Aging in the Context of Cohort Evolution and Mortality Selection

Hui Zheng
Ohio State University

Support for this project provided by a seed grant from the Institute for Population Research at the Ohio State University which is supported by a grant from the Eunice Kennedy Shriver National Institute for Child Health and Human Development (R24-HD058484)

1. How has aging process changed across cohorts?

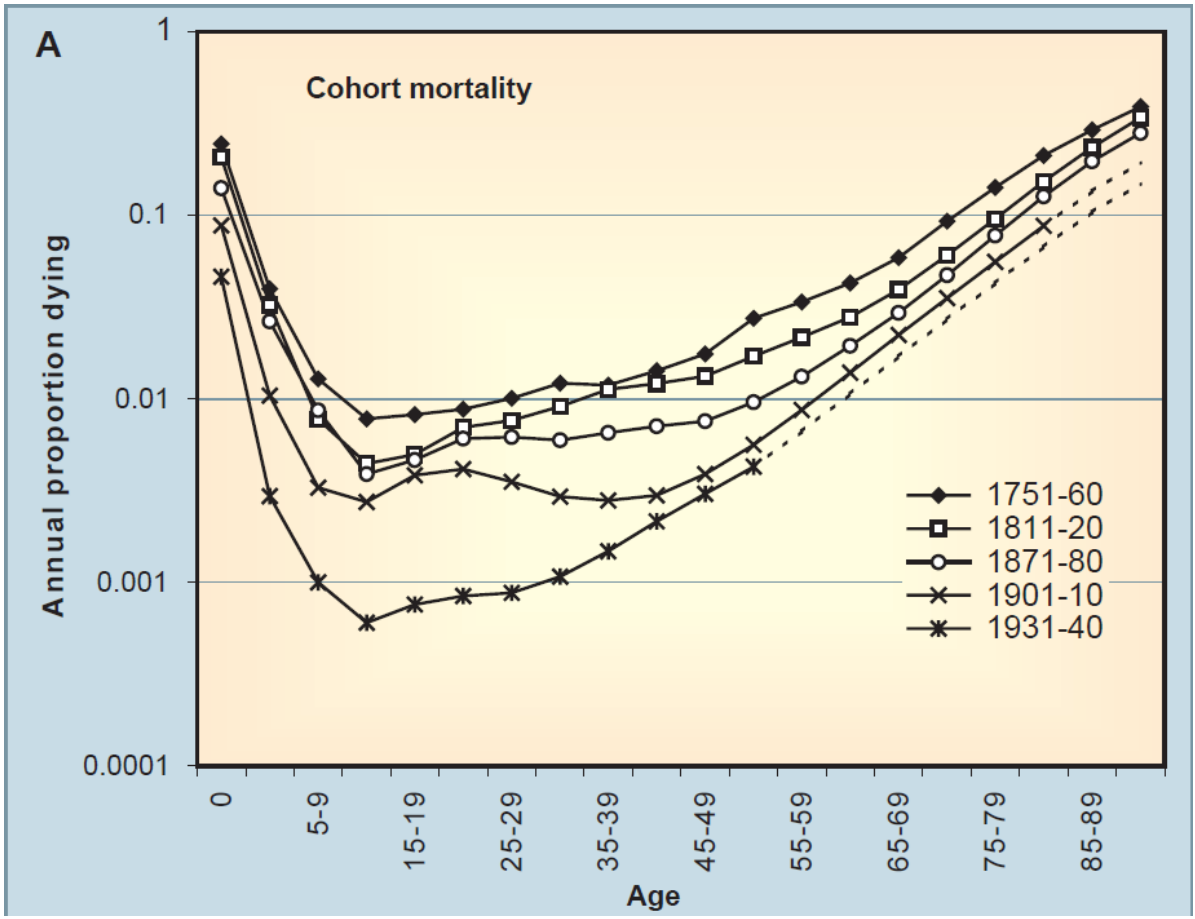
- Rate of demographic aging: the extent of acceleration in mortality rates across ages, measured by the slope of the mortality curve (Gompertz slope), i.e., α in $R_t = R_0 e^{\alpha t}$

- Rate of biological aging: the internal senescence process

- How are these two rates related across cohorts?

2. How has cohort evolution affected the aging process?

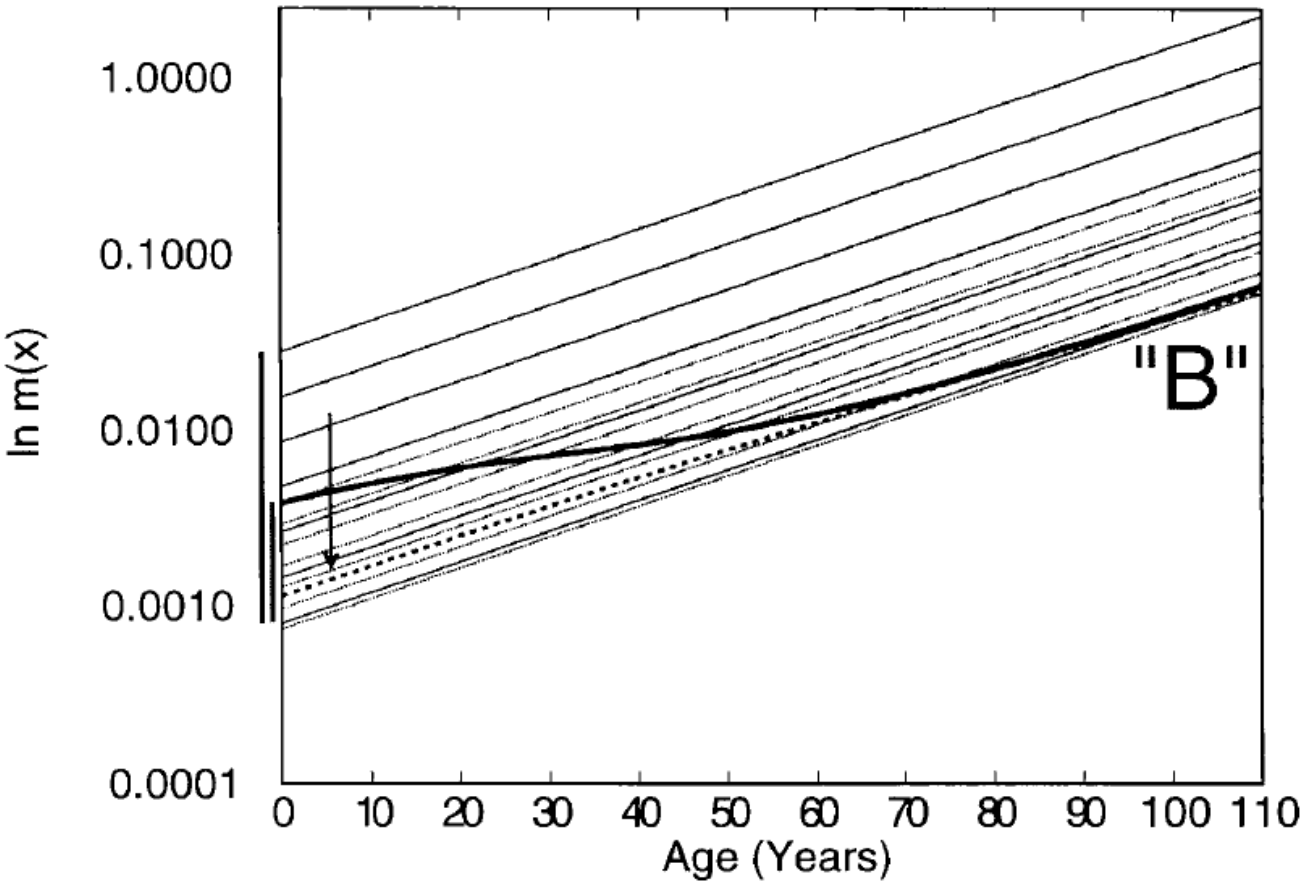
- "Cohort morbidity phenotype" (Finch and Crimmins 2004) and "technophysio evolution theory" (Fogel and Costa 1997) suggest a positive link between young and old-age mortality risk.
- Both predict that later cohorts enjoy better health in old age. **Does that mean that aging slows down in later cohorts?**



Source: Finch and Crimmins (2004), "Inflammatory Exposure and Historical Changes in Human Life-Spans." *Science* 305: 1736-1739.

3. How has mortality selection affected the aging process?

- **<u>The theory of population heterogeneity</u>**: mortality acceleration (i.e., the rate of demographic aging) is **negatively** related to the *variance of the distribution of frailty in the population*.



Source: Yashin et al. (2002), "Individual aging and mortality rate: how are they related?." *Social Biology* 49: 206-217.

- **Strehler and Mildvan (SM) general theory of mortality and aging**: the *initial mortality rate* ln(R_o) and the slope α of the logarithm of the Gompertz mortality curve ($R_t = R_0 e^{\alpha t}$) are **negatively** correlated.

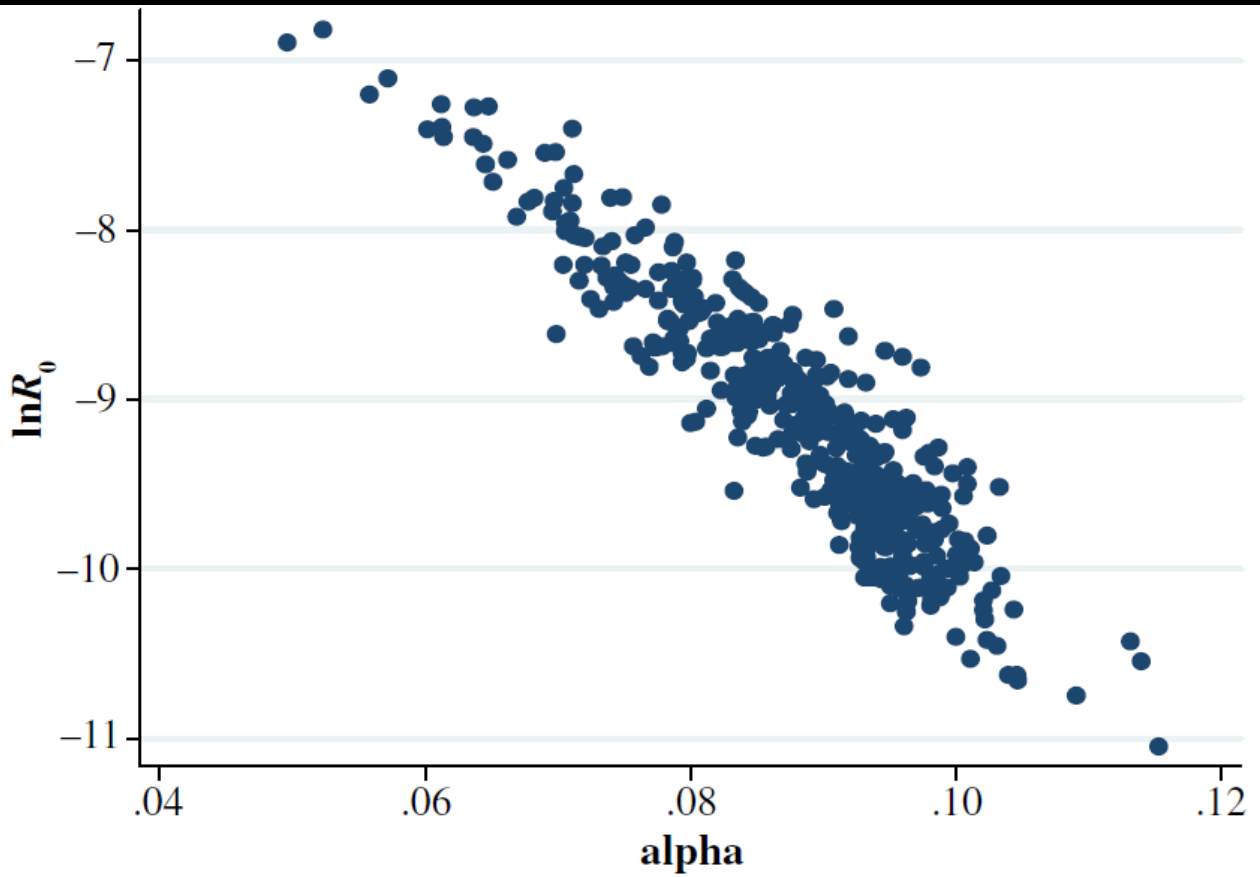


Fig. 2 The inverse relationship between lnR_0 and α for 42 countries, 1955–2003

Source: Zheng et al. (2011), "Heterogeneity in the Strehler-Mildvan General Theory of Mortality and Aging." *Demography* 48: 267-290.

- This negative correlation is expressed as $\ln(R_0) = -\frac{1}{B}\alpha + \ln(K)$, where *B* is the fractional loss each year of original vitality and *K* denotes the total number of challenges per unit time regardless of their magnitudes.

- *B* "appears to be nearly constant regardless of the environment" (Strehler and Mildvan 1960: 16-17)

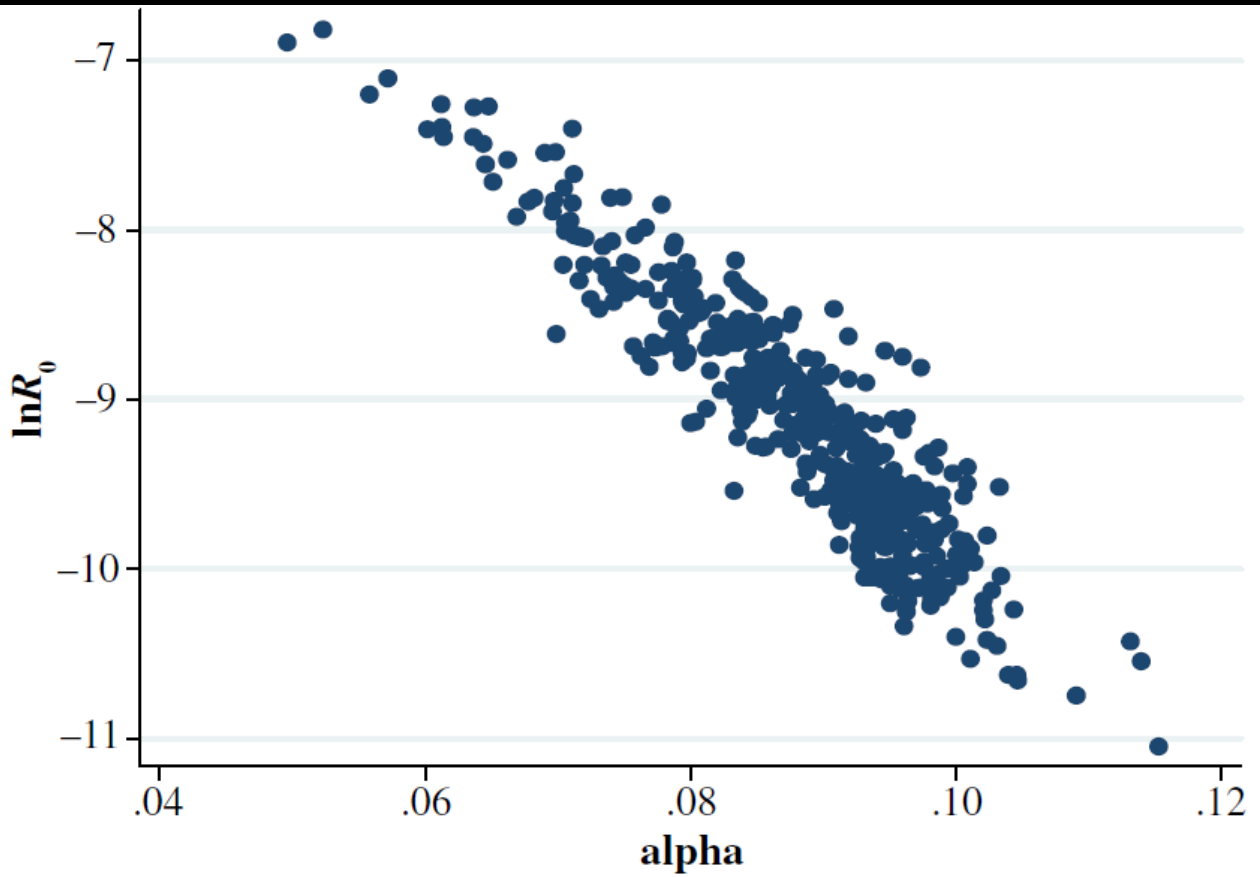


Fig. 2 The inverse relationship between $\ln R_0$ and α for 42 countries, 1955–2003

Source: Zheng et al. (2011), "Heterogeneity in the Strehler-Mildvan General Theory of Mortality and Aging." *Demography* 48: 267-290.

Delayed not decelerated senescence

- Vaupel (2010): "all older humans share a similar, and perhaps essentially the same, rate of increase in mortality with age."
- This insight is consistent with the SM theory's proposition that the rate of decline in the vitality index, denoted as *B*, is fixed.

Source: Vaupel (2010), "Biodemography of Human Aging." *Nature* 464: 536-542.

Data

- Cohort age-specific mortality data from Human mortality database: Sweden, 1751-1915; Netherlands, 1850-1914; Iceland, 1838-1915; France, 1816-1914; England, 1841-1912; Denmark, 1835-1914; and Norway, 1846-1914.

- Restricted the upper end of age to 94.

- Compute rate of demographic aging α between age 70 and 94 from $\ln(R_t) = \ln(R_0) + \alpha t$, where age-specific mortality rates R_t are available in the data.

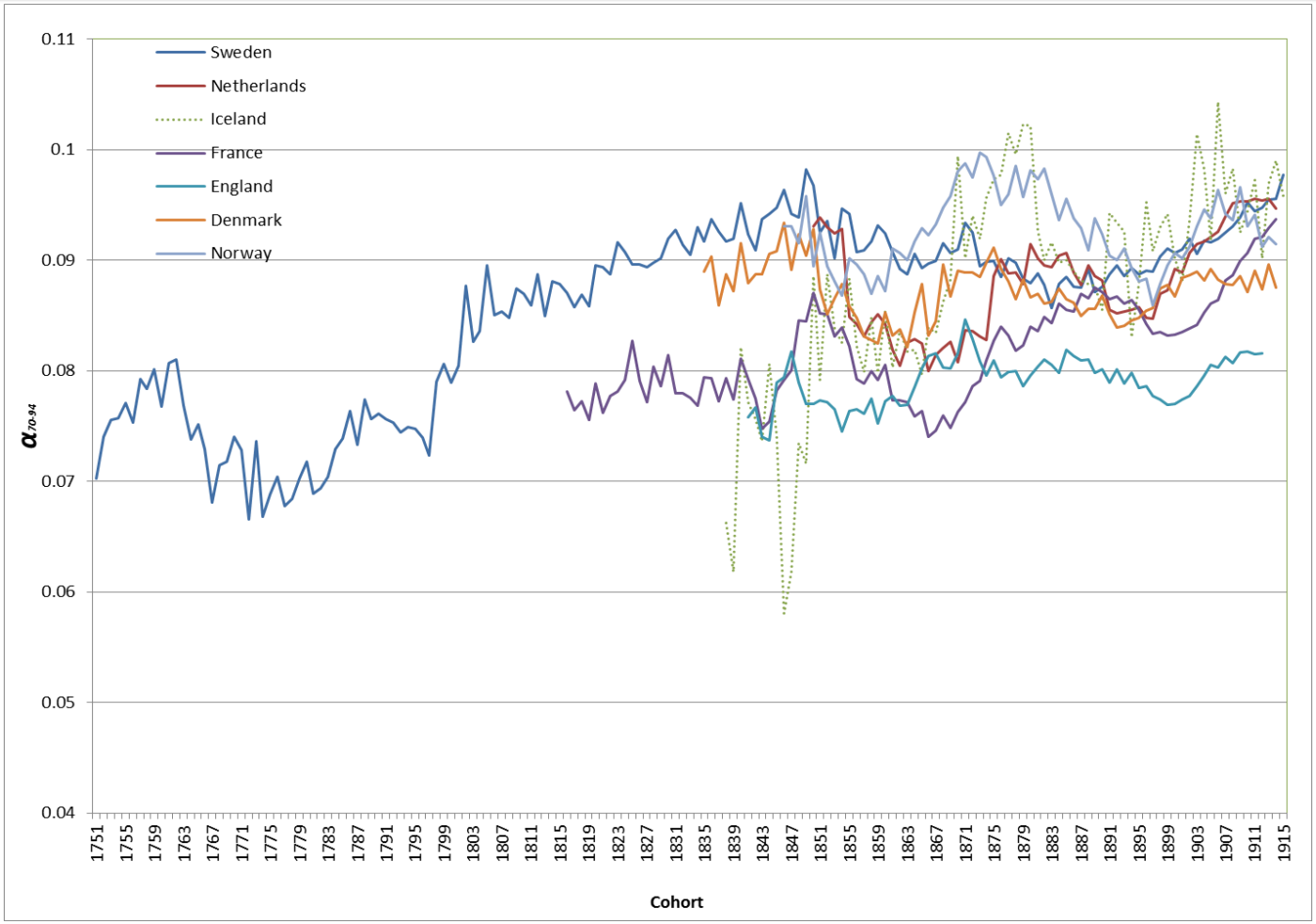
- Calculate rate of biological aging B from age 70 to age 94 using the equation $\ln(R_0) = -\frac{1}{B}\alpha + \ln(K)$ by assigning a value of K (K=1).

- The data used for the analysis are country-cohort panel data, composed of 628 country-cohort cases.

- Each country-cohort case includes measures of age-specific mortality rates from age 0-1 to age 90-94; and the values of the parameters α and B.

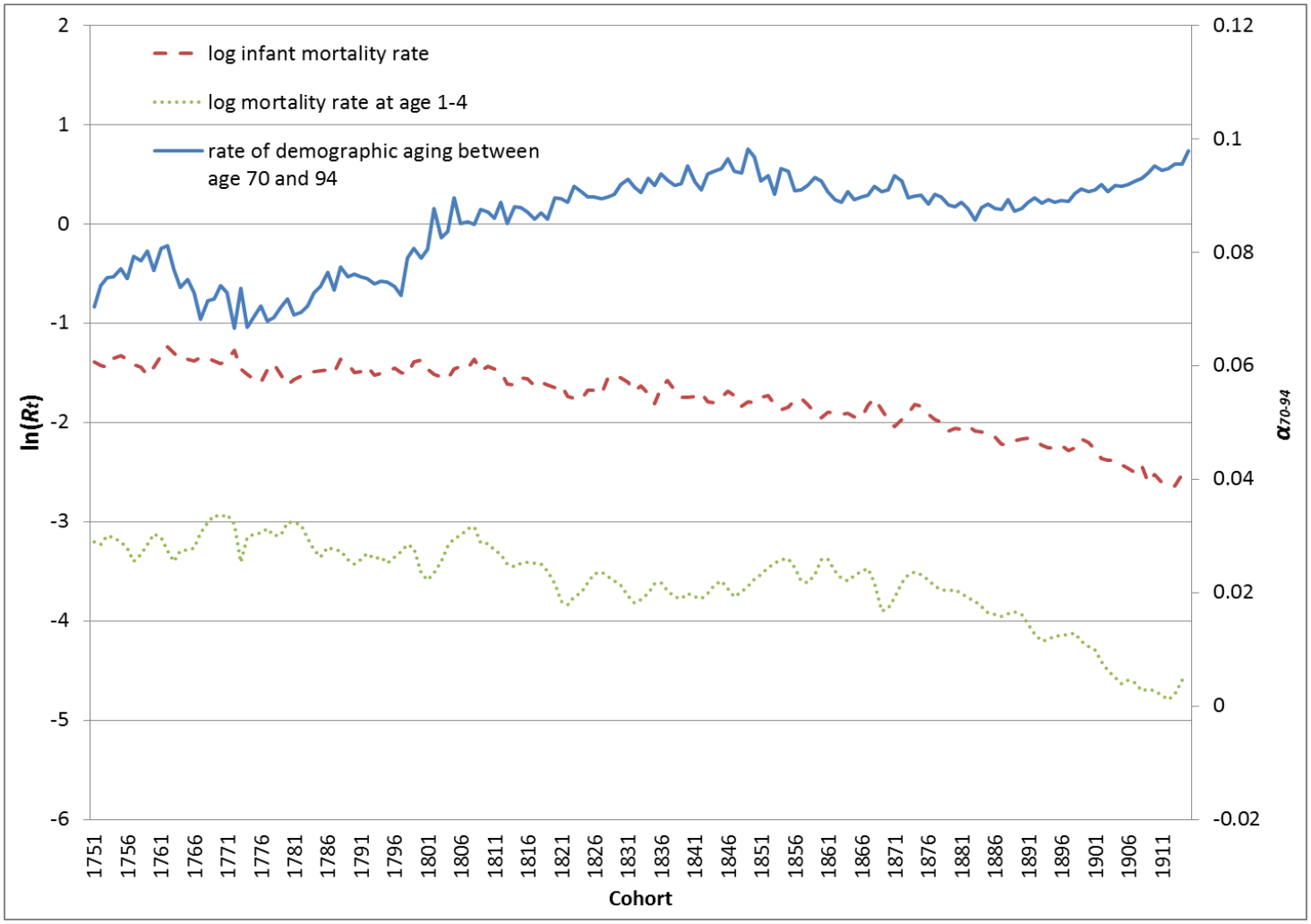
- Using country fixed effects models to eliminate unobserved heterogeneity among countries.

I. The trend in mortality acceleration (rate of demographic aging)



Note: $\alpha_{70\text{-}94}$ represents the rate of demographic aging from age 70 to 94

The trend of rate of demographic aging between age 70 and 94 ($\alpha_{70\text{-}94}$), log infant mortality rate, and log mortality rate at age 1-4 in Sweden across cohorts 1751-1915.

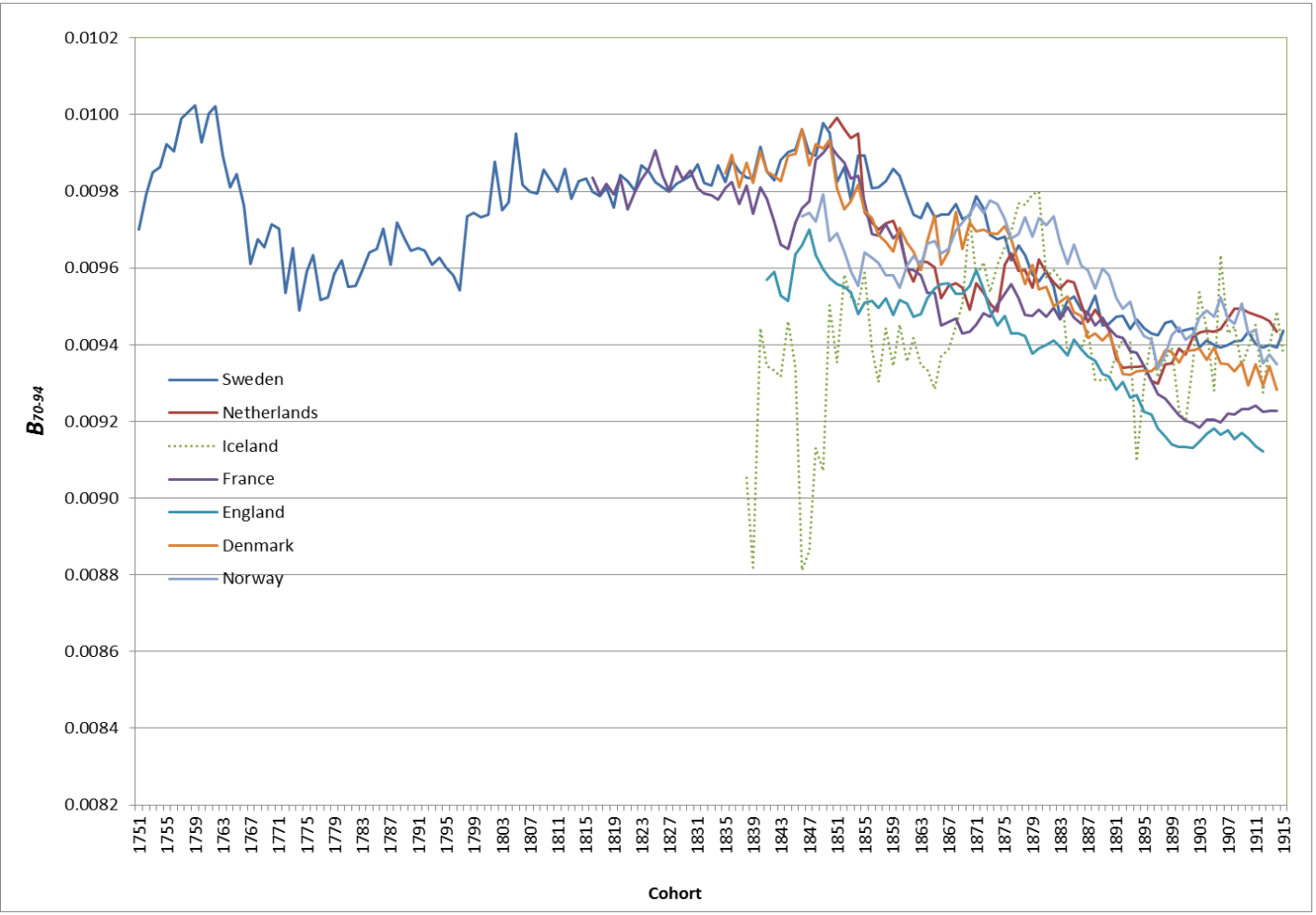


The unstandardized coefficients for regression of rate of demographic aging $\alpha_{70\text{-}94}$ on young age- and late middle age-mortality rates (standard errors in parentheses)

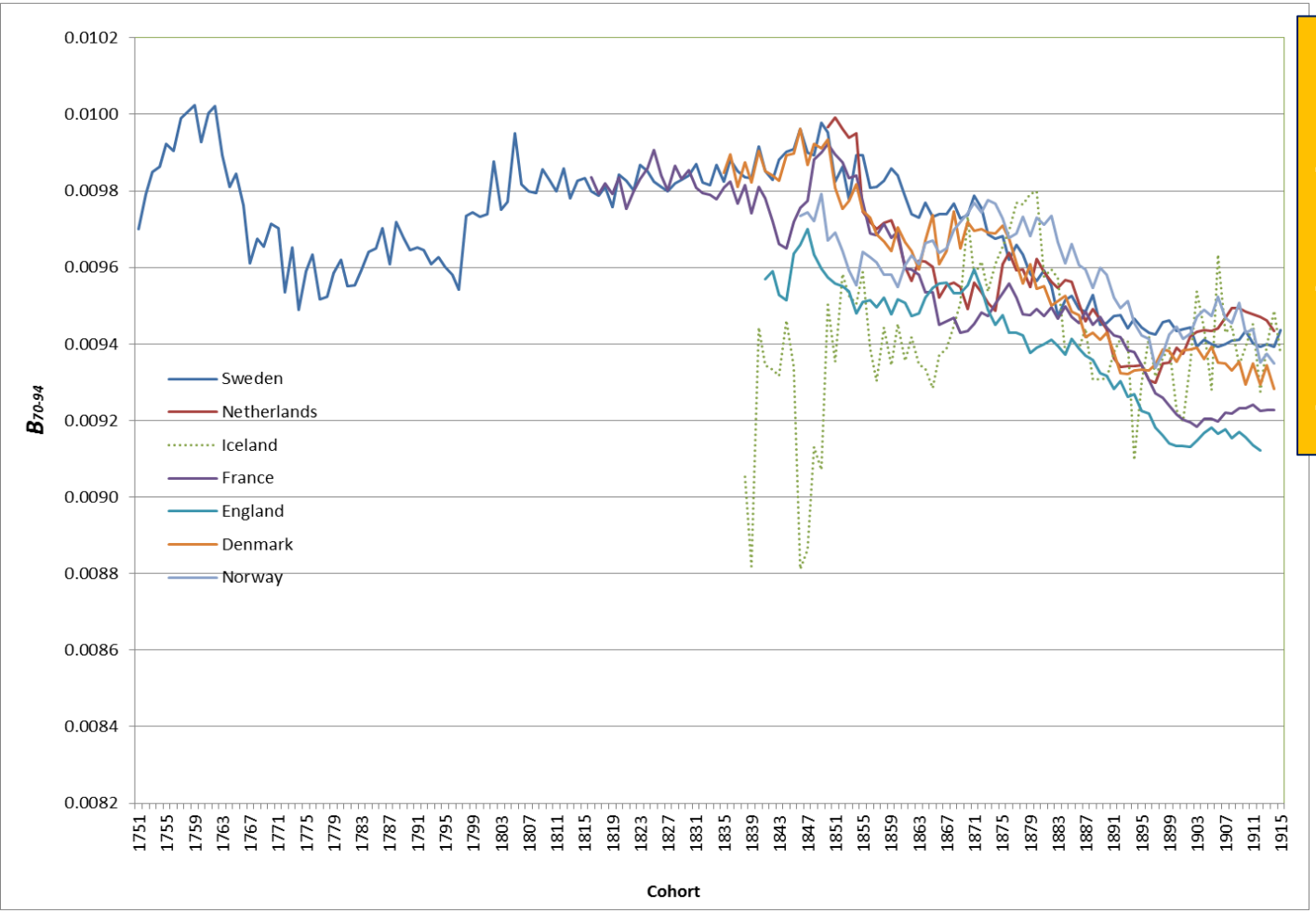
	$\alpha_{70\text{-}94}$	
$\ln(R_{0\text{-}1})$	-.012*** (.001)	
$\ln(R_{1\text{-}4})$	.002 (.001)	
$\ln(R_{5\text{-}9})$	.002 (.001)	
$\ln(R_{10\text{-}14})$	-.005*** (.001)	
$\ln(R_{55\text{-}59})$		.002 (.002)
$\ln(R_{60\text{-}64})$		.002 (.003)
$\ln(R_{65\text{-}69})$		.002 (.003)
$\ln(R_{70\text{-}74})$		-.024*** (.003)
R^2	.28	.56

Although mortality acceleration during late life is affected by mortality selection in early life, it appears to be more directly affected by selection in late life

II. The trend in the rate of biological aging

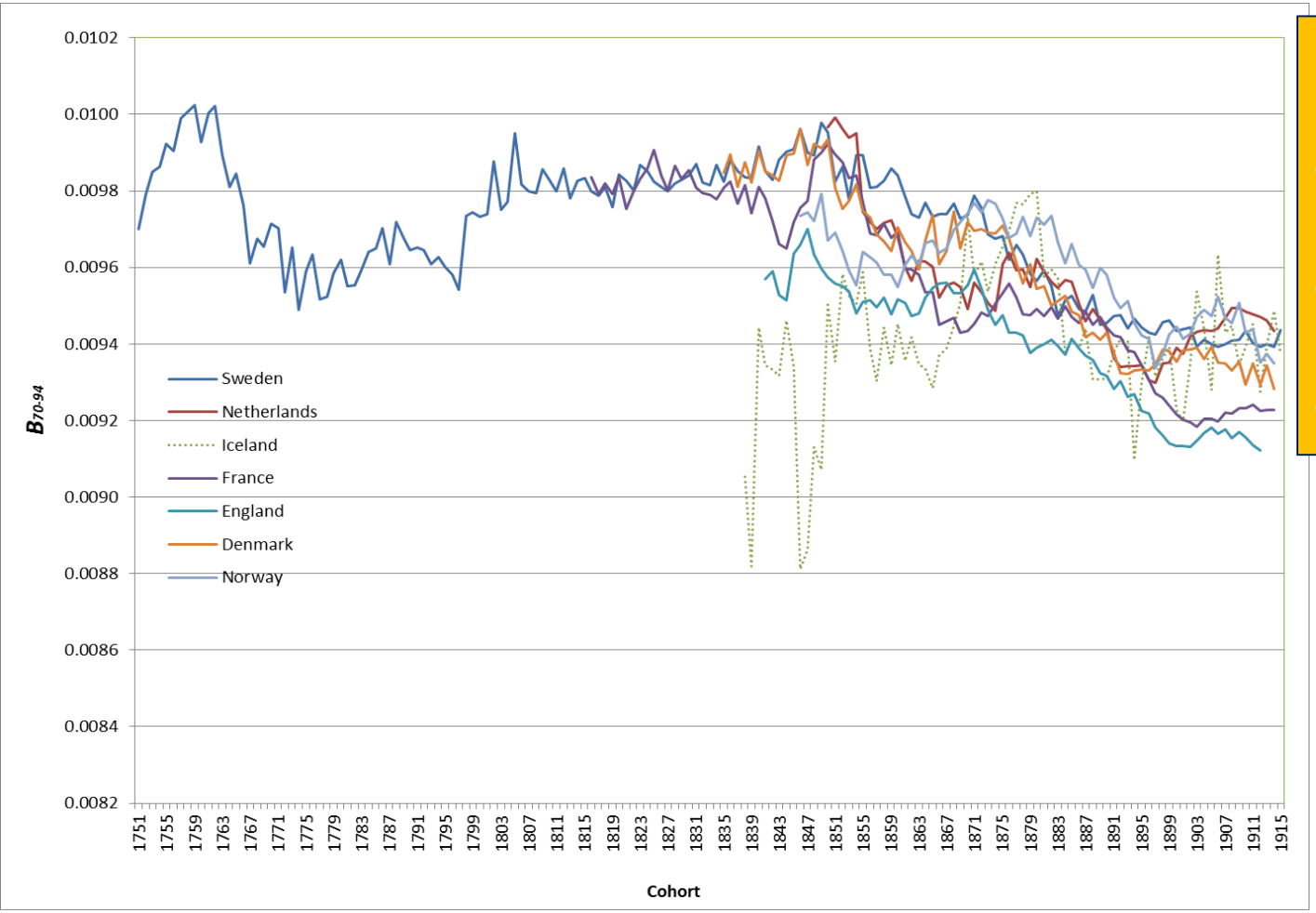


II. The trend in the rate of biological aging



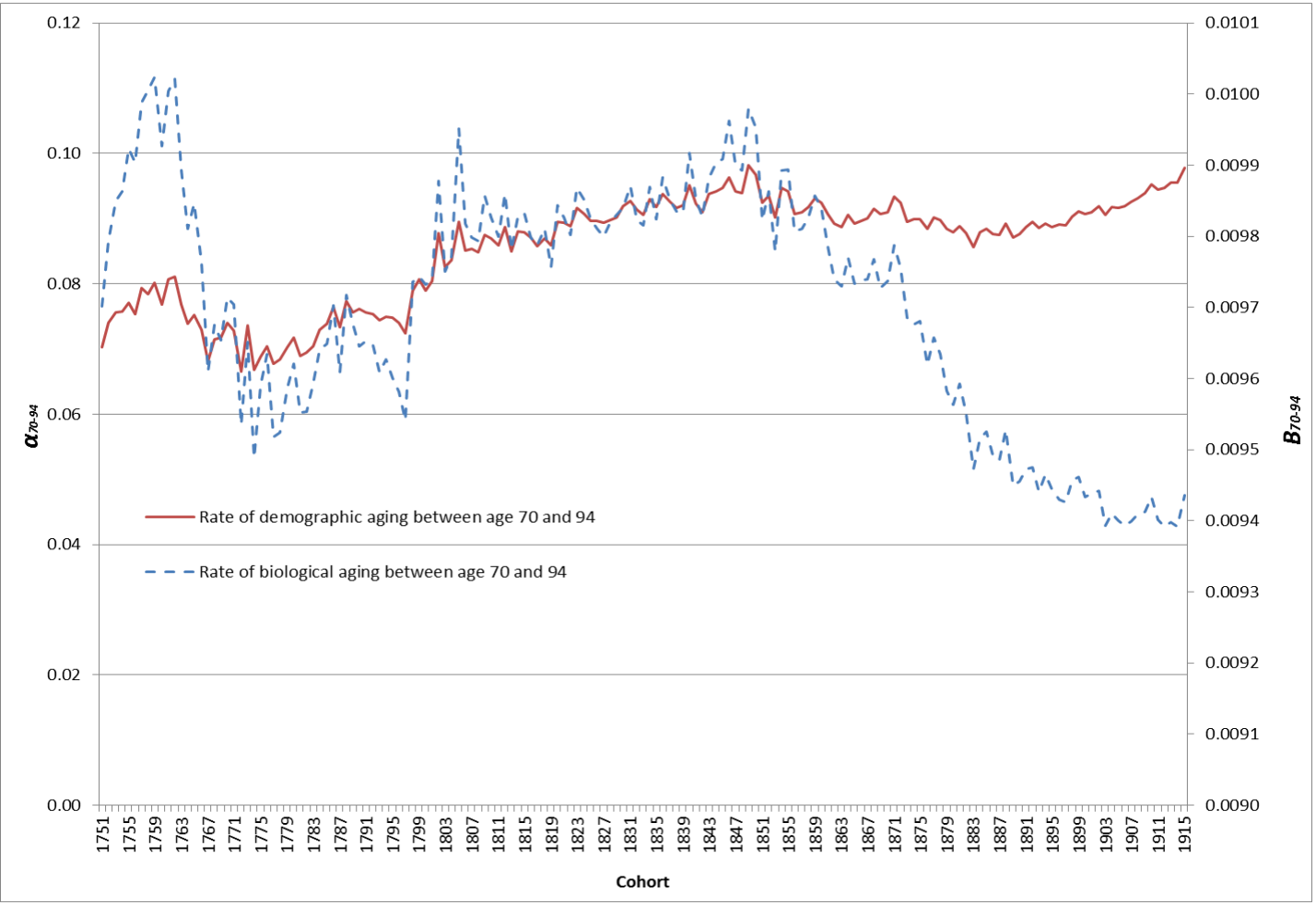
The turning points in the evolution of the rate of biological aging coincide with the stages of epidemiologic transition.

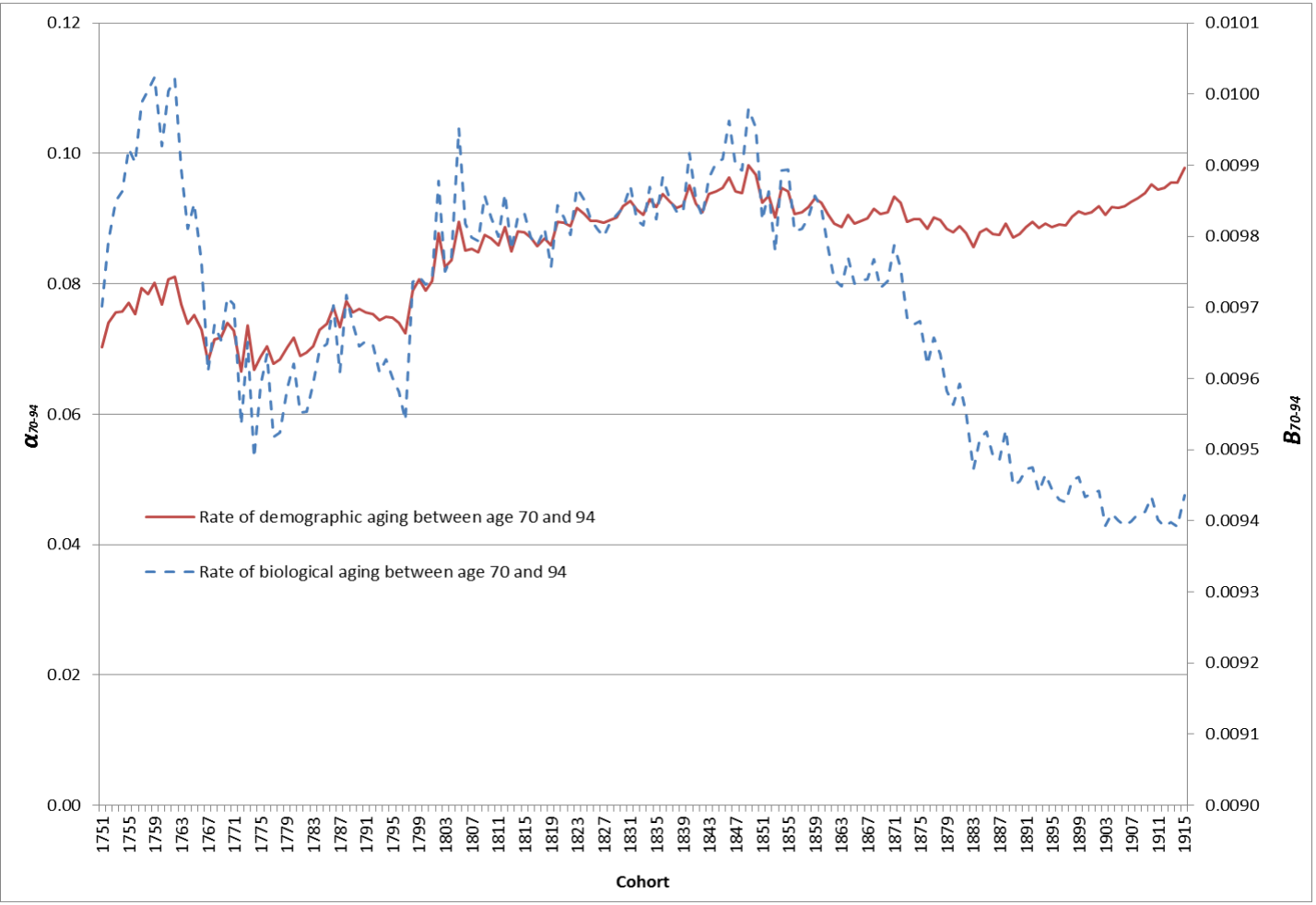
II. The trend in the rate of biological aging



The turning points in the evolution of the rate of biological aging coincide with the stages of epidemiologic transition.

the rate of biological aging is particularly affected by young-age mortality risk


0.12
0.10
0.08
0.06
0.04
0.02
0.00
$\alpha_{70\text{-}94}$
0.0101
0.0100
0.0099
0.0098
0.0097
0.0096
0.0095
0.0094
0.0093
0.0092
0.0091
0.0090
$B_{70\text{-}94}$
Rate of demographic aging between age 70 and 94
Rate of biological aging between age 70 and 94
1751
1755
1759
1763
1767
1771
1775
1779
1783
1787
1791
1795
1799
1803
1807
1811
1815
1819
1823
1827
1831
1835
1839
1843
1847
1851
1855
1859
1863
1867
1871
1875
1879
1883
1887
1891
1895
1899
1903
1907
1911
1915
Cohort



mortality selection does not contribute to the decreasing rate of biological aging

The unstandardized coefficients for regression of rate of biological aging $B_{70\text{-}94}$ on young age- and late middle age-mortality rates (standard errors in parentheses)

	$B_{70\text{-}94}$	
$\ln(R_{0\text{-}1})$	-.0002*** (.0000)	
$\ln(R_{1\text{-}4})$	.0001*** (.0000)	
$\ln(R_{5\text{-}9})$	.0002*** (.0000)	
$\ln(R_{10\text{-}14})$	.0001** (.0000)	
$\ln(R_{55\text{-}59})$		.0001 (.0001)
$\ln(R_{60\text{-}64})$		.0001 (.0001)
$\ln(R_{65\text{-}69})$		.0000 (.0001)
$\ln(R_{70\text{-}74})$		.0001 (.0001)
R^2	.52	.25

The unstandardized coefficients for regression of rate of biological aging $B_{70\text{-}94}$ on young age- and late middle age-mortality rates (standard errors in parentheses)

	$B_{70\text{-}94}$		$\alpha_{70\text{-}94}$	
$\ln(R_{0\text{-}1})$	-.0002*** (.0000)		-.012*** (.001)	
$\ln(R_{1\text{-}4})$	.0001*** (.0000)		.002 (.001)	
$\ln(R_{5\text{-}9})$	.0002*** (.0000)		.002 (.001)	
$\ln(R_{10\text{-}14})$	.0001** (.0000)		-.005*** (.001)	
$\ln(R_{55\text{-}59})$		.0001 (.0001)		.002 (.002)
$\ln(R_{60\text{-}64})$		.0001 (.0001)		.002 (.003)
$\ln(R_{65\text{-}69})$		.0000 (.0001)		.002 (.003)
$\ln(R_{70\text{-}74})$		.0001 (.0001)		-.024*** (.003)
R^2	.52	.25	.28	.56

Summary of findings

- The rate of demographic aging, or mortality acceleration, after age 70 is not fixed.
- Affected by mortality selection in early life, but more directly by mortality selection in late life.
- This causes later cohorts to have higher rate of demographic aging than earlier cohorts.

- The rate of biological aging fluctuated widely until the mid-19th century birth cohort, declined significantly, then stabilized since the early 20th century cohort.
- The turning points in the evolution of the biological aging rate are consistent with the stages of the epidemiologic transition.
- The rate of biological aging is not affected by mortality selection, but by cross-cohort changes in young-age mortality rates.
- This causes lower rates of biological aging in old age among later cohorts.

Implications

1) The rate of demographic aging, or the mortality acceleration parameter α, might be used to approximate the rate of biological aging when young-age mortality rates are very high (e.g., due to pervasive epidemics).

- But this approximation would be misleading for cohorts born in developed countries after the mid-19th century.

2) The deceleration of biological aging at the individual level provides a micro-level mechanism that explains the positive correlation between young- and old-age mortality rates across cohorts.

- enriches cohort evolution theories.

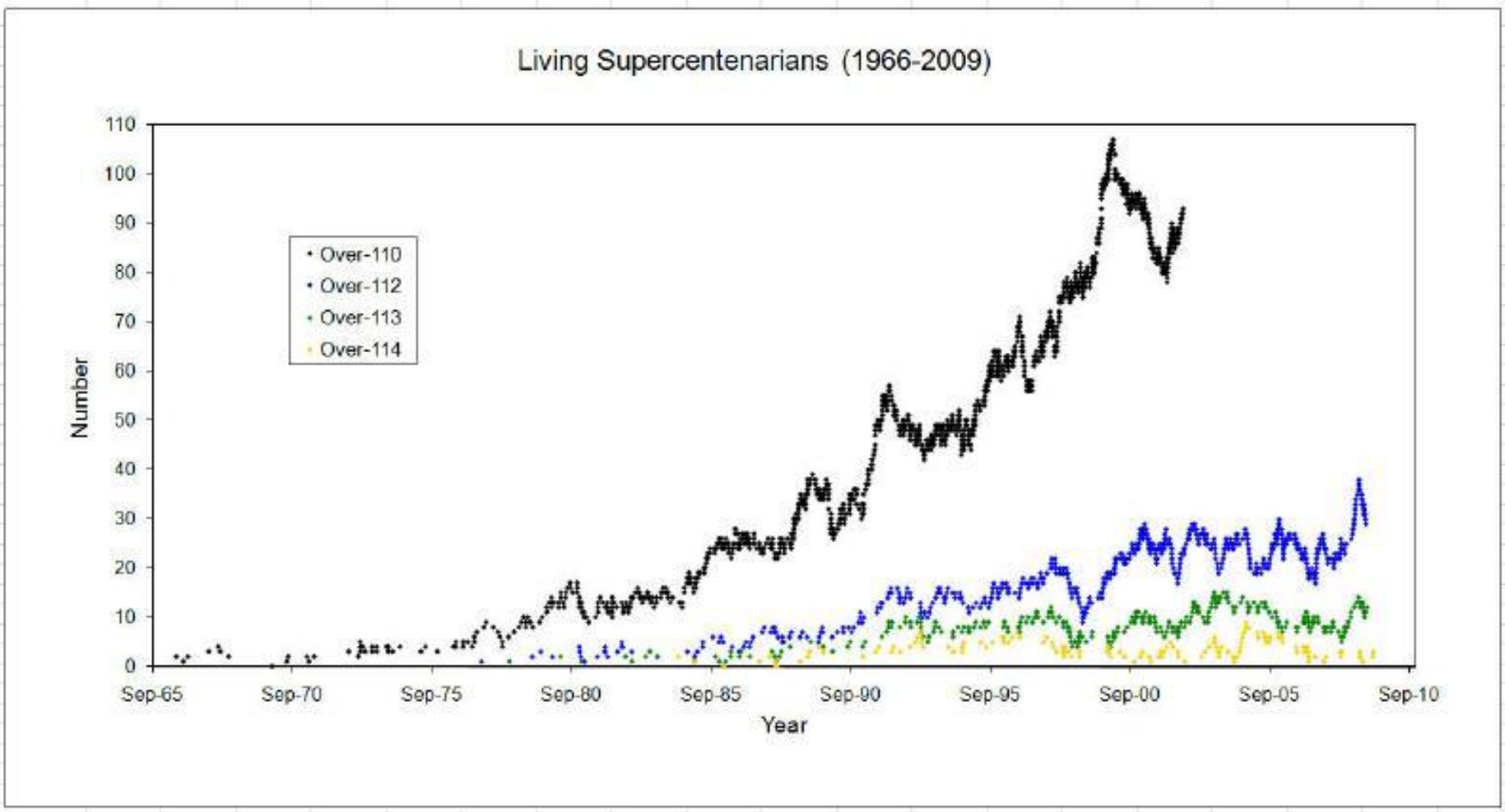
3) The rate of biological aging has not always been fixed.

- Previous studies that claimed a fixed senescence process were based on period data collected since the mid-20th century (Vaupel 2010; Strehler and Mildvan 1960).

4) Strehler and Mildvan's (1960) model states that the maximum human life span is given by the inverse of *B* (i.e., 1/*B*). My analysis suggests age 114-115 may be the limit.

- SM model is deterministic, so in empirical applications, there will be stochastic variability around this expected value.

- The expected maximum human life span for the population does not imply that all individuals must expire no later than that age (Zheng et al. 2011).



Data from Afrim Alimeti and Louis Epstein, September 9, 2009

Right now, there are about 500,000 living centenarians in the world and this number increases by 7% every year, but the number of super-centenarians over age 115 does not change.

Jeanne Calment, 122, died in 1997

Misao Okawa, 115, alive

Discussion

- What mechanisms link a cohort's mortality risk at young ages to its rate of biological aging?

- It is unclear whether the declining rate of biological aging should be attributed to reductions in infection and inflammation during early childhood, or improved nutrition in utero, during infancy or in early childhood.

- Stabilized rate of biological aging since the early 20th birth cohort despite continual declining young-age mortality rate suggests these two are no longer linked.
  - Consistent with cohort morbidity phenotype theory, suggesting reductions in infection and inflammation may be the main mechanism.
    - Having fewer infections at a young age reduces and delays the development of atherosclerotic and thrombotic conditions by reducing the lifetime inflammatory burden
    - Biological mechanism is more complicated.
      - antagonistic pleiotropy theory (Williams 1957)
      - mutation accumulation theory (Medawar 1952)

- Improved nutrition and living standards during early childhood may be also very important
  - improved nutrition can strengthen resistance to infection
  - weaken antagonistic pleiotropy and the accumulation of detrimental mutations
  - increase the resources available for the repair and maintenance of the body (disposable soma theory, Kirkwood 1977)

  - The reason why the rate of biological aging stabilized despite continual improvements in living standards during the 20th century may be because this rate has reached its minimum.

Limitations

- Data quality?
- Other measures of rate of biological aging? Biomarkers of aging?

Future?

- At this time, it is still unknown whether the stabilization of biological aging is due to diminished infections at young ages, or due to the rate of biological aging reaching a minimum.
- Future research should investigate the mechanisms linking young-age mortality risk to the rate of biological aging,
- and ascertain whether stabilization in the rate of biological aging for cohorts born in the early 20th century represents a culminating or transitory stage.