Natural Variation in the Sex Gap in Life Expectancy

Lindahl-Jacobsen, Rune; Zarulli, Virginia; Christensen, Kaare; Vaupel, James W.; Oeppen, James

Publication date: 2016

Citation for published version (APA):

Terms of use
This work is brought to you by the University of Southern Denmark through the SDU Research Portal. Unless otherwise specified it has been shared according to the terms for self-archiving. If no other license is stated, these terms apply:
• You may download this work for personal use only.
• You may not further distribute the material or use it for any profit-making activity or commercial gain
• You may freely distribute the URL identifying this open access version

If you believe that this document breaches copyright please contact us providing details and we will investigate your claim. Please direct all enquiries to puresupport@bib.sdu.dk
Natural variation in the sex gap in life expectancy

Rune Lindahl-Jacobsen1,4, Virginia Zarulli1,4, Kaare Christensen1,3,4, James W. Vaupel1,2,4,5, Jim Oeppen1,4

1 Max-Planck Odense Center on the Biodemography of Aging, University of Southern Denmark, J.B. Winsløws Vej 9B, DK-5000 Odense C, Denmark; 2 Max Planck Institute for Demographic Research, Konrad-Zuse-Str. 1, 18057 Rostock, Germany; 3 Department of Clinical Genetics and Department of Clinical Biochemistry and Pharmacology, Odense University Hospital, Sdr. Boulevard 29, 5000 Odense C, Denmark; 4 Department of Epidemiology, Biostatistics and Biodemography, University of Southern Denmark, J.B. Winsløws Vej 9B, DK-5000 Odense C, Denmark; 5 Duke University Population Research Institute, Duke University, 140 Science Drive, Gross Hall, Box 90989, Durham, NC 27708-0989, USA

Women outlive men in all countries of the world and for decades women’s life expectancy has increased more rapidly than that of males. Factors contributing to these observations are believed to be associated with the external environment and internal biological factors. It has been hypothesized that females withstand harsh environments better than males in terms of survival, partly explaining their higher life expectancy. If this hypothesis is true and females survive environmental stressors better than males then large sex differences in life expectancies could reflect the action of these environmental factors whereas small differences would reflect a lower action of the factors and approach the ‘natural’ biological level. Here we examine variability in sex differences in life expectancy in 47 historical and contemporary human populations to address our hypothesis: large sex differences in life expectancies reflect large variation in mortality across age and thus indicate larger influence from environmental factors.

Introduction

Women outlive men even in the poorest countries of the world1. The research behind this sex gap in life expectancy suggests that mixtures of biological, social, behavioral and environmental conditions and their interactions are the reasons behind the sex discrepancy in survival.

It is well established that men engage in risky behaviors more often, including use of tobacco, alcohol, and psychoactive substances, less safe driving, and less healthy diet, thus increasing elevated risks of various morbidities and death2,3. Among these risk behaviors cigarette smoking is the single largest factor for the explanation of sex differential mortality in high-income countries4–6.

Less evidence is present for the biological factors explaining sex differences in mortality. It is believed that the sex differences in mortality include hormonal and genetic differences. Sex hormones have been suggested to be important2,7 with estrogens being protective through anti-inflammatory and vasoprotective processes8–10 whereas testosterone can increase the
mortality risk for certain diseases\textsuperscript{11,12} and together with progesterone possibly have immunosuppressive effects\textsuperscript{13–15}. The double X-chromosomes of women are another possible biological advantage in relation X-linked diseases\textsuperscript{16,17}. Strong support for a major biological component comes from demographic studies of sub-populations belonging to specific religious groups or being non-smokers in which men and women have more similar lifestyles than in the general population\textsuperscript{18–21}. The rationale behind these studies is that in these sub-populations men are somewhat protected from the risk factors present in the general population thus suggesting that excess male mortality is attributable to biological factors (i.e. excluding environmental factors such as unhealthy lifestyle behavior). These studies do not however address the question why women have a biological advantage in the first place.

Women have been found to have a higher heterogeneity in frailty then males\textsuperscript{22} suggesting perhaps a better potential to withstand environmental stressors. That women better withstand harsh environments was demonstrated in a recent study where we examined mortality risk in extremely harsh environments\textsuperscript{23}. We found that even in populations with life expectancies as low as two years women outlived men thus underpinning the suggestion that females are better at surviving environmental stress than males. If females indeed survive environmental stressors better then large sex differences in life expectancies could be the reflection of the action of these environmental factors whereas small differences would reflect less action of the factors and approach the ‘natural’ biological level for a difference in life expectancy. It has been suggested that stressful environments induce an increase in both phenotypic variation in non-human organisms and that this increase in variation is likely to be manifested under stress where the mortality in a population is high\textsuperscript{24–26}. That the key to understand underlying biological mechanisms is variation is well known within the field of biology\textsuperscript{27} where variance itself is viewed as an irreducible essence\textsuperscript{27,28}.

Here we address this hypothesis by examining the variability in sex differences in life expectancy in 47 contemporary human populations. Our hypothesis is that large sex differences in life expectancies reflect larger variation in mortality across age and thus the suggestion of larger influence from environmental factors.

**Methodology**

Our analyses are based on one-year life tables from 47 countries in the human mortality database (\url{www.mortality.org}) in the period 1950 to 2005-2011 (depending on country - \url{www.mortality.org}).
For addressing the variation between in the age specific contribution to differences in life expectancy we age-decomposed the contribution to the total life expectancies by one-year calendar years and thereafter calculated the variance of the components (coefficient of variation) for these age and period specific contributions.

We first calculated age-specific contributions to the difference in life expectancies within each country and calendar year using Arriaga’s discrete decomposition technique\textsuperscript{29,30}. The difference in life expectancies at age $x$ can be estimated as:

$$\Delta_x = \frac{l_x^1}{l_0^1} \left( \frac{L_x^2}{L_x^1} - \frac{L_x^1}{l_0^1} \right) + \frac{T_{x+1}^2}{l_0^1} \left( \frac{l_x^1}{l_x^2} - \frac{l_x^1}{l_x^1} \right)$$

where $l_x$ denotes the number of survivors at age $x$, $L_x$ the number of life-years lived in age $x$, and $T_x$ the number of life-years lived at age $x$ and above. Superscripts 1 and 2 indicate the two sexes.

Secondly, we estimated the variance of the components for the calculated country ($c$), age ($x$) and period ($j$) specific contribution to differences in life expectancies.

To examine how the variance of the age components correlated with total sex differences we plotted variation as a function of ($\Delta_x$).

R 3.2.5 was used for all the analyses.

**Results**

In general the largest variation of the age components were centered around ages above 70 years (see figure 1a for examples). For some countries (Japan, Lithuania, Latvia, Poland, Estonia, Ukraine, Belarus, former East Germany) where there was a steady increase in the variation of the age components with age whereas for the rest of the countries examined the increase was followed by a decrease (see figure 1a for examples). For these countries the maximum age for the variation of the age components differed by country (figure 1a). When viewed in the temporal perspective this maximum age for the variation of the age components differed among countries with some countries having an earlier onset such as in the U.K. and the US and others such as the Netherlands and Norway having a later onset (figure 1b).
The variance of the components showed an increase with increasing female advantage in life expectancy (figure 2). The level of increase of the variance of the age components was slower for low female advantages in life expectancy and then increased.

Figure 1. Examples of ages and periods with maximum variance of components for the analyzed countries by (A) age and (B) calendar time.

Figure 2. Variance of components by age for female advantage in life expectancy in years. Each point represent the variation of age specific contributions to differences in life expectancy for a specific country within one calendar year.
Discussion and conclusion

Our results support our initial hypothesis that large sex differences in life expectancies reflect larger variation in age specific contributions to the difference. We found a clear correlation between female advantage in life expectancy and variance. This observation supports the suggestion that women survive better under greater environmental stress then males whether this external environments are self exposed (e.g. behavior) or not. Thus a bigger advantage in survival for females is reflected in larger variation. If the level of variation in mortality is a reflection of the level of environmental stress then our results suggest that women are better at withstanding environmental stress or that they expose themselves to the stressors less often (i.e. more survival safe behavior). Another implication is that if low variation reflects low environmental stress then the ‘natural’ biological sex differences (i.e. when excluding the environment for the term ‘natural’) would be at the lowest levels of variation. In our study the lowest observed advantage of women is 2.7 years at which the variation is also the lowest observed suggesting that the ‘natural’ biological differences (i.e. excluding environmental stress from natural) should be found below 2.7 years.

More interestingly, the measure of variance seems to capture the onset of the results of the smoking epidemic with a start first in the US and UK followed by different other countries illustrating the potential of the method used (figure 1b). Another interesting point is that the former Eastern European countries (results not shown) and Japan (figure 1b) show a similar pattern to the US and the Western European countries, but with a delay. This indicates that the sex difference in life expectancy will also decrease in the former Eastern European countries and Japan, as seen in the Western European countries31

Conclusion – The strategy of using variation at the population level in humans as a tool for approaching environmental influence on sex differences in life expectancies may be beneficial.

Next steps

1. Include older data and data for populations with very low female advantage in life expectancy to better approach the ‘natural’ biological difference in life expectancy.
2. Examine the contributions of the components of variation (age, period and sex)
3. Explore the possibility that countries that can minimize dispersion within a sex may also minimize dispersion between the sexes (i.e. plot life length males (e-dagger-male) versus life length females (e-dagger-female)32.


