DECELERATION IN THE AGE PATTERN OF MORTALITY AT OLDER AGES*

SHIRO HORIUCHI AND JOHN R. WILMOTH

The rate of mortality increase with age tends to slow down at very old ages. One explanation proposed for this deceleration is the selective survival of healthier individuals to older ages. Data on mortality in Sweden and Japan are generally compatible with three predictions of this hypothesis: (1) decelerations for most major causes of death; (2) decelerations starting at younger ages for more "selective" causes; and (3) a shift of the deceleration to older ages with declining levels of mortality. A parametric model employed to illustrate the third prediction relies on the distinction between senescent and background mortality. This dichotomy, though simplistic, helps to explain the observed timing of the deceleration.

It is well known that the death rate increases almost exponentially with age through most of the adult age range in humans. When age-specific death rates are plotted against age on a logarithmic scale, the points appear to fall along a straight line. A closer look at the data reveals, however, that the rate of mortality increase with age slows down at older ages (Horiuchi and Coale 1990; Manton 1992), as illustrated for Swedish females in Figure 1a. Similar and more extreme mortality decelerations have been observed for some animal species as well (Brooks, Lithgow, and Johnson 1994; Carey et al. 1992; Curtsinger et al. 1992; Economos 1980).

Evidence of this deceleration encouraged some researchers to switch from the exponential (Gompertz) to the logistic (Perks 1932) or power (Weibull) function (Rosenberg et al. 1973). In the logistic and the power functions, the rate of mortality increase slows down with advancing age. Other models that took this deceleration into consideration include the quadratic curve fitted to the logarithm of age-specific death rates at very advanced ages (Coale and Kisker 1990; Wilmoth 1995) and the exponential survival function for tails of survival curves (Witten 1988).

Why does the deceleration occur? Although an apparent slowdown can be attributed to inaccurate data for some human populations (Coale and Li 1991; Elo and Preston 1994), the trend has been observed using accurate data as well. There are at least two possible explanations for this phenomenon: the heterogeneity hypothesis and the individual-risk hypothesis (Khazaeli, Xiu, and Curtsinger 1995).

According to the heterogeneity hypothesis, the deceleration is a statistical effect of selection through the attrition of mortality: Because the more frail tend to die at younger ages, survivors to older ages tend to have favorable health endowments and/or healthy lifestyles. This argument has been supported by several studies based on mathematical models (Beard 1959; Vaupel, Manton, and Stallard 1979) and simulations (Redington 1969; Strehler and Mildvan 1960; Vaupel and Carey 1993). The extent of heterogeneity has been estimated from cohort mortality patterns (Manton, Stallard, and Vaupel 1981, 1986), and anecdotal support for the heterogeneity hypothesis has been inferred from the relatively healthy profiles of very old persons (Perls 1995).

Some parametric models on relationships between physiological changes and mortality patterns suggest that selective survival should cause decelerations of age-related increases in both mortality and disability at very old ages (Manton et al. 1994; Manton, Stallard, and Corder 1997). Furthermore, the idea of selective survival is consistent with age-related reductions in the prevalence of certain diseases and risk factors (Manton, forthcoming, and citations therein; Perls et al. 1993; Rebeck et al. 1994). Similarly, bone density declines with age at accelerated rates among individuals who are followed over time (Ensrud et al. 1995), but the age-associated decline appears to slow down at old ages in cross-sectional, aggregate data (Hui et al. 1987), suggesting that those who survive longer tend to have higher bone density.

According to the individual-risk hypothesis, the age-related increase of mortality risk for individuals slows down at older ages for one or more reasons. There are three versions of the individual-risk hypothesis: physiological, evolutionary, and reliability-theoretical. First, if the "rate of living" is slower in old age, so may be the "rate of aging." For example, there is much direct and indirect evidence of negative correlations, both between and within species, between rate-of-living measures (e.g., metabolic rate, energy expenditure, and cell proliferation) and life expectancy (Finch 1990: chap. 5; Sohal 1986). Furthermore, declines in the rate of living at old ages have been observed for a number of physiological functions (Masoro 1981, 1985), including fundamental processes such as cell division (Grove and Kligman 1983), RNA synthesis, and protein synthesis (Remmen et al. 1995). In addition, the development of some diseases is slower at older ages (Kaesberg and Ershler 1989; O'Rourke et al. 1987; Peer et al. 1993).

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Second, Mueller and Rose (1996) conducted computer simulations of the evolution of senescence. The simulations produced life tables with a steep mortality increase at later reproductive ages and a slowdown of the increase in mortality at very old ages. These simulations are based on the theory that the age-related decline in the force of natural selection may lead, over the course of evolution, to an accumulation of genes that have deleterious effects at older ages (reviewed by Rose 1991). This process should yield a negative correlation between the age-specific force of natural selection and the age-specific likelihood of adverse gene expression. Because the force of natural selection approaches zero at very old ages, the age-related decrement of this force becomes negligible, thereby reducing the corresponding increment in the risk of detrimental gene expression. The validity of these findings, however, has recently been questioned by other evolutionary biologists (Charlesworth and Partridge 1997; Pletcher and Curtsinger 1998).

The mortality deceleration is compatible with the model by Abrams and Ludwig (1995), which is based on the theory that, in the evolution of a species, a conflict should occur between the allocation of resources to reproduction and to the repair of somatic damage. A reduced allocation to repair raises mortality rates but also increases the allocation of resources to reproduction, thereby elevating the fecundity level of the species. The trade-off model implies that the mortality deceleration at older ages could occur under certain conditions of the trade-off relationship.

Lastly, some relatively simple stochastic models describe systems in which the risk of failure (death) increases nearly exponentially with age initially but levels off later on. Examples of such models include (a) a system that fails when all components of any one of its major subsystems (e.g., organs) become defective (Gavrilov and Gavrilova 1991), and (b) a system moving stepwise and irreversibly toward states that have both higher risks of failure and higher risks of further transition (Le Bras 1976).

The heterogeneity and individual-risk hypotheses may be described as demographic versus gerontological explanations: The former emphasizes the composition of the population, whereas the latter considers senescent processes in individuals.[1] In this paper, while not denying the merits of the individual-risk hypothesis, we explore in detail the heterogeneity hypothesis by testing empirically some of its predictions.[2]

1. Yashin, Vaupel, and Iachine (1994) showed that the mortality models by Beard (1959) and Le Bras (1976) lead to the same mathematical form (logistic equation) of mortality as a function of age. This illustrates difficulties in the comparative assessment of the two explanations of the mortality deceleration, as the Beard and Le Bras models are consistent with the heterogeneity and individual-risk hypotheses, respectively.

2. We do not test the heterogeneity hypothesis directly, but rather some of its predictions. These predictions are not necessarily inconsistent with the individual-risk hypothesis or some other possible explanations. In statistical terminology, our null hypothesis is that heterogeneity is a sufficient explanation of the mortality deceleration in humans. This hypothesis is rejected only if available data are plainly inconsistent with it. Of course, failing to reject the null hypothesis is not equivalent to accepting it as true. Nevertheless, from a broader scientific perspective, surviving a series of falsifiable empirical tests lends some credibility to the heterogeneity hypothesis.

PREDICTIONS OF THE HETEROGENEITY HYPOTHESIS

If the deceleration in age-related mortality increase at older ages is due to heterogeneity and selection, three predictions can be made about the pattern of deceleration. First, the deceleration should occur for most major causes of death (CODs). Epidemiological studies have shown that there are identifiable risk factors for virtually every disease. Because these risk factors vary across populations, some persons are more vulnerable to the disease than others. Those who are more vulnerable tend to die from the disease at younger ages; thus, survivors to older ages are generally less vulnerable to the disease.

A mortality deceleration is expected not only for diseases but also for external injuries, as individuals also differ in their susceptibility to accidents, homicide, and suicide. The timing of these decelerations, however, may differ by cause of death. In general, if cause-specific mortality risks are independent of one another, then the deceleration should be less pronounced for CODs with lower death rates, which eliminate vulnerable individuals more slowly. Nevertheless, notable decelerations may be observed for a number of low-mortality CODs, as risk factors of various diseases tend to overlap or to be highly correlated with each other.

The second prediction of the heterogeneity hypothesis is that the deceleration should start at younger ages for more "selective" CODs. In this paper, the selectivity of a COD refers to the extent to which the risk of death from the cause differs among individuals of the same age. If there is a special group of individuals who are highly vulnerable to a certain COD, then even a relatively small number of deaths from that cause may significantly reduce the number of the high-risk persons, thereby exerting noticeable effects on the trajectory of cause-specific death rates.

A difficulty in testing this prediction is that we do not have well-established criteria or sufficient data for assessing and comparing the selectivity of major CODs. It might be possible to judge the selectivity of a particular cause based on information about heritability: The greater involvement of genetic factors in the development of a disease should make it more selective. Although twin and family studies provide some measures of genetic impacts, we do not yet have a sufficiently comprehensive set of comparable heritability estimates of major diseases for use in constructing a formal model. Epidemiological studies tend to focus on risk factors of one or a few selected diseases, but do not usually compare effects of those risk factors across a wide variety of diseases.

Although it is difficult to test the second prediction rigorously, it is important to compare patterns of mortality deceleration for major CODs and to consider whether their differences are interpretable in terms of the heterogeneity hypothesis. In general, diseases that are strongly determined by genetic and environmental risk factors (including heritable diseases and a number of major degenerative diseases) may be considered more selective than diseases that occur fairly

randomly in the population (such as some highly contagious infectious diseases and certain types of accidents).

The third prediction of the heterogeneity hypothesis is that the mortality deceleration should shift to older ages as the level of total (all-cause) adult mortality declines. This is because the effect of selective survival on the composition of a cohort at a given age should be positively associated with the death rate at that age. In general, if only a small proportion of a cohort dies, then the composition of that cohort changes little. Thus, although the mechanism of selective survival should operate at any age, the mortality deceleration is usually seen only at older ages, where death rates are high enough to alter the composition of the cohort substantially within a relatively short period. It follows that if the overall level of adult mortality declines, then the pattern of mortality deceleration should shift to older ages. This relationship between the mortality level and the timing of mortality deceleration was demonstrated in an earlier simulation study (Vaupel and Yashin 1986). Empirical evidence of such an association, however, has not been presented previously.

In this section, three predictions of the heterogeneity hypothesis have been inferred through qualitative reasoning. Mathematical illustrations of these arguments are given in Appendix A.

DATA AND MEASUREMENT

Data

Death rates by age, sex, and cause are needed for testing the first and second predictions, and all-cause death rates by age and sex for multiple cohorts are needed for testing the third prediction. Because selective survival should operate within cohorts, we examine cohort mortality patterns, supplemented by period patterns for comparison.

We use national-level mortality data for Sweden for the period 1861–1990 and for Japan for the period 1951–1990. The long time series of Swedish mortality data, which is known to be of exceptionally high quality even at very old ages, is particularly well suited to the mortality trend analysis (Wilmoth and Lundstrom 1996). The number of deaths at old ages in Sweden, however, may be too small when the data are tabulated by age, sex, and cause of death. A relatively large number of deaths are needed to ensure that the life-table aging rate, the main statistical tool of this study, has reasonably small confidence intervals (Wilmoth 1995). Thus, the cause-specific mortality analysis is conducted with data from Japan, whose current population is about 14 times as large as that of Sweden.

The causes of death selected for this study are listed in Table 1. A difficulty in studying cause-specific mortality trajectories of cohorts is that the national statistical system of COD classification changes over time, following revisions of the International Classification of Diseases (ICD). In particular, the classification of renal-cardiovascular diseases changed significantly between ICD7 and ICD8, and between ICD8 and ICD9. To circumvent this problem, we adopt broad categories such as "heart disease" and "cerebrovascular disease."

Measurement of Mortality Deceleration

The conventional way to examine age variations in mortality is to plot the logarithm of the death rate against age. Significant patterns of mortality acceleration or deceleration, how-

TABLE 1. ICD CODES FOR CAUSES OF DEATH ANALYZED IN THIS STUDY

Causes of Death	1951–1957 (ICD6)	1958–1967 (ICD7)	1968–1978 (ICD8)	1979–1990 (ICD9)
Infectious Diseases	001–138	001–138	000–136	001–138
Malignant Neoplasms	140–205	140–205	140–209	140–208
Diabetes Mellitus	260	260	250	250
Heart Disease	410–434	410–434	393–398, 410–429	393–398, 410–429
Cerebrovascular Disease	330–334	330–334	430–438	430–438
Pneumonia	490–493, 763	490–493, 763	480–486	480–486
Peptic Ulcer	540, 541	540, 541	531–533	531–533
Gastroenteritis	543, 571, 572, 764	543, 571, 572, 764	8, 9, 535, 561–563	8, 9, 535, 555, 556, 558, 562
Chronic Liver Disease and Cirrhosis	581	581	571	571
Motor-Vehicle Accidents	E810–E835	E810–E835	E810–E823	E810–E825
Other Accidents	E800–E802, E840–E965	E800–E802, E840–E962	E800–E807, E825–E949	E800–E807, E826–E899
Suicide	E970–E979	E963, E970–E979	E950–E959	E950–E959

ever, can easily escape visual inspection of such a graph. A simple measure, the *life-table aging rate* (LAR), has proven to be powerful for detecting these patterns (Carey and Liedo 1995; Horiuchi 1983, 1997; Horiuchi and Coale 1990; Horiuchi and Wilmoth 1997; Kannisto 1996; Wilmoth 1995). The LAR at exact age x is defined as:

$$k(x) = \frac{1}{m(x)} \frac{dm(x)}{dx} = \frac{d \ln m(x)}{dx}, \quad (1)$$

where $m(x)$ is the force of mortality (instantaneous death rate) at age x for some population. Thus, the LAR measures the relative mortality increase with age: For example, an LAR of 0.05 means that the death rate is rising (at exact age x) at an exponential rate of 5% per year of age.

An age-related increase in the LAR corresponds to an acceleration in the age pattern of mortality, whereas a decrease implies a mortality deceleration. Thus, the LAR also helps to measure the age range and extent of the mortality deceleration accurately. For example, Figures 1a and 1b display the age-specific death rate and the corresponding LAR, respectively, for the Swedish female cohort born in the period 1871–1875. The starting age of deceleration is difficult to identify in Figure 1a, but is shown to be around age 72 in Figure 1b.

When data are tabulated by five-year age groups, the LAR can be estimated by

$$K(x) = \left[\ln M(x,5) - \ln M(x-5,5)\right]/5, \quad (2)$$

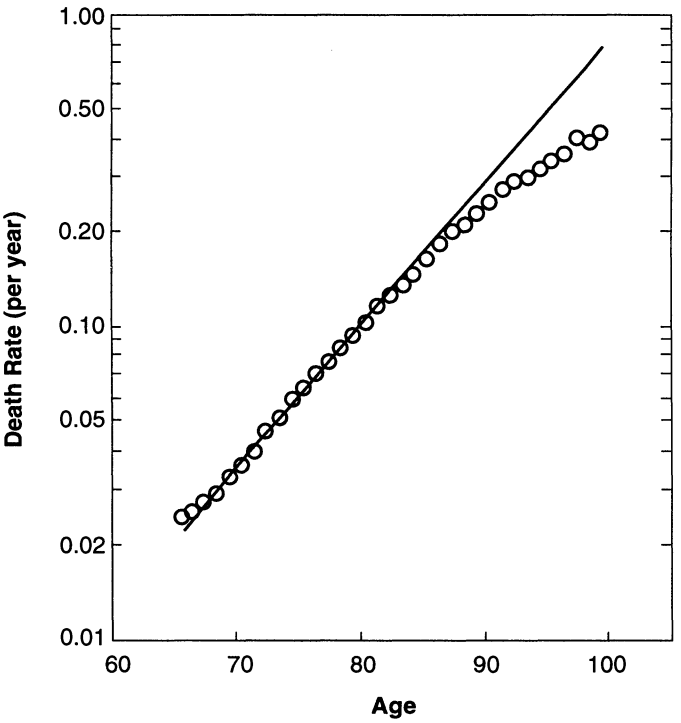
where $M(x,5)$ is the death rate for the interval between exact ages x and $x + 5$. This approximation has been shown to be sufficiently accurate (Horiuchi and Coale 1990). The standard error of this estimate of $k(x)$ can be approximated by

$$\sigma_k(x) = \frac{1}{5}\sqrt{\frac{1}{D(x,5)} + \frac{1}{D(x-5,5)}}, \quad (3)$$

where $D(x,5)$ is the number of deaths in the age interval from x to $x + 5$ (Wilmoth 1995). The LAR can be calculated for both periods and cohorts, and for all-cause mortality and each cause of death.

Because the COD data in Japan are tabulated only by five-year age groups in a period format, cohort mortality patterns must be approximated based on period data. Consider, for example, the cohort born in the period 1926–1930. On December 31, 1960, members of this cohort were aged 30–34, so we can approximate the cohort death rate in this age range by the period death rate in the surrounding 10-year interval. Thus, the mortality trajectory for the cohort born in the period 1926–1930 is approximated by a sequence of death rates for those aged 30–34 in the period 1956–1965, 35–39 in the period 1961–1970, and so on. This strategy results in a reduction of stochastic variability, as the age-period interval employed is twice as large as the age-cohort interval being approximated. (It also contributes, inevitably, to a blurring of the distinctive mortality patterns of successive cohorts.) We refer to such sequences of data as *quasi-cohorts*. We estimate cause-specific LARs in this way for each

FIGURE 1A. AGE-SPECIFIC DEATH RATES FOR SWEDISH FEMALE COHORTS BORN BETWEEN 1871 AND 1875



Notes: Circles are death rates between ages 65 and 100. The line was fitted to death rates between ages 70 and 80 by an ordinary least squares regression.

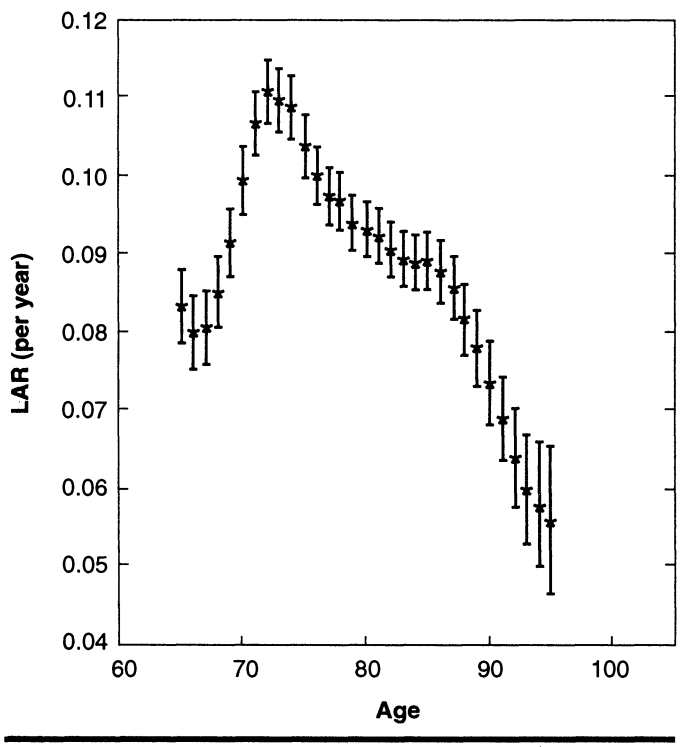
five-year birth cohort but display them only for five selected cohorts (1886–1890, 1896–1900, 1906–1910, 1916–1920, and 1926–1930) in order to simplify the presentation and interpretation of results.

A previous study indicated that cohort LARs for some CODs are strongly affected by changes in the period level of cause-specific mortality (Horiuchi and Wilmoth 1997). Development of an effective means of treating a certain disease, for example, may slow down the age-related increase in mortality from the disease for all cohorts, regardless of their ages. An accelerated decline in the period mortality level is likely to produce age-associated mortality decelerations in cohort life tables. Therefore, cohort LARs should be adjusted for changes in period mortality. A simple means of adjustment is to remove effects of time trends in age-standardized death rates from the LARs for quasi-cohorts. The form of this adjusted LAR is

$$\frac{\ln M(x,5,t) - \ln M(x-5,5,t-5)}{5} - \frac{\ln M_s(t) - \ln M_s(t-5)}{5}, \quad (4)$$

where $M(x,5,t)$ is the death rate for the age interval between x and $x + 5$ in the 10-year period centered at t; and $M_s(t)$ is

FIGURE 1B. LIFE-TABLE AGING RATES (LAR) FOR SWEDISH FEMALE COHORTS BORN BETWEEN 1871 AND 1875



Note: The confidence interval bars are two times the estimated standard errors of the LARs.

the age-standardized death rate for the same time interval.[3] This method of adjusting the LAR is crude and is not based on any particular mortality model. The time-trend–adjusted LAR is used in the analysis of cause-specific cohort LAR patterns in Japan. We employ a more formal model for all-cause mortality to adjust for the period effects on cohort mortality patterns.

PATTERNS OF MORTALITY DECELERATION BY CAUSE OF DEATH

Figure 2 displays time-trend–adjusted LAR patterns for 12 major causes of death for Japanese male cohorts born between 1886 and 1930. Overall, the results seem compatible with the first prediction that the deceleration should be observed for most major causes. The corresponding LAR patterns for females (not shown here) are generally similar to those for males.[4] The adjusted cohort LAR curves show less variability among cohorts than do the unadjusted curves. These patterns differ substantially by cause of death under age 75. Most of the LAR curves, however, tend to decline above age 75 or 80, with two notable exceptions: peptic ulcer and accidents not involving motor vehicles (called "other accidents").[5]

Figure 2 also indicates that the age at which the mortality deceleration becomes significant differs substantially among CODs. Ten of the 12 CODs considered here can be divided into the just three groups. The first group consists of malignant neoplasms, diabetes mellitus, cerebrovascular disease, and chronic liver disease and cirrhosis. For these degenerative diseases, the mortality decelerations start at relatively young ages. An early deceleration is seen not only for all cancers combined but also for each of the major cancers (not shown in Figure 2). The second group comprises infectious diseases,[6] pneumonia, and gastroenteritis. Mortality decelerations start at relatively old ages for these CODs. The third group is composed of three external injury categories (motor vehicle accidents, other accidents, and suicide). These CODs do not show notable, consistent mortality decelerations under age 75.

Overall, these patterns seem compatible with the predictions of the heterogeneity hypothesis. The deceleration starts at younger ages for most degenerative diseases for which significant effects of a number of genetic and environmental risk factors have been indicated (Boyle et al. 1995; Brass and Alberts 1995; Fujimoto 1996; Kahn, Vincent, and Doria 1996; Sherlock 1995; Stremmel et al. 1991; Wolf et al. 1991). However, the deceleration does not start early for two predominantly chronic disease categories: heart disease[7] and peptic ulcer.[8] The later timing of decelerations in the second group of CODs may be explained by their etiology. Many deaths in this group involve acute bacterial and viral infections, which may be highly contagious and/or occur fairly

3. The standardization used the unweighted average of proportional age distributions from age 30 to 94 for the period 1951–1990 as the standard age distribution.

4. LAR differences by sex have been analyzed previously by Horiuchi (1997).

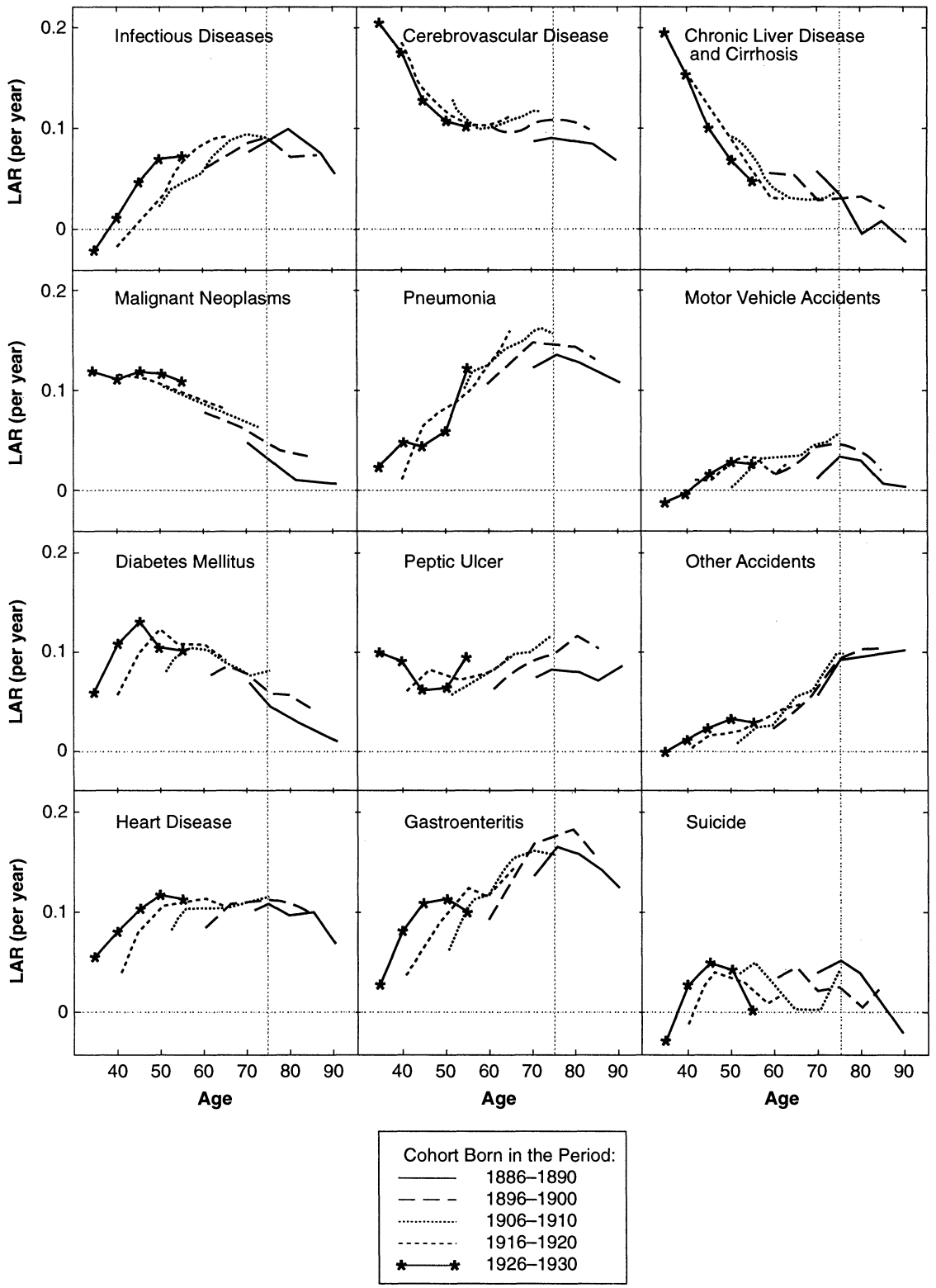
5. Mortality due to "other accidents" could be viewed as compatible with the first prediction: Although it does not decelerate over age 75, its acceleration under age 75 ceases around age 75.

6. This widely used ICD category consists mainly of highly contagious diseases prevailing in economically underdeveloped countries, but it does not include some other infectious diseases that are classified according to the organ system that is infected.

7. The lack of deceleration of heart disease mortality in the mid-adult age range may be peculiar to Japan. A previous study has shown that the period (1968–1978) LAR for ischemic heart disease declines with age noticeably at relatively early ages (late 30s and 40s) in England and Wales but not in Japan (Horiuchi 1997). The epidemiological profile of heart disease in Japan is known to be unique among economically developed countries. For example, the age-standardized death rate due to ischemic heart disease is low relative to the age-standardized total death rate (Goldman and Takahashi 1996), and the ratio of deaths from heart failure to deaths from ischemic heart disease is higher in Japan than in western Europe and North America. (Baba et al. [1994] suggest, however, that these anomalies may be partly due to inappropriate coding practices.) In addition, levels of risk factors for heart disease and their effects in Japan are different from those of other economically developed countries (Keys et al. 1984).

8. Little is known about the selectivity of peptic ulcer, which is a predominantly chronic disease. Although infection with *Helicobacter pylori* plays an important role in pathogenesis, only a small proportion of individuals infected with *H. pylori* develop peptic ulcers. No factor has been found that strongly affects the risk for an infected individual to develop a peptic ulcer (Van der Hulst and Tytgat 1996).

FIGURE 2. ADJUSTED LIFE-TABLE AGING RATES (LARS) FOR MAJOR CAUSES OF DEATH: JAPANESE MALE QUASI-COHORTS BORN BETWEEN THE PERIODS 1886–1890 AND 1926–1930



randomly. Because vulnerability to these CODs is spread more evenly across the population, survivors to older ages are less selected with respect to these CODs, and thus the mortality deceleration begins later than in the case of most degenerative diseases.

The risks of accidents and suicide vary among individuals with different psychological and lifestyle characteristics (e.g., de Chateau 1990). Nevertheless, consistent mortality decelerations are not seen under age 75 for the external injury categories. There are at least three possible explanations for this finding. First, although the risk of accidental death differs among individuals, some accidents are almost completely random and do not depend on individual characteristics. Second, as reflected by their generally low LARs, the mortality risks due to accidents and suicide rise relatively slowly with age, suggesting that external injuries are less a function of senescent processes than degenerative diseases. In general, it is not surprising that mortality decelerations tend to be less pronounced for CODs whose risks increase more slowly with age (see Appendix A for a mathematical explanation). Third, risks of accidents and suicide may not be strongly correlated with risks of degenerative diseases. Therefore, total mortality, which is dominated by degenerative diseases in economically developed countries, may do little to alter the survival prospects of individuals who are likely to have accidents or commit suicide.

CHANGING PATTERNS OF DECELERATION FOR TOTAL MORTALITY

The third prediction of the heterogeneity hypothesis states that the mortality deceleration should shift to older ages as the level of total (all-cause) adult mortality declines. To test this prediction, we display LAR patterns for successive cohorts and periods in Sweden and Japan in Figures 3 and 4. In examining these figures, it is useful to distinguish younger old ages from older old ages, taking age 75 as a somewhat arbitrary dividing point.

As a test of the third prediction, the results are mixed. Mortality patterns of recent cohorts (born after 1880) do not seem to lend strong support to this prediction: The truncated cohort LAR curves in Figure 3 show that LARs at age 75 and over rose gradually between successive cohorts of Swedish females, but not noticeably between cohorts of Swedish males, Japanese females, and Japanese males. Likewise, for earlier cohorts born in 1880 or before, no consistent time trends are evident in cohort LAR patterns at ages 75 and over for either males or females in Sweden and Japan (results not shown). This latter result may not be incompatible with the third prediction, however, as the LAR pattern should shift only when the mortality level changes significantly. Although old-age mortality has declined rapidly in recent decades (Kannisto et al. 1994), some of the cohorts born in 1880 or earlier were almost, or entirely, extinct before this period, whereas other cohorts in this group experienced the period only at very old ages.

Changes in period LAR patterns are considerably different between females and males in Sweden and Japan (Figure 4). Three phases can be identified for Swedish females: Their LAR curves (1) remained at nearly the same level between the periods 1861–1865 and 1926–1930, except for a gradual rise around age 70 (Figure 4, Panel A); (2) moved upward across the age range between the periods 1926–1930 and 1956–1960 (Figure 4, Panel B); and (3) shifted to older ages between the periods 1956–1960 and 1986–1990 (Figure 4, Panel C). In this third phase, the appearance of a lateral shift in the LAR curve was created by a decline over time in LARs at ages 55–70 combined with an increase at ages 80 and above. For Swedish females, the shift of the LAR curve during the third phase was gradual yet steady. As measured by its peak value, the curve moved (approximately) from age 70 in the 1960s to 75 in the 1970s and to age 80 in the 1980s.

The trend in the period LAR curve (Figure 4, Panel D) is substantially different for Swedish males than for Swedish females. Here, the level of the LAR at younger old ages increased appreciably during the 130-year period. Between ages 55 and 75, LARs increased over time more at younger than at older ages, which changed the slope of LAR curve in this age range from upward to flat. This LAR increase proceeded in three distinct stages: The LAR at age 55, for example, rose from around 0.06 between the periods 1861–1865 and 1916–1920 to about 0.07–0.08 between the periods 1921–1925 and 1941–1945, and further to around 0.10 between the periods 1946–1950 and 1986–1990. The LAR curve at older old ages, however, did not exhibit any discernible trend. The age pattern of mortality deceleration for Swedish males remained mostly unchanged during these 130 years (although individual LAR curves show the effects of random fluctuations, especially at the highest ages during early periods due to small numbers of deaths).

The peak of the period LAR curve for Japanese females shifted both upward and to older ages during the last four decades (Figure 4, Panel E). In this case, LARs at older old ages continued to move upward, whereas LARs at younger old ages moved upward from the 1951–1955 to the 1976–1980 period, then slightly downward from 1976–1980 to 1986–1990. Thus, the two major shifts in the LAR curve that took place in distinct phases for Swedish females occurred almost simultaneously for Japanese females during a much shorter period.

For Japanese males, the interpretation of Figure 4, Panel F is complicated by noticeable irregularities in period LAR patterns, possibly related to the aftermath of deprivations suffered by certain cohorts during the second world war (Horiuchi 1983). Amidst this confusion, however, the same two phases of change in the LAR curve are at least vaguely discernible: a shift upward from 1951–1955 to 1971–1975 and then a shift to the right from 1971–1975 to 1986–1990.

FURTHER ANALYSIS USING THE GAMMA-MAKEHAM MODEL

Upon first inspection, LAR trends for total mortality in Sweden and Japan do not seem highly compatible with the third prediction of the heterogeneity hypothesis, which states that the pattern of deceleration should be delayed as the level of

FIGURE 3. LIFE-TABLE AGING RATES (LARS) FOR FIVE-YEAR COHORTS BORN BETWEEN 1881–1885 AND 1901–1905 AND OBSERVED AND ESTIMATED LARS FOR QUASI-COHORTS BORN BETWEEN AROUND 1880 AND AROUND 1905: SWEDISH AND JAPANESE FEMALES AND MALES

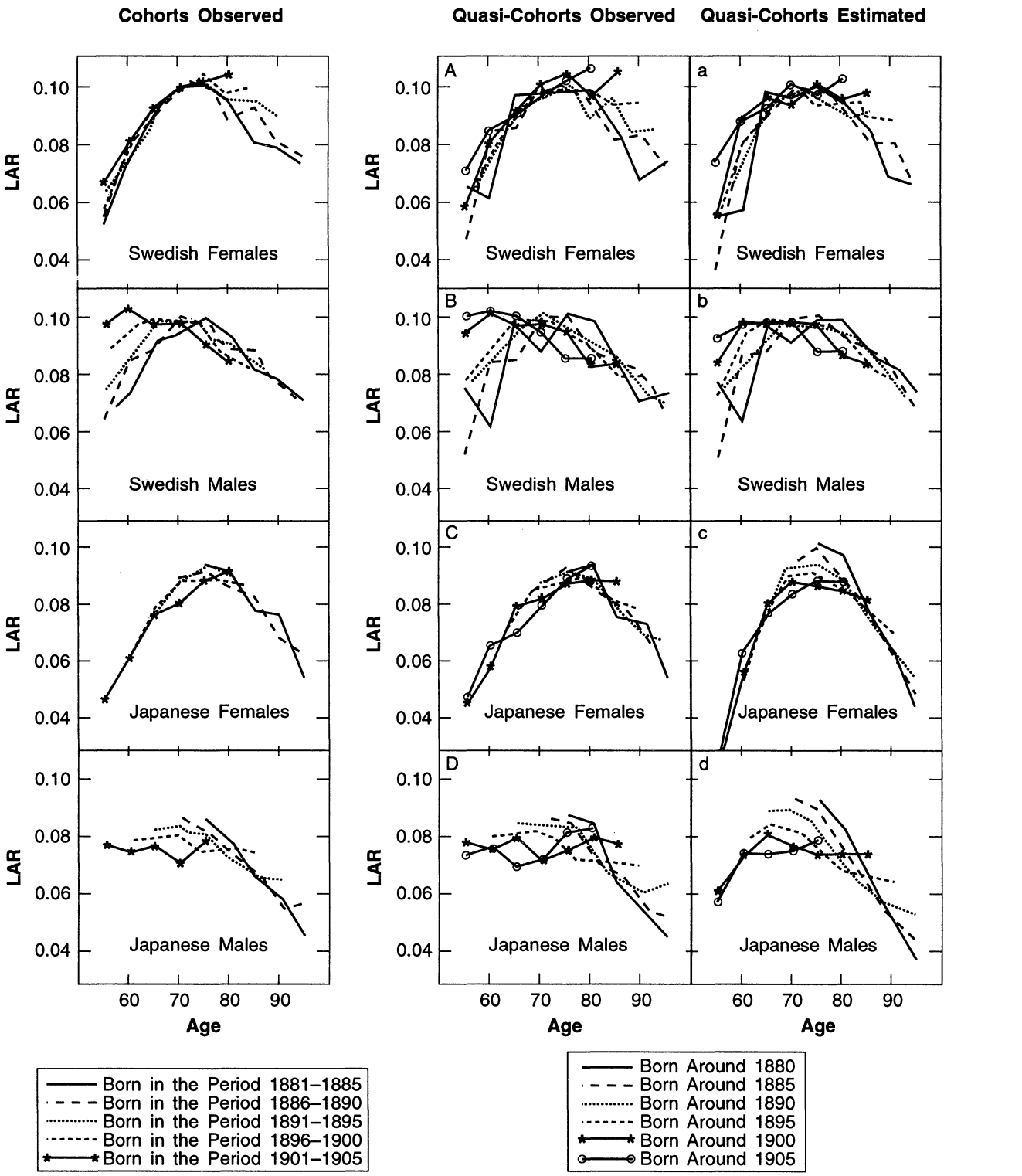
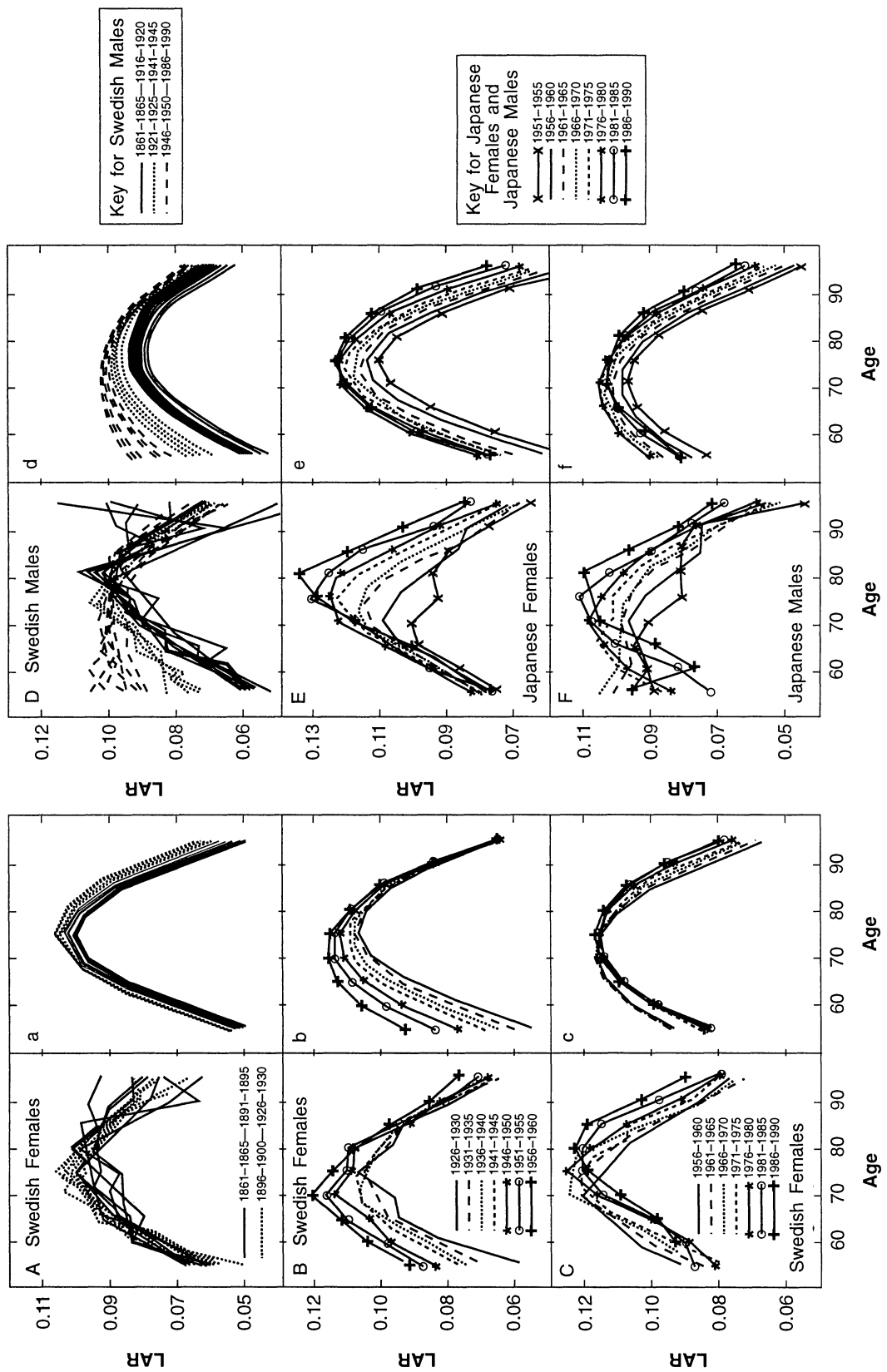


FIGURE 4. OBSERVED AND ESTIMATED PERIOD LIFE-TABLE AGING RATES FOR SWEDISH AND JAPANESE FEMALES AND MALES



mortality falls over time. Furthermore, if deceleration in total mortality is due to differential selection in the face of heterogeneous risks of death, this process of selection should be visible in cohort data, not just period data. The cohort data examined in this study, however, appear even less consistent with the third prediction than do the period data. In addition, observed changes in period LAR patterns differ considerably between Sweden and Japan, between females and males, and between successive periods.

The following three points summarize the period LAR variations documented here. First, LARs at *younger old ages* increased for Swedish females between 1926–1930 and 1956–1960, for Swedish males between 1861–1865 and 1986–1990, for Japanese females between 1951–1955 and 1976–1980, and for Japanese males between 1951–1955 and 1971–1975, but decreased for Swedish females between 1956–1960 and 1986–1990, for Japanese females between 1976–1980 and 1986–1990 (though only slightly), and for Japanese males between 1971–1975 and 1986–1990. Second, LARs at *older old ages* increased markedly for Japanese females and males between 1951–1955 and 1986–1990 and for Swedish females between 1956–1960 and 1986–1990, increased slightly for Swedish females between 1926–1930 and 1956–1960, but did not change noticeably for Swedish females between 1861–1865 and 1926–1930 or for Swedish males between 1861–1865 and 1986–1990. Third, the entire LAR pattern at older ages (50 and above) remained almost unchanged during a long period in which the level of old-age mortality declined very slowly (for Swedish females between 1861–1865 and 1926–1930 and for Swedish males between 1861–1865 and 1916–1920).

On the surface, these diverse findings seem incompatible with the third prediction of the heterogeneity hypothesis. One means of explaining these results, however, is to distinguish two types of adult mortality (Benjamin 1964; Bourgeois-Pichat 1978; Carnes, Olshansky, and Grahn 1996; Gavrilov and Gavrilova 1991; Makeham 1860) and to assume that they have different trends and age patterns. The first type of mortality risk rises steeply with age, but the second type does not vary significantly with age. These two types of mortality may be labeled *senescent mortality*, which results from the age-related deterioration of physiological functions, and *background mortality*, which is relatively independent of senescent processes (as risks of some contagious diseases and external injuries may be).[9]

Combining this dichotomy with the heterogeneity hypothesis, we can provide a plausible explanation for the observed differential LAR trends at younger and older old ages. According to the heterogeneity hypothesis, LARs at older ages should increase over time as the process of selective survival is weakened by a decline in *total* mortality. First, we need to specify whether that decline is due to changes in *background* and/or *senescent* mortality. At older old ages, total mortality is composed almost entirely of senescent mortality. Thus, assuming that the selective processes of senescent and background mortality are different (which seems likely), the rise in the LAR at older old ages must result from a general decline in senescent mortality. At these ages, trends in background mortality are irrelevant.

At younger old ages, however, the tendency for increasing LARs due to the decline in senescent mortality may be offset, or even reversed, by the changing distribution of total mortality between background and senescent components. Because background mortality is a nonnegligible fraction of total mortality at younger old ages, differential rates of decline in senescent and background mortality can have a substantial effect on the LAR curve here, but not at older old ages. Obviously, a faster reduction of senescent than background mortality decreases the proportion of total mortality due to senescent causes. This differential reduction tends to lower the LAR at younger old ages, as senescent mortality increases with age much faster than does background mortality, which is traditionally assumed constant over age (Makeham 1860). Conversely, a faster decline in background than senescent mortality would raise the LAR curve in this age range. These effects may be substantial at younger old ages, where the ratio of background to senescent mortality is relatively high, but they are negligible at older old ages, where the proportion of total mortality due to senescent causes is close to unity and not highly variable over time.

To examine the effects of differential trends in background and senescent mortality on the LAR pattern, we analyzed mortality data for Sweden and Japan using a model that takes into account both this dichotomy and individual differences in the risk of dying. In this model, the mortality risk of an individual with (fixed) frailty z (Vaupel et al. 1979), who is aged x at time t, is given by:

$$\mu(z,x,t) = A(t) + zB(t)e^{\theta x}. \quad (5)$$

The first and second terms on the right side of this equation represent background and senescent mortality, respectively. By assumption, background mortality is independent of age, whereas senescent mortality is an exponential function of age. A and B are functions of time and represent effects of the period-based factors on background and senescent mortality, respectively. These period effects reflect the level of medical services in those time periods as well as consequences of health trends that started earlier (Manton, Stallard, and Corder 1997).

Frailty, z, represents combined effects of genetic, environmental, and lifestyle characteristics of the individual upon his/her risk of senescent mortality. These characteristics are presumed to remain relatively stable over the age range of the study. The variable z in Eq. (5) is a single draw from a random variable, Z, which is assumed to follow the gamma distribution at age $x = 0$. ($x = 0$ does not necessarily refer to the moment of birth but indicates the lower bound of the age range to which this model is applied.) The mean of Z at age x

9. It is difficult to distinguish between senescent and background mortality in terms of specific causes of death, as the risk of death from most causes (including infectious diseases and accidents) rises with age. This empirical fact does not invalidate the conceptual distinction between senescent and background mortality, although it illustrates the difficulty of assigning individual deaths to one or another of the two categories.

= 0 is set to be unity, and its variance at $x = 0$ is denoted as $1/\alpha$. The shape of the gamma distribution is determined by α, with a lower value denoting greater heterogeneity at $x = 0$. The random variable, Z, follows the gamma distribution throughout the life of the cohort, but the mean and variance of Z change with age due to selective survival (Vaupel et al. 1979).

Eq. (5) is a modified version of the gamma-Makeham model (Beard 1959). In the original gamma-Makeham model, A and B remain constant throughout the life of a single cohort. In this modified version, A and B change over time and are constant within periods. Hereafter, the proposed model will be called the GMP model (gamma-Makeham model with period effects). A special case of the gamma-Makeham model in which $A = 0$ is called the gamma-Gompertz model. The original versions of the gamma-Gompertz and gamma-Makeham models are discussed in more detail in Appendix A.

It follows directly from Eq. (5) that the instantaneous death rate of the cohort aged x at time t is:

$$m(x,t) = A(t) + \bar{z}(x,t)B(t)e^{\theta x}, \tag{6}$$

where the mean of Z at age x and time t is given by

$$\bar{z}(x,t) = \frac{1}{1 + \frac{1}{\alpha}\int_0^x B(t-x+y)e^{\theta y}dy}.$$

Eq. (6) may be considered a special type of age-period-cohort model. It has an age effect ($e^{\theta x}$) and two period effects ($A(t)$ and $B(t)$). Although not a conventional cohort effect, the mean of Z is a function of the life history of the affected cohort up to time t. By design, the model follows the changing distribution of Z for each cohort as it lives through the various periods. (Alternative specifications of the GMP model are compared in Appendix B.)

The parameters of the GMP model are estimated for females and males in Sweden and Japan by weighted least squares, that is, by finding a set of values of α, θ, $A(t)$'s and $B(t)$'s that minimize

$$L = \sum_i \sum_j D_{ij}(\ln M_{ij} - \ln \hat{m}_{ij})^2, \tag{7}$$

where D_{ij} and M_{ij} are the number of deaths and the death rate, respectively, for the i^{th} age group and the j^{th} period; $\hat{m}_{ij}$ is calculated using Eq. (6). The weight, D_{ij}, is approximately equal to the inverse of the variance of $\ln M_{ij}$.[10] The criterion of optimization, L, is defined in terms of logarithmic death rates because this analysis focuses on LAR patterns, which are derived as linear functions of logarithmic death rates.

We applied the GMP model to death rates by sex for five-year age groups (50–54 to 95–99) and five-year periods (1861–1865 to 1986–1990 for Sweden, and 1951–1955 to 1986–1990 for Japan). The procedure of estimation is described in greater detail in Appendix C.

Results of the estimation are shown in Table 2 and Figure 5. In Table 2, ε_M is the square root of the mean squared error of the logarithmic death rates (weighted by the inverse of the estimated variance) for five-year age groups and five-year periods. Because ε_M is in the range of 0.02–0.04 for the four populations, the model provides estimates of individual death rates that are in error, typically, by just a few percentage points. This level of goodness-of-fit can be regarded as sufficiently accurate, given the considerable variation in death rates by age and period. Estimates of LARs are quite accurate as well. ε_K in Table 2 is the square root of the mean squared error of period LARs (weighted by the inverse of their estimated variances). Values of ε_K range from 0.0046 for Swedish males to 0.0069 for Japanese females. These ε_K values are relatively small, considering that most observed LARs are scattered widely between 0.05 and 0.13 (Figure 4).

Observed and estimated LARs are compared for quasi-cohorts in Figure 3 and for periods in Figure 4. The panels of these figures are labeled by upper- and lower-case letters denoting observed and estimated LARs, respectively. Overall, the GMP model seems to reproduce observed LAR patterns reasonably well.[11]

The estimates of α and θ in Table 2 suggest that individual differences in frailty are larger, and the rate of age-related increase in mortality risk of individuals is higher, for females than for males in both Sweden and Japan. These sex differences in heterogeneity are consistent with the results of a previous analysis of U.S. cohort mortality using the gamma-Gompertz model (Manton et al. 1986). Estimated trends of background and senescent mortality (A and B in Eq. (6)) shown in Figure 5 indicate that the lower old-age mortality for females than males is mainly due to divergent trends in senescent mortality. Levels and trends in background mortality, on the other hand, are more similar between the sexes in both countries.

Figure 5 shows that the level of the two mortality components for Swedish females passed through three distinct phases, which correspond precisely to the three stages of change in their LAR trends mentioned earlier. In the first phase (up to 1926–1930), both background and senescent mortality decreased gradually (in a logarithmic scale). In the second phase (1926–1930 to 1956–1960), background mortality plummeted, while senescent mortality held nearly constant. In the third phase (1956–1960 to 1986–1990), background mortality fluctuated without a major change of level, while senescent mortality declined at an accelerated rate.

10. Brillinger (1986) showed that the variance of an age-specific death rate, M_{ij}, can be estimated by M_{ij}^2/D_{ij}. In addition, if both D_{ij} and N_{ij} are large, the distribution of $\ln(M_{ij}/m_{ij})$, where m_{ij} is the mean of M_{ij}, is nearly identical to that of $(M_{ij}/m_{ij}) - 1$. Making use of these results, we can approximate the mean and variance of $\ln M_{ij}$ by $\ln m_{ij}$ and $1/D_{ij}$, respectively.

11. The GMP model slightly underestimated the rise in the LAR curve at older old ages for Swedish females in recent decades (between 1956–1960 and 1986–1990), as well as for Japanese females and males (Figure 4 Panels C vs. c, E vs. e, and F vs. f). On the other hand, it overestimated the almost negligible rise in the level of the LAR at older old ages for Swedish females in earlier periods (between 1861–1965 and 1926–1930), as well as for Swedish males during the entire period (Figure 4 Panels A vs. a and D vs. d). The reasons for these deviations remain unclear.

TABLE 2. SUMMARY RESULTS OF THE GMP MODEL ESTIMATION

	Sweden		Japan	
	Females	Males	Females	Males
Square Root of the Mean Squared Error in:				
Weighted log death rate[a]	0.0301	0.0238	0.0397	0.0319
Weighted LAR[b]	0.0056	0.0046	0.0069	0.0064
Percent of the Explained Variance in:				
Weighted log death rate	99.95	99.98	99.92	99.96
Weighted LAR	98.38	98.71	97.62	97.54
Parameters[c]				
α	6.26	12.46	5.31	7.06
θ	0.127	0.108	0.136	0.116

[a] $\varepsilon_M = \sqrt{\sum_i \sum_j D_{ij}(\ln M_{ij} - \ln m_{ij})^2 / \sum_i \sum_j D_{ij}}$, where D_{ij}, M_{ij}, and m_{ij} are as defined in the text. Both the variance of $\ln M_{ij}$ and that of M_{ij} can be approximated by $1/D_{ij}$.

[b] $\varepsilon_K = \sqrt{\sum_i \sum_j W_{ij}(\ln K_{ij} - \ln k_{ij})^2 / \sum_i \sum_j W_{ij}}$, where $W_{ij} = 25 / \left(\frac{1}{D_{ij}} + \frac{1}{D_{i+1,j}}\right)$, $K_{ij} = \frac{\ln M_{i+1,j} - \ln M_{ij}}{5}$, and $k_{ij} = \frac{\ln m_{i+1,j} - \ln m_{ij}}{5}$. The variance of K_{ij} can be approximated by $1/W_{ij}$.

[c] *A*'s and *B*'s are shown in Figure 5.

This transition in three phases reflects the history of health improvements in industrialized countries during the twentieth century. After a long period of slowly decreasing (though still fluctuating) mortality levels, in the early twentieth century these countries witnessed a sharp downturn of mortality due to rapid reductions in infectious and parasitic diseases. This epidemiological transition was then followed by a different type of transition in the late twentieth century characterized by a substantial reduction of mortality from degenerative diseases, in particular, cardiovascular diseases (Crimmins 1981). This "new stage of epidemiological transition" (Olshansky and Ault 1986; Rogers and Hackenberg 1987) resulted in a marked decline of old-age mortality in recent decades (Kannisto et al. 1994).

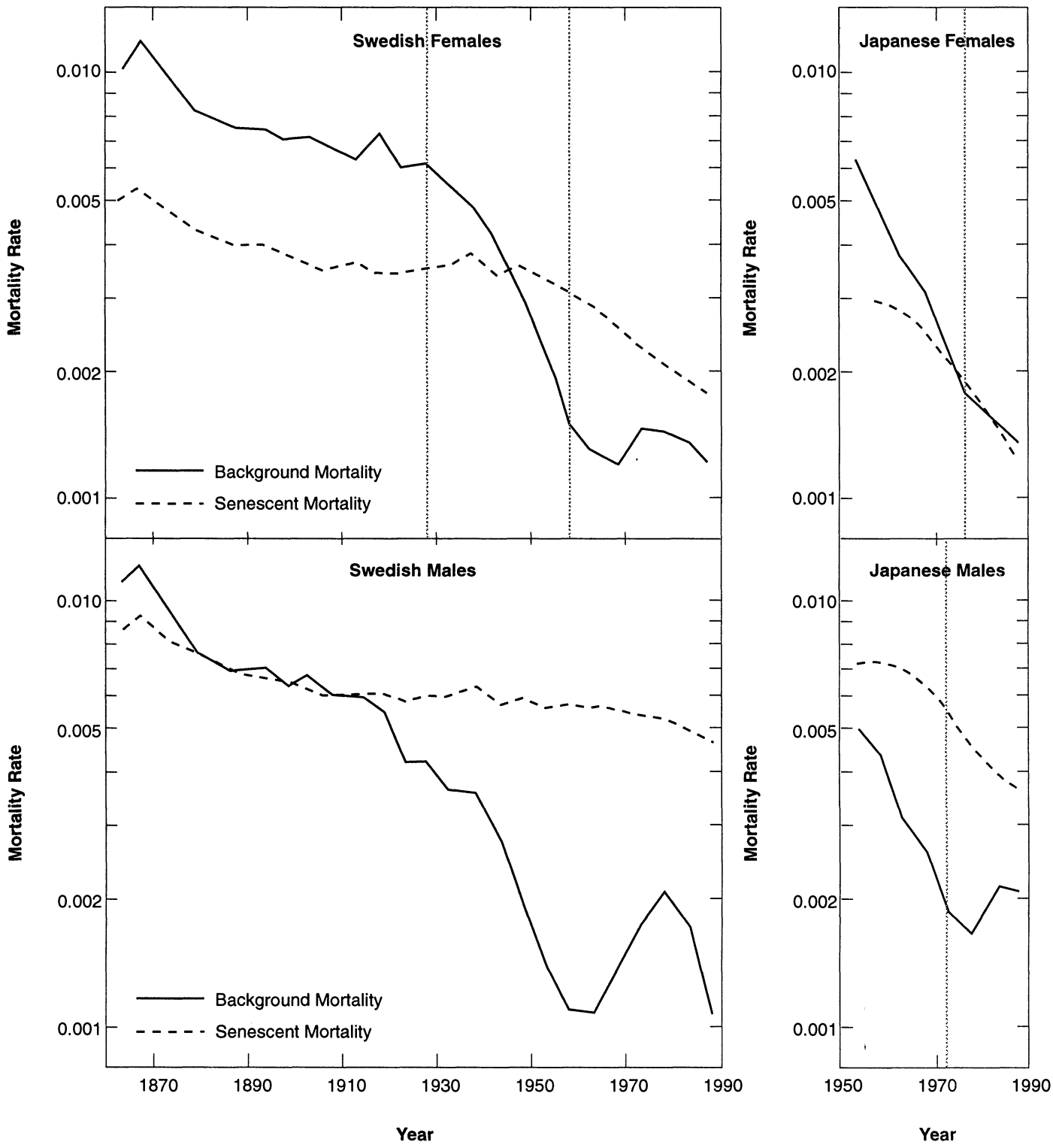
A different pattern prevailed for Swedish males, however, for whom senescent mortality declined only modestly during this 130-year period. This difference reflects the fact that the expectation of life at age 65 for Swedish males increased very slowly (for example, from 13.7 years in the period 1941–1945 to 14.1 years in the period 1974–1978); even in 1990, the increase in life expectancy was only 15.3 years, which was comparable to 15.2 years for Swedish females in the period 1956–1960 (United Nations, various years), when the substantial decline of female senescent mortality was about to start.[12]

The transition from a phase of background mortality reduction to a phase of senescent mortality decline occurred for Japanese females and males as well as for Swedish females. The shift between phases was around 1976–1980 for females and 1971–1975 for males. In postwar Japan, however, the decline in senescent mortality was substantial, even in years when the decline was outpaced by the reduction in background mortality. Thus, certain periods (1951–1955 to 1976–1980 for females and 1951–1955 to 1971–1975 for males) can be described most appropriately as a phase of rapid, simultaneous declines in both senescent and background mortality, resulting in an unprecedented reduction of total mortality in the adult age range.

The trends of background and senescent mortality shown in Figure 5 help to explain the differential LAR trends shown in Figure 4 in two ways. First, declines in senescent mortality are associated with increasing levels of the LAR at older old ages. The LAR curve at older old ages increased notably when senescent mortality declined steeply (for Swedish females between 1956–1960 and 1986–1990, and for Japanese females and males between 1951–1955 and 1986–1990), but

12. These estimates of background mortality show a recent rise for Swedish males around 1970 and, to a lesser extent, for Swedish females around 1970 and for Japanese males around 1980. This apparent resurgence of background mortality levels may reflect the effects of smoking. Smoking raises the risks of some cancers and most forms of heart disease, which are generally considered to be degenerative causes of death. Thus, smoking would normally be thought to affect senescent rather than background mortality. Doll et al. (1994) has shown, however, that the impact of smoking on mortality is significantly stronger for those aged 45–64 than for those aged 65–84. Furthermore, in a recent study on senescent mortality, lung cancer under age 50 was classified as a nonsenescent cause (Carnes et al. 1996). Therefore, it seems possible that estimates of both senescent and background mortality reflect effects of the increase in tobacco consumption. The decrease in background mortality among Swedish males during the 1980s is consistent with the recent reduction in both tobacco consumption (Nicolaides-Bouman et al. 1993) and smoking-related mortality (Peto et al. 1994) in Sweden.

FIGURE 5. ESTIMATED BACKGROUND MORTALITY AND SENESCENT MORTALITY FOR THOSE AGED 50–54: SWEDISH FEMALES AND MALES (1861–1990) AND JAPANESE FEMALES AND MALES (1951–1990)



Note: The vertical dotted lines divide the period into different phases.

increased only slightly or not at all when senescent mortality declined at a modest pace (for Swedish females between 1861–1865 and 1956–1960, and for Swedish males in the entire period). Second, the differential pace of decline in background and senescent mortality is related to changes in the level of the LAR at younger old ages. The LAR curve at younger old ages increased when background mortality declined faster than senescent mortality (for Swedish females between 1926–1930 and 1956–1960, for Swedish males in most of the period, for Japanese females between 1951–1955 and 1976–1980, and for Japanese males between 1951–1955 and 1971–1975). The direction of this change in the LAR curve was reversed when senescent mortality declined faster than background mortality (for Swedish females between 1956–1960 and 1986–1990, for Japanese females between 1976–1980 and 1986–1990, and for Japanese males between 1971–1975 and 1986–1990).

One crucial question remains: Why do cohort LARs appear to be less consistent with the third prediction of the heterogeneity hypothesis than do period LARs? To investigate this question, we decomposed estimated LARs for periods and quasi-cohorts as described in detail in Appendix D. Quasi-cohorts were used because the GMP model was applied to the data by five-year age groups and five-year periods. The results of this decomposition for Swedish females are shown in Appendix Figure D1.

These results indicate that there are at least three possible causes behind the clearer shifts in period than in cohort LARs. First, the truncation of cohort LAR curves makes cohort variations less evident than period variations. Several five-year cohorts that experienced some portion of the decline in senescent mortality after the late 1950s (when they were over age 50) were still in the middle of the study's age range (ages 50–99) in 1990, the end of our observation period. Second, the mean frailty ($\bar{z}$) tends to decrease with age more steeply in a given period than in the life history of a cohort. From a cross-sectional perspective, then, older individuals tend to be more "selected" than younger ones because of the effects of both age and cohort on selection processes: Older cohorts have been exposed to attrition longer, but also they have survived in a less favorable environment (i.e., a higher mortality regime). Third, and most important, although declines in senescent mortality raised cohort LAR curves at older old ages as well as period LAR curves, their effects on cohort LARs were masked by substantial period variations in the rate of senescent mortality decline, making cohort LAR curves look erratic.

In summary, the results of the analysis using the GMP model indicate that the data from both Sweden and Japan lend support to the third prediction of the heterogeneity hypothesis, when modified as follows: Mortality deceleration tends to shift to older ages as the level of *senescent* mortality declines.

CONCLUSION

In general, the results of this study appear broadly consistent with the heterogeneity hypothesis. It is possible, however, that they are also compatible with specific versions of the individual-risk hypothesis. For example, if deceleration results from a general slowdown in fundamental senescent processes, it should be observed for most CODs (first prediction of the heterogeneity hypothesis). Furthermore, differences between CODs in the timing of the deceleration (second prediction) could be due to currently unexplained pathophysiological factors. Finally, a shift in the pattern of deceleration to older ages (third prediction) might have been caused by a delay of senescent processes, brought about by improvements in the health of the elderly during recent decades (Manton, Corder, and Stallard 1997). In this regard, it is noteworthy that observed shifts of LAR curves to older ages appear to be greater than estimated by the GMP model (Figure 4). This discrepancy suggests that factors other than heterogeneity may play a role in these changes.

Although we cannot dismiss alternative explanations, some of the findings of this study seem to support the heterogeneity hypothesis more strongly than the individual-risk hypothesis. For example, with regard to our third prediction and associated findings (shifts in LAR patterns to older ages), an individual-risk explanation would imply that the age pattern of senescence for individual women has shifted by about 10 years within the last few decades. Even with evidence of health improvements, such an interpretation does not seem fully convincing in light of other evidence that the timing of at least some senescent processes among women has not changed significantly. For example, the average age at natural menopause in industrialized countries has been nearly constant (at around age 50) during this period (Khaw 1992; Kono et al. 1990; Luoto, Kaprio, and Uutela 1994).

Indeed, the latter hypothesis, as currently stated, is quite flexible and could be compatible with almost any observed pattern, trend, or differential mortality deceleration. In contrast, the heterogeneity hypothesis implies at least three specific predictions, as delineated in this study. If the data had deviated significantly from those predictions, then the validity of the hypothesis would have been questioned. To test the individual-risk hypothesis in a comparable fashion, we would need to specify the changes in senescent processes that account for mortality deceleration and to state falsifiable hypotheses that can be tested with available data.

Although mortality deceleration is observed for many species, implications of this study for nonhuman species are unclear. For example, mortality deceleration starts at considerably younger ages in invertebrates (e.g., fruit flies, nematodes, and beetles) than in humans if their ages are rescaled in relation to the life expectancy at puberty (Brooks et al. 1994; Carey et al. 1992; Curtsinger et al. 1992; Tatar and Carey 1994). Thus, the mechanisms underlying the mortality deceleration of invertebrates may be significantly different from those of humans. In future research, differences between species in age patterns of mortality and mortality deceleration should be studied in depth and detail.

APPENDIX A: MATHEMATICAL ILLUSTRATIONS OF THE PREDICTIONS

In this appendix, we discuss three mortality models in which the vulnerability of individuals with the same age is distributed according to a gamma distribution. These models may not represent mortality dynamics accurately in all situations, but they provide mathematical illustrations of the three predictions of the heterogeneity hypothesis.

Gamma-Gompertz Model

The gamma-Gompertz model (Beard 1959; Manton et al. 1981, 1986; Yashin et al. 1994) is based on three key assumptions: (1) the mortality risk of an individual is the product of two factors; (2) the first factor, frailty, is independent of age and follows the gamma distribution at some initial age; and (3) the second factor, the mortality profile for a "standard" individual (whose frailty equals 1), increases as an exponential function of age. Following these assumptions, the force of mortality for an individual with frailty z at age x is as follows:

$$\mu(x,z) = zBe^{\theta x}, \tag{A1}$$

where z is a single observation of a random variable, Z, which follows the gamma distribution (with a mean of 1 and variance of $1/\alpha$ at $x = 0$), and B and θ are positive constants. In this model, z represents the joint effects of genetic, environmental, and lifestyle characteristics that are relatively stable; B establishes the level of mortality at age $x = 0$; and $e^{\theta x}$ represents the combined effects of age-related physiological changes.

It follows from Eq. (A1) that the death rate for the cohort is a logistic function of age:

$$m(x) = \frac{De^{\theta x}}{1+Ce^{\theta x}}, \tag{A2}$$

where

$$C = \frac{B}{\alpha\theta - B} \text{ and } D = \alpha\theta C.$$

The derivation of Eq. (A2) from Eq. (A1) is given elsewhere (Beard 1959; Horiuchi and Coale 1990). If C is positive, $m(x)$ is a logistic function increasing from 0 to $D/C(= \alpha\theta)$. The rate of relative increase in the death rate with age is given by

$$k(x) = \frac{1}{m(x)}\frac{dm(x)}{dx} = \frac{d\ln m(x)}{dx} = \frac{\theta}{1+Ce^{\theta x}}. \tag{A3}$$

Thus, the relative increase in $m(x)$ with age slows down at advanced ages.

Eqs. (A2) and (A3) imply that either a larger α (reduced heterogeneity) or a smaller B (lower mortality) yields a smaller value of C, thereby raising $k(x)$ for any x and shifting the $k(x)$ curve to older ages. Specifically, if $k^*(x)$ is a new LAR curve found by reducing B (holding other parameters constant), then $k^*(x + \delta) = k(x)$ for all x, where δ is a positive constant. This relationship between B and the LAR is consistent with the third prediction, which states that the pattern of deceleration should shift to older ages as mortality declines.

Gamma-Makeham Model

The third prediction is also supported by the gamma-Makeham model (Beard 1959), which includes a background-mortality term. In this model, the force of mortality for an individual is assumed to be

$$\mu(x,z) = A + zBe^{\theta x}, \tag{A4}$$

where A is a positive constant. The population LAR in this case is given by

$$k(x) = \frac{\theta}{1+(A/D)e^{-\theta x}} - \frac{\theta}{1+(1/C)e^{-\theta x}}, \tag{A5}$$

where

$$C = \frac{B}{\alpha\theta - B} \text{ and } D = (A+\alpha\theta)C$$

(Horiuchi and Coale 1990). From these definitions, it is obvious that a decline in B reduces both C and D by the same proportion. As with the gamma-Gompertz model, then, a decline in the level of senescent mortality shifts the $k(x)$ curve to older ages without changing the shape of the curve.

Multiple-Decrement Gamma-Gompertz Model

The gamma-Gompertz model can be extended to multiple causes of death. Suppose that there are n causes of death and each individual has a frailty profile $\mathbf{z} = [z_1, z_2, \ldots, z_n]$ (Manton et al. 1986). We assume that the force of mortality at age x for an individual with frailty profile $\mathbf{z}$ is the sum of the cause-specific forces. Thus,

$$\mu(x,\mathbf{z}) = \sum_i \mu_i(x,z_i), \tag{A6}$$

where

$$\mu_i(x,z_i) = z_i B_i e^{\theta_i x}. \tag{A7}$$

Now μ, z, B, and θ all have a subscript for cause i, and the z_i's are single draws from (independent) random variables, Z_i's, which each follow the gamma distribution (with a mean of 1 and variance of $1/\alpha_i$ at age $x = 0$).

At a population level as well, the force of mortality is additive across causes of death:

$$m(x) = \sum_i m_i(x). \tag{A8}$$

Furthermore, if the various causes of death are independent, the cause-specific forces of mortality have the following simple form:

$$m_i(x) = \frac{D_i e^{\theta_i x}}{1+C_i e^{\theta_i x}}, \tag{A9}$$

where

$$C_i = \frac{B_i}{\alpha_i\theta_i - B_i} \text{ and } D_i = \alpha_i\theta_i C_i.$$

Thus, when causes of death are independent, the LAR for cause i has a simple form:

$$k_i(x) = \frac{\theta_i}{1 + C_i e^{\theta_i x}}. \quad \text{(A10)}$$

A few important implications are drawn from Eqs. (A9) and (A10). First, because $m_i(x)$ is a logistic function of age for any cause i, the deceleration occurs for all causes (the first prediction). Second, for smaller values of α_i, the $k_i(x)$ curve is shifted to younger ages. Thus, the mortality deceleration tends to start earlier for CODs with greater individual differences in vulnerability (the second prediction).

Some additional predictions emerge from Eq. (A10) that we do not test in this paper. For example, a smaller θ_i narrows the range of the LAR (numerator of Eq. (A10)) and slows its age-associated change (denominator), thereby making the deceleration less pronounced. Because relative levels of θ_i are especially difficult to know a priori, we chose not to test this prediction. Finally, the multiple-decrement gamma-Gompertz model predicts that the mortality deceleration starts at younger ages for CODs with higher death rates (greater B_i values). This prediction depends strongly on the assumption of independence between causes of death, however, and thus may be difficult to document empirically. The prediction might fail, for example, if the deceleration pattern of a low-mortality COD were heavily influenced by the deceleration pattern of a high-mortality COD because of a strong correlation between the two causes.

Note that the single-decrement and multiple-decrement versions of the gamma-Gompertz model (Eqs. (A2), (A8), and (A9)) are not mathematically equivalent because the sum of logistic functions is not generally a logistic function.

APPENDIX B: ALTERNATE SPECIFICATIONS OF THE GMP MODEL

There may be differences among individuals for each of the three parameters of the Makeham model: level of background mortality (A), level of senescent mortality (B), and rate of senescent mortality increase with age (θ). If all three types of individual differences are incorporated in the GMP model, then the force of mortality for a person aged x at time t is given by

$$\mu(z_A, z_B, z_\theta, x, t) = z_A A(t) + z_B B(t) \exp(z_\theta \theta x), \quad \text{(B1)}$$

where z_A, z_B, and z_θ are frailties of the individual with regard to A, B, and θ, respectively.

We consider five versions of the GMP model with different combinations of z's: z_A only (Model A); z_B only (Model B, Eq. (5)); z_θ only (Model θ); z_A and z_B (Model AB); z_A, z_B, and z_θ (Model ABθ, or Eq. (B1)). The five models were fitted to mortality data for Japanese females. In all cases, we assume that z_A, z_B, and z_θ are independent and follow a gamma distribution (with a mean of 1 and variances of $1/\alpha_A$, $1/\alpha_B$, and $1/\alpha_\theta$ in the age group 50–54).

Appendix Table B1 provides a summary of the results. The large values of α_A in Models A, AB, and ABθ, and of α_θ in Model ABθ indicate that, according to these models, the Japanese female population is nearly homogeneous with respect to z_A and z_θ. Thus, the table seems to indicate that heterogeneity needs to be considered only for z_B. Based on a comparison of standard error estimates (for each model as a whole), Model B clearly fits the data better than do Model A and Model θ, and the addition of A and θ to Model B does not improve the fit perceptibly.

A closer look at the results suggests, however, that we cannot exclude the potential importance of z_θ for several reasons. First, $\varepsilon_M = 0.0473$ for Model θ, suggesting a standard error in estimated death rates of about 4.73%, which is small and roughly comparable to $\varepsilon_M = 0.0397$ for Model B. Second, when compared graphically, estimated LAR curves for Model B (Figure 4) and those for Model θ (not shown) are hardly distinguishable. Third, although $\varepsilon_M = 0.0397$ for Model ABθ is obtained with $\alpha_B = 5.32$ and an extremely large value of $\alpha_\theta (1.77 \times 10^5)$, fairly low ε_M's can be obtained for some other combinations of α_B and α_θ. For example, the combination of $\alpha_B = 7.53$ and $\alpha_\theta = 542.40$ (together with $\alpha_A = 2.60 \times 10^{12}$ and $\theta = 0.1326$) results in $\varepsilon_M = 0.0429$. Although $\alpha_\theta = 542.40$ may seem large, it implies a coefficient of variation of z_θ around 0.043 (in the age group 50–54), which is not negligibly small. Finally, these results may also be influenced by inadequacies in our current estimation procedures, which may differentially affect the various parameters: Whereas, in the iterative algorithm, the gamma distribution of z_θ is computed at each step, and death

APPENDIX TABLE B1. SUMMARY RESULTS OF DIFFERENT VERSIONS OF THE GMP MODEL ESTIATION FOR JAPANESE FEMALES, 1951–1990

Variable	Model A	Model B	Model θ	Model AB	Model ABθ
ε_M	0.0727	0.0397	0.0473	0.0397	0.0397
α_A	4.65×10^{13}	—	—	2.63×10^{12}	2.63×10^{12}
α_B	—	5.31	—	5.32	5.32
α_θ	—	—	113	—	1.77×10^5
θ	0.114	0.136	0.130	0.136	0.136

Note: ε_M is defined as in Footnote a to Table 2.

rates must be found by numerical integration with respect to z_θ, simple formulae are used for z_A and z_B. These complexities suggest that our estimates may be less stable for α_θ than for α_A and α_B, although further study is needed to confirm or disprove this conjecture. In summary, it remains unclear whether the heterogeneity in senescent mortality is due mainly to individual differences in z_B, z_θ, or some combination of both.

In contrast, z_A appears to be nonessential for a model of mortality deceleration at advanced ages. Estimates of α_A in Appendix Table B1 are extremely large, suggesting little or no heterogeneity in background mortality. These estimates may also be unstable, however, because background mortality is a very small component of the total at advanced ages. It seems possible that a slight error in the estimation of the senescent component of the model could distort the estimation of heterogeneity in the background component. Therefore, the best argument for the unimportance of considering heterogeneity in the background component is that this component is too small at advanced ages relative to senescent mortality for its individual differences to have a significant effect on the age pattern of total mortality.

APPENDIX C: APPLICATION OF THE GMP MODEL

Estimation Using Discrete Data

By modifying Eq. (6) for discrete data, the death rate for the ith five-year age group and jth five-year period is estimated by:

$$m_{ij} = A_j + \bar{z}_{ij} B_j e^{5\theta(i-1)}, \qquad \text{(C1)}$$

where

$$\bar{z}_{ij} = \frac{1}{1 + \frac{1}{\alpha}\sum_{u=1}^{i} g_u B_{j-i+u} e^{5\theta(u-1)}}.$$

$\bar{z}_{ij}$ is the mean frailty for the ith age group and jth period. We can assume $\bar{z}_{ij}$ to be nearly equal to the age-specific mean frailty of the birth cohort that is in the ith age group at the midpoint of the jth period. The age trajectory of the cohort can be approximated by the corresponding sequence of combinations of five-year age groups and five-year periods. The second term of the denominator of $\bar{z}_{ij}$ reflects the previous attrition of the cohort that occurred between the first and ith age categories. g_u is the number of years for which the cohort was exposed to the risk of senescent mortality in the uth age group. Because five-year age categories are used here, usually $g_u = 5$ except for the first and ith age groups, for which $g_u = 2.5$. The mean frailty of the cohort currently in the first age group is set to be 1. Therefore, $g_u (u = 1,\ldots,i)$ is defined as follows: if $i > 1$, $g_u = 2.5$ for $u = 1$ and i, and $g_u = 5$ for the other u's; if $i = 1$, then $g_1 = 0$. The FMINS program in MATLAB for UNIX 4.2c is used for minimizing L in Eq. (7).

Parameter Estimates for Earlier Periods

To estimate $\bar{z}$'s for different age groups in the initial period (1861–1865 for Sweden and 1951–1955 for Japan), we must provide estimates of B for $N_i - 1$ periods preceding the initial period, where N_i is the number of age groups, which is 10 in this analysis. There are at least three ways to determine the values of these previous B's. First, they can be assumed constant and set to be equal to B for the initial period, which is iteratively estimated by the weighted least-squares procedure. Second, they can be included in the GMP model as additional unknown parameters and estimated simultaneously with the other parameters. Third, if some data are available for the preceding periods, the trend of those B's up to the initial period can be estimated directly from the data. We experimented with all three options, and the estimates of the major parameters (α, θ, and A's and B's for the initial period and after) were not sensitive to the choice of option. However, the constancy of senescent mortality in the first approach may be too strong an assumption for Sweden and Japan in those periods. In the second approach, the weighted least-square estimates of these previous B's implied questionable trends (such as mortality increase) in some cases, even though the estimates of the later B's were reasonable. Thus we adopted the third approach: These B's are assumed to have followed the trend in the mean death rate between ages 60 and 80, calculated by $-\ln(l(80)/l(60))/20$, between 1816–1820 and 1861–1865 for Sweden and between 1906–1910 and 1951–1955 for Japan. $l(60)$ and $l(80)$ in these periods are drawn or interpolated from life tables prepared by Keyfitz and Flieger (1968) and Kobayashi and Nanjo (1988). In this way, the ratios of B's for the preceding periods to B for the initial period are predetermined and fixed during the iterative estimation process. Similarly, the trend of A for the preceding periods is estimated using $l(30)$ and $l(50)$ for the models that include z_A (see Appendix B).

Constant Parameters

To avoid a large number of parameters and to simplify the model, we assumed both α and θ to be constant for all cohorts. There is no compelling reason to assume that the initial frailty distribution should vary significantly among successive cohorts in the same national population. Thus, we hold α constant over cohorts.

The assumption of a constant θ may not seem compatible with the notable period LAR variations observed in this study or with previous findings that the slope parameter of the Gompertz equation fitted to period death rates changes notably over time (e.g., Riggs 1992). However, θ is the unobserved rate of mortality increase with age *for individuals*. If θ reflects some constant, genetically determined rate of biological senescence, then it will not vary notably among cohorts. Nevertheless, *for populations* the rate of mortality increase with age (measured by the LAR) could change markedly among cohorts and periods, as LARs are determined by interactions among the biological rate of senescence (reflected in θ), heterogeneity (α), and environmental factors (A and B). In fact, our analysis using the GMP model shows that substantial LAR variations by age, period, and cohort could result from a constant θ.

Another important choice was to limit the analysis to mortality above age 50. First, we thought that age 50 would

be sufficiently young as a lower boundary of "old ages." Second, the bell-shaped section of the LAR curve, which characterizes old-age mortality patterns of many populations, tends to start around age 50. Finally, the age pattern of adult mortality under age 50 varies notably because it is often affected significantly by special conditions of certain CODs, such as tuberculosis, homicide, and complications of pregnancy and childbirth. Because of the five-year approximation, the starting age in Eq. (6) (such that $x = 0$) corresponds to age 52.5.

One final assumption that deserves comment is our choice to hold the mean frailty ($\bar{z}$) for the age group 50–54 constant for all cohorts. This assumption could be in error for two opposing reasons. On the one hand, it is possible that later cohorts are less selected, due to mortality decline before age 50. Thus, the average frailty of individuals aged 50–54 should increase over time. On the other hand, it is possible that later cohort are less debilitated by the adverse experience of disease before age 50 (especially during infancy and childhood). Thus, the average frailty of individuals aged 50–54 should decrease over time. There is scattered evidence in support of both of these perspectives (Barker et al. 1993; Elo and Preston 1992; Manton, Stallard, and Corder 1997; Vaupel et al. 1979), but there is also some suggestion that the correlation between early- and late-life mortality is close to 0 (Kannisto, Christensen, and Vaupel 1997). It is possible that both effects are present but that they largely cancel each other out. Therefore, it seemed prudent to adopt the simplest assumption possible—namely, a constant level of frailty at ages 50–54.

APPENDIX D: DECOMPOSITION OF THE LIFE-TABLE AGING RATE

The third prediction of the heterogeneity hypothesis states that the pattern of mortality deceleration should shift to older ages as the mortality level declines. Here we demonstrate why cohort LAR patterns appear to be less consistent with this prediction than do period patterns. For this purpose, we develop a decomposition of both period and cohort LARs.

The GMP model (Eq. (6)) implies that the period LAR (k_p) and the cohort LAR (k_c) can be decomposed as follows:

$$k_p = p_B\theta + p_B\lambda_p, \tag{D1}$$

and

$$k_c = p_A r_A + p_B r_B + p_B\theta + p_B\lambda_c, \tag{D2}$$

where

$$p_A = \frac{A(t)}{A(t)+\bar{z}B(t)e^{\theta x}},\ p_B = \frac{\bar{z}B(t)e^{\theta x}}{A(t)+\bar{z}B(t)e^{\theta x}},$$

$$r_A = \frac{d\ln A(t)}{dt},\ r_B = \frac{d\ln B(t)}{dt},$$

$$\lambda_c = \lambda_p + \lambda_t,\ \lambda_p = \frac{\partial \ln \bar{z}}{\partial x}, \text{ and } \lambda_t = \frac{\partial \ln \bar{z}}{\partial t}.$$

p_A and p_B are the proportions of the total death rate attributable to background and senescent mortality, respectively; r_A and r_B are the relative rates of change (over time) in the levels of background and senescent mortality; λ_p and λ_c are the relative rates of change (over age) in mean frailty by period and cohort; and λ_t is the relative rate of change (over time) in the mean frailty. k_p, k_c, p_A, p_B, λ_c, λ_p, λ_t, and $\bar{z}$ are functions of both age (x) and time (t); r_A and r_B are functions of time (t) only. (x,t) and (t) are omitted from these terms to avoid unnecessary complexities.

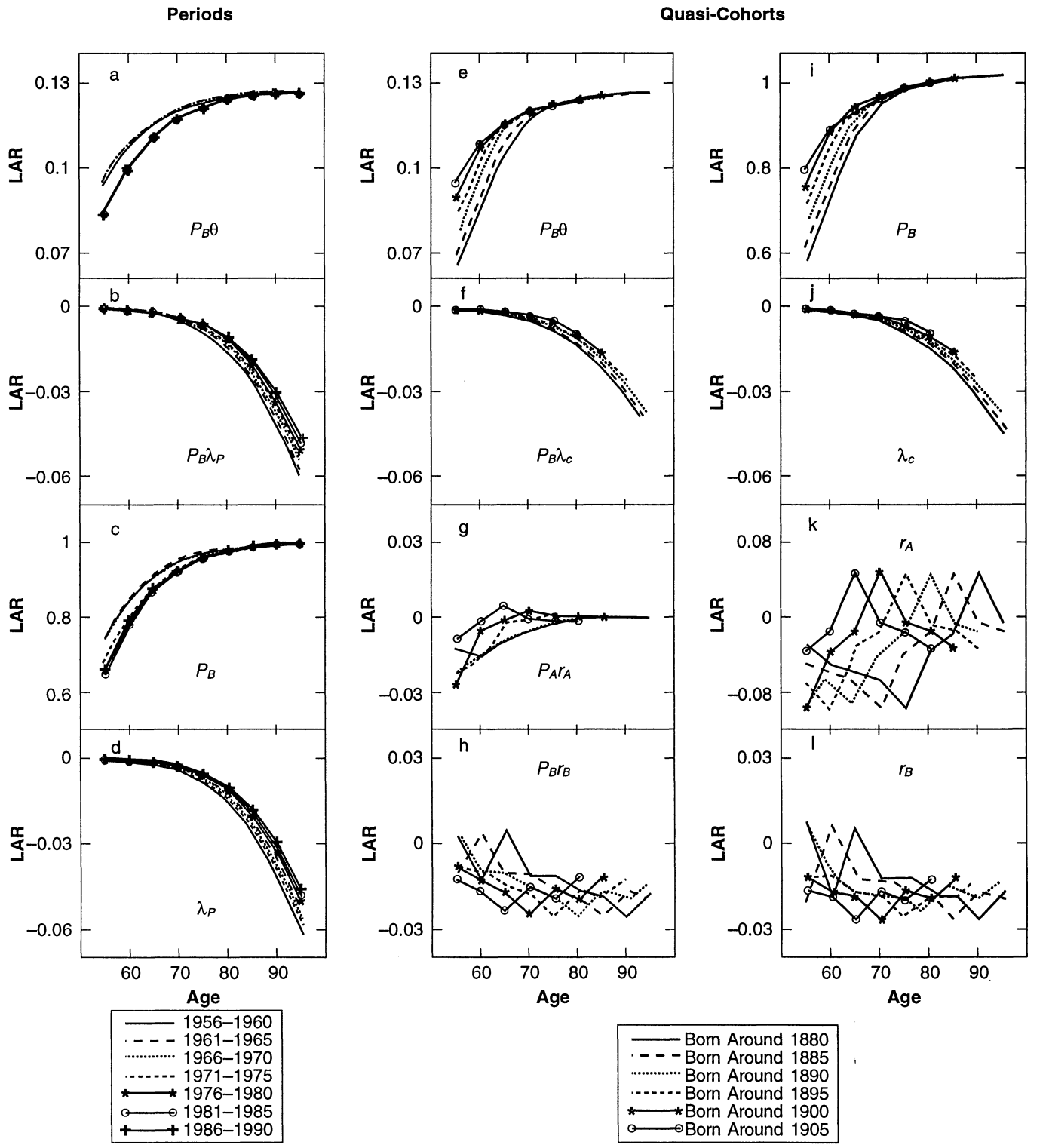
Results of the LAR decomposition for Swedish females are shown in Appendix Figure D1. Panels a–d of the figure show components of the estimated LAR curves for the periods between 1956–1960 and 1986–1990, which are displayed in Figure 4, Panel c. Panels e–l of the figure show components of the estimated LAR curves for quasi-cohorts born between around 1880 and around 1905, which are exhibited in Figure 3, Panel a.

The components of the period LAR from the GMP model illustrate why these curves are bell-shaped and why they tend to shift over time to older ages. As shown in Eq. (D1), the period LAR is the sum of two terms. The decomposition reveals that the bell-shaped curve of the period LAR results from two opposing tendencies: One of the two terms ($p_B\theta$) rises rapidly with age at younger old ages (Appendix Figure D1, Panel a), and the other ($p_B\lambda_p$) falls rapidly with age at older old ages (Appendix Figure D1, Panel b). Because θ is constant, the age-associated rise of the first term, $p_B\theta$, reflects the age pattern of the proportion of senescent mortality (p_B), which increases steeply at younger old ages but flattens as it approaches one at older old ages (Appendix Figure D1, Panel c). The left arm of the p_B curve moves downward over time, thereby lowering the LARs at younger old ages. This downward shift is due to a combination of declining senescent mortality and stagnant background mortality.[13]

The second term of the decomposition of the period LAR, $p_B\lambda_p$, decreases with age. This decrease is due to an accelerating decline in mean frailty ($\bar{z}$) with age, which is caused by the more rapid attrition of mortality at older ages (λ_p in Appendix Figure D1, Panel d). The right arm of this λ_p curve moves upward over time, thereby raising LARs at older old ages. This upward shift reflects the slower age-related decrease in mean frailty during recent periods, which is caused by the lesser attrition brought about by the secular decline in senescent mortality. Therefore, while the left arm of the period LAR curve decreases over time, the right arm increases, producing the appearance of a lateral shift to the right. It is the time trend of the λ_p curve, in particular, that corresponds to the third prediction of the heterogeneity hypothesis.

13. The age-related LAR rise at younger old ages has been discussed previously in relation to menopause, as the LAR rise was steeper among females than among males for many economically developed countries in the late twentieth century (Horiuchi 1997). The historical data in this study, however, reveal that the LAR rise for Swedish males at younger old ages is more noticeable in the nineteenth century than in the late twentieth century. Therefore, although menopause remains one of the potentially important determinants of old-age mortality patterns, consideration should be given to other factors, including p_B, that could explain the LAR rise among both females and males.

APPENDIX FIGURE D1. DECOMPOSITION OF THE ESTIMATED LARS FOR PERIODS AND QUASI-COHORTS: SWEDISH FEMALES



Note: p_A is not shown, as it is simply $1-p_B$.

The cohort LAR is more complicated than its period counterpart because it is the sum of four terms (Eq. (D2)). Again, however, the bell shape of the cohort LAR is attributable to two opposing factors: the rapid rise in the first term ($p_B\theta$ in Appendix Figure D1, Panel e) at younger old ages, reflecting the changing proportion of senescent mortality (p_B in Appendix Figure D1, Panel i); and the rapid fall of the second term ($p_B\lambda_c$ in Panel f) at older old ages, reflecting the accelerating decline of mean frailty with age (λ_c in Panel j).

The trend in the LAR curve over time is somewhat different for cohorts than for periods: The cohort p_B curve moves upward over time (Appendix Figure D1, Panel i), whereas the period curve moves downward (Panel c). These different trends are not due to a fundamental difference between periods and cohorts, but rather to changes in dominant mortality trends over time. When the cohorts in question were at younger old ages, background mortality was declining faster than senescent mortality; during the periods in question, however, the opposite occurred. Thus, unlike the period pattern, the left arm of the cohort LAR tends to move upward over time. Like the period pattern, the right arm of the cohort LAR tends to move upwards over time due to changes in λ_c (Panel j). The upward shift in the right arm of the cohort LAR is consistent with the third prediction of the heterogeneity hypothesis.

Unlike the period LAR, however, the cohort LAR has two more terms ($p_A r_A$ in Panel g, and $p_B r_B$ in Panel h), which introduce fluctuations into the cohort LAR curves. These fluctuations are due to period variations in the rate of change in senescent mortality (r_B in Panel l) and, to a lesser extent, background mortality (r_A in Panel k). For example, the annual rate of senescent mortality decline between consecutive five-year periods from 1961–1965 to 1986–1990 followed a fluctuating series: 1.89%, 2.65%, 1.65%, 1.94%, and 1.23%. These ups and downs affect cohort LAR curves, which would otherwise reflect more clearly the changes (over both age and time) in the proportion of senescent mortality (p_B) and the rate of change in mean frailty (λ_c).

The expected trend of an upward shift over time of LARs at older old ages is more clearly seen in period than in cohort data (e.g., Figure 4, Panel C and Figure 3, Panel A). According to the decomposition results, one of the major reasons for this difference is that period variations in background and senescent mortality introduce erratic patterns into cohort LAR curves. Thus, the assumption that A and B are functions of time, which leads to estimates of r_A and r_B, seems useful in explaining the puzzling difference between the cohort and period results.

Similar conclusions are drawn from decomposition results for Swedish males and Japanese females and males (not shown here). In addition, the faster proportional declines of senescent mortality for Japanese females and males in more recent years move the r_B curves downward over time, counteracting the upward time trends of the right arms of the λ_c curves. This also makes the cohort LAR curves appear less compatible with the third prediction than do the period LAR curves.

REFERENCES

Abrams, P.A. and D. Ludwig. 1995. "Optimality Theory, Gompertz' Law, and the Disposable Soma Theory of Senescence." *Evolution* 49:1055–66.

Baba, S., H. Ozawa, Y. Sakai, A. Terao, M. Konishi, and K. Tatara. 1994. "Heart Disease Deaths in a Japanese Urban Area Evaluated by Clinical and Police Records." *Circulation* 89:109–15.

Barker, D.J., P.D. Gluckman, K.M. Godfrey, J.E. Harding, J.A. Owens, and J.S. Robinson. 1993. "Fetal Nutrition and Cardiovascular Disease in Adult Life." *Lancet* 341:938–41.

Beard, R.E. 1959. "Note on Some Mathematical Mortality Models." Pp. 302–11 in *CIBA Foundation Colloquia on Ageing, The Life Span of Animals 5*, edited by G.E.W. Wolstenholme and M. O'Connor. Boston: Little, Brown and Company.

Benjamin, B. 1964. "Demographic and Actuarial Aspects of Ageing, With Special Reference to England and Wales." *Journal of the Institute of Actuaries* 90:211–38.

Bourgeois-Pichat, J. 1978. "Future Outlook for Mortality Decline in the World." *Population Bulletin of the United Nations* 11:12–41.

Boyle, P., C.L. Vecchia, P. Maisonneuve, T. Zheng, and G.R. MacFarlane. 1995. "Cancer Epidemiology and Prevention." Pp. 199–273 in *Oxford Textbook of Oncology*, edited by M. Peckham, H.M. Pinedo, and U. Veronesi. New York: Oxford University Press.

Brass, L.M. and M.J. Alberts. 1995. "The Genetics of Cerebrovascular Disease." *Baillieres Clinical Neurology* 4:221–45.

Brillinger, D.R. 1986. "The Natural Variability of Vital Rates and Associated Statistics." *Biometrics* 42:693–734.

Brooks, A., G.J. Lithgow, and T.E. Johnson. 1994. "Mortality Rates in a Genetically Heterogeneous Population of *Caenorhabditis elegans*." *Science* 263:668–71.

Carey, J.R. and P. Liedo. 1995. "Sex-Specific Life Table Aging Rates in Large Medfly Cohorts." *Experimental Gerontology* 30:315–25.

Carey, J.R., P. Liedo, D. Orozco, and J.W. Vaupel. 1992. "Slowing of Mortality Rates at Older Ages in Large Medfly Cohorts." *Science* 258:458–61.

Carnes, B.A., S.J. Olshansky, and D. Grahn. 1996. "Continuing the Search for a Fundamental Law of Mortality." *Population and Development Review* 22:231–64.

Charlesworth, B. and L. Partridge. 1997. "Ageing: Levelling of the Grim Reaper." *Current Biology* 7:R440–42.

Coale, A.J. and E.E. Kisker. 1990. "Defects in Data on Old-Age Mortality in the United States: New Procedures for Calculating Mortality Schedules and Life Tables at Highest Ages." *Asian and Pacific Population Forum* 4(1):1–31.

Coale, A.J. and Li Shaomin. 1991. "The Effect of Age Misreporting in China on the Calculation of Mortality Rates at Very High Ages." *Demography* 28:293–301.

Crimmins, E.M. 1981. "The Changing Pattern of American Mortality Decline, 1940–77, and Its Implications for the Future." *Population and Development Review* 7:229–54.

Curtsinger, J.W., H.H. Fukui, D.R. Townsend, and J.W. Vaupel. 1992. "Demography of Genotypes: Failure of the Limited Life-Span Paradigm in *Drosophila melongaster*." *Science* 258:461–

63.
de Chateau, P. 1990. "Mortality and Aggressiveness in a 30-year Follow-Up Study in Child Guidance Clinics in Stockholm." *Acta Psychiatrica Scandinavica* 81:472–76.
Doll, R., R. Peto, K. Wheatley, R. Gray, I. Sutherland. 1994. "Mortality in Relation to Smoking: 40 Years' Observations on Male British Doctors." *British Medical Journal* 309:901–11.
Economos, A.C. 1980. "Kinetics of Metazoan Mortality." *Journal of Social Biological Structures* 3:317–29.
Elo, I.T. and S.H. Preston 1992. "Effects of Early-Life Conditions on Adult Mortality: A Review." *Population Index* 58:186–212.
———. 1994. "Estimating African-American Mortality from Incomplete Data." *Demography* 31:427–58.
Ensrud, K.E., L. Palermo, D.M. Black, J. Cauley, M. Jergas, E.S. Orwoll, M.C. Nevitt, K.M. Fox, and S.R. Cummings. 1995. "Hip and Calcaneal Bone Loss Increase With Advancing Age: Longitudinal Results From the Study of Osteoporotic Fractures." *Journal of Bone and Mineral Research* 10:1778–87
Finch, C.E. 1990. *Longevity, Senescence, and the Genome.* Chicago: The University of Chicago Press.
Fujimoto, W.Y. 1996. "Overview of Non-Insulin-Dependent Diabetes Mellitus (NIDDM) in Different Population Groups." *Diabetic Medicine* 13(9 Suppl. 6):S7–10
Gavrilov, L.A. and N.S. Gavrilova. 1991. *The Biology of Life Span: A Quantitative Approach.* New York: Harwood.
Goldman, N. and S. Takahashi. 1996. "Old-Age Mortality in Japan: Demographic and Epidemiological Perspectives." Pp. 157–81 in *Health and Mortality Among Elderly Populations*, edited by G. Caselli and A.D. Lopez. New York: Oxford University Press.
Grove G.L. and A.M. Kligman. 1983. "Age-Associated Changes in Human Epidermal Cell Renewal." *Journal of Gerontology* 38:137–42.
Horiuchi, S. 1983. "The Long-term Impact of War on Mortality: Old-Age Mortality of World War I Survivors in the Federal Republic of Germany." *Population Bulletin of the United Nations* 15:80–92.
———. 1997. "Postmenopausal Acceleration of Age-Related Mortality Increase." *Journal of Gerontology: Biological Sciences* 52A:B78–92.
Horiuchi, S. and A.J. Coale. 1990. "Age Patterns of Mortality for Older Women: An Analysis Using the Age-specific Rate of Mortality Change With Age." *Mathematical Population Studies* 2:245–67.
Horiuchi, S. and J.R. Wilmoth. 1997. "Age Patterns of the Life-Table Aging Rate for Major Causes of Death in Japan, 1951–1990." *Journal of Gerontology: Biological Sciences* 52A:B67–77.
Hui, S.L., C.W. Slemenda, C.C. Johnston, and C.R. Appledorn. 1987. "Effects of Age and Menopause on Vertebral Bone Density." *Bone and Mineral Research* 2:141–46
Kaesberg, P.R. and W.B. Ershler. 1989. "The Change in Tumor Aggressiveness With Age: Lessons From Experimental Animals." *Seminars in Oncology* 16:28–33.
Kahn, C.R., D. Vicent, and A. Doria. 1996. "Genetics of Non-Insulin-Dependent (Type-II) Diabetes Mellitus." *Annual Review of Medicine* 47:509–31.
Kannisto, V. 1996. *The Advancing Frontier of Survival: Life Tables for Old Age.* Odense, Denmark: Odense University Press.
Kannisto, V., K. Christensen, and J.W. Vaupel. 1997. "No Increased Mortality in Later Life for Cohorts Born During Famine." *American Journal of Epidemiology* 145:987–94.
Kannisto, V., J. Lauristen, A.R. Thatcher, and J.W. Vaupel. 1994. "Reduction in Mortality at Advanced Ages." *Population and Development Review* 20:793–810.
Keyfitz, N. and W. Flieger. 1968. *World Population. An Analysis of Vital Data.* Chicago: University of Chicago Press.
Keys, A., A. Menotti, C. Aravanis, H. Blackburn, B.S. Djordevic, R. Buzina, A.S. Dontas, F. Fidanza, M.J. Karvonen, and N. Kimura. 1984. "The Seven Countries Study: 2,289 Deaths in 150 Years." *Preventive Medicine* 13:141–54.
Khaw, K.T. 1992. "Epidemiology of the Menopause." *British Medical Bulletin* 48:249–61.
Khazaeli, A.A., L. Xiu, and J.W. Curtsinger. 1995. "Stress Experiments as a Means of Investigating Age-Specific Mortality in *Drosophila melongaster.*" *Experimental Gerontology* 30:177–84.
Kobayashi, K. and Z. Nanjo. 1988. *Generation Life Tables for Japan Based on Period Life Tables Covering the Years 1891–1986.* Tokyo: Nihon University Population Research Institute.
Kono, S., Y. Sunagawa, H. Higa, and H. Sunagawa. 1990. "Age of Menopause in Japanese Women: Trends and Recent Changes." *Maturitas* 12:43–49.
Le Bras, H. 1976. "Lois de Mortalite at Age Limite." *Population* 31:655–92.
Luoto, R., J. Kaprio, and A. Uutela. 1994. "Age at Natural Menopause and Sociodemographic Status in Finland." *American Journal of Epidemiology* 139:64–76.
Makeham, W.M. 1860. "On the Law of Mortality and the Construction of Annuity Tables." *Journal of the Institute of Actuaries* 8:301–10.
Manton, K.G. 1992. "Mortality and Life Expectancy Changes Among the Oldest Old." Pp. 157–82 in *The Oldest Old*, edited by R.M. Suzman, D.P. Willis, and K.G. Manton. New York: Oxford University Press.
———. Forthcoming. "The Future of Old Age." In *Textbook of Geriatric Medicine and Gerontology,* 5th edition, edited by J. C. Brocklehurst. London: Churchill Livingstone.
Manton, K.G., L.S. Corder, and E. Stallard. 1997. "Chronic Disability Trends in Elderly United States Populations: 1982–1994." *Proceedings of the National Academy of Sciences* 94:2593–98.
Manton, K.G., E. Stallard, and L.S. Corder. 1997. "Changes in the Age Dependence of Mortality and Disability: Cohort and Other Determinants." *Demography* 34:135–58.
Manton, K.G., E. Stallard, and J.W. Vaupel. 1981. "Methods for Comparing the Mortality Experience of Heterogeneous Populations." *Demography* 18:389–410.
———. 1986. "Alternative Models for the Heterogeneity of Mortality Risks Among the Aged." *Journal of American Statistical Association* 81:635–44.
Manton, K.G., E. Stallard, M.A. Woodbury, and J.E. Dowd. 1994. "Time-Varying Covariates in Models of Human Mortality and Aging: Multidimensional Generalization of the Gompertz." *Journal of Gerontology* 49(4):B169–90.

Masoro, E.J. 1981. *Handbook of Physiology of Aging.* Boca Raton, FL: CRC Press.

———. 1985. "Metabolism." Pp. 540–63 in *Handbook of the Biology of Aging,* 2nd edition, edited by C.E. Finch and E.L. Schneider. New York: van Nostrand Reinhold.

Mueller, L.D. and M.R. Rose. 1996. "Evolutionary Theory Predicts Late-Life Mortality Plateaus." *Proceedings of the National Academy of Sciences* 93:15249–53.

Nicolaides-Bouman, A., N. Wald, B. Forey, and P. Lee. 1993. *International Smoking Statistics.* New York: Oxford University Press.

Olshansky, S.J. and A.B. Ault. 1986. "The Fourth Stage of the Epidemiologic Transition: The Age of Delayed Degenerative Diseases." *Milbank Memorial Fund Quarterly* 64:355–91.

O'Rourke, M.A., J.R. Feussner, P. Feigl, and J. Laszlo. 1987. "Age Trends of Lung Cancer Stage at Diagnosis." *Journal of American Medical Association* 258:921–26.

Peer, P.G.M., J.A.A.M. van Dijck, J.H.C.L. Hendriks, R. Holland, and A.L.M. Verbeek. 1993. "Age-Dependent Growth Rate of Primary Breast Cancer." *Cancer* 71:3547–51.

Perks, W. 1932. "On Some Experiments in the Graduation of Mortality Statistics." *Journal of the Institute of Actuaries* 63:12–40.

Perls, T.T. 1995. "The Oldest Old." *Scientific American* 272(1):70–75.

Perls, T.T., J.N. Morris, W.L. Ooi, and L.A. Lipsitz. 1993. "The Relationship Between Age, Gender and Cognitive Performance in the Very Old: The Effect of Selective Survival." *Journal of the American Geriatric Society* 41:1193–201.

Peto, R., A.D. Lopez, J. Boreham, M. Thun, and C. Heath, Jr. 1994. *Mortality From Smoking in Developed Countries, 1950–2000.* New York: Oxford University Press.

Pletcher, S.D. and J.W. Curtsinger. 1998. "Mortality Plateaus and the Evolution of Senescence: Why Are Old-Age Mortality Rates So Low?" *Evolution* 52:454–64.

Rebeck, G.W., T.T. Perls, H.L. West, P. Sodhi, L.A. Lipsitz, and B.T. Hyman. 1994. "Reduced Apolipoprotein Epsilon 4 Allele Frequency in the Oldest Old Alzheimer's Patients and Cognitively Normal Individuals." *Neurology* 44:1513–16.

Redington, F.M. 1969. "An Exploration Into Patterns of Mortality." *Journal of the Institute of Actuaries* 95:243–98.

Remmen, H.V., W.F. Ward, R.V. Sabia, and A. Richardson. 1995. "Gene Expression and Protein Degradation." Pp. 171–234 in *Handbook of Physiology, Section 11, Aging,* edited by E.J. Masoro. New York: Oxford University Press.

Riggs, J.E. 1992. "The Dynamics of Aging and Mortality in the United States, 1900–1988." *Mechanisms of Ageing and Development* 66:45–57.

Rogers, R.G. and R. Hackenberg. 1987. "Extending Epidemiologic Transition Theory: A New Stage." *Social Biology* 34:234–43.

Rose, M.R. 1991. *Evolutionary Biology of Aging.* New York: Oxford University Press.

Rosenberg, B., G. Kemeny, L.G. Smith, I.D. Skurnick, and M.J. Bandurski. 1973. "The Kinetics and Thermodynamics of Death in Multicellular Organisms." *Mechanisms of Ageing and Development* 2:275–93.

Sherlock, S. 1995. "Alcoholic Liver Disease." *Lancet* 345:227–29.

Sohal, R.S. 1986. "The Rate of Living Theory: A Contemporary Interpretation." Pp. 23–44 in *Insect Aging: Strategies and Mechanisms,* edited by K.G. Collatz and R.S. Sohal. Berlin: Springer.

Strehler, B.L. and A.S. Mildvan. 1960. "General Theory of Mortality and Aging." *Science* 132:14–21.

Stremmel, W., J. Schwarzendrube, C. Niederau, and G. Strohmeyer. 1991. "Epidemiology, Clinical Course and Treatment of Chronic Viral Hepatitis." *Hepato-Gastroenterology* 38(1):22–8.

Tatar, M. and J.R. Carey. 1994. "Sex Mortality Differentials in the Bean Beetle: Reframing the Question." *American Naturalist* 144:165–75.

United Nations. Various years. *Demographic Yearbook.* New York: United Nations.

Van der Hulst, R.W. and G.N. Tytgat. 1996. "*Helicobacter pylori* and Peptic Ulcer Disease." *Scandinavian Journal of Gastroenterology* (Suppl.) 220:10–18.

Vaupel, J.W. and J.R. Carey. 1993. "Compositional Interpretations of Medfly Mortality." *Science* 260:1666–67.

Vaupel, J.W., K.G. Manton, and E. Stallard. 1979. "The Impact of Heterogeneity in Individual Frailty on the Dynamics of Mortality." *Demography* 16:439–54.

Vaupel, J.W. and A.I. Yashin. 1986. "Cancer Rates Over Age, Time and Place: Insights From Stochastic Models of Heterogeneous Populations." IIASA Working Paper wp-86–59. Laxenburg, Austria: International Institute for Applied Systems Analysis.

Wilmoth, J.R. 1995. "Are Mortality Rates Falling at Extremely High Ages? An Investigation Based on a Model Proposed by Coale and Kisker." *Population Studies* 49:281–95.

Wilmoth, J.R. and H. Lundstrom. 1996. "Extreme Longevity in Five Countries: Presentation of Trends With Special Attention to Issues of Data Quality." *European Journal of Population* 12:63–93.

Witten, M. 1988. "A Return to Time, Cells, Systems, and Aging: V. Further Thoughts on Gompertzian Survival Dynamics—The Geriatric Years." *Mechanisms of Ageing and Development* 46:175–200.

Wolf, P.A., R.B. D'Agostino, A.J. Belanger, and W.B. Kannel. 1991. "Probability of Stroke: A Risk Profile From the Framingham Study." *Stroke* 22:312–18.

Yashin, A.I., J.W. Vaupel, and I.A. Iachine. 1994. "A Duality in Aging: The Equivalence of Mortality Models Based on Radically Different Concepts." *Mechanisms of Ageing and Development* 74:1–14.