
Romola Davenport
Oxford Institute of Ageing
(Institute of Human Sciences, Oxford)
The Inflammatory Hypothesis

• Exposure to infections (estimated from mortality) in childhood increases risk of chronic disease mortality (esp. heart disease and stroke) in adulthood ( Finch & Crimmins, Science, 2004)

• Later modified to exclude cohorts born after ca. 1900, who experienced major improvements in late adult health due to period improvements in treatment (Crimmins & Finch, PNAS, 2006)
Sweden, 1751-1899

France, 1806-1899

England & Wales, 1841-1907

Cohort mortality 0-14 was strongly associated with cohort late adult mortality (70-74), but association was weak or negative for youngest ages.

<table>
<thead>
<tr>
<th>England (1841–1899)</th>
<th>Coefficient</th>
<th>Standard Error</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.19</td>
<td>(0.02)***</td>
</tr>
<tr>
<td>$q_{(0-1)}$</td>
<td>$-0.31$</td>
<td>(0.14)*</td>
</tr>
<tr>
<td>$q_{(1-4)}$</td>
<td>0.02</td>
<td>(0.13)</td>
</tr>
<tr>
<td>$q_{(5-9)}$</td>
<td>1.72</td>
<td>(0.58)*</td>
</tr>
<tr>
<td>$q_{(10-14)}$</td>
<td>3.14</td>
<td>(0.95)*</td>
</tr>
<tr>
<td>$N = 58$</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$R^2 = 0.96$

Proportion of variance explained by model

Mortality of infants and one year olds differed from older children in England & Wales

- Infant mortality did not improve until ca. 1900
- Mortality at ages 1-14 improved from ca. 1860
- Rate of improvement was ~constant, and same for ages 2-14
- Mortality improvement was half as fast in one year olds as older ages
Cohort childhood (0-14) highly correlated ($r^2=0.911$, $P<0.001$) with adult (70-74) cohort mortality.

But the timing of initiation of decline is earlier for adult mortality, and there is no hiatus 1880-1900. And adult mortality decline in C20th is paralleled by simultaneous decline in period child mortality.
Test the inflammatory hypothesis using cause-specific mortality data for England and Wales

Null hypothesis:

The inflammatory hypothesis is correct:

- Childhood infectious disease mortality is more highly correlated with cohort adult mortality than is all-cause or other non-infectious mortality in childhood.
- Adult mortality from ‘chronic’ diseases is more highly associated with cohort childhood mortality than is other mortality in adulthood.
- Timing of initiation of mortality decline is similar for adult and child mortality by cohort
Cause-specific mortality data were reported annually for England & Wales from 1848, by age and sex.

- 1901-2003 - ONS
- 1848-1900 - made machine-readable with BA grant

Advantages of national annual dataset:
- Annual data by age - can construct cohorts
- Migration relatively low - can construct stable cohorts
- Can calculate sex ratios for cause specific mortality
- Can calculate annual rates by age, and analyse annual fluctuations
- Can follow individual causes, and construct consistent major categories spanning coding changes
**Cause-specific mortality data are least reliable for infants and oldest adults**

- **Cohort childhood mortality 0-14** - need to allocate ill-defined infant deaths
- **Cohort adult mortality 40-69**
- **Females, to avoid effects of WWI etc**

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**Cohort $5q_x$ regressed against cohort $15q_0$**

- **Slope**
- **$r^2$ value**
Infectious disease mortality (period):

- Is highest in infants, but only 30% of deaths
- Is ca. 70% of deaths in children 2-14, and declines, i.e. is a major contributor to mortality decline for most of period 1860-1910

*Childhood infectious diseases, tuberculosis, smallpox, skin diseases; NOT respiratory, except pulmonary TB (phthisis)*
Mortality of infants and one year olds follows same pattern as older children for most infectious diseases.
Infants differ from older children in lack of improvement in diarrhoeal mortality - the main reason why the infant infectious disease rate did not decline.

Mortality from diarrhoeal diseases was very high in infants and one year olds and did not decline as it did for older ages.
If diarrhoeal deaths are excluded, then infectious disease rates decline for all ages from at least 1870.

Infectious disease mortality, excluding Diarrhoea, Dysentery & Gastroenteritis.
Excluding diarrhoeal deaths improves the fit after 1880, but does not change the timing of initiation of improvement in childhood mortality.
Test whether chronic disease mortality in adulthood fits predictions of hypothesis better than all-cause mortality.

Cohort probability of dying aged 40-69 by cause, 1850-1896

Circulatory diseases are a major component of female mortality and decline by birth cohort for cohorts born 1850-1896.
Does mortality from circulatory diseases show greater association with childhood mortality than other causes in adulthood? (NO)

circulatory 40-69 vs childhood all cause

![Graph showing the probability of dying at ages 40-69 vs cohort year of birth with an $r^2=0.852$.]

all-cause 40-69 vs childhood all cause

![Graph showing the probability of dying at ages 40-69 vs cohort year of birth with an $r^2=0.922$.]

circulatory 40-69 vs childhood infectious

![Graph showing the probability of dying at ages 40-69 vs cohort year of birth with an $r^2=0.917$.]

all-cause 40-69 vs childhood infectious

![Graph showing the probability of dying at ages 40-69 vs cohort year of birth with an $r^2=0.953$.]
Conclusions

- Although all-cause cohort childhood and adult mortality appear highly correlated, they differ in the timing of initiation of mortality decline.
- Using childhood infectious disease mortality improves fits slightly but not timing.
- Using adult chronic disease mortality does not improve fits relative to all-cause mortality.
- Neither all-cause mortality nor cause-specific mortality data support the hypothesis of a causal relationship between childhood mortality and adult chronic disease mortality.
Acknowledgements

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