

Are reproductive and somatic senescence coupled in humans? Late, but not early, reproduction correlated with longevity in historical Sami women

Samuli Helle^{1*}, Virpi Lummaa² and Jukka Jokela³

¹*Section of Ecology, Department of Biology, University of Turku, FIN-20014 Turku, Finland*

²*Department of Animal and Plant Sciences, University of Sheffield, Sheffield S10 2TN, UK*

³*Department of Biology, University of Oulu, POB 3000, FIN-90014 Oulu, Finland*

Evolutionary theory of senescence emphasizes the importance of intense selection on early reproduction owing to the declining force of natural selection with age that constrains lifespan. In humans, recent studies have, however, suggested that late-life mortality might be more closely related to late rather than early reproduction, although the role of late reproduction on fitness remains unclear. We examined the association between early and late reproduction with longevity in historical post-reproductive Sami women. We also estimated the strength of natural selection on early and late reproduction using path analysis, and the effect of reproductive timing on offspring survival to adulthood and maternal risk of dying at childbirth. We found that natural selection favoured both earlier start and later cessation of reproduction, and higher total fecundity. Maternal age at childbirth was not related to offspring or maternal survival. Interestingly, females who produced their last offspring at advanced age also lived longest, while age at first reproduction and total fecundity were unrelated to female longevity. Our results thus suggest that reproductive and somatic senescence may have been coupled in these human populations, and that selection could have favoured late reproduction. We discuss alternative hypotheses for the mechanisms which might have promoted the association between late reproduction and longevity.

Keywords: evolution; longevity; life history; *Homo sapiens*; natural selection

1. INTRODUCTION

Evolutionary theories of senescence based on life-history trade-offs highlight the adverse effects of high and early reproductive effort on late-life survival (Williams 1957; Kirkwood & Rose 1991). These predictions are upheld in a variety of animals (e.g. Partridge & Barton 1993; Kirkwood & Austad 2000; Partridge & Gems 2002). By contrast, evidence for the reproduction-mediated decrease of human lifespan is equivocal (Appendix A). Surprisingly, the most frequently reported relationship between reproduction and post-reproductive survival in humans is between late reproduction and longevity, with advanced age at last reproduction being associated with improved longevity (see Appendix A). Likewise, many studies have shown that higher age at menopause is associated with prolonged female post-reproductive lifespan (Snowdon *et al.* 1989; van der Schouw *et al.* 1996; Cooper & Sandler 1998; Jacobsen *et al.* 1999, 2003). In addition, a recent study showed that the delaying of an entire reproductive effort to late ages covaried with the enhanced post-reproductive survival of mothers (Helle *et al.* 2002). Thus, previous results in humans appear to contradict theoretical expectations of trade-offs between early reproduction, total fecundity and late-life survival.

The causal link between late reproduction and increased female post-reproductive survival is unclear, but it has been

proposed to reflect slow overall senescence of both reproductive and somatic systems as natural selection aims to maximize the period when women can bear offspring (Perls *et al.* 1997; Perls & Fretts 2001). However, the association between late rather than early reproduction and longevity, and the positive sign of this relationship is problematic from both a technical and theoretical viewpoint. First, environmental variation among individuals may be so large that early reproduction, late reproduction and long lifespan are all expressed by the same individuals with good condition, effectively hiding the true genetic constraints among life-history traits (van Noordwijk & de Jong 1986). Second, late reproduction in women is not expected to be favoured by natural selection owing to decrease in offspring survival and quality, and maternal survivorship from childbirth (e.g. Wood 1994; Tarin *et al.* 1998), which would jeopardize the survival of all dependent offspring produced and hence female fitness. Third, because the sensitivity of natural selection on reproductive effort declines with age (Medawar 1952; Hamilton 1966), early reproduction should be favoured over late reproduction, especially in growing populations (Houston & McNamara 1999) and in constant environments (Tuljapurkar 1990). In other words, reproductive output early in life should outweigh late reproduction in terms of evolutionary fitness, and therefore have a greater impact on late-life survival.

At the present, we have no proper estimates on the intensity of natural selection on extended reproductive lifespan by the means of delayed age at last reproduction in

* Author for correspondence (samuli.helle@utu.fi).

Table 1. Mean (\pm s.d.) for studied life-history traits among historical post-reproductive Sami women in three study populations ($n = 306$).

life-history trait	Utsjoki	Inari	Enontekiö
lifetime reproductive success	4.64 \pm 1.96	4.85 \pm 1.99	5.61 \pm 2.30
number of offspring born	5.23 \pm 2.04	5.67 \pm 2.09	6.94 \pm 2.57
percentage of surviving offspring to age 18	82.8	83.3	79.1
lifespan	74.82 \pm 9.57	71.06 \pm 10.20	72.19 \pm 11.43
age at first reproduction	29.31 \pm 5.06	27.02 \pm 4.95	26.05 \pm 5.25
age at last reproduction	41.59 \pm 4.59	41.72 \pm 3.55	42.14 \pm 3.80
mean inter-birth interval (years)	3.06 \pm 0.95	3.31 \pm 0.92	2.90 \pm 0.84
spouse's age at death	69.08 \pm 12.24	67.28 \pm 12.27	69.98 \pm 11.83
number of observations	61	144	101

natural-fertility human populations (for age at menopause in contemporary populations, see Kirk *et al.* 2001). Although young age at first reproduction has previously been suggested to be one of the most important determinants of female fitness in both historical and present-day populations (Käär *et al.* 1996; Kirk *et al.* 2001), advanced models of natural selection incorporating both the ages at first and last reproduction are currently lacking. Therefore, we are unable to estimate accurately the evolutionary significance of late reproduction, and accordingly, its importance for the evolution of female post-reproductive survival.

We investigate the intensity of natural selection on female reproductive timing, and whether advanced age at last reproduction was related to female post-reproductive survival in historical Sami populations. In particular, we concentrate on the fitness effects of late reproduction by estimating the selection differential of age at last reproduction and the potential costs of childbearing at advanced age in terms of offspring survival to adulthood and maternal death at childbirth.

2. MATERIAL AND METHODS

(a) Demographic data

We used demographic data from the three seventeenth to nineteenth century Sami populations of Northern Scandinavia (Utsjoki, Inari and Enontekiö) collected from the Finnish parish registers (e.g. Helle *et al.* 2002, 2004a,b). These socially monogamous, but demographically and partly culturally different Sami populations depended on reindeer herding, fishing and hunting for their livelihood, and experienced natural mortality owing to the lack of advanced medical care (Itkonen 1948; Käär *et al.* 1996). In Enontekiö, towards the end of the nineteenth century the majority of the inhabitants were agriculturalists and of Finnish origin (Itkonen 1948). Each population occupied large partly overlapping geographical areas, with the inhabitants living in small family groups or villages (Itkonen 1948). Population size in the populations studied generally increased during the study period (e.g. in Utsjoki and Inari populations between 1750 and 1860, the increment in population size was 54% and 65%, respectively; Itkonen 1948), suggesting that early reproduction could have been important for individual fitness in these populations (Houston & McNamara 1999).

From these data we recorded fitness and key life-history traits for the Sami women (born 1679–1839), who married once (table 1). Only those women who lived beyond the age at which 99% of all women in a population had ceased their reproduction (i.e. the post-reproductive women) and for whom complete life histories

were known, were included in the analyses (n at maximum: 322), unless indicated otherwise (see § 2b). This ensured avoidance of spurious positive correlations between reproductive output and lifespan arising from the fact that women dying young also had fewer opportunities to bear offspring.

(b) Statistical methods

The intensity of natural selection on age at last reproduction (i.e. selection differential, Lande & Arnold (1983); Arnold & Wade (1984)), while controlling for other key reproductive traits including age at first reproduction, total number of offspring born, average length of inter-birth intervals and spouse's age at death, was estimated using path analysis performed on the variance-covariance matrix (e.g. Kingsolver & Schemske 1991; Mitchell 1993; Hatcher 1994; Scheiner *et al.* 2000). In our path model, ages at first and last reproduction, mean inter-birth interval and spouse's lifespan were assumed to be intercorrelated and have a direct causal effect on total fecundity, which, in turn, has a direct causal effect on fitness. As a surrogate of fitness, we used lifetime reproductive success (i.e. the number of offspring raised to age 18 years). Spouse's age at death was included to control for the effects of male survival on female reproductive performance. All non-significant path coefficients ($\alpha < 0.05$) were constrained to zero in the final path model presented here. For these Sami women, Käär *et al.* (1996) have already shown that age at first reproduction was an important component of female fitness. However, their model did not include age at last reproduction.

In a path analysis, the estimated selection differential is the sum of direct and indirect selection on a trait relating to fitness (Scheiner *et al.* 2000). Direct selection on a trait is estimated by its direct effect and effects through intermediate steps on fitness, whereas indirect selection on a focal trait is estimated by its effects via (non-causal) correlations with other traits at the same level of hierarchy in the model (Scheiner *et al.* 2000). In path analysis, one cannot directly assess the statistical significance of direct selection on a trait if it involves intermediate steps to fitness or indirect selection. Instead, one evaluates the fit of the entire path model using structural equation modelling (SEM) by comparing the expected and observed covariance matrices by different goodness-of-fit tests and indexes (Mitchell 1993; Hatcher 1994). For example, a particular path model describes the data well if the χ^2 goodness-of-fit test is non-significant; otherwise the model should be rejected or modified (Hatcher 1994; Scheiner *et al.* 2000). Complementary, and in some cases necessary (e.g. Hatcher 1994), goodness-of-fit indices often used in assessing the fit of a path model are the non-normed-fit index (NNFI) and the comparative fit index (CFI) (Hatcher 1994). If these indices exceed 0.9 (CFI ranges from zero to unity, whereas NNFI can

Table 2. Selection differential decomposed to direct and indirect selection for studied life-history traits in Sami women.

life-history trait	selection differential	direct selection	indirect selection
age at last reproduction	0.363	0.486	-0.123
age at first reproduction	-0.563	-0.668	0.105
mean inter-birth interval	-0.395	-0.396	0.001
spouse's age at death	0.144	—	0.144
number of offspring born	0.877	0.877	—

exceed unity), the fit of a path model is regarded as acceptable (Hatcher 1994). In addition, path analysis is sensitive to multicollinearity (Petraitis *et al.* 1996). We thus calculated variance inflation factors and tolerance values for independent variables in our path model. The largest inflation factor was 1.1 and the smallest tolerance value was 0.9, indicating that collinearity was not a problem.

The path analysis was conducted on pooled data over the three populations, because there were no statistically significant interactions ($p > 0.13$ in all cases) between study population and the life-history traits studied. Although the strength of selection on age at last reproduction and mean inter-birth interval varied through the study period ($p < 0.0001$), the sign and the statistical significance of these traits remained constant over the study period.

We used generalized linear mixed model (GLMM) to assess whether female age at delivery affected offspring survival probability to adulthood (age 18 years). This analysis controlled for sex, length of previous birth interval, delivery type (twin or singleton), and birth population and cohort of offspring. Because our data included offspring from the same mothers, family identity was included as a random term into the model to account for the correlated measures of offspring survival within mothers. This was done by fitting the model using the generalized estimating equations (GEEs) with binomial errors and logit-link function (Zeger & Liang 1986; McCulloch & Searle 2001). All second- and third-order interactions between explanatory variables were first added into the model and, if statistically significant ($\alpha < 0.05$), included in the final model using the backward model fitting method. In addition, using logistic regression (Hosmer & Lemeshow 1994), we examined how female age at delivery affected her probability of dying at childbirth, or shortly after the birth (i.e. within the following 12 months from the delivery) by taking offspring sex into account (male births may be more risky to the mother, see Eogan *et al.* 2003). Note that when studying the effects of advanced maternal age on offspring survival and maternal risk of dying at childbirth, we included all women with adequate information available ($n = 1519$), and not only post-reproductive women as was done in path analysis and the following maternal post-reproductive survival analyses (see following paragraph).

Finally, we examined the effect of age at last reproduction on female post-reproductive survival, while controlling for age at first reproduction, total number of offspring born, birth population and cohort, and spouse's age at death using Cox proportional hazards regression (Allison 1995; Collet 2003). Here, spouse's age at death was included to control for the effects of shared environmental and socio-economic factors acting simultaneously on the longevity of both sexes within a family (Gavrilov & Gavrilova 2001). Second-order interactions between female life-history variables and birth population were first added into the model. If these interaction terms, as well as the main terms, were not statistically significant ($\alpha < 0.05$) using the log-likelihood ratio test for comparing nested models (Collet 2003), they were omitted from the final minimal model. Assumption of proportional hazards

was checked by including time-dependent covariates of the explanatory variables in the model (Allison 1995). No evidence of time dependence for the effects of independent variables was found, and thus the assumption of proportional hazards was satisfied. All analyses above were conducted with SAS statistical package version 8.02 (SAS Institute Inc., Cary, NC, USA).

3. RESULTS

(a) Selection on age at last reproduction

The path analysis showed that the most important component of female fitness (i.e. the highest selection differential) was the number of offspring produced (table 2; figure 1). Timing of reproduction was also essential for fitness: women gained higher fitness if they began reproducing earlier, had shorter inter-birth intervals and continued reproducing later (table 2; figure 1). Covariation between female life-history traits indicated that women who started to reproduce early also ceased reproduction early, and that inter-birth intervals were largely independent of both ages at first and last reproduction (figure 1). Spouse's survival also indirectly contributed to female fitness through positive correlation with age at last reproduction and a weak negative correlation with age at first reproduction (table 2; figure 1). This model showed a good fit to the data: p -value of χ^2 test was non-significant, and both CFI and NNFI were close to unity.

If we also included those mothers who were known to have died before their post-reproductive years ($n = 493$) in our path model, the strength of selection on age at last reproduction (selection differential = 0.460) increased in relation to age at first reproduction (selection differential = -0.485) and mean inter-birth intervals (selection differential = -0.322). This result strengthens our conclusion that age at last reproduction was an important life-history trait in the Sami women studied.

(b) Age-specific costs of reproduction

We found no indication to suggest that reproducing at a late age incurred costs to Sami mothers. First, female age at delivery was unrelated to probability of offspring survival to adulthood (table 3). Furthermore, offspring survival depended on the type of delivery (twin or singleton; see Helle *et al.* (2004a) for further details), sex (sons had poorer survival), and birth population and cohort, but not on the length of previous birth interval (table 3). This result remained unchanged when mothers were divided to age classes (less than 25, 25–35 and more than 35 years of age) based on their age at each delivery to account for the potential non-linearity in female age effects ($\chi^2_2 = 1.14$, $p = 0.57$). Second, only 69 out of 1519 (4.5%) Sami mothers included here died within the next 12 months after giving birth, and this risk was neither associated with maternal age ($\chi^2_1 = 0.15$, $p = 0.48$), offspring sex

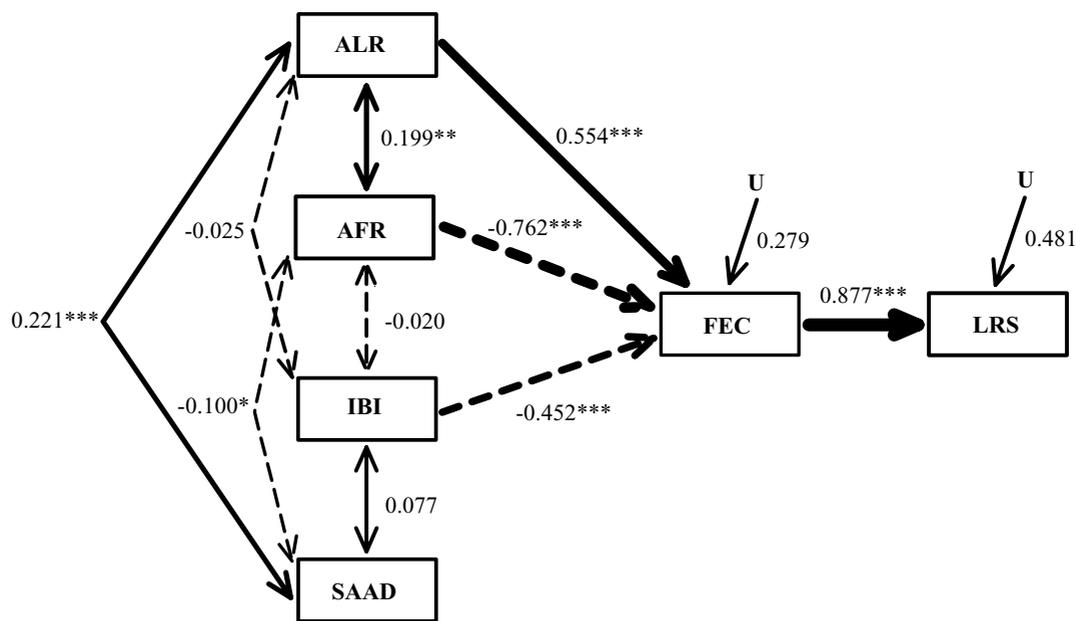


Figure 1. Path model describing linear selection gradients (i.e. standardized partial regression coefficients) on age at last reproduction (ALR), age at first reproduction (AFR), mean inter-birth intervals (IBI), spouse's age at death (SAAD) and total fecundity (FEC) on lifetime reproductive success (LRS) in historical post-reproductive Sami women. Single-headed arrows represent causal relationships, whereas double-headed arrows represent non-causal correlations between two variables. Positive selection gradients and correlations are shown in solid lines and negative selection gradients in dashed lines, and the thickness of each arrow represents the magnitude of that relationship. Insignificant selection gradients constrained to zero are omitted from the path model shown. R^2 values for total fecundity and lifetime reproductive success were 0.922 and 0.768, respectively. U denotes the unexplained error variation in dependent variables. (** $p < 0.0001$, ** $p < 0.001$, * $p < 0.08$). Goodness of fit: CFI = 0.999; NNFI = 0.997; $\chi^2 = 6.27$; d.f. = 5; $p > 0.28$.

($\chi_1^2 = 0.13$, $p = 0.72$) nor their interaction ($\chi_1^2 = 0.20$, $p = 0.65$). Similarly, this result did not change if we again divided mothers to age classes (see above) to account for nonlinearity in female age effects ($\chi_2^2 = 2.84$, $p = 0.24$).

(c) Age at last reproduction and post-reproductive survival

Those women who continued childbearing until advanced ages enjoyed the highest post-reproductive survival (table 4; figure 2). The magnitude of this effect corresponded to a 28% reduction in post-reproductive mortality for every additional year that females delayed their last birth (table 4). Female post-reproductive survival was also positively correlated with the length of her spouse's lifespan (table 4). By contrast, age at first reproduction, total number of offspring born, birth cohort and population had no effect on female post-reproductive survival (table 4). In addition, the post-reproductive survival of childless married mothers did not differ from that of mothers who had offspring (hazard ratio = 0.754(0.439–1.297), $\chi_1^2 = 1.04$, $p = 0.31$, controlling for birth population and spouse's age at death).

If the model was re-run without age at last reproduction, both age at first reproduction (hazard ratio = 0.971 (0.944–0.988), $\chi_1^2 = 4.49$, $p = 0.034$) and the total number of offspring born (hazard ratio = 0.931(0.874–0.991), $\chi_1^2 = 4.97$, $p = 0.026$) revealed significant positive effects on female post-reproductive survival. This suggests that one might have drawn the wrong conclusions about the effects of age at first reproduction and total fecundity on

female longevity, had we failed to take the effect of age at last reproduction into account.

Finally, we also conducted the survival analysis by replacing the age at first and last reproduction with the length of female reproductive lifespan. However, female post-reproductive survival was independent of the length of her reproductive lifespan ($\chi_1^2 = 0.35$, $p = 0.55$). This result shows that long female post-reproductive lifespan was related to their age at last reproduction, and not to the extended reproductive lifespan as such.

4. DISCUSSION

Natural selection favoured high fecundity, and early age at first, and late age at last, reproduction in historical Sami women. Surprisingly, these women did not pay direct costs of delayed reproduction in terms of increased maternal death risk at childbirth or decreased offspring survival to adulthood. Despite the strong selection for greater fecundity, earlier age at first reproduction and delayed age at last reproduction, only age at last reproduction contributed to maternal post-reproductive survival, by being associated with improved female longevity. These findings suggest a more important role for late rather than early reproduction for female longevity in the populations studied.

Our analysis provides, to our knowledge the first estimates of the intensity of natural selection on age at last reproduction in historical women. While fecundity and age at first reproduction were unsurprisingly the most important components of female fitness (Käär *et al.* 1996; Kirk *et al.* 2001), our results also revealed an important role

Table 3. Factors explaining offspring survival probability to adulthood in historical Sami populations. (Note that in this analysis we included all women with adequate information available ($n = 1519$) and did not restrict our analysis only to post-reproductive mothers. Number of offspring included in the analysis is 5834.)

independent variable	$b \pm \text{s.e.}$	d.f.	χ^2	p
maternal age at delivery	0.0054 \pm 0.007	1	0.66	0.42
sex	—	1	3.74	0.053
previous birth interval (months)	0.0014 \pm 0.002	1	0.43	0.51
delivery type (twin/singleton)	—	1	12.15	0.0005
population	—	2	11.98	0.0025
birth cohort	—	9	61.58	< 0.0001

Table 4. Cox proportional hazard model for the effects of age at first and last reproduction, number of offspring born, spouse's age at death, and birth cohort and population on the post-reproductive survival of the women studied ($n = 322$). (Terms in bold represent the final minimal model including only statistically significant terms. CI: confidential intervals for hazard ratios. $-2 \log$ -likelihood of the null model was 2202.88.)

independent variable	$-2LL^*$	d.f.	χ^2	p	hazard ratio (95% CI)
spouse's age at death	2192.83	1	10.05	0.0016	0.986 (0.977–0.994)
age at last reproduction	2188.65	1	4.183	0.0408	0.972 (0.946–0.998)
population	2184.67	2	3.982	0.14	—
age at first reproduction	2184.59	1	0.079	0.78	0.997 (0.977–1.018)
number of offspring born	2184.09	1	0.499	0.48	0.962 (0.864–1.071)
birth cohort	2182.06	4	2.025	0.73	—

for delayed last parturition on the fitness of Sami women without any detectable costs. This result is unexpected, because late age at reproduction is not generally believed to be favoured by natural selection owing to its adverse effects on both the survivorship of the mother and the offspring (Wood 1994; Tarin *et al.* 1998; see Hill & Hurtado 1996 for an alternative view). However, because maternal death at childbirth and shortly after the birth was a rare event among Sami (4.5%), it is unlikely that such deaths have played a major role in age-dependent reproductive costs in these populations. We may, nonetheless, have underestimated the long-term cost of delayed parenthood, as we were unable to assess the reproductive performance and longevity (i.e. quality) of offspring born to older parents.

Despite the obvious selection for extended reproductive lifespan among Sami women, as indicated by selection for earlier start and later cessation of reproduction, births seemed to be scheduled either to early or late ages (figure 1). This was indicated as a positive correlation between age at first and last reproduction, which suggests that females were generally unable to maximize their fitness by both starting reproducing early and continuing reproducing later. In other words, long reproductive lifespan yielded the highest fitness, but the potential trade-off between early and late reproduction may have limited such a response to selection. Another way to interpret these results is that females starting their reproduction late were able to compensate the fecundity loss by continuing to reproduce until older age. Thus, this result may also imply a parental preference for a desired family size rather than a physiological constraint between early and late reproduction.

Evolution of senescence is believed to result from life-history optimization, where long lifespan is traded for high reproductive success at an earlier age (Williams 1957; Kirkwood & Rose 1991; Partridge & Barton 1993). It was thus not expected that female post-reproductive survival

would be independent of the two most important components of fitness, total fecundity and age at first reproduction, but instead correlated to age at last reproduction irrespectively of the length of reproductive lifespan. More generally, in humans evidence for such trade-offs is very mixed, with results varying according to the population studied (see Appendix A). However, this result together with our earlier finding that late average age of reproduction was related to the improved post-reproductive survival of Sami mothers (Helle *et al.* 2002) suggests that late reproduction was more strongly coupled with female longevity than early reproduction in these populations.

Covariation between late reproductive effort and long lifespan has been suggested to indicate both slow reproductive and somatic senescence (Perls *et al.* 1997; Perls & Fretts 2001). There is experimental evidence that reproductive system may directly influence the rate of somatic senescence in a variety of taxa, including nematodes (Hsin & Kenyon 1999; Arantes-Oliveira *et al.* 2002), medflies (Carey *et al.* 2002) and mice (Gargill *et al.* 2003). Such an effect, for example, has been proposed to be mediated via hormonal signals (through insulin/insulin-like growth factor) from the reproductive system that set the pace for subsequent somatic senescence (Hsin & Kenyon 1999). Favourable effects of delayed late reproduction on female lifespan may also come through the extended period of endogenous oestrogen production, which may modify later mortality to various diseases (Mikkola & Clarkson 2002). Nevertheless, causation from these kinds of phenotypic correlations is hard to determine, and it is thus possible that there is some unknown underlying mechanism affecting both the reproductive and somatic senescence. Another, but evolutionarily unlikely explanation (Kaplan 1994; Lee 2003) for such a correlation is that increased female longevity would be a by-product of care provided from late offspring to their mother (Wolf 1994). It should also be

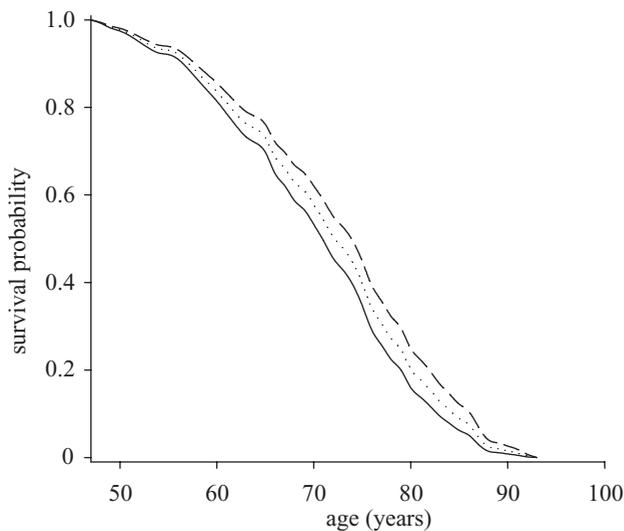


Figure 2. Estimated survival probability curves for post-reproductive Sami women as a function of age at last reproduction at age 35 (solid line), age 40 (dotted line) and age 45 (dashed line), adjusting for spouse's age at death.

noted that late reproduction and post-reproductive survival may covary, because the mothers of high quality may have been able to reproduce until old ages and live long post-reproductively (van Noordwijk & de Jong 1986). However, one would expect that high-quality individuals should also have started their reproduction early, which we did not observe (figure 1). In our analyses, we also controlled for the confounding environmental effects by controlling the birth cohort and population of an individual and the survival of her spouse (see Gavrilov & Gavrilova 2001).

Because our conclusions are based on the phenotypic correlations between different female life-history traits without information on the underlying genetic correlations and heritabilities, we are unable to determine the evolutionary response to selection on the traits studied. However, one may argue that in these Sami populations selection on age at first reproduction was less likely to lead to response to selection than selection on age at last reproduction. In common with many other European populations of that time, variation in age at first reproduction of Sami women probably did not reflect their age at maturation, which usually takes place at *ca.* 12–16 years of age, depending also on the environmental resource availability (Ellison 2001). Rather, variation in age at first reproduction was determined by social and cultural factors, as indicated by high average age at first reproduction in these women (table 1). In the Sami studied, age at marriage was largely determined by the wealth of both the wife and the husband and the special marriage customs of the Sami population in question: for example, there was a minimum acceptable marriage age for women (often between 18 and 20 years of age), and the process of proposal usually took 1 to 3 years before the actual wedding (Itkonen 1948). Hence, selection on age at first reproduction probably demonstrates selection on the social component of that trait, and not on biological age at maturity. By contrast, response to selection on age at last reproduction may have been more likely, because it can be taken to reflect the true age-specific decline of female fertility towards the menopause in natural-fertility populations such as those studied

here (Wood 1994; Holman & Wood 2001). In other words, even if a negative genetic correlation existed between age at maturity and rate of senescence, it was unlikely to be under natural selection owing to high cultural influence on age at first reproduction among these Sami women. By contrast, age at last reproduction may not have been socially constrained to that extent, and thus an association between late reproduction and longevity may have evolved.

The above explanations for the evolution of late reproduction and female post-reproductive survival do not require that female post-reproductive survival is adaptive: the correlation arises simply because of the selection on later reproduction and its positive pleiotropic effects on subsequent survival. By contrast, females may have gained fitness benefits through considerably outliving their own reproductive capacity by improving the reproductive success of their offspring and the survival of their grand-offspring (Williams 1957; Hawkes *et al.* 1998; Lee 2003; Lahdenperä *et al.* 2004). Such positive fitness effects of long post-reproductive lifespan would intensify the selection for pleiotropic genes affecting positively both to late reproduction and longevity.

In conclusion, we found no support for the predicted long-term survival costs of high and early reproduction among the Sami women studied. Rather, long female post-reproductive lifespan was related to late age at last reproduction, which was also favoured by natural selection. This may indicate synchronized senescence of both reproductive and somatic systems, but in different time schedules: senescence of physiological functions lagged almost 30 years behind the reproductive functions. The reason for this lag might be the continued positive selection on prolonged female vigour and viability beyond menopause owing to helping behaviour towards own offspring and grand-offspring. It remains, however, to be plausibly shown why and how the rate of reproductive senescence exceeded that of somatic senescence in our evolutionary past.

The authors thank Andy Russell, Toni Laaksonen, Tapio van Ooik, Mirkka Lahdenperä and three anonymous reviewers for their valuable comments on this manuscript. This study was financially supported by Emil Aaltonen foundation (S.H.), The Royal Society (V.L.) and The Academy of Finland (S.H., V.L. and J.J.).

APPENDIX A

This is a summary of previous studies in humans on the associations between reproduction and longevity. The study period (where available) is given in parentheses after the study population. Symbols (+) and (–) represent statistically significant positive or negative correlation between different aspects of reproductive effort and female lifespan, respectively. Zero means that the reproductive effort and female lifespan were unrelated. Two symbols separated by a slash indicate that the results of the study are not straightforward, but depend on data selection (e.g. restriction of age or study period), population, or on the finer-scale measure of reproductive effort. Note that all of these studies are not directly comparable to each other owing to variation in statistics used and the coding of measured variables (categorical versus continuous). Only studies concerning the post-reproductive survival of women and measuring total mortality are shown.

study population	sign of correlation	reference
total fecundity and longevity		
England and USA	+	Beeton <i>et al.</i> (1900)
New England	+	Bell (1918)
New South Wales, Australia (1898–1902)	–/+	Powys (1905)
USA (1625–1825)	+	Freeman (1935)
New South Wales, Australia (1909–1928)	+	Dorn & McDowell (1939)
Quebec, Canada (1800–1880)	0	Philippe & Yelle (1976)
Ostfriesland, Germany (1700–1800)	+	Voland & Engel (1986, 1989)
nationwide sample (1600–1800)	0/+	Bideau (1986)
Germany (1700–1800)	0	Knodel (1988)
Quebec, Canada (1608–1765)	0	Le Bourg <i>et al.</i> (1993)
USA (1880–1929)	–/0	Friedlander (1996)
Paraguay (1977–1990)	0	Hill & Hurtado (1996)
England (1580–1837)	0	Wrigley <i>et al.</i> (1997)
British aristocracy (740–1875)	–	Westendorp & Kirkwood (1998)
Israel (1902–1992)	+	Manor <i>et al.</i> (2000)
Global data census (1992)	–	Thomas <i>et al.</i> (2000)
England, Wales, Austria (1971–1996)	–	Doblhammer (2000)
Finns, European nobles (1700–1899)	–/0	Korpelainen (2000)
Krummhörn, Germany (1720–1870)	–/0	Lycett <i>et al.</i> (2000)
Norway (1970)	–	Kumle & Lund (2000)
Matlab, Bangladesh (1982–1992)	–/0	Mostafa & Ginneken (2000)
Quebec, Canada (1600–1800)	+	Müller <i>et al.</i> (2002)
Sami of Scandinavia (1700–1900)	0	Helle <i>et al.</i> (2002)
Finns (1870–1949)	0	Korpelainen (2003)
Mormons, USA (1800–1900)	–	Smith <i>et al.</i> (2003)
British aristocracy (1641–1850)	–	Doblhammer & Oeppen (2003)
Bangladesh (1975–1979)	0	Menken <i>et al.</i> (2003)
Germany (1600–1900)	0	Kemkes-Grottenthaler (2004)
Swedes (1766–1895)	–	Dribe (2004)
European aristocracy (1500–1875)	0	Gavrilova <i>et al.</i> (2004)
Finns (1702–1859)	0	Helle <i>et al.</i> (2004b)
percentage of studies finding the predicted outcome	22 or 39%	
age at first reproduction and longevity		
Quebec, Canada (1608–1765)	0	Le Bourg <i>et al.</i> (1993)
British aristocracy (740–1875)	+	Westendorp & Kirkwood (1998)
England, Wales, Austria (1971–1996)	+	Doblhammer (2000)
Norway (1970)	0	Kumle & Lund (2000)
Finns, European nobles (1700–1899)	0	Korpelainen (2000)
Mormons, USA (1800–1900)	0	Smith <i>et al.</i> (2003)
Finns (1870–1949)	0	Korpelainen (2003)
British aristocracy (1641–1850)	0	Doblhammer & Oeppen (2003)
Bangladesh (1975–1979)	0	Menken <i>et al.</i> (2003)
Swedes (1766–1895)	0	Dribe (2004)
Finns (1702–1859)	0	Helle <i>et al.</i> (2004b)
percentage of studies finding the predicted outcome	18%	
age at last reproduction and longevity		
Ostfriesland, Germany (1700–1800)	+	Voland & Engel (1986)
USA (1896)	+	Perls <i>et al.</i> (1997)
USA (1867–1923)	0	Egan <i>et al.</i> (1997)
England, Wales, Austria (1971–1996)	+	Doblhammer (2000)
Finns, European nobles (1700–1899)	0	Korpelainen (2000)
Norway (1970)	+	Kumle & Lund (2000)
Quebec, Canada (1600–1800)	+	Muller <i>et al.</i> (2002)
Finns (1870–1949)	0	Korpelainen (2003)
Mormons, USA (1800–1900)	+	Smith <i>et al.</i> (2003)
Bangladesh (1975–1979)	+	Menken <i>et al.</i> (2003)
British aristocracy (1641–1850)	0	Doblhammer & Oeppen (2003)
Swedes (1766–1895)	+	Dribe (2004)
Chinese (1988–2000)	+	Zeng & Vaupel (2004)
Finns (1702–1859)	+	Helle <i>et al.</i> (2004b)
percentage of studies finding the predicted outcome	71%	

REFERENCES

- Allison, P. D. 1995 *Survival analysis using the SAS system: a practical guide*. Cary, NC: SAS Institute Inc.
- Arantes-Oliveira, N., Apfeld, J., Dillin, A. & Kenyon, C. 2002 Regulation of life-span by germ-line stem cells in *Caenorhabditis elegans*. *Science* **295**, 502–505.
- Arnold, S. J. & Wade, M. J. 1984 On the measurement of natural selection and sexual selection: theory. *Evolution* **38**, 709–719.
- Beeton, M., Yule, G. U. & Pearson, K. 1900 Data for the problem of evolution in man V: on the correlation between duration of life and number of offspring. *Proc. R. Soc.* **67**, 159–179.
- Bell, A. G. 1918 *The duration of life and conditions associated with longevity: a study of the Hyde genealogy*. Washington, DC: Genealogical Record Office.
- Bideau, A. 1986 Fertility and mortality at ages 45 and over. The contribution of research in historical demography. *Population* **41**, 59–72.
- Carey, J. R., Liedo, P., Harshman, L., Liu, X., Müller, H.-G., Partridge, L. & Wang, J.-L. 2002 Food pulses increase longevity and induce cyclical egg production in Mediterranean fruit flies. *Funct. Ecol.* **16**, 313–325.
- Collett, D. 2003 *Modelling survival data in medical research*, 2nd edn. Boca Raton, FL: Chapman & Hall/CRC.
- Cooper, G. S. & Sandler, D. P. 1998 Age at natural menopause and mortality. *Ann. Epidemiol.* **8**, 229–235.
- Doblhammer, G. 2000 Reproductive history and mortality later in life: a comparative study of England and Wales and Austria. *Popul. Stud.* **54**, 169–176.
- Doblhammer, G. & Oeppen, J. 2003 Reproduction and longevity among the British peerage: the effect of frailty and health selection. *Proc. R. Soc. B* **270**, 1541–1547. (doi:10.1098/rspb.2003.2400)
- Dorn, H. F. & McDowell, A. J. 1939 The relationship between fertility and longevity. *Am. Soc. Rev.* **4**, 234–246.
- Dribe, M. 2004 Long-term effects of childbearing on mortality. *Popul. Stud.* **58**, 297–310.
- Egan, K. M., Giovanucci, E., Titus-Ernstoff, L., Newcomb, P. & Stampfer, M. 1997 Mixed blessing for middle-aged mothers. *Nature* **389**, 922.
- Ellison, P. 2001 *On fertile ground*. Cambridge, MA: Harvard University Press.
- Eogan, M. A., Geary, M. P., O'Connell, M. P. & Keane, D. P. 2003 Effect of fetal sex on labour and delivery: retrospective review. *Br. Med. J.* **326**, 137.
- Freeman, B. C. 1935 Fertility and longevity in married women dying after the end of reproductive period. *Hum. Biol.* **7**, 392–418.
- Friedlander, N. J. 1996 The relation of lifetime reproduction to survivorship of women and men: a prospective study. *Am. J. Hum. Biol.* **8**, 771–783.
- Gargill, S. L., Carey, J. R., Müller, H.-G. & Anderson, G. 2003 Age of ovary determines remaining life expectancy in old ovariectomized mice. *Aging Cell* **2**, 185–190.
- Gavrilov, L. A. & Gavrilova, N. S. 2001 Epidemiology of human longevity: the search for appropriate methodology. *J. Anti-Aging Med.* **4**, 13–30.
- Gavrilova, N. S., Gavrilov, L. A., Semyonova, V. G. & Evdokushkina, G. N. 2004 Does exceptional human longevity come with a high cost of infertility? *Ann. NY Acad. Sci.* **1019**, 513–517.
- Hamilton, W. D. 1966 The moulding of senescence by natural selection. *J. Theor. Biol.* **12**, 12–45.
- Hatcher, L. 1994 *A step-by-step approach to using SAS® for factor analysis and structural equation modeling*. Cary, NC: SAS Institute Inc.
- Hawkes, K., O'Connell, J. F., Jones, N. G., Alvarez, H. & Charnov, E. L. 1998 Grandmothering, menopause, and the evolution of human life histories. *Proc. Natl Acad. Sci. USA* **95**, 1336–1339.
- Helle, S., Käär, P. & Jokela, J. 2002 Human longevity and early reproduction in pre-industrial Sami populations. *J. Evol. Biol.* **15**, 803–807.
- Helle, S., Lummaa, V. & Jokela, J. 2004a Selection for increased brood size in historical human populations. *Evolution* **52**, 430–436.
- Helle, S., Lummaa, V. & Jokela, J. 2004b Accelerated immunosenescence in preindustrial twin mothers. *Proc. Natl Acad. Sci. USA* **101**, 12 391–12 396.
- Hill, K. & Hurtado, A. M. 1996 *Ache life history: the ecology and demography of a foraging people*. Hawthorne, NY: Aldine de Gruyter.
- Holman, D. J. & Wood, J. W. 2001 Pregnancy loss and fecundity in women. In *Reproductive ecology and human evolution* (ed. P. T. Ellison), pp. 15–38. Hawthorne, NY: Aldine de Gruyter.
- Hosmer, D. W. & Lemeshow, S. 1994 *Applied logistic regression*. New York: Wiley.
- Houston, A. I. & McNamara, J. M. 1999 *Models of adaptive behaviour*. Cambridge University Press.
- Hsin, H. & Kenyon, C. 1999 Signals from the reproductive system regulate the lifespan of *C. elegans*. *Nature* **399**, 362–366.
- Itkonen T. 1948 *The Lapps of Finland*. vol. 2. Provo, Finland: WSOY.
- Jacobsen, B. K., Knutsen, S. F. & Fraser, G. E. 1999 Age at natural menopause and total mortality and mortality from ischemic heart disease: the Adventist health study. *J. Clin. Epidemiol.* **52**, 303–307.
- Jacobsen, B. K., Heuch, I. & Kvåle, G. 2003 Age at natural menopause and all-cause mortality: a 37-year follow-up of 19 731 Norwegian women. *Am. J. Epidemiol.* **157**, 923–929.
- Käär, P., Jokela, J., Helle, T. & Kojola, I. 1996 Direct and correlative phenotypic selection on life-history traits in three pre-industrial human populations. *Proc. R. Soc. B* **263**, 1475–1480.
- Kaplan, H. K. 1994 Evolutionary and wealth flows theories of fertility: empirical tests and emerging models. *Popul. Dev. Rev.* **20**, 753–791.
- Kemkes-Grottenthaler, A. 2004 God, faith, and death: the impact of biological and religious correlates on mortality. *Hum. Biol.* **75**, 897–915.
- Kinsolver, J. G. & Schemske, D. W. 1991 Path analyses of selection. *Trends Evol. Ecol.* **6**, 276–280.
- Kirk, K. M., Blomberg, S. P., Duffy, D. L., Heath, A. C., Owens, I. P. F. & Martin, N. G. 2001 Natural selection and quantitative genetics of life-history traits in western women: a twin study. *Evolution* **55**, 423–435.
- Kirkwood, T. B. L. & Austad, S. N. 2000 Why do we age? *Nature* **408**, 233–238.
- Kirkwood, T. B. L. & Rose, M. R. 1991 Evolution of senescence: late survival sacrificed for reproduction. *Phil. Trans. R. Soc. B* **332**, 15–24.
- Knodel, J. E. 1988 *Demographic behavior in the past*. New York: Cambridge University Press.
- Korpelainen, H. 2000 Fitness, reproduction and longevity among European aristocratic and rural Finnish families in the 1700s and 1800s. *Proc. R. Soc. B* **267**, 1765–1770. (doi:10.1098/rspb.2000.1208)
- Korpelainen, H. 2003 Human life histories and the demographic transition: a case study from Finland, 1870–1949. *Am. J. Phys. Anthropol.* **120**, 384–390.
- Kumle, M. & Lund, E. 2000 Patterns of childbearing and mortality in Norwegian women. A 20-year follow-up of women aged 40–96 in the 1970 Norwegian census. In *Sex and longevity: sexuality, gender, reproduction, parenthood* (ed. J. M. Robine, T. B. L. Kirkwood & M. Allard), pp. 117–128. Berlin: Springer.

- Lahdenperä, M., Lummaa, V., Helle, S., Tremblay, M. & Russell, A. F. 2004 Fitness benefits of prolonged post-reproductive lifespan in women. *Nature* **428**, 178–181.
- Lande, R. & Arnold, S. J. 1983 The measurement of selection on correlated characters. *Evolution* **37**, 1210–1226.
- Le Bourg, E., Thon, B., Légaré, J., Desjardins, B. & Charbonneau, H. 1993 Reproductive life of French-Canadians in the 17–18th centuries: a search for a trade-off between early fecundity and longevity. *Exp. Gerontol.* **28**, 217–232.
- Lee, R. 2003 Rethinking the evolutionary theory of aging: transfers, not births, shape senescence in social species. *Proc. Natl Acad. Sci. USA* **100**, 9637–9642.
- Lycett, J. E., Dunbar, R. I. M. & Voland, E. 2000 Longevity and the costs of reproduction in a historical human population. *Proc. R. Soc. B* **267**, 31–35. (doi:10.1098/rspb.2000.0982)
- McCulloch, C. E. & Searle, S. R. 2001 *Generalized, linear, and mixed models*. New York: Wiley.
- Manor, O., Eisenbach, Z., Israeli, A. & Friedlander, Y. 2000 Mortality differentials among women: the Israel longitudinal mortality study. *Soc. Sci. Med.* **51**, 1175–1188.
- Medawar, P. B. 1952 *An unsolved problem of biology*. London: H. K. Lewis.
- Menken, J., Duffy, L. & Kuhn, R. 2003 Childbearing and women's survival: new evidence from rural Bangladesh. *Popul. Dev. Rev.* **29**, 405–426.
- Mikkola, M. S. & Clarkson, T. B. 2002 Estrogen replacement therapy, atherosclerosis, and vascular function. *Cardiovasc. Res.* **53**, 605–619.
- Mitchell, R. J. 1993 Path analysis: pollination. In *Design and analysis of ecological experiments* (ed. S. M. Scheiner & J. Gurevitch), pp. 211–231. New York: Chapman & Hall.
- Mostafa, G. & van Ginneken, J. K. 2000 Trends in and determinants of mortality in the elderly population of Matlab, Bangladesh. *Soc. Sci. Med.* **50**, 763–771.
- Müller, H.-G., Chiou, J., Carey, J. R. & Wang, J. 2002 Fertility and lifespan: late children enhance female longevity. *J. Gerontol. A Biol. Sci. Med. Sci.* **57**, B202–B206.
- Partridge, L. & Barton, N. H. 1993 Optimality, mutation and the evolution of ageing. *Nature* **362**, 305–311.
- Partridge, L. & Gems, D. 2002 Mechanism of ageing: public or private? *Nature Rev. Genet.* **3**, 165–175.
- Perls, T. T. & Fretts, R. C. 2001 The evolution of menopause and human lifespan. *Ann. Hum. Biol.* **28**, 237–245.
- Perls, T. T., Alpert, L. & Fretts, R. C. 1997 Middle-aged mothers live longer. *Nature* **339**, 133.
- Petratis, P. S., Dunham, A. E. & Niewiarowski, P. H. 1996 Inferring multiple causality: the limitations of path analysis. *Funct. Ecol.* **10**, 421–431.
- Philippe, P. & Yelle, L. 1976 Effect of family size and mother's longevity. *Ann. Hum. Biol.* **3**, 429–431.
- Powys, A. O. 1905 Data for the problem of evolution in man: on fertility, duration of life and reproductive selection. *Biometrika* **4**, 233–285.
- Scheiner, S. M., Mitchell, R. J. & Callahan, H. S. 2000 Using path analysis to measure natural selection. *J. Evol. Biol.* **13**, 423–433.
- Smith, K. R., Mineau, G. P. & Bean, L. L. 2003 Fertility and post-reproductive longevity. *Soc. Biol.* **49**, 55–75.
- Snowdon, D. A., Kane, R. L. & Beeson, W. L. 1989 Is early natural menopause a biological marker of health and ageing? *Am. J. Pub. Hlth* **79**, 709–714.
- Tarin, J., Brines, J. & Cano, A. 1998 Long-term effects of delayed parenthood. *Hum. Reprod.* **13**, 2371–2376.
- Thomas, F., Teriokhin, A. T., Renaud, F., De Meeûs, T. & Guégan, J. F. 2000 Human longevity at the cost of reproductive success: evidence from global data. *J. Evol. Biol.* **13**, 409–414.
- Tuljapurkar, S. 1990 Delayed reproduction and fitness in variable environments. *Proc. Natl Acad. Sci. USA* **87**, 1139–1143.
- van der Schouw, Y. T., van der Graff, Y., Steyerberg, E. W., Eijkemans, M. J. C. & Banga, J. D. 1996 Age at menopause and a risk factor for cardiovascular mortality. *Lancet* **347**, 714–718.
- van Noordwijk, A. J. & de Jong, G. 1986 Acquisition and allocation of resources: their influence on variation in life history tactics. *Am. Nat.* **128**, 137–142.
- Voland, E. & Engel, C. 1986 Ist das postmenopausale sterblicher variable einer fitness-maximierender reproduktionsstrategie? *Anthropol. Anz.* **44**, 19–34.
- Voland, E. & Engel, C. 1989 Women's reproduction and longevity in a premodern population Ostfriesland, Germany, 18th century. In *The sociobiology of sexual and reproductive strategies* (ed. A. E. Rasa, C. Vogel & E. Voland), pp. 194–205. London: Chapman & Hall.
- Westendorp, R. G. J. & Kirkwood, T. B. L. 1998 Human longevity at the cost of reproductive success. *Nature* **396**, 743–746.
- Williams, G. C. 1957 Pleiotropy, natural selection and the evolution of senescence. *Evolution* **11**, 398–411.
- Wolf, D. A. 1994 The elderly and their kin: patterns of availability and access. In *Demography of aging* (ed. L. G. Martin & S. H. Perston), pp. 146–194. Washington, DC: National Academy Press.
- Wood, J. M. 1994 *Dynamics of human reproduction: biology, biometry, demography*. Hawthorne, NY: Aldine de Gruyter.
- Wrigley, E. A., Davies, R. S., Oeppen, J. E. & Schofield, R. S. 1997 *English population history from family reconstitution 1580–1837*. Cambridge University Press.
- Zeger, S. L. & Liang, K. Y. 1986 Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* **42**, 121–130.
- Zeng, Y. & Vaupel, J. W. 2004 Association of late childbearing with healthy longevity among the oldest-old in China. *Popul. Stud.* **58**, 37–53.

As this paper exceeds the maximum length normally permitted, the authors have agreed to contribute to production costs.