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LETTER

Early Childhood Conditions and Old-Age Mortality

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Abstract:

Background:

Early life conditions might determine adult mortality. The literature, however, both support and contradict this proposition. In most studies, the outcome has been the mortality rates in a given period of time. These rates represent the combined result of both previous and current exposures. Therefore, it is more apt to study the rate of improvement as an outcome, rather than mortality rates in a given period of time.

Objective:

The effects of early-life conditions, assessed as mortality rates at ages 0 and 1-4, and the effects of indicators of available resources in adult life were analysed.

Methods:

The outcomes were the decrease in the national rates of mortality in three age groups, aged 24-34, 35-54 and 55-74, in 18 OECD countries over the years 1990-2010. The effects were analysed in linear multiple regression models using least squares, controlling for country-specific historical constants, which represent the mortality rates in 1990.

Results:

Among the 24-34 and 35-54 year-olds, neither early-life indicators nor resource indicators significantly affected the regression equations. Among the 55-74 year-olds, however, in the model including the mortality rate at age 0 in 1940-49, the explanatory value of the equation in question increased from 65 to 79%, and the effect of mortality rate at age 0 was statistically significant.

Conclusion:

Significant effects of early-life conditions on the rate of decrease in mortality were found, but only in the oldest age group. This finding is consistent with Gavrilov's reliability theory of aging.

Key Points

• Mortality rates have decreased almost linearly in recent decades in OECD countries.

• Most of the variation between countries seemed to be determined by past history and the catch-up of nations that have previously lagged behind.

• A significant effect of early-life conditions on the rate of decrease in mortality was found, but only in the 55-74 year-olds, not in the 24-34 and 35-54 year-olds.

Keywords: Childhood, Aging, Mortality rate, Cross-national study, Time trend, OECD countries.

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1. INTRODUCTION

Since the mid-19th century, the mortality rates have decreased in most countries. The decrease has continued, even in present high-income countries. Although health status varies between nations, health levels tend to converge over time with the catch-up of nations that have lagged behind [1, 2]. The reasons for the continuing decrease in mortality have not been well understood [3], although it has been ascribed, for example, to improved living conditions, improved medical care, and innovations in general [4]. The challenge involved in discerning specific explanations is partly due to the simultaneous change over time of potential determinants: increases in GDP, spending on health care, quality of health care, social spending, *etc.* Thus, our current understanding of general determinants is not sufficient for the devising of health policies.

Ouellette *et al*. suggested that a dominant force behind mortality trends in high-income countries during the latter part of the 20th century has improved health conditions during early life [5]. Beltran-Sancheza *et al.* stated that, in cohorts born in the 19th and early 20th centuries in Europe, 78% of the variation in mortality due to aging was explained by early-life mortality [6]. Finch *et al*. considered improvements in early-life conditions to be a major cause of the current decrease in old-age mortality [7].

There is a substantial literature supporting the proposition that early-life conditions affect adult health and mortality [8]. As early as in 1934, Kermack *et al*. stated that adult mortality in historical cohorts in England and Sweden seems to have been affected by early-life conditions [9]. Van den Berg found significant effects on old-age mortality of exposure to famines during the early years in Europe in the 20th century [10]. Yet, a number of authors have not found any effects of early-life conditions on adult mortality. For example, Gagnon *et al*. did not find any effect on old-age mortality of early-life conditions in Canadian cohorts born in the 17th and 18th centuries [11]. Hayward *et al.* presented similar findings in Finnish cohorts born in the 18th and 19th centuries [12]. Vaiserman [13] refers to studies of the Dutch famine of 1944–1945, the Ukrainian famine of 1932–1933, the Finnish famine of 1866–1868 and the Chinese famine of 1959–1961, all of which failed to find any effects of early-life famine on mortality later in life. Thus, the impact of early-life conditions on later-life mortality is far from being agreed upon.

The conflicting findings might partly be due to the design of the studies. In cohort studies, the outcome is partly dependent on the quality of confounder control. Thus, we should look at studies with comprehensive control of confounders. Among such studies, Elo *et al.* found that early-life conditions influence later health mainly through compromised adult socioeconomic attainment [14]. Ploubidis *et al.* found that current socioeconomic position was the dominant effect on later-life physical health in participants under 65 [15], and Myrskyla *et al*. found that the effect of advanced parental age was mainly explained by adult social factors [16].

Natural experiments may be better than cohort studies at establishing a causal relationship. Yet, such a relationship was not found in the famine studies referred to above. One research group has, however, shown effects of economic recessions during early childhood on mortality above 60 years of age [17, 18].

1.1. Mechanisms

Several mechanisms that may mediate the effect of early-life conditions on adult mortality have been considered [8]. Some authors emphasize early-life infections [7, 19, 20], while others highlight nutritional deprivation [13, 21]. Another mechanism might be selection. Individuals who have survived harsh conditions during their early years may be more robust, which, at adult ages, may give rise to lower mortality [22]. Yet, no systematic study of this mechanism in human populations has been presented.

The biological mechanisms underlying links between malnutrition during early life and adult health status may involve persistent epigenetic changes [23]. Yet, early-life exposures typically produce relatively small effects on DNA methylation [23a]. An additional mechanism may be telomere shortening, which accelerates cellular senescence [24].

1.2. The Gompertz–Makeham Law of Mortality

It seems to be hard to identify a specific mechanism for early-life effects on adult mortality. Accordingly, it seems reasonable to approach the question in various ways. A starting point may be the varying rates of mortality improvements in different age groups. In high-income countries, mortality improvements have been most noticeable in the youngest and oldest age groups. In OECD countries during the period 1990-2010, mortality rates decreased annually at ages 0, 1-4, 5-14, 15-24, 25-34, 35-54 and 55-74 years by 2.8, 2.7, 2.5, 2.0, 2.0, 1.4 and 2.0%, respectively [2, 25].

There is no apparent reason for the faster decrease at old age than at middle age, which may be a mere coincidence. Yet, it makes sense in light of Gavrilov's reliability theory of aging [26].

Gavrilov's theory takes its point of departure in the classical Gompertz–Makeham law of mortality, which states that the human mortality rate is the sum of an age-independent component (the Makeham component) and an age-dependent component that increases exponentially with age (the Gompertz component) [27]. Gavrilov thinks that the exponential increase in mortality by age (the Makeham component) is the result of stochastic processes, with an accumulation of errors in different organ systems. When a critical number of errors have occurred in an organ system that is essential for survival, the individual will die. Accordingly, the initial level of redundancy in different organ systems will affect the age at which a critical number of errors have occurred and the individual dies.

Improvements to the two Gompertz–Makeham components may be expected to have different effects in separate age groups. In young and middle-aged individuals, the effects of the age-independent component (the Makeham component) will dominate, while the effects of the age-dependent component (the Gompertz component) will dominate in old age. This expectation was confirmed in a decomposition study of mortality in high-income countries during the previous century [28].

The age-dependent component (the Gompertz component) will be affected by initial organ redundancy, but this is not the case for the age-independent component (the Makeham component). Thus, the decrease of mortality among individuals aged 55-74 years may be partly affected by the level of initial redundancy, which is not the case for individuals aged 35-54 and below [29].

This view is supported by the findings of Ploubidis *et al.* [15]. In a cohort study of the effects of social conditions on adult physical health, they found that current socioeconomic position dominated the effect in participants under 65, while early-life conditions had a prominent effect at ages 75 and above. Further, Richards *et al.* analysed the effect of year of birth in the UK during the period 1915-1950 [30]. Cohorts born during specific periods, *e.g.,* around 1931, exhibited lower adult mortality. This effect was most noticeable in old age.

1.3. The Present Study

Although previous studies have presented conflicting results, there are still both theoretical arguments and empirical findings supporting the proposition that early-life conditions affect old-age mortality. Most published studies have had a cohort design, and an important limitation of such studies is unmeasured confounding. Natural experiments are more reliable, but require instruments that measure early-life conditions and not conditions during adulthood. Famines meet these requirements but are not relevant to high-income countries today. Economic recessions are an alternative, but there is a dearth of suitable instruments. Accordingly, it is justifiable to use a design that enables the analysis of current inter-country variations. From a policy perspective, these variations are very important.

In most studies of the determinants of health at national level, the outcome considered has been the mortality rate over a given period of time. Yet, an essential characteristic of mortality rates during the last century is a regular, often linear, rate of decrease [31]. During any one study period, different nations start at varying levels. Thus, the mortality rate at a given point in time may be understood as the combined result of previous and current exposures [25]. Accordingly, in analysing determinants, it is appropriate to study the rate of improvement in mortality as an outcome, rather than the mortality rate during a given period of time. Yet, such studies of the effects of early-life conditions on adult mortality have not been presented.

This study uses multiple regression analyses to investigate the effect of early-life conditions on the rates of improvement in mortality in high-income countries (in the Organisation for Economic Co-operation and Development, OECD) over the period 1990-2010, with historical levels of mortality taken into account. Since macro level determinants might confound the effect of early life conditions, four macro-level determinants were also included in the analyses.

2. METHODS

2.1. Countries

Eighteen OECD members were selected for analysis: Australia, Austria, Belgium, Canada, Denmark, Finland, France, Italy, Japan, the Netherlands, New Zealand, Norway, Portugal, Spain, Sweden, Switzerland, the United Kingdom, and the United States. Six OECD members were excluded: Chile, Mexico and Turkey due to Gross Domestic

Product (GDP) per capita, Purchasing Power Parity **(**PPP) and current prices being less than 50% of the OECD average in 2010; and Estonia, Iceland and Luxemburg due to small populations, of less than 1.5 million in 2010. Further, the Czech Republic, Germany, Greece, Hungary, Ireland, Israel, Korea, Poland, Slovakia and Slovenia were excluded due to a lack of data on infant mortality in 1940-49 in the Human Mortality Database.

2.2. Outcomes

The outcomes studied were the national rates of decrease in mortality in the period 1990-2010 in three age groups, 24-34, 35-54 and 55-74 year-olds. Data were obtained from the WHO Mortality Database [32].

Mortality rates were assumed to decrease as linear functions of time. The outcome investigated was the national rate, in each age group, of the decrease in the mortality rate over the period 1990-2010, assessed as the slope (*ß value*) of the linear regression line for each country.

The regression equations also included an assessed constant, which corresponded to the computed mortality rate in the year 1990, *i.e.*, the intercept of the regression line in 1990 (named *H1990)*, and an estimate of the variance that the regression equation explains, R^2. An alternative way of assessing the mortality rate in 1990 would have been to use the actual mortality rate in 1990. The disadvantage of this approach is the lack of precision of single-year assessments of mortality rates, especially in countries with small populations.

2.3. Determinants

Six indicators of early-life conditions were selected: mortality at age 0 and 1-4, in 1940-49, 1950-59 and 1960-69. Four macro level determinants were also selected, based on current understanding of the most important determinants of mortality. They all relate to available resources and their distribution [33]: GDP per capita, distribution of resources assessed as Gini coefficients, poverty rates, and public-funded health care as a percentage of GDP. These determinants, and the data sources used are listed in Supplementary Table **1**.

Supplementary Table 1. Potential determinants.

Group	*Determinant*	*Year*	*Mean*	*Coefficient of Variation*	*Source*	*Remark*
Early life conditions	Mortality age 0, per 1000	1940-49	62.9	0.4688	The Human Mortality Database	Austria, Japan 1947-49; New Zeeland 1948-49
	Mortality age 0 per 1000	1950-59	37.9	0.4963	The Human Mortality Database	
	Mortality age 0 per 1000	1970-79	16.6	0.4629	The Human Mortality Database	
	Mortality age 1-4 per 1000	1940-49	7.32	0.4824	The Human Mortality Database	Austria, Japan 1947-49; New Zeeland 1948-49
	Mortality age 1-4 per 1000	1950-59	2.52	0.9746	The Human Mortality Database	
	Mortality age 1-4 per 1000	1970-79	0. 803	0.4521	The Human Mortality Database	
General resources	GDP per capita. 1000 US $, PPP, current prices	2000	27.0	0.1738	OECD, 2016	
Distribution of resources	Gini index	Around 2005	32.1	0.1285	World Bank, 2015	No data: New Zeeland, Portugal
	Poverty rate	1990-2010	0.1019	0.3294	OECD, 2016	
Health specific resources	Publicly funded health care, % of GDP	2000	5.8	0.1292	OECD, 2016	

2.4. Analytic Strategy

The analyses were performed in Microsoft Excel and the StatPlus supplement to Excel. Prerequisites for the application of multiple linear regression analysis are linear relationships between the outcomes and the historical constant, H1990, and also the selected determinants. Therefore, bivariate scatter plots between the outcomes and the determinants, including H1990, were constructed and inspected visually. All correlations were found to be linear and normally distributed. No correlation was better described by logarithmic or exponential transformation of the

determinants. An additional prerequisite for linear multiple regression analysis is a relatively even distribution of the equation residuals around the value zero. These residuals were therefore inspected. In the analyses that were carried out, all residuals were found to be relatively evenly distributed around zero. A level of $p<0.05$ was considered to be statistically significant.

3. RESULT

The main outcomes that studied the annual rates of decrease in mortality (ß), are presented in Table **1**. The annual rates of decrease, expressed as percentages of the calculated rates in 1990 (H1990) are given in Column 5. They ranged between 2.0% for the 55-74 year-olds and 1.4% for the 35-54 year-olds. The country-specific linear regression equations, which described rates of decrease, explained on average between 80% of the annual variations in the 25-34 year-olds, and 97% in the 55-74 year-olds (Column 4). Thus, the linear equations seemed sufficient to explain the country-specific variations in the development of mortality rates over the study period. Accordingly, no separate analyses of unmeasured unit heterogeneity and serially-auto correlated errors seemed to be called for.

Table 1. Mortality rates in 18 OECD countries in three age groups during the period 1990-2010. Results from country specific linear regression analyses: assessed rates in 1990 (H1990), annual rates of decrease (ß), explanatory values of the linear regression equations (R2) and rate of decrease as percentage of H1990.

Age group	*Mortality rate in 1990 (H1990) per 100000, assessed, mean (SD)*	*Annual rate of decrease of mortality (ß), mean (SD)[Coefficient of Variation]*	*Explanatory values of the country specific linear regression equations (R2), mean (SD)*	*Mean ß/Mean H1990 (%) (Rate of decrease/rate in (1990), mean (SD)*
25-34 years	104.06 (29.83)	-2.22 (1.371) [-0.6174]	0.7981 (0.1866)	-1.989 (0.877)
35-54 years	279.32 (49.63)	-3.857 (1.529) [-0.3965]	0.8751 (0.1113)	-1.383 (0.475)
55-74 years	1 773.91 (275.7)	-35.79 (9.672) [-0.2703]	0.9645 (0.025)	-1.995 (0.36)

In Tables (**2** , **3** and **4**), the results of applying the multiple regression models to the age groups, 25-34, 35-54 and 55-74 years, are presented. All tables start with results from Model 0 assessments, *i.e.,* models that include only the rate of decrease in mortality (ß) as the outcome and the history variable (H1990) as a determinant. In the 25-34, 35-54 and 55-74 year-olds, the model 0s explained 72, 17 and 65% of the cross-national variation, respectively. Thus, in the youngest and oldest age groups, most of the cross-national variation of rates of decrease in mortality were explained by mortality rates in 1990.

Table 2. Multivariate regression models with annual rate of decrease of mortality (ß) at age 25-34 years in 18 different OECD countries as dependent variable.

Modell	*Determinant*	*Coefficient*	*SE*	*p-level*	*R2*
Modell 0					0.7208
	History (H1990)	-0.039	0.0061	<0.001	
Modell 1					0.7221
	History	-0.0406	0.0087	<0.001	
	Mortality at age 0 in 1970-79	8.739	33.63	0.7985	
Modell 2					0.7259
	History	-0.0415	0.0078	<0.001	
	Mortality at age 1-4 in 1970-79	337.1	638.1	0.605	
Modell 3					0.7277
	History	-0.0373	0.0068	<0.001	
	GDP per capita	0.0255	0.0414	0.5467	
Modell 4					0.7019
	History	-0.0469	0.0088	<0.001	
	Gini index	0.0661	0.0524	0.2296	
Model 5					0.733
	History	-0.0408	0.0065	<0.001	
	Poverty rate	4.783	5.777	0.4207	
Modell 6					0.7208
	History	-0.039	0.0063	<0.001	
	Publicly funded health care	-0.0014	0.2425	0.9955	

Table 3. Multivariate regression models with annual rate of decrease of mortality (ß) at age 35-54 years in 18 different OECD countries as dependent variable.

Modell	*Determinant*	*Coefficient*	*SE*	*p-level*	*R2*
Modell 0					0.1686
	History (H1990)	-0.0126	0.007	0.0906	
Modell 1					0.1697
	History	-0.0122	0.0078	0.136	
	Mortality at age 0 in 1950-59	-2.871	19.95	0.8875	
Modell 2					0.1726
	History	-0.013	0.0074	0.0973	
	Mortality at age 1-4 in 1950-59	40.207	148.44	0.7902	
Modell 3					0.1695
	History	-0.0125	0.0073	0.1096	
	GDP per capita	0.0097	0.0745	0.8979	
Modell 4					0.3869
	History	-0.0129	0.0071	0.0918	
	Gini index	0.1734	0.0828	0.0565	
Model 5					0.3421
	History	-0.01	0.0066	0.1507	
	Poverty rate	19.3863	9.7456	0.0652	
Modell 6					0.2128
	History	-0.0105	0.0074	0.1765	
	Publicly funded health care	-0.4387	0.4778	0.3731	

Table 4. Multivariate regression models with annual rate of decrease of mortality (ß) at age 55-74 years in 18 different OECD countries as dependent variable.

Modell	*Determinant*	*Coefficient*	*SE*	*p-level*	*R2*
Modell 0					0.6462
	History (H1990)	-0.0282	0.0052	<0.001	
Modell 1					0.7896
	History	-0.0263	0.0042	<0.001	
	Mortality at age 0 in 1940-1949	121.9	38.122	0.006	
Modell 2					0.7048
	History	-0.0256	0.0052	<0.001	
	Mortality at age 1-4 in 1940-1949	489.1	283.6	0.1051	
Modell 3					0.6578
	History	-0.0279	0.0053	<0.001	
	GDP per capita	-0.213	0.2996	0.4879	
Modell 4					0.6895
	History	-0.0275	0.0052	<0.001	
	Gini index	0.3592	0.3554	0.3306	
Model 5					0.6645
	History	-0.0269	0.0054	<0.001	
	Poverty rate	40.4	44.74	0.3809	
Model 6					0.6498
	History	-0.0283	0.0054	<0.001	
	Publicly funded health care	0.7523	1.918	0.7004	

In the 25-34 year-olds, when added to the regression equations, neither the early-life indicators nor the resource indicators seemed significant to increase the explanatory power of the equations, and none reached statistical significance. In the 35-54 year-olds, the early-life indicators did not seem significant to increase the explanatory power of the equations. That was, however, the case for the resource indicators, but none reached statistical significance.

In the 55-74 year-olds, the pattern was different. In the year 2000, the 55 year-olds were born in 1945. In the model

where the mortality rate at age 0 in 1940-49 was added, the explanatory value of the equations increased from 65 to 79%, and the mortality rate at age 0 was statistically significant. In the model where the mortality rate at age 1-4 years in 1940-49 was added, the model also increased the explanatory value, but the added determinant did not reach statistical significance. Two models were also explored with mortality rates at age 0 and 1-4 in 1930-1939 added as determinants. These models were limited by data only being available for 14 countries. The age-0 determinant increased the explanatory value of the equation from 65 to 73% and the beta coefficient reached statistical significance; the age 1-4 determinant increased the explanatory value of the equation to 64%, but the beta coefficient did not reach statistical significance (data not shown). The resource indicators, used as determinants, did not significantly increase the explanatory power of the equations.

4. DISCUSSION

The mortality rates decreased in all age groups. The relative rate of decrease was larger in the youngest and oldest age groups to be compared with the middle-aged. This finding is consistent with the trend in high-income countries in general during the period 1950-2010 [34]. Significant effects of early-life conditions on the rate of decrease in mortality were found in the oldest age group, aged 55-74 years, but that was not the case for the 25-34 and 35-54 year-olds. In all age groups, some or most variation between countries was explained by the previous history. Thus, in countries with high initial mortality in 1990, the rate of decrease was generally faster than in countries with a relatively low mortality in that year. In fact, in 25-34 year-olds, 72% of the inter-country variation was explained in this way, which left little room for other explanations. This phenomenon, often named beta-convergence, has previously been demonstrated [2, 35].

Yet, the lack of effect of early-life conditions in 35-54 year-olds cannot be explained in the same way, since only 17% of the inter-country variation was explained by the initial mortality rates in 1990, and neither the early-life indicators nor the resource-related determinants reached statistical significance.

Four potential macro-level determinants were included in the analyses. A correlation between favourable early life conditions and low old age mortality might be confounded by an effect of favourable early life conditions on economic growth in a country which in turn might affect old age mortality. Similarly, cultural characteristics might both affect early life conditions and distribution of resources that in turn affect old age mortality. The analyses, however, did not support any effect of macro-level determinants on old age mortality.

Since there was no predetermined relationship between the main determinant, early life conditions, and the rate of old age mortality improvement. The study supports the notion that early-life conditions mainly affect individuals at age 55 and above. This finding is consistent with Gavrilov's reliability theory of aging [26], and also the findings of an English study by Ploubidis *et al.* [15]. The conflicting results in previous studies may partly be due to the inclusion of outcomes in individuals below 55 years of age.

The results can hardly be explained by selection, *i.e.*, decreased mortality in individuals who survive relatively harsh conditions during their early years. If that were the case, the effects of early-life conditions would be expected in all adult groups. Gavrilov's reliability theory of aging presents a better explanation; that is, less favourable early-life conditions result in less redundancy in different organ systems [26].

Another potential source of variation between the different age groups might lie in the amount of variation in the outcome variable, *i.e.,* the rate of mortality decreases during the period 1990-2010. The coefficients of variation are given in Table **1**. These coefficients decrease with age, which limits the potential for significant findings in the oldest age group.

A limitation of the study is the use of aggregated data at national level, for age groups and for periods of observation. These aggregations, however, would be expected to decrease the chances of detecting significant effects. The number of observation units, countries, is also limited. Having a small number also decreases the chances of detecting effects.

A strength of the study lies in the employment rate of decrease in mortality as an outcome rather than mortality in a specific year. Another strength is that the study data reflect the current situation in high-income countries.

CONCLUSION

The results add to our understanding that efforts to improve early-life conditions not only better childhood health

but also decrease old age mortality. The study, in fact, suggests that early life living conditions are more important for improvement of old age mortality than poverty rate and general resources for health care during adulthood. In high-income countries, there is a competition of resources for dependent age groups, *i.e.* minors and seniors. The results indicate that improvements during early-life, in the long run, will benefit all age groups while that is obviously not the case for betterments at the end of life.

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ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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HUMAN AND ANIMAL RIGHTS

No Animals/Humans are used for studies that are bases of this research.

CONSENT FOR PUBLICATION

Not applicable.

CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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