Comment on "Inflammatory Exposure and Historical Changes in Human Life-Spans"

Finch and Crimmins (*1*) hypothesized that "decreased inflammation during early life has led directly to a decrease in morbidity and mortality resulting from chronic conditions in old age." Various early-life factors have been shown to affect late-life mortality (*2*, *3*). However, demographic and epidemiological studies suggest that the effect is modest (*3*–*6*). Research on twins indicates that less than 10% of the variation in how long twins live is attributable to variation in shared health conditions early in life (*7*, *8*).

To buttress their claim, Finch and Crimmins examined the trajectories of mortality over age up through old age for people born in four decades starting between 1751 and 1901. Successive cohorts suffer lower death rates: The trajectories are approximately parallel after age 60. In contrast, age trajectories of mortality "tend to converge at older ages" in the periods corresponding to the birth dates of the cohorts. As shown in Fig. 1, however, mortality at all ages between 40 and 90 shifted downward by roughly the same amount over the second half of the 20th century.

To understand the relative importance of cohort versus period effects, it is useful to analyze patterns of death rates over age and time. Such studies reveal that period effects have generally been more important than cohort effects (*9*, *10*). In particular, in developed countries, progress in reducing old-age mortality accelerated somewhat around 1950 and accelerated further around 1970, simultaneously at all older ages (*4*).

If the level of infant mortality determined the level of mortality for the elderly in corresponding birth cohorts, then differences in infant death rates between two populations should forecast differences in death rates among the elderly decades later. Figure 2 compares infant and old-age mortality in Italy and Sweden. Like Finch and Crimmins (*1*), we chose age 70 for our analysis. Italian infant mortality reached the Swedish level around 1990, whereas Italian death rates at age 70 fell to Swedish levels four decades earlier. Infant mortality in Italy for people born around 1880 was almost twice the Swedish rate, but 70 years later, death rates at age 70 were almost the same in Italy and Sweden.

Finch and Crimmins, in unpublished work adumbrated in their article and central to their argument (*1*), compare infant mortality 70 years ago with current infant mortality as a way of predicting death rates at age 70. For Sweden, they analyzed cohort data for infants who were born between 1751 and 1927 and who reached age 70 between 1821 and 1997. For comparison, they examined the relationship of infant mortality from 1751 to 1927 to death rates at age 70 in the same years. Alternatively, they could have analyzed infant mortality from 1821 to 1997 versus death rates at age 70 during this period. It is also informative to examine the probability of death among 1-year-olds to determine the late-life impact of early inflammation. Figure 3, A to F, presents the various comparisons, using data available for Sweden up through 2002. Finch and Crimmins claim that there is a much stronger association of death rates at age 70 with infant mortality 70 years earlier than there is with current infant mortality. Our plots show that this claim is an overstatement. Contrary to prediction of the inflammatory hypothesis, the cohort correlation (Fig. 3, B and D) is weakest when the level of infant mortality is highest. In any case, the correlation of death rates at two ages does not demonstrate causal linkage; less simplistic analyses (*4*–*10*) suggest that period effects are more important than cohort effects.

Finch and Crimmins concluded their study with speculation that "future increases in life expectancy from reduced inflammatory causes may be relatively small, particularly in populations that have had low levels of childhood infection for many decades…." Some readers may draw the dubious implication that future increases in life expectancy in developed countries are likely to be slow. Life expectancy has increased over the past two centuries as a result of a successive series of new kinds of mortality reductions. As various acute diseases were conquered, improvements in chronic-disease mortality accelerated. When, around 1950, infant and childhood mortality reached very low levels, death rates among the elderly started to decline (*11*). It is clear that future increases in life expectancy will not largely be due to further reductions in inflammatory causes in childhood. Rather,

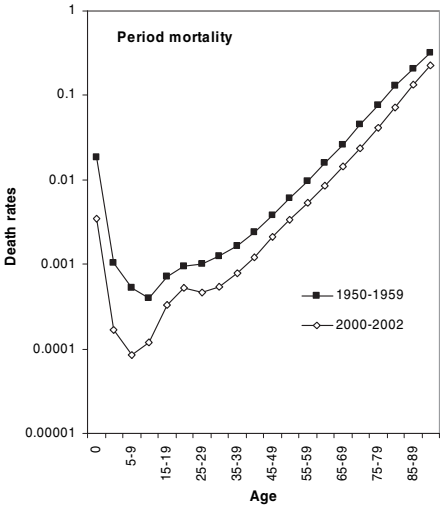

Fig. 1. Age-specific mortality over the life span, Sweden, 1950 to 1959 and 2000 to 2002 (semilogarithmic plots). Data source: Human Mortality Database (www.mortality.org).

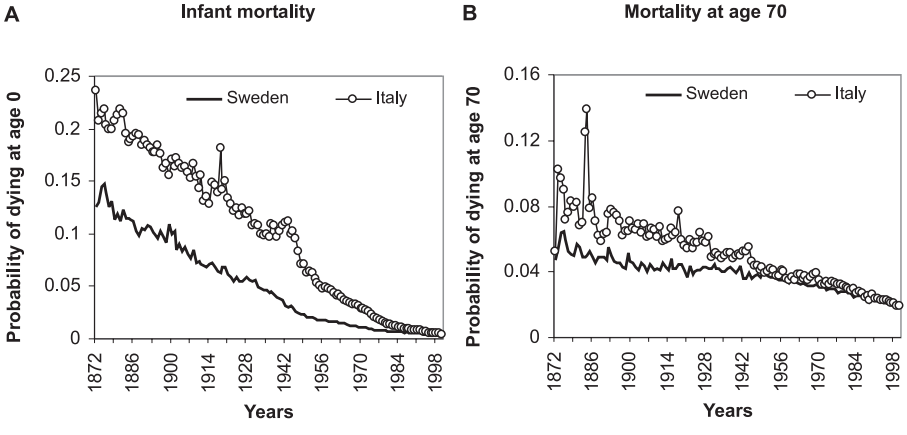

Fig. 2. Infant and old-age mortality in Italy and Sweden, 1872 to 2000. (**A**) Probabilities of dying at age 0. (**B**) Probabilities of dying at age 70. Data source: Human Mortality Database (www.mortality.org).

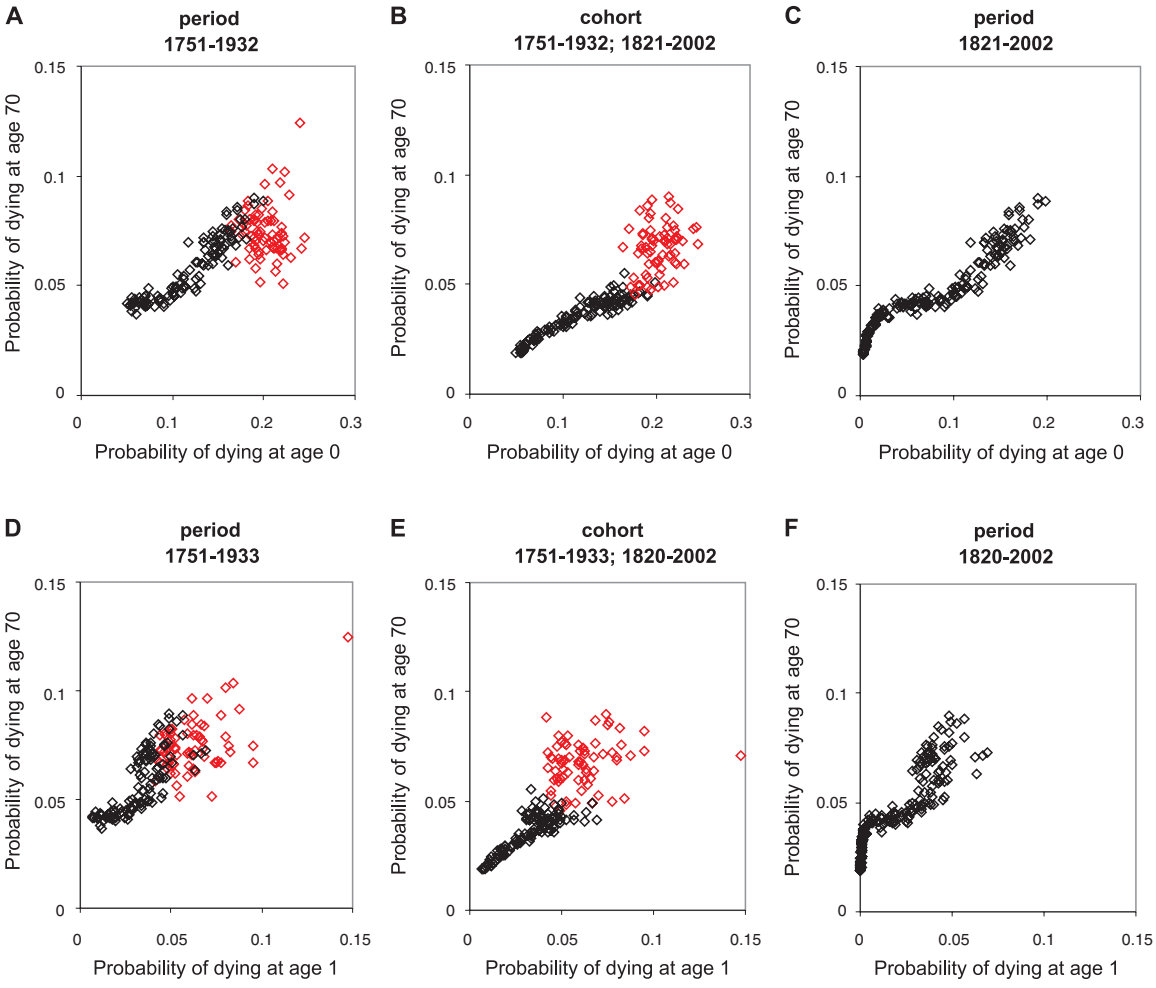

Fig. 3. Scatter plots of probabilities of death at age 70 ($q70$) versus probabilities of death at age 0 ($q0$) or at age 1 ($q1$). The red points pertain to infant mortality in 1820 and earlier. (**A**) $q0$ from 1751 to 1932 versus $q70$ in the same years. (**B**) $q0$ from 1751 to 1932 versus $q70$ between 1821 and 2002. (**C**) $q0$ from 1821 to 2002 versus $q70$ in the same years. (**D**) $q1$ from 1751 to 1933 versus $q70$ in the same years. (**E**) $q1$ from 1751 to 1933 versus $q70$ between 1820 and 2002. (**F**) $q1$ from 1820 to 2002 versus $q70$ in the same years. Data source: Human Mortality Database (www.mortality.org).

improvements will come from advances in fighting diseases that occur at older ages, including cancer, cardiovascular disease, and Alzheimer's disease. Emerging knowledge of genetics will permit individualized interventions. Regeneration and rejuvenation research and nanotechnology may also, in coming decades, help improve health and longevity.

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