

Response to Comment on “Inflammatory Exposure and Historical Changes in Human Life-Spans”

Barbi and Vaupel (1) argue that period effects have generally been more important than cohort effects in contributing to the historical decline in old-age mortality. We

respond by summarizing key points in our initial article and providing data that was mentioned but not discussed in detail (2). Our analysis extends the 70-year literature of young-old cohort mortality associations (3–7) with new historical data interpreted in light of the pathophysiology of inflammation. Our analysis excludes modern birth cohorts, individuals of which have benefited from immunizations and the use of antibiotics.

The historical demography of Sweden offers unique profiles of mortality across the life span, beginning before the industrial revolution when mortality was high from birth into old age. The age-specific mortality trajectories from 1751 to 1940 show that old-age mortality declined in a cohort fashion,

not a period fashion across all ages [see figure 1 in (2)]. These historical cohorts retain a coherent mortality trajectory, which we described as the “cohort morbidity phenotype” (2).

The comment by Barbi and Vaupel (1) incorrectly implies that death rates among the elderly in developed countries declined only after 1950. The life expectancy at age 70 in Sweden was improving by 1850 (Fig. 1). These early improvements are hypothesized to result from better public health and hygiene, which began to reduce infection and inflammation long before modern medicine.

We hypothesize that inflammation associated with vascular disease and cancer [the incidence of which is attenuated by modern drugs with anti-inflammatory activities (2)] is the strongest mechanistic link between early and later cohort mortality. These cohort inflammatory mechanisms are most active when mortality from infections is high. As childhood infection decreases because of immunization, public health advances, and antibiotics, the early inflammatory exposure has much less impact on cohort old-age mortality. Thus, although figure 1 in (1) shows the period effects of age-specific mortality for recent Swedish periods, it cannot identify cohort effects.

Barbi and Vaupel also ignore recognized cohort mortality effects (3–7) and instead argue, based on period mortality changes in Sweden after 1950, that the period explains the change in late-age mortality. However, these recent data are not appropriate for testing our hypothesis. Therefore, we replotted Swedish mortality by period and birth cohorts [figure 3 in (1)] but excluded data after 1879. As shown in Fig. 2, the correlations of early- and old-age mortality are much stronger for cohort than for period. The regression coefficients (R^2) for appropriate historical phases refute their assertion, for which they provided no statistics, that “this claim is an overstatement...the cohort correlation is weakest when the level of infant mortality is highest.”

Moreover, a graph of period and cohort mortality from 1751 to 1889 (Fig. 3) shows that mortality at the young and old ages declined similarly in these cohorts, despite the seven-decade gap in dates. The mortality trends at age 70 in the specified calendar year, or the period mortality trend in old age, does not resemble the trend for the young age group. After an initial rise, mortality declines were first significant in the 1791 cohort at both young and old ages. Period mortality first declined significantly among the old in 1861 to 1870, which is the same cohort wherein the decline was observed. Again, child mortality trends correlate less with old-age mortality

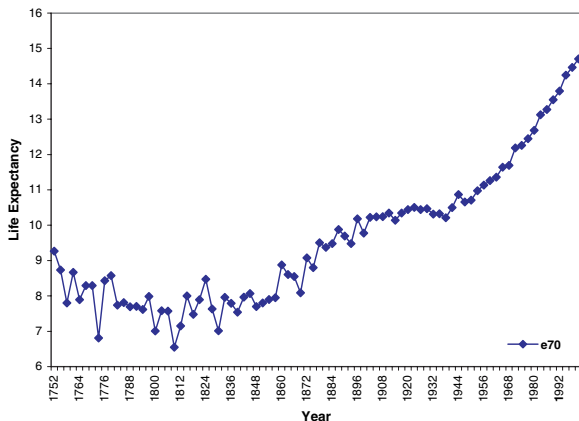


Fig. 1. Life expectancy at age 70 in Sweden (3-year moving average). Data source: Human Mortality Database (www.mortality.org)

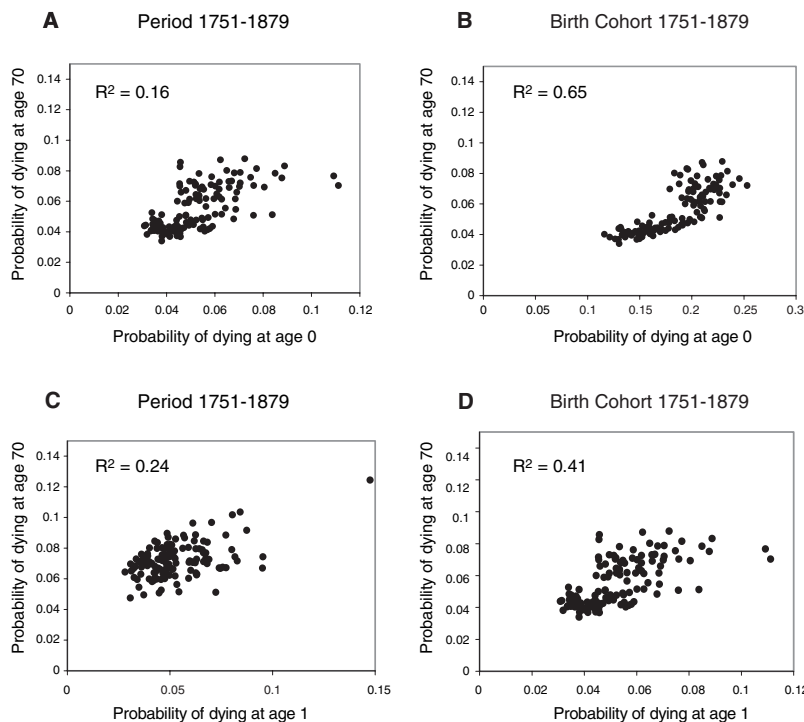


Fig. 2. Scatter plots of probabilities of death at age 70 (q_{70}) versus probabilities of death at age zero (q_0), or at age 1 (q_1). (A) q_0 from 1751 to 1879 versus q_{70} in the same years. (B) q_0 from 1751 to 1879 versus q_{70} for the same cohort 70 years later (1821 to 1949). (C) q_1 from 1751 to 1879 versus q_{70} in the same years. (D) q_1 for birth cohorts 1751 to 1879 versus q_{70} for the same cohorts.

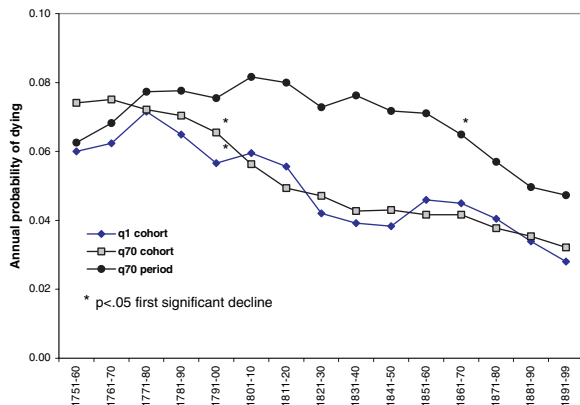


Fig. 3. Child and old-age mortality in Sweden, 1751 to 1899. q1 cohort, probability of dying at age 1 for cohorts born in specified years (10-year average); q70 cohort, probability of dying at age 70 for cohorts born in specified years (10-year average); q70 period, probability of dying at age 70 in a specified calendar year (10-year average). Data source: Human Mortality Database (www.mortality.org). Regressions of annual mortality rate against decade showed that significant decline ($P < 0.05$) from the 1771 to 1780 decade occurred first in the 1791 to 1800 birth cohort at both ages 1 and 70. Period regressions indicated that the first significant decline occurred among those reaching 70 in 1861 to 1870.

trends in the same year (period effect) than with mortality trends seven decades later.

Barbi and Vaupel (1) also cite studies that are not germane to explaining these historical

to fully resolve period and cohort effects. Mortality change in any period can reflect combinations of period and cohort effects, which can shift with local conditions. None-

theless, the present evidence and prior analyses (3–7) clearly document the existence of cohort effects before 1900. Our analysis (2) builds new relationships between biology and demography by identifying pathophysiological explanations for the recognized cohort mortality relationships.

Twin studies indicate that <10% of the longevity variation is attributable to shared health conditions in early life. Because these twins lived mostly in the 20th century and because any twin pair by definition originates from the same cohort, the variance in their mortality is not the same as for a population over time. Factors explaining the variability of longevity at one time may not explain historical time trends, and vice versa. Both genetics and season of birth may cause differences at one time but do not explain historical changes. The comparison of Italy and Sweden [figure 2 in (1)] does not address our hypothesis either, because it uses mortality levels, not trends, it uses only one age group (q_0), and it extends up to 2000.

We agree that it is difficult

theless, the present evidence and prior analyses (3–7) clearly document the existence of cohort effects before 1900. Our analysis (2) builds new relationships between biology and demography by identifying pathophysiological explanations for the recognized cohort mortality relationships.

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References and Notes

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8. Supported by National Institute on Aging grants AG 17265 (E.C.), and AG 05142 and AG 14751 (C.E.F.), and the Ellison Foundation for Medical Research (C.E.F.).

10 February 2005; accepted 16 May 2005
 10.1126/science.1109017