Lifespan costs of reproduction increase during the Great Finnish Famine

Euan A Young*, Erik Postma, Virpi Lummaa^, and Hannah L Dugdale^*

Author names, ORCID ID

Euan A. Young[1*], 0000-0001-9370-9681

Erik Postma[2], 0000-0003-0856-1294

Virpi Lummaa[3^],

Hannah L. Dugdale[1^*], 0000-0001-8769-0099

1 - Groningen Institute for Evolutionary Life Sciences, University of Groningen, Groningen, The Netherlands

2 - Centre for Ecology and Conservation, University of Exeter, Penryn, United Kingdom

3 - Department of Biology, University of Turku, Turku, Finland

^ equal last authorship

* Corresponding author emails: e.a.young@rug.nl, h.l.dugdale@rug.nl

ABSTRACT

Evolutionary theory of aging predicts that women with increased reproductive effort live shorter lives, but evidence is inconsistent. These inconsistencies could be because environmental conditions influence how much reproductive behavior shapes a mother's lifespan, i.e. their lifespan cost of reproduction. Using a structural equation measurement model, we compare how reproductive effort affects lifespan of 4,684 women exposed across different life-stages, or not at all, to the Great Finnish Famine. We find that lifespan costs of reproduction became higher in mothers exposed to the famine during reproduction, and for these mothers amounted to a decreased life expectancy of ~0.5 years per child. Conversely, reproductive behavior did not shape the lifespans of mothers not exposed to the famine, or exposed post-reproduction or during development. These results suggest environment-dependent reproductive costs, which provides a biological explanation for previous inconsistent findings, and demonstrate how reproductive behavior can be an important determinant of human lifespan.

KEYWORDS: disposable soma theory of aging, reproduction-survival trade-off, early-life adversity, resource acquisition-allocation, human life-history, maternal lifespan

INTRODUCTION

Understanding why we age – defined as a decline of health in later-life – and why some of us undergo this aging process faster than others, are vital foundations for improving human health-spans[1]. One theory – the disposable soma hypothesis – predicts that aging is a consequence of natural selection honing our physiology to maximize reproduction at the cost of other organismal functions, resulting in an accumulation of damage through life that limits lifespans[2,3]. Consequently, researchers have tested if individuals who devote more resources to reproduction have shorter lifespans[4]. However, expected negative associations between reproduction and lifespans are rarely found[5] and typically only when using experimental studies (e.g., Boonekamp et al.[6]). For humans, the bearing and raising of even one child is energetically demanding for women[7], but – despite over 100 years of research[8,9] – evidence of a reproduction-survival trade-off is inconsistent[10–12] and the role that human reproductive behavior plays in shaping aging remains unclear.

There is however a difference between the theoretical predictions of the reproduction-survival trade-off, and empirical estimates of the slope of the regression of survival against reproduction – the reproduction-survival trade-off *function* – due to the presence of among-individual heterogeneity. Individual heterogeneity will weaken the observed trade-off function because: (1) among-individual variation in resource acquisition introduces a positive association between reproductive effort and lifespan that can mask the within-individual reproduction-survival trade-off (i.e., the big house and big car syndrome[13,14]; and (2) among-individual variation in frailty, meaning some women will manifest lifespan costs of reproduction more than others[12,15]. Thus, the estimated trade-off function quantifies how important reproductive behavior versus unaccounted individual heterogeneity is in shaping human lifespans. The relative importance of reproductive behavior versus individual heterogeneity in shaping lifespans factors changes both among studies/populations, and within studies/populations through time[16–18]. However, we still have a poor understanding of which biological factors drive these changes in the reproduction-survival trade-off. Understanding these biological drivers can give us insight into the mechanisms underlying this fundamental trade-off, how it manifests itself, and under what circumstance human reproductive behavior is an important factor in shaping aging.

Although the role of reproductive effort in shaping aging is uncertain, examples of environmental effects on human health are numerous[19,20]. In humans, experiencing periods of extreme environmental adversity, such as famines, can accelerate the biological aging process[21]. In fact, famine can have an array of effects, from long-term individual effects on human health, such as prenatal famine exposure increasing risk of type-2 diabetes and schizophrenia later in life[22,23], to social and economic consequences[24]. Although widely used as natural experiments in other fields, the role that famine exposure plays in shaping estimated lifespan costs of reproduction has not to our knowledge been studied.

Given the well-documented adverse effects of famines, mothers exposed to famines could show greater reductions in lifespan for a given increase in reproductive effort. However, this reduction may depend upon the life-history stage of the mother during the famine exposure. Firstly, even short-term fluctuations in early-life environmental conditions can lead to physiological differences[25] that influence the overall lifespan and realized reproduction of individuals[26,27]. Thus, women experiencing famines during development may show increased costs of reproduction. However, Nenko et al.[17] found no evidence that crop yields, spring temperatures, or infant mortality rates at birth modified the reproduction-lifespan trade-off in mothers. Instead, mothers may be especially vulnerable to resource limitations while raising children[17] due to both the calorific demands of pregnancy and lactation, and increased vulnerability to disease[7]. Indeed, Wang et al.[18] proposed that some individuals experiencing the Great Depression and Second World War while being reproductive caused the variation in costs of reproduction in the Framingham cohort study. Finally, women in post-reproductive life are particularly at risk of mortality under lower food availability[27]. Thus, mothers could suffer increased frailty due to high reproductive effort but perhaps only when combined with famine exposure during post-reproductive life would this result in reduced lifespans.

Rigorous tests of these hypotheses require detailed individual-level life-history data for a period encapsulating a major famine event. Here, we use individual life-history data across 250 years from rural Finland to quantify lifespan costs of reproduction and compare how they changed across mothers exposed to The Great Finnish Famine in different life-stages, and those not exposed at all. In the 1860s, Finland experienced a series of low harvests, which in 1867 dropped to catastrophic levels meaning a major loss of employment[28]. Widespread migration then followed as people went in search of work, which in turn triggered a large spike in infectious diseases, such as typhoid fever, typhus, and dysentery[28]. This led to an excess mortality of 110,000 (or 5-10% of Finland's population[29]) making it one of the most devastating famines in recent European history, and the worst in Finland since the 17th century [30].

Here we capitalize on the fact that this famine occurs in the middle of our dataset, allowing us to estimate the lifespan costs of reproduction before, during, and after a famine. Specifically, we compare mothers exposed to the famine during three life-stages (during their development [ages 0-19], while reproductively active [ages 19-45], and while in post-reproductive life [ages 45+]) to mothers dying before the famine and those born in the years after using a structural equation measurement model (N = 4,868, Fig. 1). We follow Helle[31] and use a measurement model using multiple indicator variables to obtain a comprehensive measure of lifetime reproductive effort. Within this structural equation model framework, we estimate the association between reproductive effort and lifespan (i.e., the reproduction-survival trade-off function) in each famine exposure group and how these lifespan costs of reproduction differed across groups, accounting for the changes in reproductive effort and lifespan in relation to famine exposure. Broadly we expected mothers exposed to the famine to show an increased lifespan

cost of reproduction, but that this cost would depend upon the life-stage of mothers during this famine exposure. Showing such a dependency would shed light on why the estimated costs of reproduction are so variable both among and within studies.

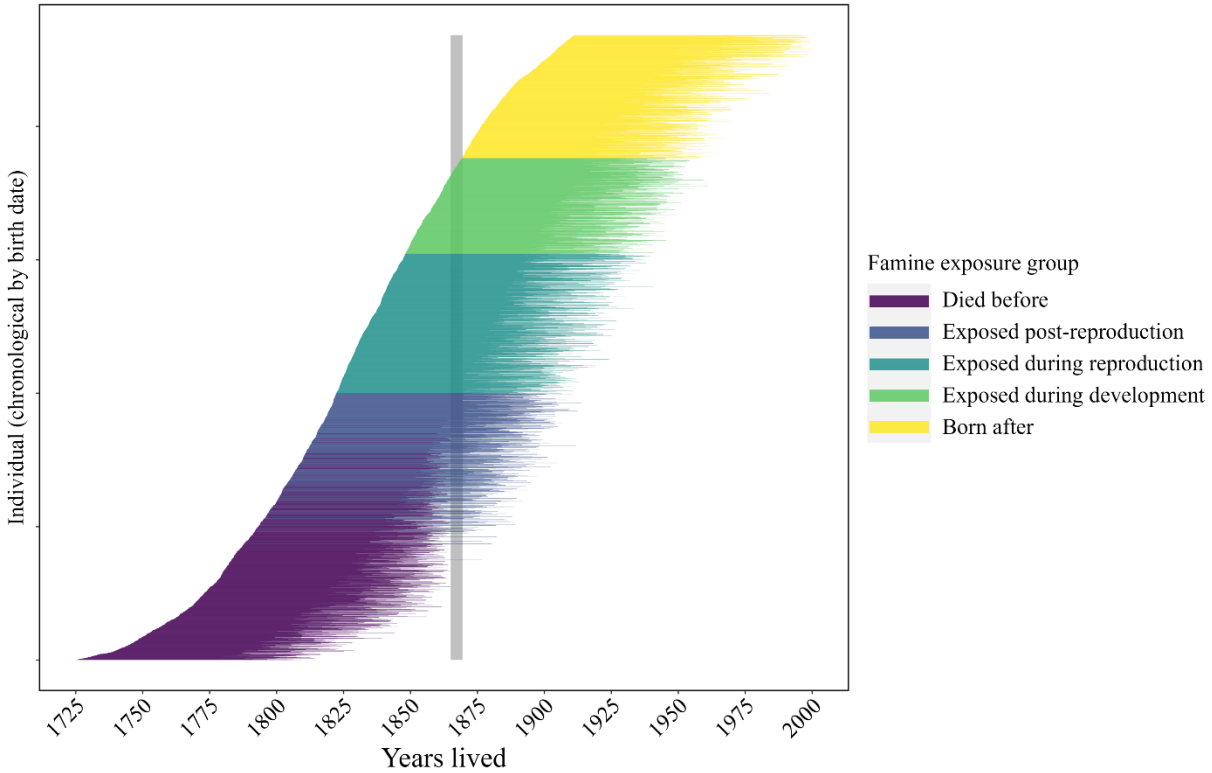

Fig. 1: Line graph showing the years lived for each mother included in the analyses, sorted chronologically by their birth date (N = 4,684). Colors indicate their exposure to the Great Finnish Famine (grey bar) and groupings in the analyses: died before (n = 1,297), exposed post-reproduction (n = 705), exposed during reproduction (n = 1,044), exposed during development (n = 716), and born after (n = 922).

RESULTS

Lifespan costs of reproduction

Exposure to the Great Finnish Famine shaped the estimated reproduction-survival trade-off (Fig. 2, Tables 1 and 2). Specifically, increases in reproductive effort were associated with a reduction in lifespan in mothers exposed to the famine while reproductively active, but not among other groups (Fig. 2; Table 2). Mothers exposed to the famine who had one child would be expected to live to age 71.6 (95% CIs 69.2 – 74.6), whereas a mother with 15 children would only be expected to live to age 64.3 (61.7-68.3), or a reduction in lifespan of half a year per child (Fig. 2, Table S1). The association between reproductive effort and lifespan in mothers exposed during reproduction was also higher than in mothers dying before the famine, mothers born after the famine, and mothers exposed to the famine in post-

reproductive life ($p < 0.05$), and marginally higher than those exposed to the famine during development ($p = 0.087$, Table 2, Fig. 2).

These results were confirmed in a complementary mixed model analysis that accounted for significant variation in lifespan amongst birth years, families, and 13 geographical regions (Table S2). Mothers again varied in the reproduction-survival trade-off function according to famine exposure, with the statistically significant association between reproductive effort and lifespan only found in mothers exposed to the famine during reproduction and was of a similar magnitude to the previous model (Tables S3 and S4). The association between reproductive effort and lifespan in mothers exposed to the famine while reproductively active was also higher than in all other groups, except for those exposed during development (Table S4).

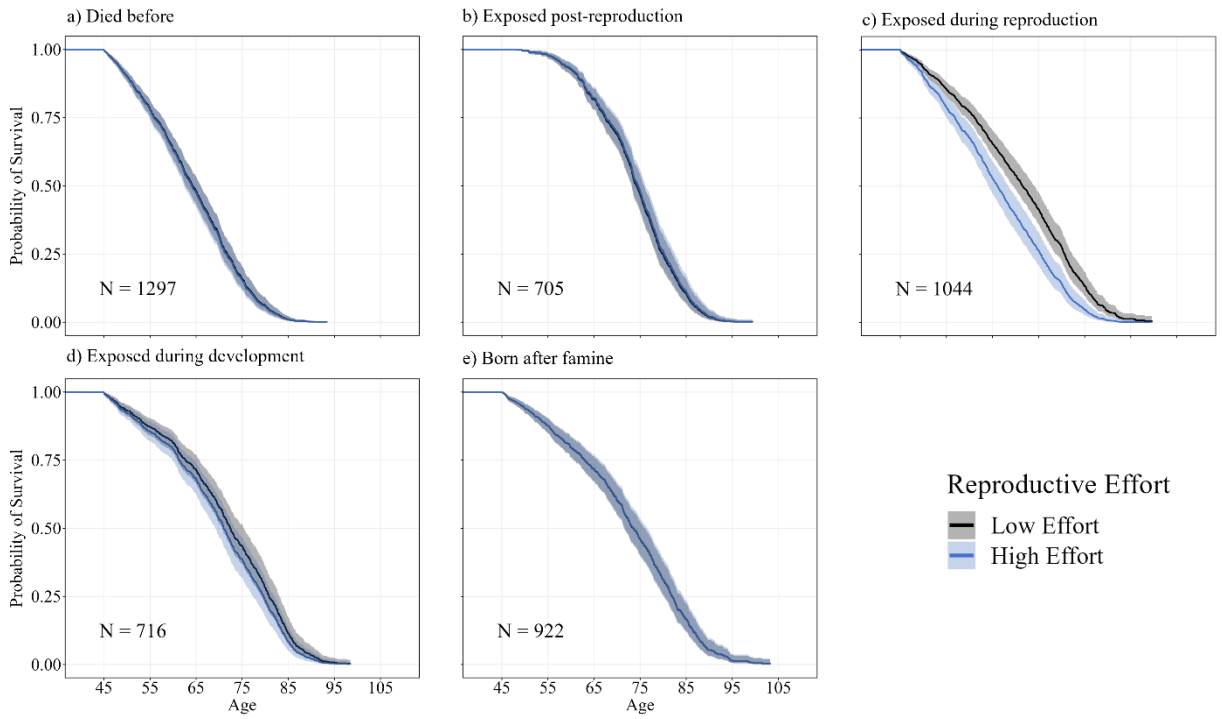

Fig. 2: Predicted survival curves for low and high reproductive effort across five famine exposure groups. Curves were generated using Cox proportional hazards models on each famine exposure group separately (see Table S1). Each panel represents a different famine exposure group: (a) died before famine, (b) exposed during post-reproduction, (c) exposed during reproduction, (d) exposed during development, and (e) born after famine. Survival curves are shown for low (5th percentile, -3.8) and high (95th percentile, 6.5) reproductive effort levels. All curves are calculated for individuals of intermediate socioeconomic status and median relative birth date within each famine group. Shaded areas represent 95% confidence intervals.

Temporal changes in lifespan

There were differences in lifespan among famine exposure groups and how lifespan changed over time *within* each group (Table 1, Table S1). Life-expectancy for mothers dying before the famine was 66 years for those born in 1777 but declined over time to 55 years for mothers born in 1819 (Table 1, Table S1). Similarly, for mothers exposed to the famine post-reproduction, life-expectancy was 79 years for those born in 1796 but declined overtime to 70 years for mothers born in 1822 (Table 1, Table S1). These trends reflect the classification of these groups: within mothers who died before the start of the famine, those born later must have lived shorter lives. Similarly, by focusing only on famine survivors, mothers born earlier among those exposed to the famine during post-reproduction cannot have had short lives, with the higher life-expectancies overall likely reflecting the loss of higher frailty women during the famine itself. Mothers exposed to the famine during reproduction had a life expectancy of 71 years which stayed similar for mothers exposed during development and did not change through time in either group (Table 1, Table S1). However, life-expectancies then increased for mothers born after the famine from 71 years in mothers born in 1869 to 78 years for mothers born in 1910 (Table 1, Table S1).

Temporal changes in reproductive effort

Mean reproductive effort did not change between mothers dying before the famine and those exposed to the famine post-reproduction, and it remained constant overtime within each group (Table 1, Fig. S1). However, for mothers exposed during reproduction, reproductive effort increased from being similar to prefamine levels for mothers born in 1822 to being 0.8 children higher in mothers born in 1848 in this group (Table 1). Reproductive effort then remained similarly high for mothers exposed during development who had on average 0.6 children more than pre-famine levels, which did not change over time (Table 1). Reproductive effort then declined rapidly in mothers born after the famine going from mothers born in 1869 having 0.8 children more than mothers dying before the famine, to mothers born in 1911 having 1.8 children fewer than prefamine levels (Table 1).

Socioeconomic status effects

Socioeconomic status did not modify the association between reproductive effort and lifespan (Table S5). However, there were differences in both lifespan and reproductive effort across socioeconomic status groups, with the magnitude of these differences changing according to famine exposure (Table 1, Table S1). No differences in lifespans were found in mothers dying before the famine between higher and middle socioeconomic statuses and these effects did not change across famine exposure groups (Table 1). However, lower socioeconomic status mothers had lower life-expectancies of around three years compared with intermediate socioeconomic status mothers (Table 1). This difference in life-expectancies between lower and intermediate socioeconomic status mothers remained similar across famine exposure groups, except in lower socioeconomic status mothers exposed to the famine during

development who did not have lower lifespans than mothers of intermediate socioeconomic status (Table 1).

Upper socioeconomic status mothers dying before the famine had higher reproductive effort than mothers of intermediate socioeconomic status, amounting to 0.6 more children (Table 1). These differences gradually decreased through time until mothers born after the famine, where upper and intermediate socioeconomic status mothers had identical reproductive effort (Table 1). Mothers from lower socioeconomic statuses had lower reproductive effort amounting to 0.6 fewer children in mothers dying before the famine. This difference in reproductive effort between lower and intermediate socioeconomic status mothers remained stable, except for mothers exposed during reproduction, where the difference increased to 1.2 fewer children.

DISCUSSION

Using life-history records for 4,684 Finnish women, we find evidence that adverse environmental conditions increase the importance of reproductive behavior in shaping lifespan (Fig. 2, Table 2). Specifically, mothers exposed to the Great Finnish Famine (1866-68) while reproductively active showed reduced lifespans of approximately 0.5 years per child as estimated through a structural equation measurement model. On the other hand, mothers not exposed to the famine (i.e., mother who died before, or were born after) or those exposed to the famine in post-reproductive life or during development did not pay a lifespan cost. Although the effects of famines on human health and aging are well documented (e.g. Cheng et al.[21]), this is, to the best of our knowledge, the first evidence of a famine event modifying the reproduction–survival trade-off function in humans. In addition to previously highlighted methodological explanations (detailed in: Helle et al.[32]; Helle[33]), our findings provide a biological explanation for why several studies have shown variation in costs of reproduction over time[16–18]: fluctuations in environmental conditions experienced by mothers while reproductively active impact the estimated trade-off function. This strengthens the evidence for the existence of lifespan costs of reproduction and gives insight into under what circumstances human reproductive behavior is an important driver of aging.

The role of the environment in shaping reproduction-survival trade-off function has been demonstrated in non-human animal studies[34,35], but in humans the evidence has been less clear. A recent study using data for preindustrial Canada showed that only mothers having both high reproductive effort (i.e. a high numbers of sons) and high lifetime infant mortality showed increased lifespan costs of reproduction[36]. While this change in the reproduction-survival function across mothers is in line with our findings, Invernizzi et al.[36] did not explore how environmental conditions drive variation in infant mortality among mothers beyond showing an effect of a mother's birth year (see Invernizzi, et al.[36], Supplementary Table 1). In contrast, and in line with a previous study on the same population but a different time period[17], we found no strong support for the early-life environment shaping the

reproductive–survival trade-off function, with the lifespan costs of reproduction being small and statistically non-significant (Fig. 2, Table 2). Nevertheless, given the well-established importance of the early-life environment on human health[37], and in modifying the reproduction–survival trade-off function in wild animal populations[38], early-life adversity may modify lifespan costs of reproduction in other ways and remains worthy of further study.

In addition to famine exposure, we found that demographic and cultural factors were important drivers of reproductive effort, lifespan, and their association. Differences across socioeconomic groups were consistent with previous results, with lower socioeconomic status mothers having lower realized reproduction[30] and shorter lives[39], but not increased lifespan costs of reproduction (Supplementary Table S5, Helle[31], but see Lycett et al.[40]). We also found that mothers exposed to the famine during reproduction lived shorter lives than those exposed during development, and those exposed during development lived shorter lives than mothers born after the famine. Rather than being a direct effect of famine exposure, this is probably a symptom of increased industrialization, which, in line with country-wide trends, started during this period[41]. These improvements in lifespan through, for example, vaccination[42], combined with a reduction in overall reproductive effort, are probably why the importance of the reproductive-survival trade-off decreased in mothers born after the famine. This is analogous to results for the Netherlands[43], but future studies could test how lifespan costs of reproduction change across the demographic transition outwith northern European countries.

Our finding that only mothers exposed to the famine while reproductively active showed lifespan costs of reproduction could be due to the increased energetic demands of bearing and raising children during a period of high environmental adversity. When pregnant, mothers must increase their caloric consumption by on average 300 kcal d-1 to sustain a healthy pregnancy, which rises to 460-630 kcal d-1 during breastfeeding[44]. If the mother's pregnancy or breastfeeding coincides with a famine it could mean that these increases in metabolic demands are paid by themselves through lowering basal metabolism, and thus slowing or shutting down other important functions[11,45], resulting in a decline in health and shorter lifespans. Specifically, circulating estrogen levels – which are important for cardiovascular health[46] – during breastfeeding are very low[47]. These levels are even lower in mothers with poor nutrition[48], which could mean that cardiovascular disease risk (which is already a risk factor of high parity[49]) could be even higher in mothers of high reproductive effort experiencing poor nutrition while reproducing. Although we can speculate, ultimately the underlying mechanisms are difficult to disentangle in genealogical studies but are worthy areas of exploration for studies using human biobank data or non-human species in experiments.

Although high reproductive effort during the famine may have affected individual health directly, among-individual processes, such as selective disappearance, may still have influenced the reproduction–survival trade-off function. Because the reproduction–survival trade-off function will weaken with higher individual heterogeneity[13–15], higher mortality rates during The Great Finnish

Famine may have driven higher mortality of frailer individuals (as suggested by previous studies[50]), reducing individual heterogeneity in mothers sampled after completing reproduction, and increasing the strength of the estimated trade-off function. In our study, selective disappearance due to the famine will have occurred in all groups exposed to the famine because we focused only on survivors of the famine, and on post-reproductive life. Furthermore, given that the effects of the famine on mortality are biased towards the very young and old[51], the selective disappearance should have been highest in the development and post-reproductive exposures – even after accounting for adverse conditions potentially increasing maternal death during childbirth[52]. Our finding that the trade-off function was strongest in mothers reproducing during the famine disagrees with this prediction. However, if selective disappearance removes the frailest mothers who are most susceptible to the trade-off, this leaves a more robust subset of mothers for whom reproduction is less costly, and the trade-off function is thus predicted to become weaker with greater selective disappearance. This may explain why women of lower socioeconomic status have lower lifespan, but not if they have been exposed to the famine during development. If negative effects of environmental adversity are more difficult to detect in low-frailty survivors, selective disappearance may hence explain why no moderating effects of the early-life environment have been found here and elsewhere[17]. Therefore, while we cannot rule out the effects of selective disappearance on the trade-off function, a direct negative within-individual effect of famine exposure while reproducing is the most parsimonious explanation, or at least the major driving factor.

We emphasize that our findings should be interpreted within the context of this being an observational study occurring over a single famine event that will have coincided with other historical events that may have shaped reproduction and lifespan. Albeit the largest (as measured by death rates[30,53]), the Great Finnish Famine is only one of many societal perturbations faced by Finns between the 18th century and present day. Principally, the Finnish War (1808-1809), severe epidemics and crop failures (1832–1833), the Finnish Civil War (1918), and World War II may all have shaped the reproduction and longevity of individuals in our study population[54,55]. Although we were able to account for some demographic trends in reproductive effort and lifespan both within and among famine groups, there are limitations. Most importantly, because Finland began to industrialize soon after the famine (i.e. in the 1870s), we had no group of women born after the famine whose demography was comparable to the time preceding the start of industrialization. Thus, nailing down the causality of the Great Finnish Famine (1866-68) shaping the trade-off function is difficult within our system, but it may be possible in other datasets.

After over 100 years of research, human observational studies have provided mixed evidence for lifespan costs of reproduction, leading some to believe that reproductive behavior is not important in shaping human aging. Contrary to this, we provide evidence for a life-history trade-off between reproductive effort and lifespan and demonstrate that – under certain circumstances – reproductive effort is an important driver of individual variation in lifespan. For example, although reproductive behavior may shape the lifespans of mothers exposed to adverse environments while reproducing, it appears less

important in contemporary Finland where investment in reproduction is far lower, and modern medicine may alleviate many potential costs. Due to unaccounted variation in individual heterogeneity, our study will still underestimate the underlying trade-off, and future research should focus on the underlying mechanisms or within-individual measures of aging (e.g., Ryan et al.[56]). Lifespan is the ultimate outcome of many underlying factors, and reproductive behavior in particular can have different effects on different diseases: for example, high reproductive effort increases the risk of cardiovascular disease[49] but very low reproductive effort increases the risk of some breast cancer subtypes[57]. Therefore, future studies focusing on specific diseases or using biomarkers would be best placed to study how individual reproductive behavior shapes aging.

METHODS

Study population

To investigate how a mother's reproductive behavior affects her lifespan, we used long-term individual life-history data from rural Finland. Data were adapted from Parish records across rural Finland dating back to the 16th century. These records were maintained by the Lutheran Church and include birth, marriage, and death certificates, but also yearly attendances of religious services, which from 1749 onwards were required by law to be recorded for tax purposes. This allows complete life-histories to be precisely constructed, including the migration of individuals between parishes. These individual records were then linked across generations resulting in a genealogical dataset of 100,598 people born from 1536 to 2012.

The majority of individuals in these data were born in a preindustrial period where agriculture employed 90% of the population[28]. Preindustrial farming techniques, combined with particularly tough crop growing conditions in Finland, meant that during this period yearly yields of the two main crops, rye and barley, varied a lot with the climatic conditions[26]. Consequently, the population was characterized by high birth and death rates due to limited access to healthcare and contraception, and infectious diseases such as smallpox, typhus, and typhoid fever[55]. In our records, mothers on average had 4 children, but 38% of children died before their 15th birthday. On average, women had their first child at age 25 and 95% had their last child before age 45. Like other pre-industrial European populations, the mating system was patrilocal and highly monogamous. Divorce was forbidden[58] and infidelity severely punished[59], with recent genetic studies confirming that ~1% of children were born outside of marital ties[60,61].

Industrialization began in Finland in the 1870s – relatively late by European standards – and developed gradually, with manufacturing still employing only 20% of the population by 1910[28]. Throughout this period, access to healthcare improved and vaccination of children against smallpox was relatively common by the 1880s[42]. Consequently, life expectancy in Finland increased from 32 years at birth in

1865 to 70 for those born in 1965 and is now above the European average[53]. In this period, access to contraception also improved and cultural preferences changed, with the fertility transition beginning around 1910 where birth rates declined from ~30 births per 1000 people to ~12 by the 1970s[41].

Quantification of lifespans

All data handling was performed in R 4.3.2[62], within RStudio 2023.12.1[63], using *tidyr* 1.3.1[64]. We calculated the lifespan of all individuals with a recorded birth (99%) and death (43%). For those with recorded years but missing months and/or days the middle value was used (1% and 2% of recorded births and deaths, respectively). Individuals with missing death dates were then assigned a last-seen date of the final year they were known to have been alive in the data (available for 97% of individuals missing death dates), which could include a last-known birth of child or attendance of religious services. As the precise date of these services was often unknown, we standardized the date across individuals and treated all individuals as at least being alive on January 1st of their year of last appearance. Lifespans were then calculated in decimal years using the *lubridate* package 1.9.2[65] giving a median of 24 (range = 0-108). We also recorded whether this lifespan was calculated from known death dates or dates of last appearance which would be accounted for using a survival analysis in statistical analyses (see *Statistical analyses*).

Quantification of reproductive traits

We recorded six aspects of a woman's reproductive history thought to capture a mother's reproductive effort, defined as the total amount of resources – accounting for both direct and indirect reproductive costs[66] – devoted to bearing and raising offspring to independence[31,67]. These variables included the four variables that Helle[31] used to measure reproductive effort: number of children born, number of child-years experienced, ages at last reproduction, and reproductive tenure (i.e., the time between first and last reproduction). Additionally, we included the number of sons born, and the number of children born that were twins or triplets (hence multiple births), which are both associated with increased reproductive effort[68–71]. We also modified the definition of child-years experienced from the cumulative time that a mother co-survived with her children while they were younger than age 18 to age 5, because the effort of bearing and raising offspring is relatively low and children are more independent after age 5[72], even helping to raise younger siblings thereafter[73]. Thus, if a mother survived at least 5 years after her last birth and had 3 children, one of which died at age 1, another age 10, and another age 60, her child years experienced would be (1+5+5=) 11.

The median number of children for known mothers in our population was 3, ranging from 1 to 18. We estimated the ages at last reproduction and reproductive tenure for all mothers with a known child-birth date, which had medians of 35 (range, 16–51) and 8 (0–31), respectively. Sex of children was known in 99.4% of children, with mothers having 0–12 sons, with population-level birth sex ratios approximately 50:50. Multiple birth status was assigned to 99.3% of cases. Six percent of mothers had at least one set

of twins or triplets, but one mother had 3 sets of twins. In cases where children or mothers had unknown death dates before age 5 (81%), the year of last appearance was used to calculate the child-years experienced. Median child years experienced were 12 (0-75).

Assigning famine exposure groups

All individuals were grouped according to whether – and in what life stage – they were exposed to the Great Finnish Famine. We first assigned the start and end dates of the famine as February 1st 1865 and May 31st 1869 which is the period of elevated excess mortality observed country-wide in Finland due to the famine[28]. Based on these dates we categorized all women surviving to adulthood (19.1yr, 5th percentile for age at first reproduction) into 3 groups: individuals dying before the famine (n = 3,694), individuals exposed to the famine at some point in their live (n = 9,337), and individuals born after the famine (n = 15,036). We then further divided individuals exposed to the famine into three groups based on when they were exposed to the famine: when they were developing, reproductively active, or post-reproductive. We defined women as reproductively active during the famine if – at the midpoint of the famine (i.e., March 31st 1867) – they were older than the 5th percentile of age at first reproduction (19.1 yr) but younger than the 95th percentile of age at last reproduction (44.9 yr) calculated from mothers reproducing before the fertility transition in 1911[41]. Individuals younger than 19.1 years at the famine's midpoint were assigned the developing group (n = 4,231) and individuals older than 44.9 at the midpoint were assigned the post-reproductive group (n = 1,612), with those aged in between assigned to the reproductively active group (n = 3,494). 1,052 women could not be assigned a famine category, due to missing birth or last seen dates.

Assigning socioeconomic status groups

To account for a source of individual heterogeneity that can influence the lifespan and reproductive effort of women[51,74], we grouped women surviving to adulthood into three socioeconomic status groups: upper, including mostly landowners and merchants (n = 6,591); intermediate, including mostly craftsmen, such as smiths, and fishermen (n = 7,764); and lower, consisting of landless families and servants (n = 6,750). In cases where a woman's occupation was missing but the husband's occupation was present, we assigned it based on the husband's occupation (n = 2,357). If both were present but different (n = 590), the highest socioeconomic status was used. In total, socioeconomic status could be determined for 76% of adult women.

Data selection

For women surviving to adulthood, we first excluded childless women (n = 9,275) because of the substantial differences in health of childless females in preindustrial populations that make comparisons to reproductive females (henceforth mothers) challenging[12]. We then excluded mothers that had not been tracked throughout their entire reproductive period (n = 6,658) to ensure the precise estimation of reproductive effort. We further excluded mothers who died before completing their reproductively

active period (age 44.9, as defined above) because we wanted to estimate the long-term lifespan costs of reproduction and minimize frailty heterogeneity (n = 2,204). However, we accept that this may lead to an underestimation of the total costs of reproduction by excluding those who died directly after reproducing and by including only the most robust mothers that survived to post-reproductive life[16,33]. This left 9,930 women. Before 1725 the coverage of the data was very low and after 1911 there were increasing numbers of missing individuals because they are still alive, both of which could bias lifespans, so were removed (n = 1,906). We were also only interested in the long-term effects of the famine, and so excluded those dying during the famine period itself (n = 478). We further controlled for individual heterogeneity by excluding mothers who were twins or triplets (n = 119), multiple marriers (n = 612), and women without recorded childbirth dates (n = 4) or socioeconomic statuses (n = 410) as done in other studies[75]. This data selection is summarized in Fig. S2.

Finally, we examined the proportion of individuals with known death dates versus those that had only a last seen date (i.e. were censored) across the years lived for each of our famine exposure groups. Survival analyses (as used here) allow the combining of censored and uncensored data to estimate lifespans but can become biased if the proportion of censoring is biased with respect to lifespan across predictors in a survival model[76]. We found that the percentage of censored individuals was much higher in the groups of individuals exposed to the famine while reproductively active (43%), while developing (51%), and those born after the famine (35%), compared with those exposed post-reproduction (4%) and dying before the famine (3%; Fig. S3a), due to two spikes in the number of censored individuals between the years of 1898-1904 and 1910-11 (Fig. S3b). Because of the temporal nature of our famine exposure groups, these resulted in systematic structuring of censoring across lifespans (Fig. S4), which would result in biased lifespans. Removing lifespans censored during those two periods (n = 1717) removed these biases (Fig. S4) and resulted in a relatively even percentage of censored to non-censored individuals across famines exposure categories (2-11%; Fig. S5).

This resulted in 4684 mothers with a median lifespan of at least 68 years (range 45-103) and 5 children (1-17) (Table S6). These values are slightly higher than the full dataset (see Table S6) but remained comparable to other similar populations[36,75].

Statistical analysis

Following Helle[31] we used a confirmatory factor analysis measurement model to estimate the *latent* lifetime reproductive effort from the six indicator variables that are hypothesized to be components of a woman's reproductive effort[77–79]. Measurement models use simultaneous equations to separate the correlation between these indicator variables into the true variance in reproductive effort, and the error variance which captures the measurement error for each specific indicator variable[80]. As indicator variables we used the number of children born, number of child-years experienced, ages at last reproduction, and reproductive tenure, number of sons born, and number of children that were part of

multiple births. Indicators with factor loading p-values < 0.05 contributed to estimating lifetime reproductive effort. The number of children born was used to scale the *latent* reproductive effort so that each unit increase in reproductive effort could be interpreted as equivalent to the total resources used in raising one child. The latent reproductive effort was mean centered at 0 so values could be negative, and indicate lower than average reproductive effort.

All reproductive variables significantly contributed to estimating reproductive effort (p-value < 0.001, *loadings*, Table 1). Specifically, increases in one unit of reproductive effort was associated with 0.536 (95% CIs = 0.523-0.548) more sons, 1.238 (1.187-1.289) years increase in ages at last reproduction, 2.131 (2.092-2.170) years longer reproductive tenures, 3.878 (3.811-3.945) years increase in child-years experienced, and 0.052 (0.044-0.059) more multiple births (Table 1). The number of children was clearly the most important component of the reproductive effort variable and showed a correlation with the estimated reproductive effort of 0.99 (see Fig. S6).

This measurement model was incorporated within a structural equation model (SEM) estimated using simultaneous equations and restricted maximum likelihood in the software *Mplus* 8.8[81]. This model was used to examine how reproductive effort, lifespan, and the direct effect of reproductive effort on lifespan changed across mothers exposed to the Great Finnish Famine. Lifespan was estimated using a semiparametric continuous-time survival model which approximates a Cox-proportional hazards model[82]. This combines the number of years individuals were known to have lived and whether these individuals had a recorded death date or had been censored. By using a survival analysis, the SEM estimates how the log-hazard mortality risk changes according to each covariate. Hence, positive coefficients indicate an increased risk of mortality with an increase in the covariate, and thus a reduction in survival probability or lifespan. The model included the direct effects of reproductive effort on lifespan while simultaneously estimating the differences in reproductive effort and lifespan across predictors. Separating these effects is a key strength of the SEM, which cannot be done in other models (such as linear mixed models). We also modelled the differences in lifespan and reproductive effort across socioeconomic statuses and temporal changes occurring in each famine exposure group by including a birth year effect relative to the middle birth year in each famine exposure group, and by allowing the effects of relative birth year to vary across groups. We also tested if the effect of reproductive effort on lifespan depended on socioeconomic status. P-values less than 0.05 were deemed significant and non-significant interactions were removed from final models, least significant first, to aid interpretation of lower-order effects. Pairwise comparisons between categories were done by swapping the reference groups in the SEM. Collinearity of between variables used in models was checked using *corvif()* from *Highstat* 10[83]. The variance inflation factors were all < 1.5. For illustration and quantification purposes, we extracted the estimated reproductive effort for mothers and ran Cox proportional hazard models with the same predictors for each famine exposure group separately,

allowing us to estimate and present the predicted effect of changing reproductive effort on lifespan under a given famine exposure.

Mplus does not allow for the inclusion of random effects if some groups only have one sample[81]. Therefore, we also used the extracted reproductive effort estimates for each mother from the SEM in mixed effect Cox proportional hazard models using *Coxme* 2.2-20[84] to see if our results were robust when accounting for shared family, region, and birth year effects among mothers. For these analyses we retained all but four individuals of unknown region. Mothers with unknown parents were assumed to have come from different families (44%) as sisters would have been identifiable in the data. *Coxme* models cannot model the direct effects of factors such as famine exposure on reproductive effort, but they represent a useful robustness check and still account for such dependencies when estimating the marginal effects. For *Coxme* models, we used likelihood ratio chi-squared tests comparing models with and without a given predictor to test for the significance of predictors with a threshold of $p < 0.05$.

The SEMs were run in *Mplus*[81], implemented in R 4.3.0[62] using *MplusAutomation* 1.1.0[85]. *ggplot2* 3.3.5[86] and *ggpubr* 0.4.0[87] were used for plotting, *ggeffects* 1.5.1[88] was used for estimating marginal effects. *survival* 3.5.7 [89] was used for estimating life-expectancies which were calculated as the predicted age at which survival probability was 50%, using median values for variables and an intermediate socioeconomic status if not specified.

COMPETING INTERESTS

The authors declare no competing interests.

ACKNOWLEDGEMENTS

E.A.Y.'s PhD was funded by the University of Groningen, through a Rosalind Franklin Fellowship awarded to H.L.D. V.L. was funded by the Strategic Research Council of the Academy of Finland (grant nos. 345185 and 345183). We thank Mirkka Lahdenpera, Mila Solonen, Dinos Sevdalakis, Aida Nitsch, and the University of Exeter's Quantitative Genetics Club for feedback throughout the project. We thank Samuli Helle for helping with the SEM approach and other detailed methodological feedback, and Yuheng Sun, Maaike A Versteegh, and Janet Chik for comments on the writing.

AUTHOR CONTRIBUTION

All authors designed the research; VL collected the data; EAY wrangled the data and performed all analyses; EAY drafted the main text and supplementary material; EP, VL, and HLD commented and edited versions of this text.

REFERENCES

1. Flatt, T. & Partridge, L. Horizons in the evolution of aging. *BMC Biology* **16**, 1–13 (2018).
2. Kirkwood, T. B. L. Evolution of ageing. *Nature* **270**, 301–304 (1977).
3. Kirkwood, T. B. L. & Rose, M. R. Evolution of senescence : late survival sacrificed for reproduction. *Philosophical Transactions: Biological Sciences* **332**, 15–24 (1991).
4. *Mechanisms of Life History Evolution: The Genetics and Physiology of Life History Traits and Trade-Offs*. (Oxford University Press, 2011). doi:10.1093/acprof:oso/9780199568765.001.0001.
5. Chang, C., Moiron, M., Sánchez-Tójar, A., Niemelä, P. T. & Laskowski, K. L. What is the meta-analytic evidence for life-history trade-offs at the genetic level? *Ecology Letters* **27**, e14354 (2024).
6. Boonekamp, J. J., Salomons, M., Bouwhuis, S., Dijkstra, C. & Verhulst, S. Reproductive effort accelerates actuarial senescence in wild birds: an experimental study. *Ecology Letters* **17**, 599–605 (2014).
7. Jasienska, G. Costs of reproduction and ageing in the human female: Reproduction and ageing in women. *Philosophical Transactions of the Royal Society B: Biological Sciences* **375**, (2020).
8. Beeton, M., Yule, U. & Pearson, K. Data for the problem of evolution in man. V. On the correlation between duration of life and the number of offspring. *Proc. R. Soc. Lond.* **67**, 159–179 (1901).
9. Bell, A. G. *The Duration of Life and Conditions Associated with Longevity: A Study of the Hyde Genealogy*. (Genealogical Record Office, 1918).
10. Bolund, E. The challenge of measuring trade-offs in human life history research. *Evolution and Human Behavior* **41**, 502–512 (2020).
11. Gagnon, A. Natural fertility and longevity. *Fertility and Sterility* **103**, 1109–1116 (2015).
12. Hurt, L., Ronsmans, C. & Thomas, S. L. The effect of number of births on women's mortality: Systematic review of the evidence for women who have completed their childbearing. *Population Studies* **60**, 55–71 (2006).

13. Reznick, D., Nunney, L. & Tessier, A. Big houses, big cars, superfleas and the costs of reproduction. *Trends in Ecology and Evolution* **15**, 421–425 (2000).
14. van Noordwijk, A. J. & de Jong, G. Acquisition and Allocation of Resources: Their Influence on Variation in Life History Tactics. *The American Naturalist* **128**, 137–142 (1986).
15. Doblhammer, G. & Oeppen, J. Reproduction and longevity among the British peerage: The effect of frailty and health selection. *Proceedings of the Royal Society B: Biological Sciences* **270**, 1541–1547 (2003).
16. Hsu, C. H., Posegga, O., Fischbach, K. & Engelhardt, H. Examining the trade-offs between human fertility and longevity over three centuries using crowdsourced genealogy data. *PLoS ONE* **16**, 1–20 (2021).
17. Nenko, I., Hayward, A. D., Simons, M. J. P. & Lummaa, V. Early-life environment and differences in costs of reproduction in a preindustrial human population. *PLoS ONE* **13**, 1–16 (2018).
18. Wang, X., Byars, S. & Stearns, S. Genetic links between post-reproductive lifespan and family size in Framingham. *Evol Med Public Health.* (2013) doi:10.1093/emph/eot013.
19. Riley, J. C. *Rising Life Expectancy: A Global History*. (Cambridge University Press, 2001).
20. Vermeulen, R., Schymanski, E. L., Barabási, A.-L. & Miller, G. W. The exposome and health: Where chemistry meets biology. *Science* **367**, 392–396 (2020).
21. Cheng, M. *et al.* Accelerated biological aging six decades after prenatal famine exposure. *Proceedings of the National Academy of Sciences* **121**, e2319179121 (2024).
22. Lumey, L. H., Li, C., Khalangot, M., Levchuk, N. & Wolowyna, O. Fetal exposure to the Ukraine famine of 1932–1933 and adult type 2 diabetes mellitus. *Science* **385**, 667–671 (2024).
23. Lumey, L. H., Stein, A. D. & Susser, E. Prenatal Famine and Adult Health. *Annu. Rev. Public Health* **32**, 237–262 (2011).
24. Chen, Y. & Zhou, L.-A. The long-term health and economic consequences of the 1959–1961 famine in China. *Journal of Health Economics* **26**, 659–681 (2007).
25. Barker, D. J. P. *Mothers, Babies and Disease in Later Life*. (Churchill Livingstone, Edinburgh; New York, 1998).

26. Hayward, A. D., Holopainen, J., Pettay, J. E. & Lummaa, V. Food and fitness: Associations between crop yields and life-history traits in a longitudinally monitored pre-industrial human population. *Proceedings of the Royal Society B: Biological Sciences* **279**, 4165–4173 (2012).
27. Rickard, I. J. *et al.* Food availability at birth limited reproductive success in historical humans. *Ecology* **91**, 3515–3525 (2010).
28. Voutilainen, M. Poverty, Inequality and the Finnish 1860s Famine. (2016).
29. Pitkänen, K. J. & Mielke, J. H. Age and sex differentials in mortality during two nineteenth century population crises. *European Journal of Population* **9**, 1–32 (1993).
30. Salonen, M., Lahdenperä, M., Rotkirch, A. & Lummaa, V. Fertility resilience varies by socioeconomic status and sex: Historical trends in childlessness across 150 years. *iScience* **27**, 1–13 (2024).
31. Helle, S. Search for a resource-based trade-off between lifetime reproductive effort and women's postreproductive survival in preindustrial Sweden. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences* **74**, 642–647 (2019).
32. Helle, S., Lummaa, V. & Jokela, J. Are reproductive and somatic senescence coupled in humans? Late, but not early, reproduction correlated with longevity in historical Sami women. *Proceedings of the Royal Society B: Biological Sciences* **272**, 29–37 (2005).
33. Helle, S. Selection bias in studies of human reproduction-longevity trade-offs. *Proceedings of the Royal Society B: Biological Sciences* **284**, (2017).
34. Garnier, A., Gaillard, J. M., Gauthier, D. & Besnard, A. What shapes fitness costs of reproduction in long- lived iteroparous species? A case study on the Alpine ibex. *Ecology* **97**, 205–214 (2016).
35. Robert, A., Paiva, V. H., Bolton, M., Jiguet, F. & Bried, J. The interaction between reproductive cost and individual quality is mediated by oceanic conditions in a long-lived bird. *Ecology* **93**, 1944–1952 (2012).
36. Invernizzi, L., Bergeron, P., Pelletier, F., Lemaître, J.-F. & Douhard, M. Sons Shorten Mother's Lifespan in Preindustrial Families with a High Level of Infant Mortality. *The American Naturalist* 000–000 (2024) doi:10.1086/731792.

37. Hughes, K. *et al.* The effect of multiple adverse childhood experiences on health: a systematic review and meta-analysis. *The Lancet Public Health* **2**, e356–e366 (2017).
38. Cartwright, S. J., Nicoll, M. A. C., Jones, C. G., Tatayah, V. & Norris, K. Anthropogenic Natal Environmental Effects on Life Histories in a Wild Bird Population. *Current Biology* **24**, 536–540 (2014).
39. Pettay, J. E., Helle, S., Jokela, J. & Lummaa, V. Natural Selection on Female Life-History Traits in Relation to Socio-Economic Class in Pre-Industrial Human Populations. *PLoS ONE* **2**, (2007).
40. Lycett, J. E., Dunbar, R. I. M. & Voland, E. Longevity and the costs of reproduction in a historical human population. *Proceedings of the Royal Society B: Biological Sciences* **267**, 31–35 (2000).
41. Mitchell, B. International Historical Statistics, Brian Mitchell (2013) – processed by Our World in Data. "International Historical Statistics (Births per 1,000) (Brian Mitchell (2013))" [dataset]. International Historical Statistics, Brian Mitchell (2013) [original data]. (2013).
42. Ukonaho, S., Lummaa, V. & Briga, M. The Long-Term Success of Mandatory Vaccination Laws After Implementing the First Vaccination Campaign in 19th Century Rural Finland. *American Journal of Epidemiology* **191**, 1180–1189 (2022).
43. Kaptijn, R. *et al.* The Trade-Off between Female Fertility and Longevity during the Epidemiological Transition in the Netherlands. *PLoS ONE* **10**, e0144353 (2015).
44. Butte, N. F. & King, J. C. Energy requirements during pregnancy and lactation. *Public Health Nutr.* **8**, 1010–1027 (2005).
45. Jasienska, G. Reproduction and lifespan: Trade-offs, overall energy budgets, intergenerational costs, and costs neglected by research. *Am. J. Hum. Biol.* **21**, 524–532 (2009).
46. Saltiki, K. & Alevizaki, M. Coronary heart disease in postmenopausal women; the role of endogenous estrogens and their receptors. *Hormones* **6**, 9–24 (2007).
47. Heinig, M. J. & Dewey, K. G. Health effects of breast feeding for mothers: a critical review. *Nutr. Res. Rev.* **10**, 35–56 (1997).
48. Shin, Y.-A. & Lee, K.-Y. Low estrogen levels and obesity are associated with shorter telomere lengths in pre- and postmenopausal women. *J Exerc Rehabil* **12**, 238–246 (2016).

49. Li, W., Ruan, W., Lu, Z. & Wang, D. Parity and risk of maternal cardiovascular disease: A dose–response meta-analysis of cohort studies. *Eur J Prev Cardiolog* **26**, 592–602 (2019).
50. Doblhammer, G., Van Den Berg, G. J. & Lumey, L. H. A re-analysis of the long-term effects on life expectancy of the Great Finnish Famine of 1866–68. *Population Studies* **67**, 309–322 (2013).
51. Hayward, A. D., Rickard, I. J. & Lummaa, V. Influence of early-life nutrition on mortality and reproductive success during a subsequent famine in a preindustrial population. *Proceedings of the National Academy of Sciences of the United States of America* **110**, 13886–13891 (2013).
52. Hammel, E. A. & Gullickson, A. Kinship structures and survival: Maternal mortality on the Croatian–Bosnian border 1750–1898. *Population Studies* **58**, 145–159 (2004).
53. Wilmoth, J. R. *et al.* Human Mortality Database. Available at www.mortality.org. (2021).
54. Statistics Finland. Official Statistics of Finland (OSF): Deaths [online publication]. *Helsinki: Statistics Finland* (2024).
55. Turpeinen, O. Regional differentials in finnish mortality rates 1816-1865. *Scandinavian Economic History Review* **21**, 145–163 (1973).
56. Ryan, C. P. *et al.* Pregnancy is linked to faster epigenetic aging in young women. *Proc. Natl. Acad. Sci. U.S.A.* **121**, e2317290121 (2024).
57. Aktipis, C. A., Ellis, B. J., Nishimura, K. K. & Hiatt, R. A. Modern reproductive patterns associated with estrogen receptor positive but not negative breast cancer susceptibility. *Evolution, Medicine and Public Health* **2015**, 52–74 (2015).
58. Moring, B. Nordic family patterns and the north-west European household system. *Continuity and Change* **18**, 77–109 (2003).
59. Sundin, J. Sinful Sex: Legal Prosecution of Extramarital Sex in Preindustrial Sweden. *Social Science History* **16**, 99–128 (1992).
60. Larmuseau, M. H. D., Matthijs, K. & Wenseleers, T. Cuckolded Fathers Rare in Human Populations. *Trends in Ecology and Evolution* **31**, 327–329 (2016).
61. Larmuseau, M. H. D. *et al.* A Historical-Genetic Reconstruction of Human Extra-Pair Paternity. *Current Biology* **29**, 4102-4107.e7 (2019).

62. R Core Team. R: A language environment for statistical computing. R Foundation for Statistical Computing (2020).
63. Allaire, J. RStudio: integrated development environment for R. *Boston, MA* **770**, 165–171 (2012).
64. Wickham, H. *et al.* Welcome to the tidyverse. *Journal of Open Source Software* **4**, 1686 (2019).
65. Grolemund, G. & Wickham, H. Dates and Times Made Easy with {lubridate}. *Journal of Statistical Software* **40**, 1–25 (2011).
66. Ginther, S. C., Cameron, H., White, C. R. & Marshall, D. J. Metabolic loads and the costs of metazoan reproduction. *Science* **384**, 763–767 (2024).
67. Helle, S. Accounting for measurement error in human life history trade-offs using structural equation modeling. *American Journal of Human Biology* **30**, 1–9 (2018).
68. Galbarczyk, A., Klimek, M., Nenko, I. & Jasienska, G. Sons may be bad for maternal health at older age: New evidence for costs of reproduction in humans. *Journals of Gerontology - Series A Biological Sciences and Medical Sciences* **74**, 648–651 (2019).
69. Galbarczyk, A. *et al.* Inflammaging: Blame the sons. Relationships between the number of sons and the level of inflammatory mediators among post-reproductive women. (2021) doi:10.1002/ajpa.24295.
70. Helle, S., Lummaa, V. & Jokela, J. Sons reduced maternal longevity in preindustrial humans. *Science* **296**, 1085 (2002).
71. Helle, S. & Lummaa, V. A trade-off between having many sons and shorter maternal post-reproductive survival in pre-industrial Finland. *Biology letters* **9**, 20130034 (2013).
72. Riswick, T. & Hsieh, Y.-H. Between rivalry and support: The impact of sibling composition on infant and child mortality in Taiwan, 1906–1945. *DemRes* **42**, 615–656 (2020).
73. Crognier, E., Villena, M. & Vargas, E. Helping patterns and reproductive success in Aymara communities. *Am. J. Hum. Biol.* **14**, 372–379 (2002).
74. Högnäs, R. S., Roelfs, D. J., Shor, E., Moore, C. & Reece, T. J-Curve? A Meta-Analysis and Meta-Regression of Parity and Parental Mortality. *Popul Res Policy Rev* **36**, 273–308 (2017).

75. Gagnon, A. *et al.* Is there a trade-off between fertility and longevity? A comparative study of women from three large historical databases accounting for mortality selection. *Am. J. Hum. Biol.* **21**, 533–540 (2009).
76. Leung, K.-M., Elashoff, R. M. & Afifi, A. A. Censoring issues in survival analyses. *Annu. Rev. Public Health* **18**, 83–104 (1997).
77. Bollen, K. *Structural Equations With Latent Variables*. (Wiley, New York, 1989).
78. Heck, R. H. & Thomas, S. L. Chapter 5 Defining multilevel latent variables. in *An introduction to multilevel modelling techniques: MLM and SEM approaches using Mplus* 133–181 (Routledge, New York, 2015).
79. Muthén, B. O. Beyond SEM: General Latent Variable Modeling. *Behaviormetrika* **29**, 81–117 (2002).
80. Kilne, R. *Principles and Practice of Structural Equation Modeling*. (The Guilford Press, New York, 2016).
81. Muthén, L. K. & Muthén, B. O. *Mplus: User's Guide*. (Muthén & Muthén, Los Angeles, CA, 1998).
82. Asparouhov, T. & Muth, B. Continuous - Time Survival Analysis in Mplus. 1–22 (2018).
83. Zuur, A. F. *et al. Mixed Effects Models and Extensions in Ecology with R*. vol. 574 (Springer, 2009).
84. Therneau, T. M. *Coxme: Mixed Effects Cox Models*. (2024).
85. Hallquist, M. H. & Wiley, J. F. MplusAutomation: An R Package for Facilitating Large-Scale Latent Variable Analyses in Mplus. *Structural Equation Modeling* **25**, 621–638 (2018).
86. Wickham, H. ggplot2: Elegant Graphics for Data Analysis. (2016).
87. Kassambara, Alboukadel. ggpubr: 'ggplot2' Based Publication Ready Plots. (2020).
88. Lüdecke, D. ggeffects: Tidy Data Frames of Marginal Effects from Regression Models. *JOSS* **3**, 772 (2018).
89. Therneau, T. A Package for Survival Analysis in R. R package version 3.2-7. 2020. *URL https://CRAN. R-project. org/package= survival* (2020).

Table 1: Structural equation model showing effects on lifetime reproductive effort and lifespan (as measured by log-hazard mortality risk) from 4,684 mothers. Factor loadings, mean values (*Intercept*), and residual variance for indicator variables used to estimate lifetime reproductive effort in the measurement model are shown. Estimates are shown with 95% confidence intervals and p-values. Significant effects ($p < 0.05$) are in bold. Effects of famine exposure are compared to women who died before the famine. Socioeconomic statuses are compared to intermediate statuses. Relative birth date is scaled by year and centered by the middle birth date for each group.

Variable	Estimate (95% CI)	P-value
Lifetime reproductive effort loadings		
Number of children born	1 (1-1)	-
Number of sons born	**0.536 (0.523-0.548)**	**<0.001**
Age at last reproduction	**1.238 (1.187-1.289)**	**<0.001**
Reproductive tenure	**2.131 (2.092-2.17)**	**<0.001**
Child-years experienced	**3.878 (3.811-3.945)**	**<0.001**
Number of multibirth children born	**0.052 (0.044-0.059)**	**<0.001**
Effects on reproductive effort		
Exposure group (exposed post-reproduction)	0.125 (-0.442-0.691)	0.666
Exposure group (exposed during reproduction)	*0.386 (-0.006-0.778)*	*0.054*
Exposure group (exposed during development)	**0.551 (0.080-1.022)**	**0.022**
Exposure group (born after)	**-0.504 (-0.922--0.086)**	**0.018**
Relative birth date	-0.004 (-0.013-0.004)	0.343
Relative birth date x Exposure group (exposed post-reproduction)	0.022 (-0.005-0.049)	0.108
Relative birth date x Exposure group (exposed during reproduction)	**0.033 (0.008-0.057)**	**0.010**
Relative birth date x Exposure group (exposed during development)	0.019 (-0.018-0.057)	0.308
Relative birth date x Exposure group (born after)	**-0.061 (-0.078--0.044)**	**<0.001**
Socioeconomic status (lower)	**-0.541 (-1.020--0.062)**	**0.027**
Socioeconomic status (lower) x Exposure group (exposed post-reproduction)	-0.470 (-1.228-0.287)	0.224
Socioeconomic status (lower) x Exposure group (exposed during reproduction)	**-0.653 (-1.299--0.008)**	**0.047**
Socioeconomic status (lower) x Exposure group (exposed during development)	-0.132 (-0.875-0.611)	0.728
Socioeconomic status (lower) x Exposure group (born after)	-0.335 (-1.010-0.339)	0.330
Socioeconomic status (upper)	**0.609 (0.243-0.975)**	**0.001**
Socioeconomic status (upper) x Exposure group (exposed post-reproduction)	-0.010 (-0.594-0.574)	0.974

Socioeconomic status (upper) x Exposure group (exposed during reproduction)	-0.113 (-0.655-0.429)	0.683
Socioeconomic status (upper) x Exposure group (exposed during development)	-0.265 (-0.890-0.359)	0.405
Socioeconomic status (upper) x Exposure group (born after)	**-0.583 (-1.157--0.008)**	**0.047**
Effects on mortality risk		
Exposure group (exposed post-reproduction)	**0.333 (0.283-0.392)**	**<0.001**
Exposure group (exposed during reproduction)	**0.694 (0.593-0.812)**	**<0.001**
Exposure group (exposed during development)	**0.600 (0.508-0.711)**	**<0.001**
Exposure group (born after)	**0.462 (0.397-0.538)**	**<0.001**
Lifetime reproductive effort	1.003 (0.985-1.021)	0.733
Lifetime reproductive effort x Exposure group (exposed post-reproduction)	0.994 (0.966-1.023)	0.682
Lifetime reproductive effort x Exposure group (exposed during reproduction)	**1.041 (1.009-1.073)**	**0.011**
Lifetime reproductive effort x Exposure group (exposed during development)	1.009 (0.977-1.041)	0.599
Lifetime reproductive effort x Exposure group (born after)	0.996 (0.964-1.028)	0.794
Relative birth date	**1.026 (1.022-1.029)**	**<0.001**
Relative birth date x Exposure group (exposed post-reproduction)	1.005 (0.998-1.012)	0.161
Relative birth date x Exposure group (exposed during reproduction)	**0.970 (0.962-0.980)**	**<0.001**
Relative birth date x Exposure group (exposed during development)	**0.972 (0.961-0.984)**	**<0.001**
Relative birth date x Exposure group (born after)	**0.960 (0.954-0.967)**	**<0.001**
Socioeconomic status (lower)	**1.305 (1.095-1.553)**	**0.003**
Socioeconomic status (lower) x Exposure group (exposed post-reproduction)	1.027 (0.811-1.303)	0.822
Socioeconomic status (lower) x Exposure group (exposed during reproduction)	1.130 (0.878-1.455)	0.342
Socioeconomic status (lower) x Exposure group (exposed during development)	**0.752 (0.579-0.976)**	**0.032**
Socioeconomic status (lower) x Exposure group (born after)	0.866 (0.674-1.113)	0.260
Socioeconomic status (upper)	1.110 (0.974-1.264)	0.118
Socioeconomic status (upper) x Exposure group (exposed post-reproduction)	0.967 (0.801-1.165)	0.720
Socioeconomic status (upper) x Exposure group (exposed during reproduction)	0.873 (0.715-1.066)	0.183
Socioeconomic status (upper) x Exposure group (exposed during development)	0.872 (0.705-1.078)	0.206
Socioeconomic status (upper) x Exposure group (born after)	1.121 (0.91-1.381)	0.282
Intercepts		
Number of children born	**5.265 (4.978-5.552)**	**<0.001**

Number of sons born	**2.695 (2.539-2.852)**	**<0.001**
Age at last reproduction	**38.133 (37.762-38.504)**	**<0.001**
Reproductive tenure	**11.872 (11.254-12.49)**	**<0.001**
Child-years experienced	**21.131 (20.016-22.245)**	**<0.001**
Number of multibirth children born	**0.211 (0.187-0.235)**	**<0.001**
Residual variances		
Number of children born	**0.344 (0.276-0.411)**	**<0.001**
Number of sons born	**1.348 (1.283-1.412)**	**<0.001**
Age-at-last reproduction	**19.315 (18.463-20.166)**	**<0.001**
Reproductive tenure	**10.771 (10.128-11.415)**	**<0.001**
Child-years experienced	**27.365 (24.856-29.875)**	**<0.001**
Number of multibirth children born	**0.439 (0.397-0.481)**	**<0.001**
Lifetime reproductive effort	**8.298 (7.995-8.602)**	**<0.001**

Table 2: Pairwise comparisons of the association between reproductive effort and mortality risk across famine exposure groups. Diagonal values show the hazard ratio (95% Confidence Intervals) for the effect of reproductive effort on mortality within each group. Off-diagonal values show p-values for pairwise differences in this association between groups. Significant differences or associations ($p < 0.05$) are highlighted in bold; marginally significant associations ($p > 0.05$ and < 0.10) are italicized. Results are from a structural equation model of the same structure as Table 1 but with different reference groups to estimate p-values and associations.

	Died before famine	Exposed post-reproduction	Exposed during reproduction	Exposed during development	Born after famine
Died before famine	1.003 (0.985 - 1.021)				
Exposed post-reproduction	0.682	0.997 (0.975 - 1.019)			
Exposed during reproduction	**0.011**	**0.007**	**1.044 (1.018 - 1.069)**		
Exposed during development	0.599	0.404	*0.087*	1.012 (0.986 - 1.039)	
Born after famine	0.794	0.926	**0.018**	0.5	0.999 (0.972 - 1.026)