Gender Specific Effects of Early-Life Events on Adult Lifespan

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Abstract

The idea of fetal origins of adult degenerative diseases and early-life programming of late-life health and survival is being actively discussed in the scientific literature. Can this new fascinating concept also be useful to understand (at least partially) the observed sex disparities in adult health and longevity? Are the long-lasting effects of early-life conditions identical for both sexes, or, on the contrary, they are sex-specific? These questions stimulated us to conduct the present pilot exploratory study on the gender specificity of late-life health outcomes for early-life effects. In this study we addressed these scientific problems by studying the effects of early-life conditions on adult lifespan of men and women separately, using the methodology of historical prospective study of extinct birth cohorts.

In this study we found that sex differences in adult life span are modulated by early-life events and conditions. Specifically, we found that such variables as

1. father's age at person's conception,
2. maternal lifespan
3. month of birth,
4. birth order (first-born status)

have a profound effects on adult lifespan (life expectancy at age 30) in females, but not in males. Daughters born to particularly young fathers (below 25 years) or old fathers (above 45 years) live significantly shorter lives, while sons are less affected by paternal age at conception. The dependence of progeny lifespan on maternal lifespan is non-linear with particularly steep slope for long-lived mothers (above 90 years) and female sex of the progeny. Women born in May or December live longer compared to those born in February or August, while male lifespan is less affected by the season of birth. The results of this pilot exploratory study justifies the need for further full-scale research project on gender-specific outcomes of early-life effects and conditions.

Introduction

The idea of fetal origins of adult degenerative diseases and early-life programming of late-life health and survival is being actively discussed in the scientific literature (Lucas, 1991; Barker, 1992; 1998; Kuh & Ben-Shlomo, 1997; Leon *et al*., 1998; Lucas *et al*., 1999; Blackwell *et al*., 2001). Can this new fascinating concept also be useful to understand (at least partially) the observed sex disparities in adult health and longevity? Are the long-lasting effects of early-life conditions identical for both sexes, or, on the contrary, they are sex-specific? These questions stimulated us to conduct the present pilot exploratory study on the gender specificity of late-life health outcomes for early-life effects.

The study of sex differences in late-life responses has also important methodological implications for research work on early-life effects. This is because in many cases the available datasets are limited in their size and/or the studied outcomes are rare events, thus creating a temptation to pool data for both sexes together in order to increase the statistical power (Blackwell *et al*., 2001). It is important, therefore, to find out whether gender differences in response to early-life events are indeed similar (so that the data could be pooled together with simple adjustment for sex just by one indicator variable), or they are fundamentally and qualitatively different (so that each sex should be studied separately).

In this study we addressed these two scientific problems (fundamental and methodological) by studying the effects of early-life conditions on adult lifespan of men and women separately, using the methodology of historical prospective study of extinct birth cohorts. We discovered the profound sex differences in late-life responses to early-life effects in our pilot exploratory study that justifies the need for further full-scale research project on related topic.

Data and Methods

Main Data Source.

In this study we collected, computerized and analyzed the detailed genealogical records on lifespan of about 12,000 adult persons (survived by age 30) and their parents, using particularly reliable and complete data on European royal and noble families for extinct birth cohorts (born 1800-1880). The main advantage of these data is their high accuracy, reliability and completeness (to be discussed later). Another advantage of this kind of data is the relative homogeneity of this Caucasian population regarding social class and educational background. Since this privileged social group lived in favorable conditions for many centuries, one could expect less influence of adverse social factors (poverty, for example) on life span and hence lower bias caused by these factors. This kind of data allows us to minimize the social heterogeneity of the population under study. Thus, although the sample analyzed in this study does not represent the whole human population (as laboratory animals do not represent species in the wild), it is one of the best possible samples to test biodemographic hypotheses since the effects of population heterogeneity are minimized with regard to social status.

The database on European royal and noble families (a family-linked database) was developed and already used in our previous studies (Gavrilov, Gavrilova, 1997a; b; 1999; 2000a; 2001a; Gavrilov et al., 1997; Gavrilova et al., 1998). To develop this database, we have used one of the best professional sources of genealogical data available - the famous German edition of the *Genealogisches Handbuch des Adels* (Genealogical Yearbook of Nobility). This edition is known world wide as the *Gotha Almanac* - "Old Gotha" published in Gotha in 1763-1944, and "New Gotha" published in Marburg since 1951 (see Gavrilova, Gavrilov, 1999, for more details). Data from the *Gotha Almanach* were often used in early biodemographic studies of fertility (see Hollingsworth, 1969, pp. 199-224, for references) and are used now in the studies of human longevity (Gavrilova et al., 1998; Gavrilov, Gavrilova, 1997a; 2001a).

Each volume of the *New Gotha Almanach* contains about 2,000 genealogical records dating back to the 14-16th centuries (to the founder of a particular noble genus). More than 100 volumes of this edition are already published, so more than 200,000 genealogical records with well-documented genealogical data are available from this data source. The high quality of information published in this edition is ensured by the fact that the

primary information is drawn from the German Noble Archive (*Deutsches Adelsarchiv*). The Director of the *German Noble Archive* (Archivdirektor) is also the Editor of the *New Gotha Almanach*. Our own experience based on cross-checking the data, has demonstrated that the number of mistakes (mostly misprints) is very low in the *New Gotha Almanac* (less than 1 per 1000 records), so this source of data is very accurate compared to other published genealogies.

The information on noble families in the *New Gotha Almanac* is recorded in a regular manner. The description of each particular noble genus starts with information on 2-3 generations of founders of male sex only. Then three to four the most recent generations are described in more detail, including information on individuals (e.g., first and last names; event data: birth, death, marriage dates and places; descriptive data: noble degrees, occupation if available, information on death circumstances if available), information on parents (e.g., first and last names; event data: birth and death dates and places), information on spouse(s) (e.g., first and last names; birth and death dates and places; first and last names of parents) and information on children (detailed as for each individual).

The process of data computerization was started from the most recent volumes of the *New Gotha Almanac* (published in 1990-1994) and reached now the volumes published ten years earlier. The database on European aristocratic families comprises more than 20,000 personal records and is growing further.

Supplementary Data Sources.

Some other supplementary sources of data were used in the development of database. These data sources included two computerized data files on European royalty and British peerage (computerized database "Royal92" distributed on the Internet by Brian C. Tompsett at University of Hull, UK, and database on British Peerage distributed on CD by S&N Genealogy Supplies), as well as over 100 genealogical publications on Russian nobility listed elsewhere (Gavrilov et al., 1996). These data were used as a supplement to the main data source since their quality was not as high compared to the *Gotha Almanac*. Although data on European royalty were recorded in computerized data sources ("Royal92", British Peerage CD, see above) with sufficient completeness, data on lower rank nobility (landed gentry) were less complete and accurate. The same was true for the data on Russian nobility. All supplementary data were matched with the *Gotha Almanac* data, in order to cross-check the overlapping pieces of information. This cross-checking procedure allowed us to increase the completeness of the database by complementation of information taken from different sources.

The Structure of the Database on European Aristocracy.

The database approach used in this study is similar to the approach used for existing family-linked databases, such as the *Utah Population Database* (Skolnick et al., 1979), *Laredo Epidemiological Project* (Buchanan et al., 1984) or other historical databases (Gutmann et al., 1989). Initially the information computerized from each volume of the *New Gotha Almanac* is stored in two files: the Individual File and the Marriage File. Then these two files are merged into one rectangular file with information on up to 4 spouses. Since marriages with 5th and higher orders comprise less than 0.1% of all marriages, the potential loss of information on spouses after data merge is negligible. Then these merged files are linked to the Master File (main database).

In the Master File each record is related to the duration of an individual's life. Each record represents an individual's event data (birth and death dates and places) and individual's descriptive information (identification number, sex, first and last names, nobility rank, occupation, birth order, cause of death (violent/nonviolent), ethnicity, marital status, data source code number, data source year of publication). Individual information is supplemented by data for parents (identification numbers, first and last names, birth, death and marriage dates, cause of death) and spouses. Thus, the database that is used in this project is organized in the form of triplets (referred to as the "ego" and two parents). This structure of records is widely used in human genetics and is adequate for studies of parent-child relationships. Similar database structure was used in the recent study of kinship networks (Post et al., 1997).

Data Quality Control.

Data quality control was an important part of our study designed to develop high quality family-linked databases for longevity studies.

The genealogical data sets were checked for:

(1) *completeness* in reporting birth and death dates, which is crucial for calculating individual life span - the variable of particular interest in our study.

(2) *accuracy* - whether the percentage of mistakes and inconsistencies between reported dates (such as, for example, birth by the dead mother) is low enough to be acceptable.

(3) *representativeness* - whether the characteristics of investigated data sets (distribution by age, sex, marital status, age at death, etc.) is close enough to demographic characteristics of populations in similar geographic areas, historical periods and social groups.

In our study we referred to the well-known publication by Thomas Hollingsworth (1962) on British peerage as a standard for European aristocracy, to check for data representativeness.

The completeness in birth and death dates reporting in the *New Gotha Almanac* was very high: dates of all vital events were reported for nearly 95% of all persons. Such high completeness is not common for many other genealogical data sources. For example, for British Peerage data published in Burke almanac in most cases there are no birth dates for women, which makes the calculation of their life span impossible. In fact, this problem with British aristocratic women was first noticed by Karl Pearson a century ago (Beeton and Pearson, 1899, 1901). He used the British Peerage data to study the longevity inheritance and had to exclude women from his consideration for the following reason: "The limitation to the male line was enforced upon us partly by the practice of tracing pedigrees only through the male line, partly by the habitual reticence as to the age of women, even at death, observed by the compilers of peerages and family histories" (Beeton and Pearson, 1901, pp.50-51).

The accuracy of data published in the *New Gotha Almanac* is also very high: the frequency of inconsistent records is less than 1 per 1000 records while for many other genealogical data sources it falls within 1 per 300-400 records. Comparison of our data with Hollingsworth's analysis of British peerage (Hollingsworth, 1962) revealed good agreement between his findings and our data on mortality patterns, including male/female gap in life expectancy.

The genealogies for the members of European aristocratic families presented in the *Gotha Almanac* are of descending type, tracing almost all the descendants of relatively few founders. This is an important advantage of this data source over other genealogies that are often of ascending type (pedigrees). It is known in historical demography that the ascending genealogies are biased, over-representing more fertile and longer-lived persons who succeed to become ancestors, and for this reason such genealogies should be treated with particular caution (Jetté and Charbonneau, 1984; Fogel, 1993).

Thus, the genealogical data published in the Gotha Almanac are characterized by high quality and accuracy. We have, however, encountered some problems regarding the data completeness that are discussed below, along with proposed solutions.

Censored, truncated observations and missing death dates.

Our study revealed that the percentage of cases with unreported death dates is rather small in our main data sources (*Gotha Almanac*), and is caused mainly by right censoring of long-lived persons who were still alive by the date of data collection and publication. The percentage of non-reported death dates varies from 0 to 7% in extinct birth cohorts (1800-1880), while it is higher in later birth cohorts (1880-1899) - 23% for women and 8% for men, since some individuals were still alive by the date of data collection and volume publication. Note that women, who live longer, have a higher proportion of right-censored observations. The high proportion of censored observations in genealogies is not desirable, since the exact dates of censoring are often unknown.

This uncertainty creates problems for data analysis, so the researchers working with genealogies prefer to use non-censored, extinct birth cohorts in their studies (Mayer, 1991; Pope, 1992; Kasakoff and Adams, 1995). We also used extinct (non-censored) birth cohorts in our study. For this purpose only those birth cohorts were used in the study that were born at least 100 years before the year of data publication (to be sure that the birth cohort under study is almost extinct).

Under reporting of women and children.

In many genealogical books and databases non-married women as well as children died in infancy are often missed or reported with less completeness. Since genealogical records are focused on family names which are transmitted by males only, women could be lost in genealogies when they marry and change their family names (Hollingsworth, 1976). Also, in many cases data for women do not contain information on their birth and death dates resulting in biased sex ratio in the sample with complete dates. We have also encountered this problem in our studies although for somewhat different reason. Our analysis revealed that the main cause of the sex bias in the *New Gotha Almanac* is related to the manner of data representation: more recent generations are presented completely, while the earlier generations are limited mainly to the male ancestors (in order to avoid repetitive publication of individuals already presented in previous volumes). That is why, the sex ratio among early birth cohorts (1800-1860) is biased in favor of males while for more recent birth cohorts (1880-1899) it is within normal range. Since in our previous studies the most recent volumes of the *New Gotha Almanac* (published after 1980) were computerized and analyzed (in order to avoid censoring), the proportion of males in the database was substantially higher than expected (Gavrilov, Gavrilova, 1997a; b; 1999; 2000a; 2001a; Gavrilov et al., 1997; Gavrilova et al., 1998). Sex bias is an important issue, particularly when gender differences are studied (as it is done in the present study). Therefore, every effort is made to ensure that the dataset used in this particular study is sex-balanced (see Table 1).

Table 1. Characteristics of the dataset

Birth cohort (year of birth)	Mean Age at Death* ± Standard Error (years)	
	Daughters	Sons
1800-1809	66.2 ± 0.8 (398)	64.2 ± 0.7 (396)
1810-1819	66.1 ± 0.8 (426)	62.9 ± 0.7 (469)
1820-1829	66.1 ± 0.7 (543)	63.4 ± 0.7 (504)
1830-1839	67.7 ± 0.7 (548)	62.7 ± 0.6 (573)
1840-1849	69.8 ± 0.6 (611)	63.7 ± 0.5 (682)
1850-1859	71.7 ± 0.6 (777)	63.8 ± 0.5 (899)
1860-1869	74.4 ± 0.4 (1,132)	66.1 ± 0.4 (1,207)
1870-1879	76.4 ± 0.4 (1,660)	65.7 ± 0.4 (1,611)

* Data refer to adult lifespan for those who survived by age 30.

To our knowledge, this is the first study of the family history datasets for European aristocratic families, where the sex bias is at last eliminated.

The under reporting of children died in infancy may be also a serious problem, especially for studies that include fertility analysis. Fortunately, in the *Gotha Almanac* the noble families are described with remarkable completeness, especially those families which belong to the higher nobility rank (kings, princes, earls). In particular, all ever born children are recorded, including those who died the same day. Another indicator of data completeness is the normal sex ratio at birth (101 to 108) observed among these families (according to our sample analysis). In our database over 90 aristocratic genuses belonging to the upper nobility were recorded completely, although data for lower rank nobility were not yet completed. Under reporting of children is not a problem for this particular study that is focused on adult life span for those who survive by age 30 years.

Analytical Methods.

Since the data used in this study are characterized by remarkable accuracy and completeness, it was possible to apply simple and straightforward methods of data analysis without making heavy assumptions. In particular, since the length of life is known for every person (there were no right censored observations) it was possible to analyze the duration of life directly as a dependent, outcome variable in linear regression model. There was no need to apply the Cox proportional hazard model and to make a strong assumption about multiplicative effects of covariates on hazard rate. Instead, the persons' lifespan is studied directly as a dependent outcome variable and a function of other explanatory and potentially confounding predictor variables (see later).

In this study we applied a multiple regression analysis with nominal variables which is a very flexible tool to control for effects of both quantitative and qualitative (categorized) variables. This method also allows one to accommodate for complex non-linear and non-monotonic effects of predictor variables. We used the data for extinct birth cohorts (born in 1800-1879) free of censored observations and tested a long list of explanatory and potentially confounding variables (described below) to consider all possible artifacts.

Life span of adult (30+) progeny (sons and daughters separately) was considered as a dependent outcome variable in multi-variate regression with dummy (0-1) variables using the SAS statistical package (procedure REG). The independent predictor variables included 12 types of binary variables:

(1) calendar year of birth (to control for historical increase in life expectancy as well as for complex secular fluctuations in lifespan). The whole birth year period of 1800-1879 was split into 5-year intervals (16 intervals) presented by 15 binary (0-1) variables with reference level set at 1875-1879 birth years.

(2) maternal lifespan (to study maternal lifespan effects through combined genetic effects and shared environment). The maternal lifespan data were grouped into 5-year intervals (15 intervals) with the exception of the first (15-29 years) and the last (95+ years) longer intervals with small number of observations. The data were coded with 14 dummy variables with reference level set at 75-80 years for maternal lifespan.

(3) paternal lifespan (to study paternal lifespan effects through combined genetic effects and shared environment). The data were grouped and coded in a way similar to maternal lifespan (see above).

(4) maternal age when a person (proband) was born. This variable is used to study possible confounding effects of maternal age on offspring lifespan. The data for mother's age were grouped in 5-year intervals (7 intervals to cover the age range of 15-60 years) with the exception of the last longer interval of 45-59 years with small number of observations. Maternal age of 25-29 years is selected as a reference.

(5) father's age when a person was born. This variable is used to study paternal age effects on offspring lifespan. The data were grouped and coded in 5-year intervals (9 intervals to cover the age range of 15-80 years) with the exception of the first (15-24 years) and the last (60-79 years) longer intervals with small number of observations. Paternal age of 40-44 years is selected as a reference.

(6) birth order. This variable is represented by binary variable coded as 1 when individual was a first-born child and coded as zero otherwise.

(7) nationality. The nationality of individual is represented by a set of 6 categories - Germans, British, Italians, Poles, Russians and 'others'. Germans (the largest group in our sample) is selected as a reference group.

(8) cause of death ('extrinsic' versus 'natural'). The death is coded as extrinsic or premature in following cases: (1) violent cause of death (war losses, accidents, etc.), (2) death in prison and other unfavorable conditions (concentration camp, etc.), (3) death from acute infections (cholera, etc.) and (4) maternal death (for women only). Deaths from all other causes combined were considered as a reference outcome.

(9) loss of the father in the formative years of life (before age 15). This is a binary variable coded as 1 when father was lost before the age 15 and coded as zero otherwise.

(10) loss of the mother before age 15. This binary variable is coded as 1 in those cases when mother was lost before the age 15 and coded as zero otherwise.

(11) loss of both parents (orphanhood) before age 15. This binary variable is coded as 1 in those cases when *both* parents were lost before the age 15 and coded as zero otherwise.

(12) month of birth. This variable was included into analysis, because previous studies indicated that month of birth may be an important predictor of adult lifespan (Gavrilov, Gavrilova, 1999; Doblhammer, 1999), particularly for daughters (Gavrilov, Gavrilova, 1999). This variable was represented as a set of 11 dummy variables with those born in February considered as a reference group. The main focus of this particular study is on sex-differences in the month-of-birth effects that were not studied before.

Results and Discussion

The characteristics of analyzed dataset are presented at Table 1. There are several notable features to mention here. First, the numbers of males and females are rather similar in all studied birth cohorts (no apparent sex bias). Second, the values for mean lifespan are rather high - more than 62 years for males and 66 years for females. It indicates that lifespan in this socially elite population is comparable with modern lifespan values observed now in some countries of the world. Thus, observations made on these historical data may be applicable, with some caution, to contemporary populations. Third, there is a significant increase in lifespan during the studied historical period, particularly for women (over 10 years gain). Therefore, the data should be adjusted for secular trends in lifespan (which has been done in this study). Finally, the temporal changes in lifespan are clearly not linear, and sometimes even not monotonic which justifies the method of analysis used in this study (multiple regression with nominal variables and treating the year of birth as categorized predictor variable). (Table 1appears earlier.)

Table 2 presents striking data that the month of birth is an important predictor for the life expectancy of adult women (30 years and above). In particular, women born in May and December tend to live 2-3 years longer on average compared to those born in February (significant at $p < 0.01$). The effects of the months of birth are expressed in Table 2 as a difference from the reference level in February and are point estimates of the differential intercept coefficients adjusted for other variables.

The month of birth remains an important predictor for women's lifespan, even after adjustment for the effects of all other explanatory variables mentioned earlier in the "Data and Methods" section.

The fact that such an early circumstance of human life as month of birth may have a significant effect 30 years later on the chances of human survival is quite remarkable. It indicates that there may be critical periods early in human life particularly sensitive to seasonal variation in living conditions in the past (e.g., vitamin supply, etc.). It is known that the deficiency of vitamins B_{12}, folic acid, B_6, niacin, C, or E, appears to mimic radiation in damaging DNA by causing single- and double-strand breaks, oxidative lesions, or both, and may contribute to premature aging (Ames, 1998). The seasonal lack of these vitamins in late winter/early spring, in coincidence

with one of the two critical periods in fetus or child development (the second month of pregnancy and the first months after birth), may explain a dramatic life span shortening among those born in August and February. Our finding is also consistent with the reliability theory of aging which emphasizes the importance of the initial level of damage that determines the future length of human life (Gavrilov, Gavrilova, 1991; 2001b).

Table 2. Female lifespan as a function of month-of-birth

Month-of-birth	Net effect	Standard Error	P value
February	0.00	Reference level	
March	1.04	0.99	0.2914
April	1.35	0.98	0.1676
May	**2.63**	**0.97**	**0.0065**
June	1.72	0.96	0.0737
July	1.69	0.97	0.0833
August	0.99	0.96	0.3029
September	1.20	0.98	0.2198
October	**1.92**	**0.97**	**0.0473**
November	**2.19**	**1.00**	**0.0290**
December	**3.23**	**0.97**	**0.0009**
January	0.70	0.99	0.6598
February	0.00	Reference level	

These general explanations, however, do not match with data for males presented in Table 3. In contrast to females, the male lifespan does NOT depend on month of birth, at least in this particular dataset. This observation is the first example in our study when gender differences in response to early-life conditions are observed.

Table 3. Male lifespan as a function of month-of-birth

Month-of-birth	Net effect	Standard Error	P value
February	0.00	Reference level	
March	-0.38	0.91	0.6809
April	-1.05	0.92	0.2566
May	1.08	0.91	0.2369
June	1.56	0.91	0.0888
July	-0.70	0.89	0.4314
August	-0.60	0.90	0.5053
September	0.23	0.89	0.8000
October	-0.09	0.92	0.9258
November	-1.11	0.93	0.2310
December	-0.32	0.93	0.7288
January	0.40	0.91	0.6646
February	0.00	Reference level	

The dependence of female lifespan on paternal age at reproduction (when daughter was born) is presented in Table 4. Note that there is an optimal age to father a daughter, which is rather late - about 40-44 years (considered as a reference level in this study). Daughters born to older or younger fathers tend to live about 2 years shorter lives on average (significant, see Table 4).

Table 4. Female lifespan as a function of paternal age at reproduction

Paternal Age	Net effect (point estimate)	Standard Error	P value
15-24	-2.29	1.30	0.0771
25-29	**-2.05**	**0.84**	**0.0141**
30-34	-1.19	0.73	0.1052
35-39	-0.23	0.71	0.7405
40-44	0.00	Reference level	
45-49	-1.18	0.92	0.2028
50-54	**-2.44**	**1.18**	**0.0382**
55-59	-2.47	1.81	0.1729

Shorter lifespan of daughters conceived to older fathers is usually explained by age-related accumulation of mutations in DNA of paternal germ cells (Crow, 1997; Gavrilov, Gavrilova, 2000a; 2001a). It is more difficult to explain, why daughters born to particularly young fathers also live shorter lives. Standard social explanation, that low-income males without education start reproducing earlier seems not to be easily applicable to this socially elite group of royal and noble families.

Analysis of the scientific literature suggests that there may be a fundamental biological explanation of the "young father - short daughters' lifespan" paradox. It was found that the risk of congenital heart defects (ventricular septal defects, VSD, and atrial septal defects, ASD) is increased not only among the offspring of the older fathers, but also among the offspring of particularly young fathers - below 20 years (Olshan et al., 1994). Children born to younger fathers (under 20 years) have increased risk of neural tube defects, hypospadias, cystic kidney, and Down syndrome (McIntosh et al., 1995).

In laboratory mouse, offspring born from older mature fathers exhibit better behavioural performances (for spontaneous activity in both sex and learning capacity in males) than those born from particularly young post-pubescent fathers (Auroux et al., 1998). Similar results were obtained for humans in the study that involved the distribution of scores obtained in psychometric tests by 18-year-old male subjects, according to their father's age at the time of their birth. The curve of such scores produced an inverted U-shape, with poor scores for those conceived to particularly young or old fathers. Maternal age did not appear to play a part in this event. These results pose the problem of identifying genetic and/or biosocial factors associated with young fathers, which might have an impact on the quality of the conceptus (Auroux et al., 1989).

The practical importance of these findings is obvious: the age constrains for the donors of sperm cells in the case of IVF (in vitro fertilization) should be probably revised to exclude not only the old donors, but also those donors who are too young (below 25 years).

Again, all these interesting ideas fail when data on males are analyzed (see Table 5). In contrast to females, the male lifespan does NOT depend on paternal age at person's birth, at least in this particular dataset. This observation is the SECOND example in our study when gender differences in response to early-life conditions are observed.

Table 5. Male lifespan as a function of paternal age at reproduction

Paternal Age	Net effect (point estimate)	Standard Error	P value
15-24	-1.17	1.23	0.3414
25-29	0.28	0.78	0.7198
30-34	-0.52	0.68	0.445
35-39	0.43	0.66	0.5129
40-44	0.00	Reference level	
45-49	1.09	0.84	0.1945
50-54	1.36	1.16	0.2426
55-59	0.05	1.77	0.9760

Note: Data for Tables 4 and 5 are calculated for subset where the progeny of long-lived fathers (80+ years) was excluded from the analysis for the reasons described elsewhere (Gavrilov, Gavrilova, 2000a).

The third example of sex differences in response to early-life conditions refers to effects of birth order on adult lifespan (Table 6). Specifically, the first-born daughters tend to live 1.6 years longer compared to later-born daughters (statistically significant at $p<0.005$, see Table 6), while sons again demonstrate no response at all. This is kind of strange, because the first-born sons are most likely to inherit parental property in the studied aristocratic families and, therefore, should benefit most from their first-born status. From this perspective, the results are completely opposite to expectations based on socio-economic explanations. As for possible biological explanations, it is interesting to note the results of 17-year demographic study of 315 yellow baboons at Mikumi National Park, Tansania (Wasser, Norton, 1993). This study found that female, but not male, infant survival was inversely correlated with birth order, that matches to some extent with our findings on aristocratic families.

Table 6. Effect of the birth order (first-born status) on adult lifespan of males and females

Sex	Net effect of first-born status (point estimate)	Standard Error	P value
Males	0.19	0.49	0.6961
Females	**1.62**	**0.57**	**0.0043**

The last, forth example of gender-specific effects refers to familial transmission of longevity from mother to child (Tables 7 and 8). Here again, daughters proved to be highly responsive while sons demonstrate virtually no response. Specifically, daughters born to long-lived mothers (95+) tend to live 8 years longer on average compared to daughters born to 'normal' mothers (lived 75-79 years, reference level). In contrast to daughters, son's response to maternal longevity is negligible (Table 8).

Table 7. Female lifespan as a function of maternal lifespan

Maternal Lifespan	Net effect (point estimate)	Standard Error	P value
40-44	-0.61	1.29	0.6353
45-49	-0.84	1.07	0.4351
50-54	-0.35	0.97	0.7199
55-59	-1.15	0.92	0.2087
60-64	-0.96	0.82	0.2428
65-69	0.11	0.78	0.8921
70-74	0.54	0.71	0.4445
75-79	0.00	Reference level	
80-84	1.16	0.75	0.1202
85-89	1.49	0.85	0.0808
90-94	**4.46**	**1.29**	**0.0005**
95+	**8.05**	**2.86**	**0.0049**

Table 8. Male lifespan as a function of maternal lifespan

Maternal Lifespan	Net effect (point estimate)	Standard Error	P value
40-44	-1.18	1.20	0.3234
45-49	-0.22	1.02	0.831
50-54	**-1.89**	**0.89**	**0.0330**
55-59	-0.59	0.86	0.4904
60-64	-1.29	0.75	0.0851
65-69	-0.61	0.73	0.4039
70-74	0.17	0.65	0.801
75-79	0.00	Reference level	
80-84	0.50	0.68	0.4625
85-89	1.03	0.81	0.2066
90-94	2.41	1.25	0.0544
95+	-0.08	2.68	0.9764

Of course, all these findings should be interpreted with great caution and need to be replicated on other datasets. However, the results of this pilot exploratory study clearly indicate the need for separate analysis of data for males and females when late-life consequences of early-life conditions and events are explored. There is a definite need for subsequent full-scale studies of gender-specific outcomes of early-life events and conditions and our pilot study presented here justifies the need of further work in this direction.

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