inexorably increases at ages after maturity (9, *17*). Previously unpublished data on three species from a different genus and a species from a different order (Fig. 3C) demonstrate that mortality decline is not unique to medflies. Theories of aging will have to confront the vexing observation of mortality decline.

Mortality deceleration can be an artifact of compositional change in heterogeneous populations (*18*). Previously unpublished *Drosophila* data (Fig. 3D) demonstrate that a leveling off of death rates can occur even when heterogeneity is minimized by rearing genetically homogeneous cohorts under very similar conditions.

The mortality trajectories for *C. elegans* (Fig. 3E) are based on data from experiments more extensive than earlier ones. The trajectory for the wild-type strain decelerates when about a quarter of the cohort is still alive, similar to observations for *Drosophila*. For *age-1* mutants mortality remains low throughout life, which demonstrates that simple genetic changes can alter mor-

tality schedules dramatically.

Data from about 10 billion individuals in two strains of *S. cerevisiae* were used to estimate mortality trajectories (Fig. 3F). Because the yeast were kept under conditions thought to preclude reproduction, death rates were calculated from changes in the size of the surviving cohort. Although they need to be confirmed, the observed trajectories suggest that for enormous cohorts of yeast, death rates may rise and fall and rise again.

The trajectories in Fig. 3 differ greatly. For instance, human mortality at advanced ages rises to heights that preclude the longevity outliers found in medflies (*3*, *16*, *17*). Such differences demand explanation. But the trajectories also share a key characteristic. For all species for which large cohorts have been followed to extinction (Fig. 3), mortality decelerates and, for the biggest populations studied, even declines at older ages. A few smaller studies have found deceleration in addition-

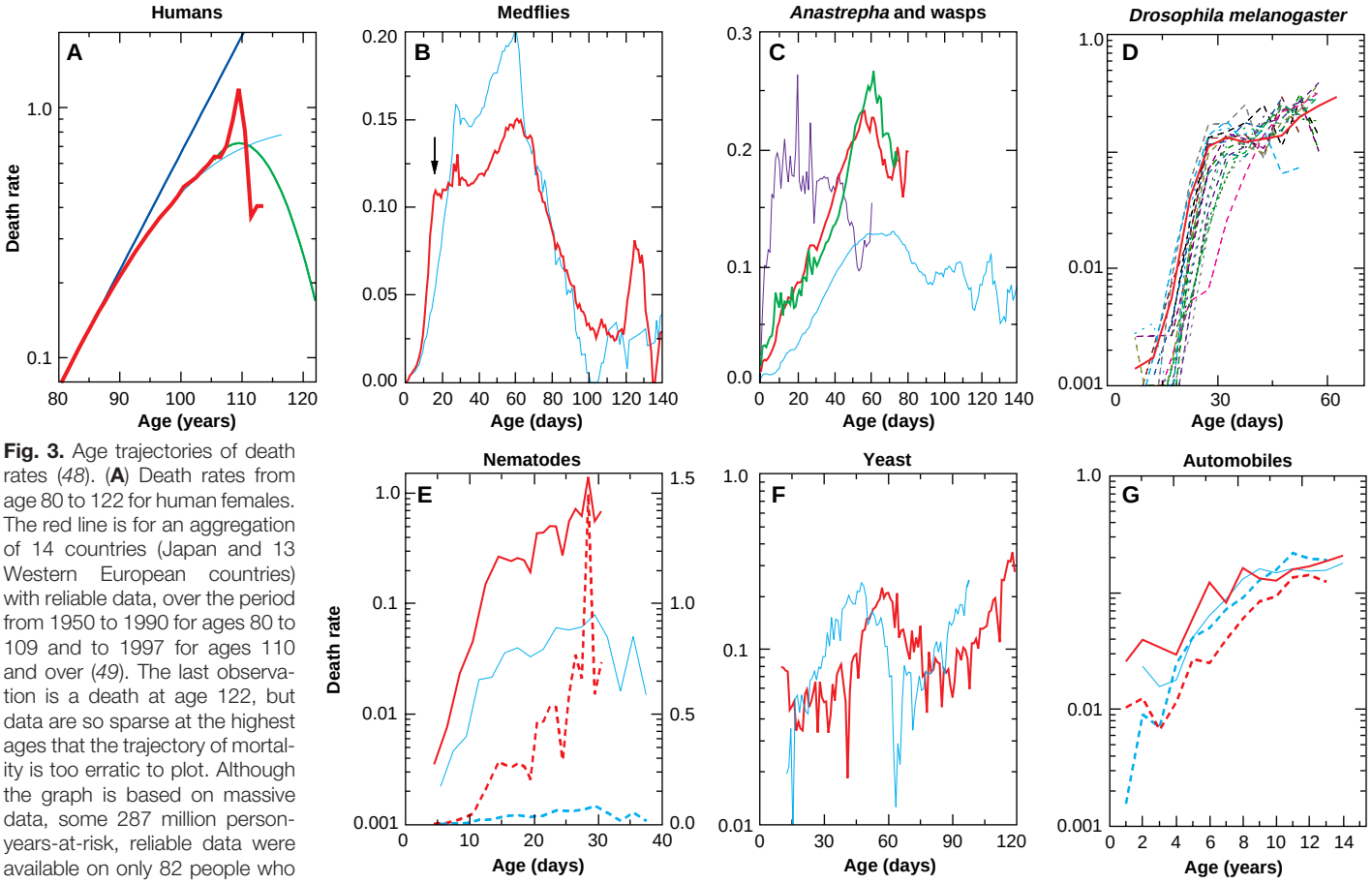

Fig. 3. Age trajectories of death rates (*48*). (**A**) Death rates from age 80 to 122 for human females. The red line is for an aggregation of 14 countries (Japan and 13 Western European countries) with reliable data, over the period from 1950 to 1990 for ages 80 to 109 and to 1997 for ages 110 and over (*49*). The last observation is a death at age 122, but data are so sparse at the highest ages that the trajectory of mortality is too erratic to plot. Although the graph is based on massive data, some 287 million person-years-at-risk, reliable data were available on only 82 people who survived past age 110. The exponential (Gompertz) curve that best fits the data at ages 80 to 84 is shown in black. The logistic curve that best fits the entire data set is shown in blue (*16*). A quadratic curve (that is, the logarithm of death rate as a quadratic function of age) was fit to the data at ages 105 and higher; it is shown in green. (**B**) Death rates for a cohort of 1,203,646 medflies, *Ceratitis capitata* (*17*). The red curve is for females and the blue curve for males. The prominent shoulder of mortality, marked with an arrow, is associated with the death of protein-deprived females attempting to produce eggs (*51*). Until day 30, daily death rates are plotted; afterward, the death rates are averages for the 10-day period centered on the age at which the value is plotted. The fluctuations at the highest ages may be due to random noise; only 44 females and 18 males survived to day 100. (**C**) Death rates for three species of true fruit flies, *Anastrepha serpentina* in red (for a cohort of 341,314 flies), *A. obliqua* in green (for 297,087 flies), and *A. ludens* in light blue (for 851,100 flies), as well as 27,542 parasitoid wasps, *Diachasmimorpha longiacaudtis*, shown by the thinner dark blue curve. As for medflies, daily death rates are plotted until day 30; afterward, the death rates are for 10-day periods. (**D**) Death rates for a genetically homogeneous line of *Drosophila melanogaster*, from an experiment by A.A.K. and J.W.C. The thick red line is for a cohort of 6338 flies reared under usual procedures in J.W.C.'s laboratory. The other lines are for 17 smaller cohorts with a total of 7482 flies. To reduce heterogeneity, eggs were collected over a period of only 7 hours, first instar larvae over a period of only 3 hours, and enclosed flies over a period of only 3 hours. Each cohort was maintained under conditions that were as standardized as feasible. Death rates were smoothed by use of a locally weighted procedure with a window of 8 days (*52*). (**E**) Death rates, determined from survival data from population samples, for genetically homogeneous lines of nematode worms, *Caenorhabditis elegans*, raised under experimental conditions similar to (*53*) but with density controlled (*21*). Age trajectories for the wild-type worm are shown as a solid red line (on a logarithmic scale given to the left) and as a dashed red line (on an arithmetic scale given to the right); the experiment included about 550,000 worms. Trajectories for the *age-1* mutant are shown as a solid blue line (on the logarithmic scale) and as a dashed blue line (on the arithmetic scale), from an experiment with about 100,000 worms. (**F**) Death rates for about 10 billion yeast in two haploid strains: D27310b, which is a wild-type strain, shown in red; and EG103 (DBY746), which is a highly studied laboratory strain, shown in blue (*34*). Surviving population size was estimated daily from samples of known volume containing about 200 viable individuals. Death rates were calculated from the estimated population sizes and then smoothed by use of a 20-day window for the EG103 strain and a 25-day window for the D27310b strain. Because the standard errors of the death-rate estimates are about one-tenth of the estimates, the pattern of rise, fall, and rise is highly statistically significant. (**G**) Death rates for automobiles in the United States, estimated from annual automobile registration data. An automobile "dies" if it is not re-registered (*26*, *54*). The blue and dashed blue lines are for Chevrolets from the 1970 and 1980 model years; the red and dashed red lines are for Toyotas from the same years.

al species (*19*). For humans, the insects, and the worms, the deceleration occurs at ages well past normal reproductive ages.

If older individuals contribute to the reproductive success of younger, related individuals, then they promote the propagation of their genes. Hence, in social species, the effective end of reproduction may be much later than indicated by fertility schedules (*20*). The deceleration of human mortality, however, occurs after age 80 and the leveling off or decline after age 110, ages that were rarely if ever reached in the course of human evolution (*8*) and ages at which any reproductive contribution is small.

In our early experiments, flies and worms were held in containers, with the density of living individuals declining with age. To check whether mortality deceleration could be an artifact of such changes in crowding, we held density constant—and still observed deceleration (*21*).

Biodemographic Explanations

It is not clear how to reconcile our two key findings—that mortality decelerates and that human mortality at older ages has declined substantially—with theory about aging. The proximate and ultimate causes of postreproductive survival are not understood (*12*, *22*). Theories that leave "nonzero late survival . . . unexplained" are unsatisfactory (*13*). Three biodemographic concepts—mortality correlation, heterogeneity in frailty, and induced demographic schedules—point to promising directions for developing theory.

Mortality correlation. Demographers have long known that death rates at different ages are highly correlated across populations and over time (*23*). In addition to environmental correlation, there may be genetic correlation: Mutations that raise mortality at older ages may do so at younger ages as well, decreasing evolutionary fitness (*12*). A pioneering *Drosophila* experiment found mortality correlation and no evidence of mutations with effects only at late ages (*24*). Postreproductive life-spans might be compared with postwarranty survival of equipment (*25*). Although living organisms are vastly more complex than manufactured products, they too are bound by mechanical constraints that may impose mortality correlations. The trajectory of mortality for automobiles (Fig. 3G) decelerates, suggesting the possibility that both deceleration and mortality correlation are general properties of complicated systems (*26*).

Heterogeneity in frailty. All populations are heterogeneous. Even genetically identical populations display phenotypic differences. Some individuals are frailer than others, innately or because of acquired weaknesses. The frail tend to suffer high mortality, leaving a select subset of survivors. This creates a fundamental problem for analyses of aging and mortality: As a result of compositional change, death rates increase more slowly with age than they would in a homogeneous population (*18*).

The leveling off and even decline of mortality can be entirely accounted for by models in which the chance of death for all individuals in the population rises at a constant or increasing rate with age (*18*). A frailty model applied to data on the life-spans of Danish twins suggests that mortality for individuals of the same genotype and with the same nongenetic attributes (such as educational achievement and smoking behavior) at some specified age may increase even faster than exponentially after that age (*27*). On the other hand, mortality deceleration could result from behavioral and physiological changes with age.

Verification of the heterogeneity hypothesis hinges on empirical estimation of the variation in frailty within a population. If at specified ages cohorts of *Drosophila* (or some other species) could be subjected to a stress that killed the frail and left the survivors neither weaker nor stronger, then comparison of the trajectories of mortality for the stressed cohorts with the trajectories for control cohorts would reveal the degree of heterogeneity (*28*). In practice, however, stresses generally weaken some survivors and strengthen others. Experiments with multiple intensities of stress, including nonlethal levels, may permit experimental estimates of heterogeneity in frailty.

Induced demographic schedules. A key construct underlying evolutionary theory is the Lotka equation, which determines the growth rate of a population (or the spread of an advantageous mutation) given age schedules of fertility and survival (*29*). The simplistic assumption in the Lotka equation that fertility and survival schedules are fixed is surely wrong for most species in the wild: Environments in nature are uncertain and changing (*30*). Many species have evolved alternative physiological modes for coping with fluctuating conditions, including dauer states (*C. elegans*), stationary phase (yeast), diapause (certain insects), and hibernation. In social insects the same genome can be programmed to produce short-lived workers or long-lived queens (*9*). That is, alternative demographic schedules of fertility and survival can be induced by environmental conditions.

To reproduce medflies need protein—and this is only occasionally available in the wild. Medflies fed sugar and water can survive to advanced ages and still reproduce when fed protein. Regardless of when medflies begin reproducing, their subsequent mortality starts low and rises rapidly. This is a striking example of how, depending on the environment, organisms can manipulate their age-specific fertility and survival (*31*).

In nematodes, exposure to nonlethal heat shock or other stresses early in life induces increases in both stress resistance and longevity (*32*). In *Drosophila*, stress can also produce increases in subsequent longevity, attributable in part to the induction of molecular chaperones (*33*). Deletion of the *RAS2* gene in *S. cerevisiae* doubles the mean chronological life-span of yeast in stationary phase (*34*). *RAS2* mutants exhibit striking similarities to long-lived nematode mutants, including increases in stress resistance (*32*, *34*). Rodents raised on restricted diets have extended life-spans and increased resistance to environmental carcinogens, heat, and reactive oxidants (*35*). These findings suggest that stress-related genes and mechanisms may affect longevity across a broad range of species (*32*–*35*).

In sum, induced physiological change can lower mortality substantially. There is also evidence for physiological remolding to cope with damage in organisms (*9*, *36*). An individual does not face fixed fertility and survival schedules, but dynamically adopts alternative schedules as the environment and the individual's capabilities change. For this and other reasons (*30*, *37*), Lotka-based evolutionary theory needs rethinking. Post-Lotka equations should incorporate "grandparental and multigenerational terms, . . . homeostatic feedback and fluctuating environments" (*37*), as well as induced demographic schedules.

Although simplistic, the Lotka equation captures a fundamental insight: It is reproductive success that is optimized, not longevity. Deeper understanding of survival at older ages thus hinges on intensified research into the interactions between fertility and longevity (*19*, *31*, *38*).

Survival Attributes

The concepts of mortality correlation, heterogeneity in frailty, and induced demographic schedules can be tied together by a general question: How important are an individual's survival attributes (that is, persistent characteristics, innate or acquired, that affect survival chances) as opposed to current conditions in determining the chance of death? For humans, nutrition and infections in utero and during childhood may program the development of risk factors for several important diseases of middle and old age (*39*). Conflicting evidence suggests that current conditions may affect old-age survival chances much more than con-

ditions early in life (*2*, *40*).

A frailty model applied to Danish twin data sheds some even-handed light on this controversy. The model suggests that about 50% of the variation in human life-spans after age 30 can be attributed to survival attributes that are fixed for individuals by the time they are 30; a third to a half of this effect is due to genetic factors and half to two-thirds to nongenetic survival attributes (related to, for example, socioeconomic status or nutritional and disease history). The model suggests that the importance of survival attributes may increase with a person's life expectancy. For persons who at age 30 can expect to survive into their 90s, more than 80% of the variation in life-span may be due to factors that are fixed by this age (*41*).

How many survival attributes account for most of the variation in life-spans? The number required to "survive ad extrema" may be "hundreds, not tens-of-thousands" (*37*); research over the next decade may resolve this question. For nematode worms and yeast, the mutation of a single gene can result in a qualitative change in the age trajectory of mortality (Fig. 3E) (*34*). For other species, including *Drosophila* and humans, no genes with such radical demographic effects have yet been discovered, but some polymorphisms, such as ApoE alleles in humans, alter substantially the chance of surviving to an advanced age (*42*). The emerging field of molecular biodemography seeks to uncover how variation at the microscopic level of genetic polymorphisms alters mortality trajectories at the macroscopic level of entire populations.

Analyses of data on Danish twins and other populations of related individuals indicate that 20 to 25% of the variation in adult life-spans can be attributed to genetic variation among individuals; heritability of life-span is also modest for a variety of other species (*43*). The possibility that genetic polymorphisms may play an increasing role with age is supported by evidence of increases with age in the genetic component of variation in both cognitive and physical ability (*44*).

Although genes and other survival attributes are fixed for individuals, their distribution in a cohort changes with age as the frail die. Hence, it is possible to develop survival attribute assays based on demographic analysis of changes with age in the frequency of fixed attributes. In longitudinal research in progress, we are gathering information on lifestyle and environmental conditions as well as DNA from 7000 Chinese octogenarians and nonagenarians, 3000 Chinese centenarians, and 14,000 elderly Danes. Survival-attribute assays applied to these data may uncover a suite of genetic and nongenetic determinants of longevity.

Experiments with insects, worms, yeast, and other organisms permit alternative approaches for discovering survival attributes; the diet and stress experiments sketched above provide examples. That genes can alter mortality trajectories is now certain; research on the mechanisms will shed new light on aging and longevity (*45*). The importance of diet, stress, and reproduction in inducing alternative mortality schedules has been demonstrated, but the potential of such studies to clarify causal relationships is just beginning to be tapped. The emerging dialogue between biologists and demographers (*5*) is changing the terms of discourse and opening new vantage points for research on aging.

REFERENCES AND NOTES

1. In China the 60+ population in 2050 may number around half a billion people, about the number worldwide today (Table 1). To keep the proportion over 60 to a quarter that size, population size would have to rise from 1.25 to 2 billion [J. W. Vaupel and Y. Zeng, *Policy Sci.* **24**, 389 (1991); Y. Zeng, J. W. Vaupel, Z. Wang, *Math. Pop. Stud.* **6**, 187 (1997)]. More generally, see J. W. Vaupel and A. E. Gowan, *Am. J. Public Health* **76**, 430 (1986) and D. A. Wise, Ed., *Advances in the Economics of Aging* (Univ. of Chicago Press, Chicago, IL, 1996).
2. V. Kannisto, J. Lauritsen, A. R. Thatcher, J. W. Vaupel, *Pop. Dev. Rev.* **20**, 987 (1994); V. Kannisto, *Development of Oldest-Old Mortality 1950-1990* (Odense Univ. Press, Odense, Denmark, 1994); V. Kannisto, *The Advancing Frontier of Survival* (Odense Univ. Press, Odense, Denmark, 1996); J. R. Wilmoth in (*5*), p. 38.
3. B. Jeune and J. W. Vaupel, Eds., *Exceptional Longevity: From Prehistory to the Present* (Odense Univ. Press, Odense, Denmark, 1995).
4. J. W. Vaupel, *Philos. Trans. R. Soc. London Ser. B* **352**, 1 (1997).
5. K. W. Wachter and C. E. Finch, Eds., *Between Zeus and the Salmon: The Biodemography of Longevity* (National Academy Press, Washington, DC, 1997).
6. K. G. Manton and J. W. Vaupel, *N. Engl. J. Med.* **333**, 1232 (1995).
7. J. W. Vaupel and B. Jeune, in (*3*), p. 109.
8. Remaining life expectancy at age 65 for Paleolithic populations may have been about 7 years [R. E. Lee, in (*5*), p. 212]. For Swedish females in 1900, 1950, and 1995 it was 12.9, 14.3, and 19.8 years, and for Japanese females in 1995 it was over 20.8 years, triple the Paleolithic level. Remaining life expectancy at age 50 from the stone age through the middle ages may have varied from 10 to 16 years [J. R. Wilmoth in (*3*), p. 125], compared with values of 23.8, 26.4, and 33.0 for Swedish females in 1900, 1950, and 1995.
9. C. E. Finch, *Longevity, Senescence, and the Genome* (Univ. of Chicago Press, Chicago, IL, 1990).
10. P. B. Medawar, *An Unsolved Problem in Biology* (Lewis, London, 1952); G. C. Williams, *Evolution* **11**, 398 (1957); W. D. Hamilton, *J. Theor. Biol.* **12**, 12 (1966); B. Charlesworth, *Evolution in Age-Structured Populations* (Cambridge Univ. Press, New York, 1994); P. Abrams and D. Ludwig, *Evolution* **49**, 1055 (1995); L. Partridge in (*5*), p. 78. For discussion of the mixed empirical support for this theory, see (*13*); J. W. Curtsinger, P. M. Service, T. Prout, *Am. Nat.* **144**, 210 (1994); D. E. L. Promislow, M. Tatar, A. A. Khazaeli, J. W. Curtsinger, *Genetics* **143**, 839 (1996).
11. J. W. Curtsinger, *Genetica* **96**, 187 (1995); S. Tuljapurkar, in (*5*), p. 65.
12. B. Charlesworth and L. Partridge, *Curr. Biol.* **7**, R440 (1997).
13. The quote, from (*12*, p. R441), pertains to L. D. Mueller and M. R. Rose, *Proc. Natl. Acad. Sci. U.S.A.* **93**, 15249 (1996); also see S. D. Pletcher and J. W. Curtsinger, *Evolution*, in press.
14. L. Keller and M. Genoud, *Nature* **389**, 958 (1997).
15. N. Keilman, *J. Off. Stat.* **13**, 245 (1997); J. F. Fries, *N. Engl. J. Med.* **303**, 130 (1980); S. J. Olshansky, B. A. Carnes, C. Cassel, *Science* **250**, 634 (1990).
16. A. R. Thatcher, V. Kannisto, J. W. Vaupel, *The Trajectory of Mortality from Age 80 to 120* (Odense Univ. Press, Odense, Denmark, 1998).
17. J. R. Carey, P. Liedo, D. Orozco, J. W. Vaupel, *Science* **258**, 457 (1992); J. R. Carey, *Demography* **34**, 17 (1997).
18. J. W. Vaupel, K. G. Manton, E. Stallard, *ibid.* **16**, 439 (1979); J. W. Curtsinger, H. H. Fukui, D. R. Townsend, J. W. Vaupel, *Science* **258**, 461 (1992); J. W. Vaupel and J. R. Carey, *ibid.* **260**, 1666 (1993); A. I. Yashin, J. W. Vaupel, I. A. Iachine, *Mech. Aging Dev.* **74**, 1 (1994).
19. M. Tatar, J. R. Carey, J. W. Vaupel, *Evolution* **47**, 1302 (1993); D. L. Wilson, *Mech. Aging Dev.* **74**, 15 (1994). But most smaller studies have not found deceleration (*9*).
20. J. R. Carey and C. Gruenfelder, in (*5*), p. 127; S. N. Austad, *ibid.*, p. 161.
21. J. R. Carey, P. Liedo, J. W. Vaupel, *Exp. Gerontol.* **30**, 605 (1995); A.A. Khazaeli, L. Xiu, J. W. Curtsinger, *J. Gerontol.* **52**, 48 (1995); A. A. Khazaeli, L. Xiu, J. W. Curtsinger, *Genetica* **98**, 21 (1996). In our nematode experiments, the volume of the container was reduced as worms died, to keep density constant.
22. K. Christensen and J. W. Vaupel, *J. Int. Med.* **240**, 333 (1996).
23. A. Coale and P. Demeny, *Regional Model Life Tables and Stable Populations* (Academic Press, New York, 1983); R. D. Lee and L. R. Carter, *J. Am. Stat. Assoc.* **87**, 659 (1992).
24. S. D. Pletcher, D. Houle, J. W. Curtsinger, *Genetics* **148**, 287 (1998).
25. L. Hayflick, *How and Why We Age* (Ballantine Books, New York, 1994); L. S. Gavrilov and N. S. Gavrilova, *The Biology of Life Span* (Harwood, Chur, Switzerland, 1991). Contrary to J. F. Fries and L. M. Crapo [*Vitality and Aging* (Freeman, San Francisco, 1981)] and R. Dawkins [*Sci. Am.* **273**, 80 (November 1995)], reliability engineering constraints make it virtually impossible for organisms to approximate the "one-hoss shay" of Oliver Wendell Holmes, which ran perfectly until one day when all of its pieces fell apart simultaneously.
26. J. W. Vaupel, in (*5*), p. 17.
27. A. I. Yashin and I. A. Iachine, *Demography* **34**, 31 (1997).
28. J. W. Vaupel, A. I. Yashin, K. G. Manton *Math. Pop. Studies* **1**, 21 (1988); J. W. Curtsinger and A. A. Khazaeli, *Exp. Gerontol.*, in press.
29. A.J. Lotka, *Theorie Analytique des Associations Biologiques* (Hermann, Paris, 1939). The equation is $1 = \int e^{-rx} l(x) m(x) dx$, where r is the intrinsic rate of growth of the population, $l(x)$ is the proportion of females surviving to age x, and $m(x)$ is the average number of female offspring to females at age x.
30. S. Orzack and S. Tuljapurkar, *Am. Nat.* **133**, 901 (1989); M. Mangel and C. W. Clark, *Dynamic Modeling in Behavioral Ecology* (Princeton Univ. Press, Princeton, NJ, 1988).
31. J. R. Carey, P. Liedo, H.-G. Müller, J.-L. Wang, J. W. Vaupel, in preparation.
32. G. Lithgow, T. M. White, S. Melov, T. E. Johnson, *Proc. Natl. Acad. Sci. U.S.A.* **92**, 7540 (1995); S. Murakami and T. E. Johnson, *Genetics* **143**, 1207 (1996).
33. M. Tatar, A. A. Khazaeli, J. W. Curtsinger, *Nature* **390**, 30 (1997).
34. V. Longo *et al.*, in preparation.
35. E. J. Masoro and S. N. Austad, *J. Gerontol.* **51A**, B387 (1996); S. M. Jazwinski, *Science* **273**, 54 (1996).
36. C. Franceschi *et al.*, *Int. Rev. Immunol.* **12**, 57 (1995); E. G. Lakatta, *Aging* **6**, 213 (1994).
37. K. W. Wachter in (*5*), p. 1.

38. L. Partridge and M. Farquhar, *Nature* **294**, 580 (1981); L. Partridge and P. Harvey, *ibid.* **316**, 20 (1985).
39. W. Kermack, A. McKendrick, P. McKinlay, *Lancet* **1**, 698 (1934); D. J. P. Barker, *Fetal and Infant Origins of Adult Disease* (British Medical Journal, London, 1992); I. T. Elo and S. H. Preston, *Pop. Index* **58**, 186 (1992); R.W. Fogel and D. R. Costa, *Demography* **34**, 49 (1997).
40. K. Christensen, J. W. Vaupel, N. V. Holm, A. I. Yashin, *Br. Med. J.* **310**, 432 (1995); V. Kannisto, K. Christensen, J. W. Vaupel, *Am. J. Epidemiol.* **145**, 987 (1997).
41. Calculation by I. A. Iachine based on frailty model described in (*27*).
42. F. Schächter *et al.*, *Nature Genet.* **6**, 29 (1994); G. De Benedictis *et al.*, *Hum. Genet.* **99**, 312 (1997); J. Maynard Smith, *Nature* **181**, 496 (1958).
43. A. M. Herskind *et al.*, *Hum. Genet.* **97**, 319 (1996); J.W. Curtsinger *et al.*, *Annu. Rev. Genet.* **29**, 553 (1995); C. E. Finch and R. E. Tanzi, *Science* **278**, 407 (1997).
44. G. E. McClearn *et al*., *Science* **276**, 1560 (1997); K. Christensen *et al.*, in preparation.
45. A promising line of inquiry we are pursuing focuses on lines of medflies (*31*) and yeast (*34*) that survive to and reproduce at advanced ages.
46. Census Bureau International Data Base (updated 10 October 1997), available at www.census.gov/ipc/www/idbnew.html; United Nations Population Division, *World Population Prospects: The 1996 Revision*, *Annex II and III* (United Nations, New York, 1997).
47. J. W. Vaupel, Z. Wang, K. Andreev, A. I. Yashin, *Population Data at a Glance: Shaded Contour Maps of Demographic Surfaces* (Odense Univ. Press, Odense, Denmark, 1998).
48. Death rates are the so-called central death rates calculated by dividing the number of deaths at the specified age by the years or days of exposure for the population at risk.
49. Own calculations from data in the Kannisto-Thatcher Oldest-Old Database and other databases in the Archive of Population Data on Aging maintained by Odense University Medical School, Denmark [see (*2*)], as well as from data in the Berkeley Mortality Database (http://demog.berkeley.edu/wilmoth/mortality).
50. U.S. data are from the Social Security Administration. Data on U.S. whites are based on Social Security data supplied to J.W.V. by the Health Care Financing Administration. Concerning reliability and calculation methods, see (*4*, *6*); B. Kestenbaum, *Demography* **29**, 565 (1992); L. B. Shrestha and S. H. Preston, *Survey Method.* **21**, 167 (1995).
51. H.-G. Müller, J.-L. Wang, W. B. Capra, P. Liedo, J. R. Carey, *Proc. Natl. Acad. Sci. U.S.A.* **94**, 2762 (1997).
52. T. J. Hastie and R. J. Tibshirani, *Generalized Additive Models* (Chapman & Hall, New York, 1990).
53. A. Brooks, G. J. Lithgow, T. E. Johnson, *Science* **263**, 668 (1994); J. W. Vaupel, T. E. Johnson, G. J. Lithgow, *ibid.* **266**, 826 (1994).
54. Calculations by J.W.V. and C. R. Owens in manuscript on "Automobile Demography."
55. Our research was supported by the U.S. National Institutes of Health (grant AG08761), Danish Research Council, Max Planck Society, Alfred P. Sloan Foundation, and Wellcome Trust. We thank K. Andreev, K. Brehmer, C. E. Finch, L. G. Harshman, B. Jeune, P. Laslett, H. Lundström, M. K. McGue, H.-G. Müller, D. Orozco, C. R. Owens, L. Partridge, S. D. Pletcher, S. H. Preston, D. Roach, R. Suzman, M. Tatar, A. R. Thatcher, S. Tuljapurkar, N. G. Vaupel, K. W. Wachter, J.-L. Wang, J. R. Wilmoth, and the Moscamed Program in Metapa, Mexico.