The Biodemography of Aging

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Is there a looming limit to human life expectancy? Will the life expectancy of any sizable population ever exceed 85 years? These were the research questions that seized my attention in 1986. I would like to start with them by way of offering an account of the course of my life as a researcher interested in the biodemography of aging.

The question of limits to life expectancy was a hot topic in 1986, and the subject remains of considerable interest today. In 1980 James Fries wrote a widely cited article in the *New England Journal of Medicine* in which he quantified some notions that gerontologists had been talking about for a long time. Fries made the following assertions. There are two kinds of death: premature and senescent. Premature death results from accidents and various illnesses that cut life short. Senescent death strikes as an individual approaches his or her maximum potential life span. Every human is born with a maximum potential life span. This maximum differs from person to person and is normally distributed with a mean of 85 years and a standard deviation of 7 years. Nothing can be done to alter a person's maximum potential life span: it is innate, fixed, and beyond the influence of any currently conceivable environmental, behavioral, or medical intervention. When a person's age nears his or her maximum potential life span, then the person becomes increasingly susceptible to many proximate causes of death. If a person does not die of cancer today, then he or she will die of a heart attack or influenza or a serious fall or something else tomorrow. Because the maximum potential life span of individuals has a mean of 85 years, it follows that under no foreseeable conditions can a population's life expectancy exceed 85 years.

The kernel of Fries's theory can be traced back to Aristotle. Aristotle also asserted that there were two kinds of death, premature and senescent. He compared premature death to a fire extinquished by throwing water on it, and he compared senescent death to a fire burning itself out. Each individual, Aristotle wrote, was born with a fixed amount of "fuel," analogous

to the wood in a fire. No new fuel could be added. Hence, each individual has a maximum potential life span. For 24 centuries this Aristotelian view has been widely accepted and is still viewed by many experts as well as laypeople as undeniably correct. The value of Fries's contribution was to clearly specify the elements of the theory and to quantify particular values for the mean and standard deviation of the distribution of maximum potential life spans.

Evolutionary biologists, starting with Medawar, Williams, and Hamilton in the 1950s and 1960s, developed a theory of aging that is consistent with the Aristotelean notion of limited life spans. Their basic reasoning can be simply summarized. Evolution is driven by the survival of the fittest. By definition, individuals who are more fit have more descendants than those who are less fit. That is, fit individuals are more likely to survive to reproductive age and to give birth to numerous offspring who survive to reproduce as well. Hence the genes of the individuals in a population tend to be the genes of fit individuals.

But how does age affect this process? Older individuals have few if any additional progeny. Over the long course of human evolution, the elderly contributed to the survival and reproductive success of their children and grandchildren by providing them with food and other resources. Such contributions tend to diminish with age. Moreover, only a small proportion of individuals, before the twentieth century, survived to age 70 or older. Hence, individuals with mutations that increased the chances of death at older ages—but not at younger ages—were almost as fit as individuals without such mutations. As such mutations gradually occurred and were passed on from generation to generation, their frequency tended to increase. This process was accelerated for mutations that are deleterious at older ages but that reduce mortality or increase fertility at younger ages. In any case, however, harmful mutations that affect only older individuals accumulate over many generations, and this results in an increase in death rates with age. In particular, death rates reach very high levels at ages when individuals make little contribution to the survival or fertility of their descendants. This high level of mortality imposes an effective limit to any individual's life span. Because the burden of late-acting mutations affects various individuals differently, maximum potential life span also varies across individuals. For humans, it does not seem unreasonable that the mean of this distribution might be 85 years or so, perhaps with a standard deviation of roughly 7 years, because the fitness contribution of older individuals is certainly modest by age 85, very small by age 92, minuscule by age 99, and not large at age 78 or even 71.

Because Fries's arguments seemed reasonable to many people, because he expressed his views clearly, cogently, and with admirable specificity, because he presented some indirectly relevant evidence to support his position, and because his theory is consistent with the evolutionary theory of

aging, the "Fries theory" was widely accepted in the 1980s. Some scholars, however, had doubts, especially about whether 85 years was the true limit to human life expectancy but also about the general notion of limited life spans. Kenneth Wachter and Sheila Ryan Johansson at the University of California at Berkeley made a crucial contribution by organizing a stimulating research workshop in 1988 to discuss the evidence for the theory and the doubts about it.

Immediately after participating in this workshop, James Carey, Shripad Tuljapurkar, and I discussed possible analyses that might be done to test the Fries theory. At the University of Minnesota I had organized a series of weekly meetings at which scholars interested in demography could discuss their research. Following the Berkeley workshop, the Minnesota meetings increasingly focused on Fries's theory and how to test it. Working together with Carey, at the University of California at Davis, we developed a program of research. We were encouraged by various people, most importantly by Richard Suzman at the US National Institute on Aging, and also by Michael Teitelbaum at the Sloan Foundation and by Tuljapurkar, Robert Fogel, Nathan Keyfitz, Peter Laslett, and Samuel Preston, among others. Before I describe our program of research, let me briefly recount how I arrived at the University of Minnesota and how my research career there got started.

My early research career

After studying international business at Harvard Business School, getting a Master's degree in public policy, and starting Ph.D. research at the Kennedy School of Government at Harvard, I joined the public policy faculty at Duke University. At Harvard I began three Ph.D. dissertations. The first focused on mathematical methods for deciding when it is time to cease analyzing a decision dilemma. The second concerned public regulation of multinational corporations. And the third, which I finished after I started working at Duke, evaluated public policies to reduce "early death" before age 65. My interest in mortality led me to start reading and thinking about demography. This resulted in my first research article in *Demography*, a piece by Vaupel, Manton, and Stallard (1979) on the impact of heterogeneity in frailty on the dynamics of mortality. For three years, spread out over the first half of the 1980s, I was employed by the International Institute for Applied Systems Analysis (IIASA), near Vienna, Austria, where I deepened my understanding of demography by working with such outstanding researchers as Brian Arthur, Nathan Keyfitz, Andrei Rogers, Michael Stoto, and Anatoli Yashin.

At the end of my stay at IIASA, I moved to Minneapolis and began working in 1986 as a full professor at the Humphrey Institute for Public Affairs and Planning at the University of Minnesota. It was immediately made clear to me that I would have to learn how to raise grant funding. In

part because of the pressure to do so and in part because of my by-now deep interest in demography, I decided to find colleagues at Minnesota who were also interested in demography. So I used the Science and Social Science Citation Indexes to find the names of everyone in Minnesota who had written a cited article with the word "demography" or "population" in the title, abstract, or key words. I found almost 200 names. Some had left Minnesota, some lived in Minnesota but a long way from Minneapolis, and some clearly had interests that were distant from demographic research. Many, however, seemed relevant and others, such as the author of "The population of timber wolves on Isle Royale," seemed at least to be worth meeting. So I started telephoning people and asking whether they would like to have lunch with me. Very few people turned me down. Altogether I had lunch with about 100 new people over the course of my first year at Minnesota.

As it turned out, many of these people were interested in survival and longevity, in some cases for humans and in other cases for various nonhuman species. A group of about 30 of these researchers decided to meet for an hour once a week to discuss research on the demography of aging. These participants included about a dozen scholars with backgrounds in social and behavioral sciences, about half a dozen with degrees in medicine and public health, another half dozen from various branches of biology, and a final half dozen from statistics, biostatistics, and actuarial mathematics. Robert Kane, who then was Dean of the School of Public Health, offered us use of a seminar room and provided some financial support. Other financial support came from the Humphrey Institute, from the central administration of the University, and from a program directed by Michael Teitelbaum at the Sloan Foundation. We used this money to start some pilot research projects.

None of the participants was able to attend every meeting, but typically between 12 and 20 researchers came—and almost all the meetings, which started in 1987 and ended in 1991, were lively and stimulating. Numerous research projects were developed or furthered by the meetings, including David Snowdon's study of elderly Catholic nuns, the work by Steven Ruggles and Robert McCaa on census data, Richard Paine's compilation of lifetables for prehistoric European populations, Stanley Hill's evaluation of the impact of longer lives on life insurance companies, and Peter Abrams's research on evolutionary forces that shape the age trajectory of mortality for any species.

Throughout the four years of the weekly series and especially after the aforementioned Berkeley workshop, the main interest focused on Fries's theory and how to test it. As a result of our discussions, we were able to develop a multi-university program of research that we submitted to the US National Institute on Aging. Richard Suzman encouraged and facilitated this application. We started the research on 1 January 1990. Funding for the re-

search we began then has been renewed three times, and we are currently in the fifteenth year of work. Of course we are now studying new topics, and there has been considerable change in personnel as well as a shift in the location of the coordinating center of the grant from the University of Minnesota to Duke University. For a decade and a half, however, we have focused on the general topic of life span limits versus life span plasticity.

Research strategy: The Scientific Method

Let me now turn to the strategy we decided to pursue to investigate the Fries theory in general and, more specifically, whether there is a looming limit to human life expectancy at age 85. Our key decision was to adopt the so-called Scientific Method. Let me emphasize that most demographic research, including most research of the highest standards and greatest interest, is based on other strategies. Let me also admit that most of my own research is based on other approaches to knowledge, although it seems to me that my involvement in the application of the Scientific Method to the Fries theory is perhaps my biggest contribution to knowledge and, in light of this, I plan to base much of my future research on that method. Various population scientists—James Smith of the RAND Corporation comes immediately to mind—have demonstrated how powerful the Scientific Method can be in research on the demography (and economics) of aging, and I believe that demographers should emphasize this strategy more than most of us do.

The Scientific Method involves three main elements. First, a theory must be explicitly and precisely specified. Fries's contribution was to add such flesh and bones to misty gerontological speculation. Second, falsifiable predictions of the theory have to be deduced. Much of our thinking at Minnesota was devoted to formulating such testable propositions. Third, highly reliable data have to be gathered to determine whether the predictions hold true. If they do, this adds to the credibility of the theory; if not, the theory has been shown to be wrong. All theories are eventually proven wrong, but some theories are useful, at least in some contexts. Newton's theory of gravity is an example. So the crucial task in testing a theory is to develop predictions that are not only falsifiable but that are also important in terms of the purposes of the theory.

With substantial help from James Carey and from others not at the University of Minnesota, we developed four falsifiable predictions of the Fries theory. Then instead of using convenient datasets already at hand—a tempting approach to research—we thought long and hard about how to assemble the most compelling datasets to test the four predictions. We gathered the data, tested the propositions, and published refereed articles in *Science* and other outstanding journals. Various objections were raised, and we systematically pursued research to respond to each serious concern.

The first of the predictions we tested can be adumbrated as follows. According to the Fries theory, nearly all mortality at advanced ages is due to senescent death, and nothing can be done to reduce senescent death. Specifically, the prediction is that death rates after age 85 years, and especially after age 92 or 99, should be about the same today as they always have been. Fries explicitly makes this claim in his seminal article. So we decided to compile reliable statistics on the age-specific probabilities of death after age 85 over an extended period of time. The most reliable long-term data on death rates pertain to Sweden: outstanding data have been collected since 1861 and serviceable data since 1750. Although appropriate data had been collected, however, statistics on Swedish death rates after age 85 had not been systematically compiled, checked, and published. So we asked Hans Lundstrom of Statistics Sweden to undertake this task. Subsequently, the work of Roger Thatcher permitted study of long-term trends in mortality at the oldest ages in England and Wales, and the monumental efforts of Väinö Kannisto extended this work to more than a dozen additional countries. Hence we were able to test our first falsifiable prediction of Fries's theory. Have death rates above age 85, and particularly above age 100, remained more or less constant over time? In particular, have death rates at these advanced ages remained unchanged in Sweden since 1861 (and in various other countries over extended periods)?

Our second testable hypothesis ran as follows. If everyone is born with a maximum potential life span, then two identical twins should be born with the same maximum. The world's best twin registry, at least for our purposes, was in Denmark. Two professors of medicine, Mogens Hauge and Bent Harvald, set up the Danish Twin Registry, the world's first such national registry, half a century ago. They and their colleagues were able to follow nearly all Danish twins born since 1870. By 1990 the Registry had 120 years of twin data, and the dataset included many elderly twin pairs. In early 1988 I contacted Niels Holm, who was then head of the Danish Twin Registry, and invited him to visit us in Minneapolis. That summer I went to Denmark and we started to do some collaborative research on the Registry. The collaboration flourished to such an extent that I was offered a professorship at Odense University Medical School in Denmark. In June 1991 I moved to Denmark and started work as professor of epidemiology and demography, with responsibility to advance research using the Twin Registry and, more generally, to develop research on the epidemiology and demography of aging. One of my colleagues was Kaare Christensen, then a young epidemiologist and now one of the world's leading twin researchers and a well-known epidemiologist of aging.

When I started to collaborate on research using the Danish Twin Registry, the data were not computerized: the information for each person was on an index card. The first thing we did, with funding from the

US National Institute on Aging, was to computerize the data. Then we were able to undertake sophisticated analyses. In particular, we fit various survival-analysis models to the data we had on the life spans of twins. Some models included a term that captured the maximum potential life span that two identical twins were hypothesized to share. And we fit simpler models, so-called nested models, that did not have this term. The key question was whether the life span term improved the fit of the models to the data.

Our third testable prediction concerned the shape of the age trajectory of mortality. Both the Fries theory and the evolutionary theory of aging assert that mortality should increase rapidly—exponentially or even faster—at advanced ages. So we decided to use Swedish data to determine the veracity of this prediction.

Furthermore, we tested this prediction using data from some nonhuman species. The evolutionary theory of aging applies not only to humans: it is supposed to apply to all species of animals. Nor is the central notion of Fries's theory—that each individual is born with a maximum potential life span—limited to humans. We decided to try to find another species for which large numbers of individuals had been followed from birth to death. James Carey and I took the lead on this project. The largest study we were able to find was done by Raymond Pearl in the 1920s. Pearl, one of the founders of the Population Association of America, conducted demographic research on various animals as well as on humans. In one experiment he compiled life span data on a few thousand fruit flies (*Drosophila*) held in his laboratory. Until our research in the 1990s, that experiment was apparently the largest ever done to determine the distribution of life spans for any nonhuman species. Thus, little was known about the trajectory of mortality at older ages for any species except humans—and even for humans the data available on mortality at advanced ages were limited and of questionable reliability.

Carey decided which nonhuman species to investigate first and where to carry out the study. The best option was to compile data on one million Medflies in a laboratory in Tapachula, Mexico. Subsequently, large populations of several other species were also studied in this laboratory. The laboratory is housed in a factory, just over the border from Guatemala, that rears billions of Medflies that are sterilized and then released along the border. When Guatemalan Medflies attempt to invade Mexico, they mate with the sterile Mexican flies and do not have any offspring: this is a way of controlling the invasion from Guatemala. Our project staff were given use of a small corner of the factory, and local technicians were hired to follow one million Medflies from birth to death.

In our first experiment, Medflies were put, one by one, into small containers with food and water. The technicians were supposed to look at each

container daily and determine whether the Medfly was alive or dead. After they had followed about 10,000 flies, they refused to continue the work—it was too tedious. So Carey designed a second experiment with smaller containers that were assembled in blocks of several containers. Work with these devices also proved too tedious. Finally, Carey designed an experiment with sizable cages, each holding about 5,000 flies. When a fly died it fell to the floor of the cage. A technician could "aspirate" (i.e., carefully suck up through a small hose) dead flies and array them on white paper. Then the males could be separated from the females and the dead counted. When the last fly died, the cumulative count of the number of dead flies provided an accurate estimate of the initial population of flies, permitting the calculation of death rates. (That is, we used the "extinct generation" method.) This laboratory procedure held the interest of the technicians. They successfully completed the study of just over one million Medflies. Then they went on to further studies of Medflies and other insects, aspirating close to 10 million flies by now.

Let me now turn to the fourth falsifiable prediction we deduced from Fries's theory. A drawback of studies based on human twins is that there are only two members of a twin pair. Determining whether they share a common maximum potential life span therefore requires application of sophisticated statistical models. The analysis would be much more straightforward if there were thousands of individuals who were identical "twins," that is, who were genetically identical with each other. Indeed, if a population of several thousand genetically identical individuals could be followed from birth to death, then a simple test of the Fries theory would be feasible. The survival curve for such a population would gradually decline from 100 percent toward zero as premature death took its toll. When the common maximum potential life span of the genotype was approached, the survival curve should then plunge to zero, with no individual living past the maximum. Such a test of the theory is possible with inbred lines of animals. In particular, it is not difficult to rear thousands of genetically identical *Drosophila* fruitflies. James Curtsinger of the University of Minnesota undertook this experiment with several different populations of fruitflies.

Findings

We started work in 1990 on the four falsifiable predictions of the Fries theory. Within two years we had publishable results, but we continued to refine and extend our tests for several more years. Our findings can be summarized as follows.

The first falsifiable prediction we deduced from the theory was that Swedish death rates at advanced ages should have remained unchanged

over time. This is not true. Even at age 100, Swedish death rates fell substantially, being less than half as high in 1990 as they were a century earlier. Subsequent analysis of data from various other countries with long life expectancies confirmed this finding. Mortality after age 85 is not fixed: it is highly plastic and has been dramatically reduced, especially since 1950.

Fries's theory also failed our second test. Simpler statistical models of the survival of Danish identical twins fit the data as well as more complicated models that included a term that captured the effect of a shared maximum potential life span. We know that identical twins die at more similar ages than do fraternal twins. And fraternal twins die at more similar ages than do unrelated individuals. We used this information to estimate that about a quarter of the variation in adult longevity could be attributed to genetic variation among individuals (McGue et al. 1993; Herskind et al. 1996). Genes, then, do have an impact on the length of life, but we could find no evidence that they determined a maximum potential life span.

Fries's third prediction was that death rates should rise rapidly at advanced ages. Our studies revealed, however, that Swedish death rates—and death rates for other countries with reliable data at oldest-old ages—increase more and more slowly after age 85. Furthermore, the age trajectory of mortality for Medflies reached a maximum and then declined. Subsequent research that our team and others have done on large populations of various species, including nematode worms and different kinds of insects, has shown that such mortality deceleration is the rule rather than the exception. This unexpected result has led to a stream of biodemographic research aimed either at trying to rescue the current evolutionary theory of aging or at finding a more valid evolutionary theory of aging. In any case, the prediction of the Fries theory is wrong.

Finally, our fourth test of the theory was whether survival curves for thousands of genetically identical *Drosophila* are characterized by a cliff of plunging survival followed by no survival when the maximum potential life span for the genotype is reached. In James Curtsinger's experiments there was no evidence of such a cliff: the survival curves gradually fell off and petered out. Thomas Johnson subsequently replicated this negative result in large populations of genetically identical nematode worms.

In sum, our research team demonstrated that all four central predictions of Fries's theory are false.

On the other hand, I admit that our findings, especially our early findings, were not beyond reasonable criticism. Various scholars advanced legitimate caveats and objections concerning our results. After the first burst of research results in the early 1990s, marked by two major articles in *Science* (Carey et al. 1992 and Curtsinger et al. 1992), we devoted considerable effort during the rest of the decade to refining and extending our findings. As I noted above, Väinö Kannisto and Roger Thatcher compiled data on

oldest-old mortality in many countries besides Sweden and this resulted in an influential article (Kannisto et al. 1994). We replicated our studies in various species in addition to humans, Medflies, and *Drosphila.* An important concern about our insect experiments was that the density of individuals in a Medfly cage or a *Drosophila* vial declined as survival declined. Consequently, James Curtsinger's group and, to a somewhat lesser extent James Carey's group, undertook laborious experiments to hold density constant—and to hold all other conditions as constant as feasible. Another effort of ours was to replicate the Danish twin results in other populations of twins and to develop more powerful methods to analyze the data; among other investigators, Anatoli Yashin worked on this. A research report in *Science* with many coauthors summarized our main results as of the mid-1990s (Vaupel et al. 1998).

We gradually convinced ourselves—and most of our colleagues who were willing to change their minds when presented with compelling evidence—that individuals are not born with limited life spans. A key milestone was reached recently: female life expectancy in Japan in 2002 rose above 85—to 85.23 years. The diehards who believe in a looming limit to human life expectancy have retreated to higher ages—88 for instance. Jim Oeppen and I reviewed the sorry saga of broken limits to life expectancy in an article in *Science* (Oeppen and Vaupel 2002). We showed that best-practice life expectancy—that is, life expectancy in the national (female) population that holds the record—has increased linearly by three months per year since 1840, with no sign of any slowdown. If this trend continues, then the new alleged maximum of 88 years will be broached in less than a dozen years.

The future of human life expectancy is uncertain. Deadly epidemics, environmental collapse, economic depression, global war, terrorism, and various other calamities could make life once again nasty, brutal, and short. Furthermore, it is possible there will turn out to be a limit to human life expectancy at some age that few if any individuals currently reach and for some reason we do not yet understand. On the other hand, biomedical and other research may permit the acceleration of progress in reducing mortality, as well as morbidity and disability. And new kinds of health interventions, based for instance on new knowledge about genetics or about ways of regenerating or even rejuvenating organs, may lead to life expectancies far exceeding 100 years.

In this regard it seems to me that a key issue is whether to focus research on limits to longevity or on the plasticity of longevity. As James Carey, Kaare Christensen, and I recently argued (Vaupel, Carey, and Christensen 2003), data on humans and on various nonhuman species suggest that mortality is remarkably malleable, even at advanced ages and even for cohorts of individuals who have suffered poor conditions earlier in life. To what

extent and how quickly human death rates can be reduced and to what extent longevity can be extended in laboratory populations of nonhuman species are open questions that may remain of great interest for decades as the frontiers of survival are further advanced. Nematode worms typically live a week or two under favorable laboratory conditions. Genetic and environmental manipulations have led to life spans exceeding half a year. Will we soon be reading about nematode worms that live more than a year? The key question does not seem to be the one that used to be popular, namely, Why and how do evolutionary forces impose species-specific limits on longevity? Rather, the key question based on our current knowledge is, Why and how do evolutionary forces license the remarkable plasticity of death rates and longevity?

Consequently, the researchers supported by our ongoing grant from the US National Institute on Aging—and various other researchers as well—have shifted their focus away from limits and toward explaining the genetic and nongenetic factors that influence why some individuals in various species live much longer than others, why humans are living longer and longer, and, more broadly, why longevity is so plastic. This is the thrust of much of the best recent research on aging in general and on the biodemography of aging in particular.

Broadening of research

An idiosyncratic essay on my voyage of discovery in the field of the biodemography of aging is not the place to review either the history or the current status of biodemography. (See Carey and Vaupel (2004) for a recent attempt at this.) Let me mention, however, four research areas within the broad field that my colleagues and I have worked on over the past decade or so.

The first area might be called the biomedical demography of aging. With support from the US National Institute on Aging and from elsewhere, I have been principal investigator on various initiatives to survey and examine elderly people in Denmark, China, Sardinia, and Russia, and I am currently the deputy director of a very large survey, funded by the European Union, of elderly sibling pairs in Europe. My contribution to this research was only a small part of the total work; many other people deserve as much or more credit than I, including Kaare Christensen and Bernard Jeune in Denmark; Zeng Yi in China; Luca Deiana, Giovanella Baggio, and Graziela Caselli in Italy; Maria Shkolnikova in Russia; and Claudio Franceschi and others for the nascent European project.

In these surveys, older individuals were (and are being) asked to answer various questions about themselves, to perform various tests of physical and cognitive functioning, and to give blood samples for genetic and biochemical analysis. Some of the surveys, including one in Denmark and

ongoing surveys in China and Sardinia, included many centenarians. My original hope was to find a few key "secrets to longevity," among them perhaps a few genetic variants and some crucial behavioral or environmental factors. To date, however, our findings and those of other groups suggest that there are many ways of living a long, healthy life; that hundreds and perhaps thousands of genetic variants play a significant but modest role; and that beyond the advice we get from our mothers—to eat sensibly, to exercise appropriately, not to smoke, not to drink excessively, to smile and keep a good sense of humor—there is little that any of us can do to change our behavior or environment in order to live substantially longer. Life expectancy today is decades longer than it was a century or two ago, and life expectancy in the future may be decades longer than it is today—but we do not know today how to take the actions necessary to live substantially beyond current life expectancy. Careful people who follow sound advice might, on average, live five or ten years beyond the life expectancy of their national population, but not two or three decades beyond.

This does not mean I think that the findings from biomedical and demographic research are uninteresting or unimportant. On the contrary, these findings will help people live longer, healthier lives. My point is different: the findings suggest that there are not a handful of secrets of longevity, but rather that a great many genetic and nongenetic factors contribute to determining a person's life span. This multiplicity of causal mechanisms is consistent with the finding that aging is remarkably plastic. The complexity may also help explain why so many people for so many years have erroneously concluded that we are close to the ultimate limit of human life expectancy.

A second branch of the biodemography of aging that has captured much of my attention over the past decade might be called the biological demography of aging (in contrast to the biomedical demography of aging described above). As a demographer I have been able to contribute to research on longevity in various species, including several kinds of insects, nematode worms, and yeast. An important thrust of this research has been to investigate the deep relationship between mortality and fertility.

Third, I have been intrigued by paleodemography in general and by the problem of estimating age from skeletal remains in particular. At the University of Minnesota, I was given a secondary appointment as professor of ancient studies and did some teaching and research on paleodemography. Since becoming Founding Director of the Max Planck Institute for Demographic Research in Rostock, Germany, in 1996, I have organized four research workshops on methods of paleodemography, helped edit a book (Hoppa and Vaupel 2001), and set up a paleodemographic laboratory in Rostock.

Finally, two years ago my interest was seized by another branch of biodemography, namely evolutionary demography or "evodemo." In the first part of the twentieth century Alfred Lotka made seminal contributions

to this line of research. In the 1960s William Hamilton, a biologist who studied demography at the London School of Economics, made further advances. For more than a decade, Shripad Tuljapurkar has been productively tilling this field and recently Ronald Lee, Kenneth Wachter, and various others have begun to focus their attention on it. It is sometimes claimed that nothing in biology can be understood except in the light of evolution. What I have learned—and many biologists would agree with me—is that nothing in evolution can be understood except in the light of demography. As just noted, demographers have made some contributions to understanding the processes of evolution, but demographers could surely make many more.

My interest in evodemo was stimulated by research by Deborah Roach, a professor at the University of Virginia whose studies are supported in part by our grant from the National Institute on Aging. She uses *Plantago lancealota* —a common plant, indeed a weed, known as plantain—as her experimental model. As this plant gets older, it tends to get bigger, and as it gets bigger its fecundity tends to increase and its chances of morbidity and mortality tend to decrease. It seemed to me that this could be called "negative senescence" and that to understand aging it would be useful to compare species characterized by negative senescence with species, such as humans, that get weaker and less fertile with age.

William Hamilton, in 1968, published a highly influential article in which he claimed to prove that negative senescence is evolutionarily impossible. So when, a couple of years ago, I uttered the phrase "negative senescence" at a research workshop on the biology of aging, I was assaulted with hisses. This stimulated me all the more. A talented doctoral student, Annette Baudisch, with some help and encouragement from me, showed that Hamilton's "proof" is no such thing. A research team at the Max Planck Institute for Demographic Research is now developing evodemo models of positive versus negative senescence, and we have published an initial article (Vaupel et al. 2004).

The nature of demography

Let me conclude with some remarks about how the course of my research career has shaped the way I have come to see the field of demography more generally. The deepest attraction of demography for me is that it is fundamentally a mathematical discipline. We demographers can prove theorems that hold forever. For the last three winter semesters in Rostock I have taught a course on "The theory of pure demography." In each of the 28 classes in the semester, I prove at least one demographic theorem. This to my mind is the essence of demography, the core that makes demography a discipline.

It seems to me that demography is where the social sciences meet the biological sciences. Some demographers may object that their field is much

closer to sociology, economics, and history than it is to biological disciplines such as epidemiology, ecology, population genetics, evolutionary theory, or physical anthropology. This may be true according to the current affiliations of most demographers, but in terms of the scope of demography as a field of study, I would argue that our domain includes large biological as well as social science territories. Death, after all, has biological aspects, as do morbidity, disability, and aging more generally. Fertility also has biological underpinnings.

At Odense University Medical School, I was professor of epidemiology and demography—and I can testify that the two disciplines have many points of contact. The flourishing of biomedical demography has brought epidemiologists and demographers even closer together. Research on the biological demography of aging is creating ties with biologists who study nonhuman species. Demographers have much to contribute to research in the areas of population genetics, evolutionary theory, ecology, life-history biology, and various other branches of the life sciences. My hunch is that much of the future growth of the field of demography will be in the direction of our legitimate but underexplored territory in the biological sciences.

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