A Child Later in Life is not a Life Prolonging Event

Findings from the European Royalty

Ulrich Mueller, Dr.med. Dr. phil.
Professor of Medical Sociology and Social Medicine
at the Institute of Medical Sociology and Social Medicine,
Medical School,
University of Marburg, 35033 Marburg, Germany
mueller2@mailer.uni-marburg.de
fax +49-6421-2865660

Manuscript information:

162 words in the abstract
app. 6210 words, app. 37920 characters including spaces in the main text
53 references
1 table
no figures

5th July 2004

Abstract

Statistical associations between late reproduction and female longevity lead to speculations that a late child actually makes the mother's lifespan longer. The data base here includes all descendants of King George I of England (1660-1727) and his wife Sophie Dorothea (1667-1726), born in the royal dynasties in Europe up to 1939 (n=1672). In the era of British world supremacy, these descendants formed the supreme layer of the European aristocracy, occupying all royal thrones from 1850 onwards. Novel in this study is the mobilisation of pedigree information. In pairs of ever married full sisters (brothers), both surviving to 45 (50) years, both having at least one child, it is observed whether the sibling with the first – or last - child born later in life, also lived a longer life. In this design are controlled: socio-economic status; health; genetics; cohort; social support; infant mortality; environmental fluctuations. In the 157 pairs of sisters, and 191 pairs of brothers, later reproduction did not extend the lifespan.

Keywords:
Longevity, lifespan, reproduction, late, first birth, last birth

Introduction

Ultimate explanations for the physiology of human ageing, as everywhere in biology, can be found only by studying the evolution of this physiology. Since lifetime reproductive success, not longevity is selected, the links between reproductive events and mortality risks over the lifetime are the key to any evolutionary explanation of the human lifespan (Vaupel et al. 1998; Carey 2003; Carey & Tuljapurkar 2003).

There are many reports of a positive association between female lifespan and late reproduction (Perls et al. 1997, Westendorp & Kirkwood 1998; Doblhammer 2000; Lycett et al. 2000; Mueller et al. 2002; Smith et al. 2002). The mechanism behind this statistical association, however, is unclear. Traditional evolutionary theory (Kirkwood 1977; Kirkwood & Rose 1991) predicts a trade-off between investment into children and own survival. Empirical support could be found in Lund et al. 1990, Kvale et al. 1994; Friedlaender 1996; Westendorp & Kirkwood 1998; Doblhammer-Reiter 2000; Doblhammer-Reiter & Vaupel 1999; Doblhammer-Reiter & Oeppen 2003; Lycett et al. 2000. An alternative approach, also supported by empirical findings from animal and human populations (Perls et al. 1997; Carey & Judge 2001; Mueller et al 2001; 2002; Perls & Fretts 2001; Smith et al. 2002) speculates that selection for increased reproductive success simultaneously may drive the selection of longevity: A longer reproductive lifespan would allow a better adaptation of the timing of births, increasing survival of parents and offspring. Also, a longer post reproductive life span may increase total parental investment per child (Hawkes 2003).

Furthermore, health, genetics, socio-economic status, social support, parity, cohort, among others, in general population samples have to be considered as potentially powerful intervening variables:

1. Health: people living longer tend to be healthy and vigorous longer and, therefore, may stop childbearing later.
2. Socio-economic status: well educated, wealthy people are known to be healthier, live longer, and, therefore, may tend to stop – and in modern societies also to start - childbearing later.
3. Genetics: Childless siblings of women reproducing after age 40 live longer than average (Smith et al. 1999; Smith et al. 2002); twin studies demonstrate longevity to be moderately heritable (Jarvik et. 1960; Herskind et al. 1996; Iachine et al. 1998; Kerber et al. 2001; Mitchell et al. 2001); siblings and parents of centenarians live longer than average (Perls et al. 1998; 2002); there is a growing body of reports on genetic risk factors for premature ovarian failure (Santoro 2003, Spencer 2002); all this suggests a genetic association between fecund lifespan and longevity (Carey & Judge 2001).
4. Parity: people starting to reproduce later tend to have fewer children, and, if there is a trade-off between parity and lifespan (Westendorp & Kirkwood 1998; Doblhammer & Vaupel 2000; Lund et al. 1990), therefore may live longer.
5. Social support: it may be speculated that despite any trade-off between parity and longevity, women (and perhaps men) with many children may receive more support in old age, keeping them longer alive.
6. Child mortality: a child dying young may mean lower overall parental investment and therefore lower parental mortality; alternatively, parents having

lost a child may sooner go on having another one – with increased parental burden.

7. Environmental fluctuations: people are easily brought to postpone reproduction: business cycles, demographic waves on the labour and on the marriage market, epidemics, nutrition supply, war and political unrest. Such factors differ in place and time, and may considerably confound the associations between reproduction and longevity studied here.
8. Cohort: there may be periods in time when over a generation or so, life expectancy increases and – for reasons unrelated with that – mean age at parenthood or parity also increases (Mueller et al. 2002). Consequently, if the chosen time horizon for comparisons is too narrow, for some cohorts a statistical association between longevity and late fertility may be observed which does not exist in others.

All these intervening effects would more or less work in females and males alike.

If indeed late reproduction makes the female body to live longer, possible physiological mechanisms might be: high estradiol levels may decrease the cardiovascular risk (Falsetti et al 1999), with the pregnancies protecting against the risk of breast, corpus uteri, ovarian and various skin cancers (Kvale et al. 1994).

Similar causal effects in the male body could be: testosterone and cortisol level sharply decline and estradiol levels increase in dads of small children (Berg & Wynne-Edwards 2001). Testosterone is known to shorten the male life span (Nieschlag et al. 1993). Caring for infants and small children is a marker for an extended male life span among various anthropoid primate species (Allman et al. 1998). Thus, births late in life may

enhance the life span also in males, if they cohabit with these children and their mothers.

Since male investment per birth is lower and a woman's physiology changes more during pregnancy and lactation, any causal impact of late reproduction on longevity – a late baby causing the parent's body to live longer - might be weaker in males. If there is no such direct causal impact, any statistical association may be as strong in males as in females.

The question studied here is not only relevant for the biology of ageing. It also is of practical relevance for health promotion and preventive medicine. Furthermore, if a late baby makes the life of parents longer, mortality population projections would have to take ubiquitous trends toward later childbearing into account.

Data

I do have a data set very well suited to control all these possible confounders with their intricate intercorrelations. These are the 1672 births occurring in the Royal Houses of Europe to George I, King of Great Britain, France and Ireland, Elector of Hannover (1660-1727) and his wife Sophie Dorothea of Celle (1666-1726) and their direct descendants, between 1. January 1683 and 31. December 1939. The proportion of direct descendants of this couple within members of the royal dynasties of Europe increased throughout the observation span: among the births 1790-1799 it was 71%, among the births 1840-1849 83%, 1890-1899 97%, and then, from the turn of the 19th to the 20th century onwards, all crowned heads in Europe have been direct descendants of this couple. In the era of Britain world dominance, a British Royal Princess was the ultimate prize in dynastic marriage politics, like a Byzantine born-to-

the-purple princess a millennium earlier. Since there were also catholic lineages among the descendants of George and Sophie Dorothea, and since marriage candidates always could convert, the catholic dynasties of Europe were in the market, too.

The basic source was McNaughton monumental three volume "Book of Kings" (1973); the information contained there on the direct, legitimate descendants of George and Sophie Dorothea born until 31st December 1939, was checked and updated by the rich genealogical sources freely available in printed form and in the internet. Vital events until 31st December 2002 (closure of the data base) were taken into account.

Intermarrying was proverbial in this very special population. An example: „*King George V (1865 - 1936) of England was first cousin to the German Emperor, Wilhelm II; first cousin to the Tsar, Nicholas II and the Tsarina, Alexandra (Nicholas through his mother's sister, Alexandra through his father's sister); first cousin to Christian X of Denmark; to Haakon VII of Norway (who was married to George V's sister, Princess Maud, and was therefore his brother-in-law as well); to King Constantine I and Queen Sophia of Greece (the former through his maternal uncle, the latter through his paternal aunt); to Queen Marie of Romania; to Queen Victoria of Spain; and to the first wife of King Gustav VI Adolf of Sweden. George V was also closely related to all reigning Princes, Dukes, Grand Dukes in the German Empire in 1914, and he was distantly related to the Emperor Karl I of Austria, himself a direct descendant of George I*". (McNaughton 1973: IX).

Almost 50% of female and of male cases had married another member of the study population; but also of almost all the other cases, who did not intermarry (but in most cases had married an aristocrat), we have the vital data of spouses, too.

For females, the maximum age at first child was 43.25 years, maximum age at last child 47.33. Only 4 women gave birth after age 45. For males, the maximum age at first child was 59.91 years, maximum age at last child 65.51. In fewer than 8% of brother pairs there was a birth after age 50.

If not stated otherwise, only cases of ever married female survivors to age 45 and male survivors to age 50, with at least one recorded child will be considered for further analysis. By the age minimum, cases with close relation between reproductive ability/events and morbidity/mortality - leading to trivial effects – will be excluded. Mean lifespan in the selected subsample remained practically stable at 69 years for such males over the observation period, and increased from 69 to 74 for such females. The 60^{th}, 70^{th}, 80^{th}, 90^{th} percentile was reached at 72.5, 76.9, 81.7 and 86.9 years of age for such males, and at 77.5, 81.1, 84.8 and 88.2 for such females.

Research Question

The question studied here is whether a late birth actually makes the life of the mother or father longer. Most of the studies reporting such an effect explicitly or implicitly focus on the last birth.

- Here, I consider such an effect for late first and late last births separately.
- I also check whether a long reproductive life span, roughly measured by time span between first and last birth, makes the life of parents of two and more children longer.

Methods

Novel for studies like this one, for all cases pedigree information was mobilised for the analyses. For example, the present King of Spain, Juan Carlos de Borbon y de Borbon, born 1938, his brother Alfonso de Borbon y de Borbon, (1941-1956), and his two sisters Dona Maria del Pilar de Borbon y de Borbon, born 1936, and Dona Margarita de Borbon y de Borbon, born 1939, great great grandchildren of Queen Victoria of England, are all listed with their parents, Maria de las Mercedes, Princess of Borbon-Siciles (1910-2000) and Juan de Borbon y Battenberg, Count of Barcelona (1913-1993). Both parents were direct descendants of George and Sophie Dorothea. By the IDs of their parents, these four cases can be grouped and compared with each other. Similarily, their father Juan can be grouped with his 5 full siblings by the IDs of his father, King Alfonso XIII of Spain, and his mother Victoria Eugenie of Battenberg, one of the 40 grandchildren of Queen Victoria of England.

The novel approach of this study here is to check in pairs of full sisters, or in pairs of full brothers, if the sibling with a first birth or a last birth later in life or with a longer reproductive life span, also lead a longer life than the other sibling.

Among the cases in the subsample, I identified 191 pairs of full brothers, and 157 pairs of full sisters, of whom either both were already dead at the closure of the data base (December 31, 2002) or the surviving sibling was already older than the deceased sibling at the time of death. For example, the pair of full sisters Queen Elisabeth II. of England (born 1926) and Princess Margaret (1930–2002), two other great great grandchildren of Queen Victoria of England, is among those selected.

Effects were tested with Chi-square models with expected equal distribution as the Null Hypothesis. For some analyses, however, lifespan was not analysed as a censured variable. Two individuals in the study group lived beyond age 100. Thus, once lifespan was to be analysed as an uncensured variable, only pairs of sisters (brothers) were considered, in which both siblings were already dead, and, in order to avoid any selectivity against survivors in the oldest age group, had been born before January 1, 1902. Here, there were 164 such pairs of full brothers and 134 such pairs of full sisters. Multivariate OLS regressions were performed with lifespan difference as the dependent, difference in age at first or at last child, or difference in reproductive lifespan as the independent, and mean cohort fertility, mean cohort longevity, own number of children of both siblings, catholic denomination as control variables.

There is no reason to exclude cases of three and more brothers or of three and more sisters. If every individual should be considered only in one pair, from groups of three, five etc. brothers (or sisters), one individual would not be considered at all. The only non-arbitrary solution seems to take all possible pairings from groups of three and more same sex siblings. Then, if there are n full sisters (brothers) from one couple, the number of possible pairings is given by the binomial coefficient , giving the descendants of a couple with many same sex children a disproportionally higher representation in the sample. Also, since such individuals occur in more than one pair, observations are not fully independent. In order to control for that, the binomial coefficient of total number of sisters (brothers) was used as a control variable in multivariate analyses. However, introducing this weighting will not completely correct

for the effects of non-independence of observations on significance levels in test statistics[1]. This will be taken into account in the interpretation of results.

In this study design at this particular population, the confounders listed in the introductory section, are well controlled:

1. Health and Socio-economic Status: All members of the study population belonged to the most affluent stratum of their societies, enjoying the best medical care of their times, and could have supported families as large as they only could have wanted for.
2. Genetics: The study population has been a highly inbreeding group. In this network of intermarriages there is only one major divide: the catholic dynasties and the others (Anglican, Protestant, Orthodox) which, however, was not an absolute one, since there were almost equal proportions of direct descendants of George and Sophie Dorothea in catholic and non catholic dynasties. Among full siblings, there will have been less genetic variance than among any pair of full sisters (brothers) taken at random from the general population.
3. Parity: All legitimate children are well documented. Illegitimate children were virtually absent from the female part of the study population. Of altogether 482 mothers in the core data base, no one was listed as unwed at the birth of her first child. Non-paternity would make no difference for mothers, only for legal fathers. Cases of nonpaternity, however, will have been too rare in this sample (detailed review of arguments in Perusse 1993; 1994; Mueller and Mazur 2001) to worry about.

[1] I owe some of the phrasing in this paragraph to an anonymous reviewer.

Also, there are no cases of unwed fathers listed in the sources. Cases of illegitimate offspring will have been frequent among the males of the study group (although these children are rarely listed). Those, however, need not worry us either, since here, any life prolonging causal effects of fatherhood may be less effective, when such children do not live together with their biological fathers – as would have been the case here.

4. Birth control is irrelevant for the research question here, since an eventual life prolonging causal effect of a late birth would be equally observable for planned as for unplanned births.

5. Social support: Even the secondary members of the study population will have had more house servants to look after them than children[2].

6. Childhood Mortality: Infant mortality was relatively low: 8% 1700-1799, 7% 1800-1849, 5% 1850-1899, and 0.8% 1900-1939. And so was child mortality (death before 5th birthday, which dropped from 15% 1700-1799, 12% 1800-1849, 8% 1850-1899 to 0.8 % after 1900. Also, with unlimited household resources, a child's mortality risk may have been less correlated with that of siblings than in other families.

   It might be expected that death of a child, especially a young one, may induce parents to replace it with another one, and, thus, affect a parent's age at last child. In the database, however, such an effect could not be observed for any sex (total number of own children, cohort specific mean family size, cohort

[2] According to press reports from August 2003, Charles Prince of Wales, the heir to the British throne, in Clarence House, his new home just for himself and his life companion Ms. Parker-Bowles, enjoys the services of 17 valets, 3 cooks, 2 private secretaries, 2 butlers, 2 chauffeurs and 8 gardeners.

specific mean life span, and catholic denomination controlled). Apparently, child mortality issues need not be considered here.

7. Environmental fluctuations: All individual subjects in the study population were extremely well shielded against the ups and downs of business cycles, demographic waves, sex imbalances on the marriage market, nutrition supply, epidemics and the risks associated with war (some secondary male members of the study population were killed in action in wars, but all before age 45, and, thus, were not included in the sample) and political unrest (except a few assassinations 1870-1918 - such cases were excluded from analysis here), save the long term trends in life expansion and in fertility reduction. There are consistent reports that season of birth has a considerable effect on average lifespan, with people born in summer months having the shortest, people born in winter have the longest lifespan (Doblhammer & Vaupel 2001, Vaiserman et al 2002, Vaiserman & Voitenko 2003, Lerchl (in press)). The difference was found to be larger in males, and larger the poorer the country. Varying food quality and incidence of infectious diseases are considered as likely causes of this effect of season of birth on mortality. I will check lifespan differences by season of birth between sisters and brothers, which, then, might be interpreted as a coarse indicator of the study population's exposure to short term environmental fluctuations.

8. Cohort: Maximal birth year difference between pairs of full brothers or of full sisters, respectively, was 27 years. However, if we exclude just 10 parental couples, the maximum such difference drops to 14 years. Cohort effects within pairs of siblings will be weak in this data set.

Results

In all subsequent multivariate comparisons between siblings, total number of own children was used as control variables in order to neutralise the trade-off between parity and longevity. In all other multivariate analyses, also catholic denomination (catholics had more children), mean cohort specific fertility and mean cohort specific lifespan - in order to control for the secular processes of fertility decline and of lifespan extemsion - were used as control variables.

1. For women, there was a moderate trade-off between parity and lifespan, which slightly increased in effect size, when women with at least one (partial correlation coefficient -.133 $p<.033$), at least two (partial correlation coefficient -.139 $p<.038$), at least three children (partial correlation coefficient -.153 $p<.042$) or at least four children (partial correlation coefficient -.186 $p<.041$) were considered. One the other hand, once women with 6 and more children were excluded, the effect disappeared. Within the 113 pairs of full sisters with completed lifespans, when age-at-first-birth and age-at-last-birth were used as additional control variables, there was a partial correlation coefficient between difference in lifespan and difference in number of children of -.238 at $p=.015$. For men, no trade-off between parity and lifespan could be observed.
2. For women, age at first birth predicted lifespan (partial correlation coefficient $r = .1295$ at $p=.034$). An extreme value comparison, putting the first ($\leq$20 years of age) and fourth quartile ($\geq$27 years of age) in age at first child against each other, generated a similar effect size: partial regression coefficient .245 at $p = .026$. Another, more arbitrary grouping, comparing women who had their

first baby before age 25 against those who had it after age 35, produced a partial regression coefficient .144 at p = .036.

Age at last birth did not predict lifespan, neither over the full range of the age-at-last-birth variable, nor in a comparison of the first ($\leq$27 years) and fourth quartile ($\geq$37 years), nor in a comparison of women up to 30 and above 40 years of age.

For men, neither age at first child nor at last child predicted lifespan.

Also, for neither sex was length of reproductive life span (time between first and last child, for individuals with at least two children, with number of children controlled) a predictor of lifespan.

However, there was a strong correlation between age at first and age at last birth, again with the same control variables and for individuals with at least two children: r=.4675 at p=.00004 for female survivors to age 45 and r=.6709 at p=.00004 for male survivors to age 50.

3. A subject's lifespan was predicted by first spouse's lifespan with r=.238 at p=.022 for women, and r=.250 at p=.020 for men.

On the other hand, a correlation was found in the lifespan of full brothers (r=.149, p=.001) and in the lifespan of full sisters (r=.215, p=.0004), but only if we include all - childless or not - individuals surviving at least to age 15. If, however, only female survivors to 45 and male survivors to age 50, with at least one child were considered – as anywhere else in the analyses presented here - no correlation was found in the lifespan of full brothers (r=.137, p=.111) nor in the lifespan of full sisters (r=-.018, p=.844). Interestingly, childless (married and unmarried) sisters surviving at least to age 45 have their lifespan correlate

with sisters with at least one child at r=.201 at p<.039, with mean cohort lifespan and mean cohort fertility controlled. Likewise, men without legitimate children surviving at least to age 45 have their lifespan correlate with brothers with at least one child at r=.314 at p<.004.

4. I checked pairs of same sex siblings whether season (spring, summer, autumn, winter) of birth had an effect on lifespan as compared to the lifespan of the other same sex sibling, provided that sibling was born in another season. Alternatively, lifespan was compared between siblings born in autumn and spring, the minimum and maximum in season of birth dependent mortality – leading to small sample sizes, however.

   No season of birth dependent mortality differentials could be observed (ANOVA with cohort specific mean lifespan and number of children of each sibling as covariates), not even as a non-significant tendency, neither in the pairs of brothers nor of sisters.

5. I checked pairs of sisters, whether the sister with the first (or the last) child born later in life, or the sister with the longer reproductive life span will have lived a longer life than the other. The same was done with the pairs of brothers. In order to avoid trivial effects, only such pairs of sisters or brothers are considered, in which both had reached the age at which the respective births had occurred. As already mentioned, analyses were performed with the binomial coefficient of the total number of full sisters, or brothers in the sample, as control variable, which, however, never showed any effect. Apparently size of family of origin has no effect on the relations between reproductive biography and longevity investigated here.

   Once mean cohort specific family size, life span and catholic denomination were controlled, there was no correlation in age at fist birth nor in age at last birth

between sisters nor between brothers. With the same control variables, there was a moderate correlation in family size between brothers, but none between sisters.

Of all sister-sister pairs, in 82 vs. 75 cases, the sister with the later first birth lived a longer life than her sister. Female fecundity progressively declines after age 35 (Hassan & Killick 2003; Tarlatzis & Zepiridis 2003), so pairs of sisters were selected, in which at least one had her first baby after age 35: in 7 vs. 4 cases the sister with the later first birth lived a longer life than her sister. If, alternatively, we look at cases with a large difference in age at first birth, irrespective of the age of the mothers, in 25 vs. 31 cases the sister who had to wait 5 years longer for her first child than her sister, also lived a longer life; in 7 vs. 8 cases the sister who had to wait 10 years longer for her first child than her sister, also lived a longer life.

Furthermore, of all sister-sister pairs, in 77 vs. 80 cases the sister with the last birth later in life lived a longer life than her sister. In pairs of sisters in which at least one had her last child after age 35, in 33 vs. 31 cases the sister with the last child later in life lived a longer life than her sister. If, alternatively, we look at cases with a large difference in age at last birth, in 47 vs. 47 cases the sister who had her last child 5 years later in life than her sister, also lived a longer life. In 22 vs. 19 cases the sister who had her last child 10 years later in life than her sister than her sister, also lived a longer life.

Finally, in all sister-sister pairs – only mothers of two and more - in 61 vs. 67 cases the sister with the longer reproductive life span lived a longer life than her sister. In none of these nine comparisons (Chi-square models with expected equal distribution as the Null Hypothesis) the difference is significant.

Of all brother-brother pairs, in 96 vs. 95 cases, the brother with the later first birth lived a longer life than his brother. Male fecundity also declines with age (Hassan &

Killick 2003), albeit the decline starts later and fecundity may continue into the 10th decade of life (Ricklefs & Finch 1995; Pal & Santoro 2003,), so pairs of brothers were selected in which at least one had his first baby after age 45: in 11 vs. 16 cases the brother with the later first birth lived a longer life than his brother. If pairs of brothers were selected in which at least one had his first baby after age 50: in 4 vs. 9 cases the brother with the later first birth lived a longer life than his brother. If, alternatively, we look at cases with a large difference in age at first birth, in 60 vs. 52 cases the brother who had to wait for his first child 5 years longer than his brother, also lived a longer life. In 26 vs. 20 cases the brother who had to wait 10 years longer for his first child than his brother, also lived a longer life.

Furthermore, of all brother-brother pairs, in 95 vs. 85 cases[3] the brother with the later last birth lived a longer life than his brother. In pairs of brothers in which at least one had his last child after age 45, in 39 vs. 40 cases the brother with the last child later in life lived a longer life than his brother. In pairs of brothers in which at least one had his last child after age 50, in 26 vs. 16 cases the brother with the last child later in life lived a longer life than his brother If, alternatively, we look at cases with a large difference in age at last birth, in 66 vs. 53 cases the brother who had his last child 5 years later in life than his brother, also lived a longer life. In 42 vs. 30 cases the brother who had his last child 10 later in life than his brother, also lived a longer life.

Finally, in all brother-brother pairs – only fathers of two and more - in 63 vs. 58 cases the sister with the longer reproductive life span lived a longer life than her

[3] In nine pairs, one brother had his last child at a time, when the other brother, although he had also survived to age 45, was already dead. Consequently, as described above, these brother pairs were not considered here.

sister.

In none of these eleven comparisons (again Chi-square models with expected equal distribution as the Null Hypothesis) the difference is significant.

These direct pairwise comparisons were, naturally, performed without the control variables as mentioned at the beginning of this section.

The results of the sister-sister and of the brother-brother comparison are displayed in a compact way in table 1.

(insert table 1 about here)

6. Among pairs of sisters, partial correlation coefficient between difference in age at first child and difference in life span (only uncensored cases) was r=.026 at p=.776, and partial correlation coefficient between difference in age at last child and difference in life span was r=-.0034 at p=.975, with number of children, mean cohort life span, mean cohort fertility and catholic denomination controlled.

   Among pairs of brothers, partial correlation coefficient between difference in age at first child and difference in life span (again, only uncensored cases) was r=.101 at p=.234, and partial correlation coefficient between difference in age at last child and difference in life span was r=.074 at p=.384.

7. Likewise, difference in length of reproductive life span and difference in life span did not correlate in any sibling comparison, with the same control variables.

Discussion

1. This dataset is ideally suited for studying the question whether a late first or a late last baby is a life prolonging event, since any differential socio-economic factors are absent, the effects of short term environmental fluctuations (coarsely measured by season of birth) are smaller than in the general population, and – due to substantial inbreeding - genetic heterogeneity probably is smaller than in a general population sample. In studying the research question by comparing pairs of full sisters or of full brothers, cohort and genetics effects are controlled further. The correlation in lifespan between full sisters or between full brothers, if we consider all survivors beyond age 15, with a correlation coefficient higher than between DZ twins and about half as high as between MZ twins in a general population sample (Herskind et al. 1996) is no surprise for a population with uniformly excellent living conditions (Korpelainen 2000). It is known, however, that non-additive genetic factors (genetic intra-locus interactions) are important here. If, however, only survivors to at least 45 (sisters) or 50 (brothers) years of age with proven fecundity are compared, a statistical association, although expected (Herskind et al. 1996; Iachine et al. 1998; Jarvik et. 1960; Kerber et al. 2001; Mitchell et al. 2001; Perls et al. 1998; 2002) could not be observed. Obviously, in the study population, genetic factors may have a small impact on post-reproductive mortality. Perhaps in the general population samples studied so far, a substantial part of the presumed heritability of the life span in fact is a shared environment effect. Once the effects of genetics get small, environment effects become greater. The stable

association in lifespan of survivors to postreproductive age, and their spouses may have to be explained by shared environment and not by assortative mating, either by spousal genetic similarity (for which is little evidence: Eckman et al. 2002) nor by phenotypic assortment (Reynolds et al. 1996), since future mortality of spouses is hardly observable at the time of marriage.

2. Sample size can never be too large; however, 191 pairs of full brothers and 157 pairs of full sisters, all surviving to at least 50 (males) or 45 (females), and of demonstrated fecundity, is large enough a sample for either sex to detect a consistent trend, if there is one in the universe of study.

3. The trade-off between total number of children and lifespan demonstrated for individual females is present, however, only after the sixth or even a later birth (similar finding for the British peerage in Doblhammer-Reiter & Oeppen 2003). No trade-off at all was demonstrated for males.

3. A later first birth predicted a longer life in females, but not for males. A later last birth did not predict a longer life for either sex – same finding in Doblhammer-Reiter & Oeppen (2003). Also, the time span between first and last birth was not a predictor for own lifespan.

4. The comparison of sibling pairs – the central part of this study - gave no hint that the event of a late – first or last - birth makes the life of the mother or of the father longer. Among females, where the life prolonging effect of a birth later in life should be stronger anyway, the effect directions (never significant) observed are fairly even distributed between four findings pointing in one and five pointing in the opposite direction. Thus, nothing speaks for the emergence of a stable significant statistical effect once the sample size should become even

several times larger. Among males, there are more (8 vs. 3: sign test p=.132) findings pointing in the hypothesised effect direction (again none of the individual findings significant), but, given the longer reproductive life span in males, selection or differential health effects rather than genuine causal effects may play a greater role than in females anyway. Given the smaller physical and biological impact pregnancy, birth and lactation has on a father's as compared to a mother's organism, there is little reason to expect an eventual life prolonging causal effect of a baby later in life to be stronger for fathers than for mothers.

4. Since Pearls et al.'s original (1997) and some later papers found the association between lifespan and late motherhood by comparing women giving birth after age 40 with others, it might be argued that, perhaps, only such very late births have the life prolonging effect searched for here, and those indeed are too rare in the sample for any meaningful analysis. Equivalently, it might be argued, that genetics may play a more important role for the lifespan among long-lived individuals (Jarvik et. 1960; Herskind et al. 1996; Iachine et al. 1998; Kerber et al. 2001; Mitchell et al.; Perls et al. 1998; 2002), and the number of very long-lived individuals (say survivors to 85, or beyond), not to speak of very long-lived pairs of siblings, again is too small in the sample. On the other hand, female fecundity – as measured by waiting time to pregnancy, for example (Pal & Santoro 2003) - starts to decline after age 30 even among the well fed and healthy women of today's rich countries (Hassan & Killick 2003; Tarlatzis & Zepiridis 2003), and while it is conceivable that an eventual life prolonging effect of a late birth gets the stronger, the later in a woman's life that birth

actually happens, there is little reason why such an effect should start only after age 40. Rather, it should gradually emerge already after age 30, and, thus, should not go undetected in our sister-sister and brother-brother comparisons, where life span is measured in exact number of days. Nothing is known to expect that a late baby should be a life-prolonging event exclusively for people who have a genetic disposition for unusually long lives, if this disposition itself is unrelated to reproduction. It might be that there is a genetic link between dispositions for late reproduction and longevity, which can be properly studied only in very long-lived individuals. But such a hypothetical link would not predict an association between the later birth and the longer life in comparisons of full sisters or of full bothers, and, therefore, would not show up if a much larger sample of sister pairs or brother pairs were available. Such a hypothetical link would – with unchanged genotype frequencies – become more visible in phenotype analyses the more favourable the environment becomes – and therefore could be masquerading as a cohort effect – but not in the novel design of sister-sister or brother-brother comparisons applied here.

Thus, the main finding of this study, obtained from a data set which is ideally suited for studying such an eventual effect, because many potential intervening variables are controlled here, namely that neither a first baby nor a last baby later in life is a life prolonging event, neither for females nor for males, probably in the same way applies to individuals with and without a genetic disposition for unusually long lives.

Conclusions

There are three interpretations of the association between late reproduction and longevity several authors have reported:

First, the event of a late (first or last) birth directly or indirectly may make the parental organism more durable.

Second, there may be a genetic link between longevity and a disposition to start or to end reproducing later in life, inducing more durable individuals to drift later into or later out of reproduction than other individuals.

Third, the association between late reproduction and longevity could be explained by the differences between families in educational investments, and healthy lifestyles.

The findings from this study, clearly do not support the first interpretation. A child later in life apparently is not a life prolonging event.

For studying life course differences based on genetic differences – the second interpretation - this genetically homogeneous study sample is poorly suited.

Thirdly, there is a clear influence also in this study sample, of individual lifestyle factors on the life course, to be seen in the stable correlation of postreproductive lifespan between first time married spouses, as compared with the much weaker correlation between the postreproductive lifespans of full sisters / full brothers. But this possibly life style dependent variance in lifespan between full same-sex-siblings still is not associated with the timing of first or last births nor the length of the reproductive life span.

The conclusion is obvious that the positive association between late reproduction and longevity, which in general population samples was repeatedly observed, must be explained by the variance of some of the factors seemingly well controlled in this

study: by genetic heterogeneity between family lineages, or by socio-economic status based health differences, or – most likely – by a combination of both.

Literature

1. Allman J, Rosin A, Kumar K, Hasenstaub A (1998): Parenting and survival in anthropoid primates: Caretakers live longer. Proc. Natl. Acad. Sci. USA 95: 6866-6869.
2. Berg SJ, Wynne-Edwards KE (2001): Changes in testosterone, cortisol, and estradiol levels in men becoming fathers. Mayo Clinic Proceedings 76: 582-592.
3. Carey JR, Judge DS (2001): Life Span Extension in Humans Is Self-Reinforcing: A General Theory of Longevity. Population and Development Review 27: 411-436.
4. Carey JR, Tuljapurkar S (2003)(eds.): Life Span. Evolutionary, Ecological, and Demographic Perspectives. Population and Development Review 29 Supp.
5. Carey, JR (2003): Longevity. The Biology and Demography of Life Span. Princeton University Press.
6. Doblhammer-Reiter G (2000): Reproductive History and Mortality Later in Life. A Comparative Study of England & Wales and Austria. Population Studies 54: 169-176.
7. Doblhammer-Reiter G, Oeppen J (2003): Reproduction and longevity among the British Peerage: the effect of frailty and health selection. Proceedings of the Royal Society London / B 270: 1541-1547
8. Doblhammer-Reiter G, Vaupel JW (1999): Reproductive History and Mortality Later in Life for Austrian Women. Max Planck Institute for Demographic Research WP 1999-012.

9. Doblhammer-Reiter G, Vaupel JW (2001) Lifespan depends on month of birth. Proc Natl 10 Acad Sci U S A 98: 2934-2939
10. Eckman RW, Williams R, Nagoshi C (2002): Marital Assortment for Genetic Similarity. J Biosoc Sci 34: 511-523
11. Falsetti L, Scalchi S, Villani MT, Bugari G (1999): Premature Ovarian Failure. Gynecological Endocrinology 13: 189-195.
12. Finch CE (1990): Longevity, Senescence and the Genome. Chicago: University of Chicago Press.
13. Friedlaender, NJ (1996): The Relation of Lifetime Reproduction to Survivorship of Women and Men: A prospective Study. Am J Hum Biol 8: 771-783
14. Hassan MA, Killick SR (2003): Effect of male age on fertility: evidence for the decline in male fertility with increasing age. Fertil Steril. 79 Suppl 3:1520-7.
15. Hawkes K (2003): Grandmothers and the Evolution of Human Longevity. Am J. Human Biol. 15: 380-400.
16. Herskind, AM, McGue M, Holm NV, Soerensen TIA, Harvald B, Vaupel JW (1996): The Heritability of Human Longevity: a Population Based Study of 2872 Danish Twin Pairs Born 1870-1900. Human Genet 97: 319-323
17. Iachine IA, Holm NV, Harris JR, Begun AZ, Iachina MK, Laitinen M, Kaprio J, Yashin AI (1998): How Heritable is Individual Susceptibility to Death ? The Results of an Analysis of Survival Data on Danish, Swedish and Finnish Twins ? Twin Res 1: 196-205
18. Jarvik L, Falek A, Kallmann FJ, Lorge I (1960): Survival Trends in a Senescent Twin Population. Am J Hum Genet 12: 170-179

19. Kerber RA, O'Brian E, Smith KR, Cawthon RM (2001): Familial Excess Longevity in Utah Genealogies. J Gerontol A Biol Sci Med Sci 56, 130-139
20. Kirkwood TBL (1977): Evolution of Ageing. Nature 270: 301-304
21. Kirkwood TBL, Rose MR (1991): Evolution of Senescence: Late Survival Sacrificed for Reproduction. Phil Trans R Soc Lond B 332: 15-24
22. Korpelainen H (2000): Variation in the Heritability and Evolvability of Human Life Span. Naturwissenschaften 87: 566-568
23. Kvale G, Heuch I, Nilssen S (1994): Parity in Relation to Mortality and Cancer Incidence: A Prospective Study of Norwegian Women. Int J Epidemiol 23: 691-699
24. Lerchl A (in press): Month of birth and life expectancy: role of gender and age in a comparative approach. Die Naturwissenschaften.
25. Lund E, Arnesen E, Borgan JK (1990): Pattern of Childbearing and Mortality in Married Women - a National Prospective Study from Norway. J Epidemiol Community Health 44: 237-240.
26. Lycett JE, Dunbar RIM, Voland E (2000): Longevity and the Costs of Reproduction in a Historical Human Population. Proc R Soc Lond B 267: 31-35
27. McNaughton A (1973): The Book of Kings. A Royal Genealogy. 3 volumes. Garnstone Press: London.
28. Mitchell BD, Hsueh WC, King TM, Pollin TI, Sorkin J, Agarwala R, Schäffer AA, Shuldinher AR (2001): Heritability of Life Span in Old Order Amish. Am J Med Genet 102: 346-352
29. Mueller HG, Carey JR, Wu D, Liedo P, Vaupel JW (2001): Reproductive Potential Predicts Longevity of Female Mediterranean Fruitflies. Proceedings of the Royal Society London: Biological Sciences 268, 445-460.

30. Mueller HG, Chiou JM, Carey JR, Wang JL. (2002): Fertility and Life Span: Late Children Enhance Female Longevity. J Gerontol A Biol Sci Med Sci 57(5): B202-206.
31. Mueller U (2001): Is There a Stabilising Selection Around Average Fertility in Modern Human Populations? Population and Development Review 27, 469-498.
32. Mueller U, Mazur A (2001): Evidence of Unconstrained Directional Selection for Male Tallness. Behavioral Ecology and Sociobiology 50, 302-311.
33. Murphy M, Wang D (2002): The Impact Of Intergenerationally-Transmitted Fertility And Nuptiality On Population Dynamics In Contemporary Populations. in: Rogers JL, Kohler HP (eds.): The Biodemography of Human Reproduction and Fertility. Kluwer Academy Publishers.
34. Nieschlag E, Nieschlag S, Behre HM (1993): Lifespan and Testosterone. Nature 366: 215.
35. Pal L, Santoro N. (2003): Age-related decline in fertility. Endocrinol Metab Clin North Am. 2003 Sep;32(3):669-88.
36. Perls TT, Alpert L, Fretts RC (1997): Middle-aged Mothers Live Longer. Nature 389: 133.
37. Perls TT, Bubrick E, Wager CG, Vijg J, Kruglyak L. (1998): Siblings of Centenarians live longer. Lancet 351: 1560.
38. Perls TT, Fretts RC (2001): The Evolution of Menopause and Human Life Span. Annals of Human Biology 28, 237-245.
39. Perls TT, Wilmoth J, Levenson R, Drinkwater M, Cohen M, Bogan H, Joyce E, Brewster S, Kunkel L, Puca A (2002): Life-long Sustained Mortality Advantage of Siblings of Centenarians. Proc. Natl. Acad. Sci. USA, 99: 8442-8447.

40. Perusse D (1993): Cultural and Reproductive Success in Industrial Societies: Testing the Relationship at the Proximate and Ultimate Levels. Behavioral and Brain Sciences 16: 267-322.
41. Perusse D (1994): Mate Choice in Human Societies: Testing Evolutionary Hypotheses with Behavioral Data. Human Nature 5: 255-278.
42. Reynolds CA, Baker LA, Pedersen NL (1996): Models of spouse similarity: applications to fluid ability measured in twins and their spouses. Behav Genet 26: 73-88
43. Ricklefs RE, Finch CE (1995): Aging: A Natural History (Scientific Amercan Library). W H Freeman & Co.
44. Rogers JL, Kohler HP, Christensen K (2002): Genetic Variance And Human Fertility: Biology, Psychology Or Both. in: Rogers JL, Kohler HP (eds.): The Biodemography of Human Reproduction and Fertility. Kluwer Academy Publishers.
45. Santoro N (2003): Mechanisms of Premature Ovarian Failure. Ann Endocrinol 64:87-92.
46. Smith K, Mineau G, Kerber RA, O'Brian E, Cawthon RM (1999): Increased longevity in the siblings of late fertile women. Abstract 1999 Annual Meeting of the Population Association of America.
47. Smith KR, Mineau GP, Bean LL (2002): Fertility and Post-Reproductive Longevity. Social Biology 49: 185-205.
48. Spencer RP (2002): Cessation of Reproduction: an Analytic View of Menopause. Med. Hypotheses 59,406-10.
49. Tarlatzis BC, Zepiridis L (2003): Perimenopausal conception. Ann N Y Acad Sci. 2003 Nov;997:93-104.

50. Vaiserman AM, Collinson AC, Koshel NM, Belaja, II, Voitenko VP (2002) Seasonal programming of adult longevity in Ukraine. Int J Biometeorol 47: 49-52
51. Vaiserman AM, Voitenko VP (2003) Early programming of adult longevity: demographic and experimental studies. J Anti Aging Med 6: 11-20
52. Vaupel JW, Carey JR, Christensen K, Johnson TE, Yashin AI, Holm NV, Iachine IA, Kannisto V, Khazaeli AA, Liedo P, Longo VD, Zeng Y, Manton KG, Curtsinger JW (1998): Biodemographic Trajectories of Longevity. Science 280: 855-860
53. Westendorp R, Kirkwood T (1998): Human Longevity at the Cost of Reproductive Success. Nature. 396: 743-746.

Table 1: The Sister-Sister and the Brother-Brother Comparisons

Hypothesis: A child later in life makes the life of the parent longer

	Females: Hypothesis			Males: Hypothesis	
First baby	Confirmed	Not Confirmed	First baby	Confirmed	Not Confirmed
All sister pairs	82	75	All brother pairs	95	94
At least one sister older than 35 at first baby	7	4	At least one brother older than 45 at first baby	11	16
			At least one brother older than 50 at first baby	4	9
One sister has her first baby at least 5 year later in life than her sister	25	31	One brother has his first baby at least 5 year later in life than his brother	60	52
One sister has her first baby at least 10 year later in life than her sister	7	8	One brother has his first baby at least 10 year later in life than his brother	26	20
Last baby			Last baby		
All sister pairs	77	80	All brother pairs	95	85
At least one sister older than 35 at last baby	33	31	At least one brother older than 45 at last baby	39	40
			At least one brother older than 50 at first baby	26	16
One sister has her last baby at least 5 year later in life than her sister	47	47	One brother has his last baby at least 5 year later in life than his brother	66	53
One sister has her last baby at least 10 year later in life than her sister	22	19	One brother has his last baby at least 10 year later in life than his brother	43	30

Hypothesis: A longer reproductive life span makes the life of the parent longer

	Females: Hypothesis			Males: Hypothesis	
Reproductive life span	Confirmed	Not Confirmed	Reproductive life span	Confirmed	Not Confirmed
All sister pairs (only mothers of 2)	61	67	All brother pairs (only fathers of 2)	63	58