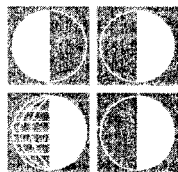


# Genealogical Data and the Biodemography of Human Longevity



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**ABSTRACT:** Biodemography of human longevity is an emerging interdisciplinary field of sociobiological research with deep historical roots. Two research questions are examined in this article: (1) What evidence is there for the familial transmission of human longevity?, and (2) what are the effects of parental age at reproduction on offspring longevity, and in particular, are there long-term adverse health consequences associated with the trend toward delayed reproduction? The ability of scientists to conduct biodemographic studies depends not only on merging theoretical and methodological elements from the biological and demographic/actuarial sciences, but unique sources of data and statistical methods must also be developed. In this article we describe how genealogical data have been used for over a century to explore basic questions about human longevity, and how similar kinds of data now being developed are driving the formation of new testable research hypotheses in the field of biodemography.

## INTRODUCTION

The biodemography of aging is an emerging interdisciplinary field of research (Carnes and Olshansky, 1993; Wachter and Finch, 1997; Gavrilov and Gavrilova, 2001a) with deep historical roots (reviewed in Olshansky and Carnes, 1997; Olshansky, 1998). The ability of scientists to conduct research in this field depends not only on merging theoretical and methodological elements from the biological and demographic/actuarial sciences, but unique sources of data and statistical methods must also be developed. In this article we describe how genealogical data have been used for over a century to explore basic questions about human longevity, and how similar kinds of data now being developed are driving the formation of new testable research hypotheses in the field of biodemography. Two of the many research questions that follow from developments in this field will be examined in this paper: (1) What evi-

dence is there for the familial transmission of human longevity?, and (2) what are the effects of parental age at reproduction on offspring longevity, and in particular, are there long-term adverse health consequences associated with the trend toward delayed reproduction?

## FAMILIAL TRANSMISSION OF HUMAN LONGEVITY

The last year of the twentieth century marked the 100th anniversary of the first systematic studies on the familial determinants of human longevity. In 1899 the founder of biometrics, Karl Pearson (1857–1936) and his student, Mary Beeton, analyzed the correlation of parent/child ages at death based on English genealogies (using data from the English peerage and landed gentry) dating back to the seventh century (Beeton and Pearson, 1899). Owing to limitations of their data, Beeton and Pearson examined only adult males age 20 and over. Their second

study was based on more extensive pedigree records of the members of the English Society of Friends and of the Friends' Provident Association—both of which included data about males and females of all ages (Beeton and Pearson, 1901). Using such data, Beeton and Pearson (1901) measured the correlation for ages at death not only for parent/child pairs, but also among siblings. As a result of their studies, these authors concluded that expectation of life is heavily influenced by the ages of death of one's relatives (Beeton and Pearson, 1901, p. 77).

The familial transmission of human longevity was also examined by the inventor of the telephone, Alexander Graham Bell (1918), using genealogical data on about 3,000 members of the Hyde family in New England. More extensive studies on the topic were subsequently conducted by Raymond Pearl (Pearl, 1931; Pearl and Dewitt, 1934; Pearl and Pearl, 1934). Raymond Pearl discovered in what is now the famous Baltimore Longevity Study that the ancestors of long-living persons (nonagenarians) had a substantially longer life span compared to a control population. Following these initial studies on the familial transmission of human longevity early in the twentieth century, a number of other scientists have addressed the same issue (Wilson and Doering, 1926; Holmes, 1928; Yuan, 1931; Preas, 1945; Dublin et al., 1949; Jalavisto, 1951; Cohen, 1964; Hawkins et al., 1965; Abbott et al., 1974, 1978; Murphy, 1978; Philippe, 1977, 1978, 1980; Welter, 1978; Wyshak, 1978; Crawford and Rogers, 1982; Swedlund et al., 1983; Vandenbroucke et al., 1984; Desjardins and Charbonneau, 1990; Bocquet-Appel and Jakobi, 1990, 1991; Brand et al., 1992; Mayer, 1991; Robine and Allard, 1997; Tallis and Leppard, 1997; Kor-

pelainen, 1999; Cournil et al., 2000; Gudmundsson et al., 2000; Kerber et al., 2001; Mitchell et al., 2001; Matthijs et al., 2002).

In addition to these traditional studies on familial longevity, others have explored the genetic and cultural contributions to inter-individual variation in human life span by evaluating the relative longevity of twins (Kallman and Sander, 1948, 1949; Kallman, 1957; Jarvik et al., 1960; Harvald and Hauge, 1965; Wyshak, 1978; Hrubec and Neel, 1981; Carmelli and Andersen, 1981; Carmelli, 1982; Hrubec et al., 1984; Hayakawa et al., 1992; McGue et al., 1993; Herskind et al., 1996; Yashin and Iachine, 1997; Ljungquist et al., 1998). A principal finding of this body of research was that the resemblance in life span among genetically identical (monozygotic) twins is higher compared to that of fraternal (dizygotic) twins, indicating the importance of genetic factors in the determination of human life span (McGue et al., 1993; Herskind et al., 1996). More recent studies on the *longevity of adopted children* have reinforced the importance of biological parents in predicting the longevity of offspring (Sorensen et al., 1988; Sorensen, 1991; Nielsen et al., 1992).

In spite of a century of research on familial longevity, there is still no consensus among scientists on many of the fundamental issues regarding familial longevity. For example, the role of genetics in familial longevity resemblance was challenged by some authors (Murphy, 1978; Philippe, 1978; Jacquard, 1982) who not only found that the familial resemblance is weak, but also emphasized the importance of social explanations. The mode of longevity inheritance in humans is also not yet determined (Carnes et al., 1999). For example, are the genes

associated with longevity dominant, recessive, or additive in their action? Are such genes autosomal or sex-linked? What is the relative importance of the maternal versus paternal longevity influence on offspring life span? Some studies suggest that human longevity is inherited more strongly along the maternal line (Pearl, 1931; Jalavisto, 1951; Abbot et al., 1978; Brand et al., 1992; Korpelainen, 1999), which is consistent with theories of aging based on the inheritance of mitochondrial DNA through the cytoplasm of maternal ova cells (e.g., Sont and Vandenbroucke, 1993; Wallace et al., 1995; Tanaka et al., 1998; Vandenbroucke, 1998). However, other studies suggest that there is a predominance of paternal longevity influence on offspring life span (Bell, 1918; Cohen, 1964; Philippe, 1978; Welter, 1978; Bocquet-Appel and Jakobi, 1990).

More recent studies suggest that it may be reasonable to revise some of the underlying assumptions behind existing controversies about maternal versus paternal inheritance, and to develop more refined methods of familial analysis of human longevity (e.g., see Gavrilov and Gavrilova, 1991). In particular, one testable hypothesis that can now be evaluated empirically with the use of genealogical data (listed in Gavrilova and Gavrilov, 1999) is the question of whether there is a *linear* relationship between offspring and parental life span (i.e., the observed ages at death of offspring are shown to rise in equal measure to the observed ages at death of their parents), as opposed to an *accelerating* relationship as suggested by Gavrilova et al. (1998). The assumption of linear dependence between offspring and parental traits is fundamental in quantitative genetics because both the theory of quanti-

tative genetics and its applications are based on this assumption (Falconer, 1989; Falconer and Mackay, 1996). Moreover, the assumption of linearity is one of the foundations for Path analysis used in studies of the mechanisms of familial transmission of quantitative traits (Neale and Cardon, 1989, p. 91).<sup>1</sup>

The methods of correlation and linear regression analyses are also based on the assumption of linearity and were used in previous familial studies of longevity (Holmes, 1928; Yuan, 1931; Dublin et al., 1949; Jalavisto, 1951; Hawkins et al., 1965; Abbott et al., 1973; Murphy, 1978; Cohen, 1964; Philippe, 1977, 1978; Welter, 1978; Wyshak, 1978; Desjardins and Charbonneau, 1990; Bocquet-Appel and Jakobi, 1990, 1991).

What are the alternatives to the linearity assumption and why are they relevant to studies of longevity inheritance? With large amounts of genealogical data it is possible to test the linearity assumption against alternative trajectories. The relationship between offspring and parental longevity may instead be based on a *decelerating* function—with a decreasing slope that may even level off (in the case of an early selection out of the parents who die prematurely, for either genetic or non-biological reasons). Thus, the population of longer-lived parents may become more homogeneous because of selection.

An alternative prediction is that dependence should be *accelerating* (more steep for the offspring of longer-lived parents)—a hypothesis derived from the evolu-

<sup>1</sup>The methods of path analysis (also known as the structural equation models) and their applications in quantitative genetics are reviewed comprehensively in Neale and Cardon, 1989, and Lynch and Walsh, 1998, and, therefore, will not be discussed in this article focused on another topic (the importance of genealogical data for biodemographic studies).

tionary theory of aging and the mutation accumulation hypothesis in particular (e.g., for a summary see Gavrilova et al., 1998). According to the evolutionary theory of aging, the equilibrium gene frequency for deleterious mutations should increase with age-at-onset of mutation action because of weaker (postponed) selection against later-acting mutations (Medawar, 1952; Finch, 1990; Rose, 1991; Partridge and Barton, 1993; Charlesworth, 1994). In accordance with this mutation accumulation hypothesis, one would expect the observed (e.g., *expressed*) genetic variability in survival (additive genetic variance) to increase with age (Partridge and Barton, 1993; Charlesworth, 1994).<sup>2</sup>

In general, both the additive genetic component of variance and the dominant component are expected to increase with age under the mutation accumulation hypothesis because in the case of traits affected by rare deleterious alleles, both components increase with increasing mutant allele frequency (Charlesworth, 1987; Falconer, 1989; Hughes and Charlesworth, 1994). As such, the ratio of additive genetic variance to the observed phenotypic variance (i.e., the heritability of longevity) may be estimated most reliably as the doubled slope of the regression line for offspring life span on parental age at death. Therefore, if longevity is indeed determined by late-acting deleterious mutations, one testable hypothesis is that this slope will become steeper for longer-lived parents (at higher parental ages at

death) (Gavrilova et al., 1998; Gavrilova and Gavrilov, 2001). It is this kind of unusual hypothesis that can be tested using data from genealogical resources (Gavrilova and Gavrilov, 1999).

Thus, biodemographic studies of the familial transmission of human longevity can be summarized in the form of three research directions and corresponding hypotheses that are amenable to evaluation using genealogical resources:

(1) What is the trajectory of the dependence of offspring longevity on parental longevity—is it linear (standard assumption in quantitative genetics), decelerating (expected in the case of early selection out of shorter-lived parents), or accelerating (predicted by the evolutionary theory of aging and by the mutation accumulation hypothesis in particular)?

(2) Is the familial transmission of longevity stronger for children born to younger (as compared with older) parents, as would be expected both for genetic reasons (higher genetic diversity of younger parents) and for cultural reasons (higher overlapping between parental and offspring life cycles)?

(3) What is the relative importance of paternal versus maternal longevity on the observed longevity of sons and daughters?

#### BIODEMOGRAPHIC STUDIES OF PARENTAL REPRODUCTIVE AGE EFFECTS ON OFFSPRING LONGEVITY

Delayed childbearing has become increasingly common in modern societies because of demographic changes (population aging), medical progress (e.g., in vitro fertilization (IVF) of older women), and personal choice. For example, in the United States the number of births to older mothers (35-39 years and 40+

<sup>2</sup>It may be difficult to observe directly this theoretically predicted age-related increase in population heterogeneity for survival probabilities. Direct testing of this theory would require identification of reliable biomarkers for individual survival probabilities (individual frailty predictors). Fortunately, it is also possible to test a related prediction of this theory regarding heritability of life span, as discussed later.

years) has more than doubled since 1980 while the number of births to younger mothers (below age 30) has not increased (U.S. Bureau of the Census, 1997).

Birth rates for older fathers (ages 45–49 and 50–54) are also increasing (U.S. Monthly Vital Statistics Report, 1997), and this trend may even accelerate in the future due to medical progress (Viagra, for example). Will the health and longevity of children born to older parents be adversely influenced by parental age at conception? While the detrimental effects of late reproduction on infant mortality and genetic diseases have been well documented (see below), little is known about the long-term health consequences for offspring born to parents who conceive later in the reproductive window.

According to existing evidence, delayed parental age at conception has many detrimental influences on the longevity of offspring (for a detailed review of this topic see Gavrilov and Gavrilova, 1997a). The major *maternal* age-related changes in humans are increases in fetal aneuploidy later in reproductive life such as Down's syndrome (trisomy 21), Klinefelter's syndrome (XXY), Edward's syndrome (trisomy 18), and Patau's syndrome (trisomy 13). Advanced maternal age also remains an important independent risk factor for fetal death.

The detrimental effect of late *paternal* reproduction is also well known: advanced paternal age has been associated with an increase in new dominant mutations in offspring that result in congenital anomalies (see Gavrilov and Gavrilova, 1997a, for review). In particular, paternal age is responsible for new dominant autosomic mutations that cause different malformations, including achondroplasia, Apert syndrome, Marfan syndrome, os-

teogenesis imperfecta, and other inherited diseases (Vogel and Motulsky, 1997; Gavrilov and Gavrilova, 1997a). Older paternal age was more common among patients with Costello syndrome, chondrodysplasia punctata, fibrodysplasia ossificans progressiva, and thanatophoric displasia (Vogel and Motulsky, 1997; Gavrilov and Gavrilova, 1997a). Advanced paternal age at reproduction is also associated with an increased risk of preauricular cyst, nasal aplasia, cleft palate, hydrocephalus, pulmonic stenosis, urethral stenosis, and hemangioma (see review by Gavrilov and Gavrilova, 1997a).

There is, however, one very important question that has yet to be addressed: does parental age at conception influence the longevity of the vast majority of the population of "healthy people," who do not suffer from aneuploidy and other obvious genetic conditions that tend to appear relatively infrequently early in life? In other words, are aging-related diseases expressed late in life associated with paternal and maternal age at conception or birth? It is possible to address this question by examining the life expectancy of adults (say, at ages 30 and older) as a function of parental age at reproduction. By adult age a substantial portion of the subpopulation suffering from lethal genetic disorders has already died. The information on potential life-shortening effects of late parental reproduction on adult offspring is notable because it addresses a possibly important gap in knowledge about the mechanisms of human longevity, the aging process itself, and the possible role of accumulated genetic damage in the germ line on aging and longevity.

The first mention in the historical literature suggesting a possible life-

shortening effect on offspring of delayed parenting was made by the French naturalist Buffon (1826), who noted that when older men procreate "they often engender monsters, deformed children, still more defective than their father" (see Robine and Allard, 1997). In 1950, Eva Jalavisto analyzed 12,786 published family records of the Finnish and Swedish middle class and nobility for those born between 1500 and 1829. Unfortunately, in this interesting study the secular changes in human life span during this long historical period were not taken into account (failure to control for secular trends can produce biases and artifacts). Also, Jalavisto (1950) did not attempt to control for the possible effects of other confounding factors (e.g., parental life span). The author concluded that offspring born to older mothers live significantly shorter lives, while the age of the father is of no importance. This observation is now amenable to verification using our developing database and related genealogical data resources (Gavrilova and Gavrilov, 1999), and by controlling for the effects of other confounding factors and historical changes in the life expectancy of birth cohorts.

In 1980, Pierre Philippe studied five birth cohorts (1800-29, 1830-49, 1850-69, 1870-79, 1880-99) from a small rural population of Isle-aux-Coudres, Quebec, Canada. Multiple discriminant analysis was used to study the effects of familial characteristics (such as parental consanguinity, maternal and paternal age at time of childbirth, birth order, time interval since the previous birth, months of birth, viability of the preceding infant, etc.) on offspring age at death. Surprisingly, possibly the most evident and important predictors of offspring longevity (paternal

and maternal *life spans*) were not included in the analysis for unknown reasons. Also, the authors noted that "taking into consideration the possibility of differential emigration" from this small rural area (Isle-aux-Coudres), the results of their analysis "must certainly be regarded cautiously" (Philippe, 1980, p. 215). Indeed, in many cases the results of this analysis were not statistically significant, perhaps because of the small size of the birth cohorts (105-298 cases only in each cohort), and also because of possible overloading of the analysis by too many variables (up to 26 binary variables were included). In spite of these problems, the authors of this study made an intriguing observation that increased maternal age at time of childbirth (35 years and above) is the main factor common to both early (0-5 years) and late (70 years and above) death (Philippe, 1980). By contrast, increased father's age was uncommon for long-lived offspring (Philippe, 1980).

These important observations can be re-evaluated by using larger sample sizes and controlling for parental longevity. Control for parental longevity is important, because it has been demonstrated that among long-lived women the proportion of those able to become mothers after 40 years is four times higher compared to women who stop childbearing at younger ages (Peris et al., 1997). Thus, increased offspring longevity might not be due to the older age of mother at childbirth *per se*, but due to higher longevity of such late-reproducing mothers and the inheritance of longevity-related traits by their offspring. This hypothesis could also be explored in future studies.

Biodemographic studies of parental age effects on offspring longevity can be summarized in the form of four research

objectives driven by corresponding hypotheses (see below):

(1) Do persons born to older fathers live shorter lives (as predicted by the hypothesis of age-related accumulation of spontaneous mutations in paternal germ cells)?—a research question that can be tested more appropriately using a larger sample size (Gavrilov and Gavrilova, 1997a, 1997b, 2000; Gavrilov et al., 1997), and do only daughters born to older fathers have a shorter life expectancy relative to daughters born to younger fathers (consistent with hypothesis of the critical importance of mutation load on paternal X chromosome inherited by daughters only)?

(2) What is the effect, if any, of mother's age at conception on offspring longevity in relation to the hypothesis that there is an age-related accumulation of oxidative damage to mitochondrial DNA in maternal ova cells?

(3) It would be interesting to examine the prediction of the X-chromosome hypothesis that there should be a specific life-shortening effect among grandchildren (grandsons in particular) if their mother was born to an older grandfather. Preliminary studies have demonstrated the sex-specific decrease of daughters' longevity when born to older fathers—a finding consistent with the mutation load hypothesis and the critical role of the X-chromosome transmitted from father to daughter only (Gavrilov and Gavrilova, 1997a, 1997b, 2000). This X-chromosome hypothesis provides a specific prediction that we propose to test in future studies. Since the grandfather's X-chromosome is inherited through the mother's side only, one might expect a specific effect of the reproductive age of the maternal grandfather. Specifically, this hypothesis predicts that *grandchildren (grandsons in particu-*

*lar) should live shorter lives if their mother was born to an older grandfather.*

(4) The parental support hypothesis is that among the offspring of longer-lived parents, the parental age effects will be less expressed. According to this hypothesis, children born to older parents may live shorter lives because they lose their parents too early, in the formative years of their lives.

#### GENEALOGICAL DATA AND THEIR USE IN BIODEMOGRAPHIC STUDIES

There are some genealogical data sets already in use in biodemographic studies, some of which have already been mentioned. We are in the process of creating a comprehensive computerized genealogical database for biodemographic studies based on the NIH/NIA-sponsored review of the feasibility of this kind of research (Gavrilov and Gavrilova, 1998). Several factors support the continued development of this source of data. There are two mutually exclusive constraints on data sources that should be taken into account in biodemographic studies: On the one hand, in order to have complete data on parental life span (for heritability studies or for their use as control variables), it is necessary to go back in history for about a century in order to have extinct parental birth cohorts. On the other hand, the historical genealogical databases are often criticized because the genealogical longevity data collected in the pre-antibiotic era and particularly in the pre-public health era are often considered to be irrelevant to current low-mortality populations (Cohen, 1964; Smith, 1993). This is thought to be the case because living conditions were quite different in the past. For example, there used to be ex-

tremely high mortality from infectious diseases (tuberculosis and pneumonia, in particular), under-nutrition and sometimes even starvation were common (see Carnes et al., 1996; Fogel and Costa, 1997), the poverty rate was high and poor sanitary conditions prevailed, and high seasonal mortality was common (especially in winter).

There is, however, one fortunate exception that perfectly fits the purpose of biodemographic studies—socially elite aristocratic families, which are reasonably homogeneous and in which social deprivation has not interfered unduly with the chances of survival. Based on pilot studies already conducted using data of this sort (Gavrilova et al., 1998), it has been determined that the modal age at death for parents in these socially elite families in the nineteenth century is remarkably high (70–75 years for fathers and 75–80 years for mothers)—which is comparable with that of modern low-mortality populations.

Another important advantage of this kind of data is their high reliability, accuracy, and completeness, since data for aristocratic families were recorded in great detail for many centuries. Moreover, these data are widely published by numerous independent publishers, thus creating a unique opportunity to cross-check the information with other data sources to ensure the highest possible data quality and completeness (see Gavrilov and Gavrilova, 1998; Gavrilova and Gavrilov, 1999).

One unique feature of this data set is that it contains a significant sample of males who achieved fatherhood later in life—a product of the fact that older kings and princes often married much younger women. For example, Queen Victoria of England, who passed the he-

mophilic gene to further royal generations, was born to an older father (Duke of Kent, 52 years), and received the hemophilic gene most probably as a result of paternal sperm mutation (Strickberger, 1976). Such cases of late fatherhood provide a unique opportunity to help discriminate between paternal and maternal age effects on offspring health and longevity later in life.

Since this privileged social group lived in rather favorable conditions for many centuries, one could expect less influence of adverse social factors (poverty, for example) on life span and hence reduced environmental variation in longevity caused by these factors. This kind of data allows the researchers to minimize the social heterogeneity of the population under study and to limit socioeconomic diversity, compared to other data sets where a mixture of families with different social status is analyzed. Thus, although this data set does not represent the whole human population (as laboratory animals do not represent species in the wild), it is an ideal source of data to test biodemographic hypotheses about the familial transmission of human longevity because the effects of population heterogeneity are minimized with regard to social status (which can also be controlled for by indicator socioeconomic variables such as nobility rank and the life span of spouses who share the same familial environment). This is particularly important for testing biological theories of aging using data on humans.

While discussing the generalizability concerns, it is also important to understand the difference between the analytical and the descriptive studies (Levy and Lemeshow, 1999). Analytical studies that intend to test specific hypotheses (for example, biodemographic hypotheses



described in this article) are less dependent on data representativeness than the descriptive studies, which intend to describe "a whole population" (Levy and Lemeshow, 1999).

Also, all the cases of familial inbreeding (consanguinity) are well documented for noble families, so the data can be used to study the effects of consanguinity, too (Gavrilov and Gavrilova, 2001b). It is interesting to note that in one study of inbred families there was no significant effect of inbreeding on survival curves and heritability of human longevity (Mayer, 1991). Mayer (p. 56) concluded that his study "indicates negligible 'inbreeding depression' with respect to longevity."

Recently, arguments in favor of historical genealogical databases for aristocratic families have received increasing recognition in the scientific community. In particular, *Nature* has published an article based on biodemographic analysis of the life span and fertility data for British aristocratic families (Westendorp and Kirkwood, 1998). Specific reference was made in the Westendorp and Kirkwood paper (1998, p. 746) to our identification of the database used in the study. (For further discussion of this *Nature* article, see Gavrilov and Gavrilova, 1999a, 2002; Gavrilova and Gavrilov, 1999.) By now, we, in collaboration with Russian colleagues (Victoria Semyonova, Ph.D., and Galina Evdokushkina, M.Sc.), have computerized more than 15,000 complete genealogical records ("European Aristocratic Families" database for 1800–1880 birth cohorts) that are already being used in biodemographic studies (Gavrilov and Gavrilova, 1997a, 1997b, 1999b, 2001a; Gavrilov et al., 1997; Gavrilova et al., 1998; Gavrilova and Gavrilov, 2001). The main difficulties with developing this

type of data set are related to the need for extensive data cross-checking with many different sources, which is very laborious and time-consuming (but produces high-quality data). Some of the new preliminary results obtained with this database are described in the Appendix.

The studies on biodemography of human longevity are progressing rapidly and such progress can be enhanced by the identification and use of new and novel databases that permit investigators to test research hypotheses that were difficult to test in the past. We have been developing a new database just for this purpose with the initial funding from the NIH/NIA—a database that will be made available to the research community once complete (publicly available data resources are reviewed in Gavrilova and Gavrilov, 1999). For now, preliminary results are interesting enough to warrant the expansion and continued use of such databases.

## APPENDIX

### PRELIMINARY FINDINGS

Preliminary research already conducted with the use of data on European aristocratic families has produced some interesting results (see Table 1). First, we have tested the validity of the general assumption of the linear dependence between offspring life span and parental life span. For this purpose, the sample was split into two parts with approximately equal numbers of cases: one subset with longer-lived parents (above 70 years) and another subset with shorter-lived parents (below 70 years). The regression slopes for linear regression of offspring life span (pre-adjusted for secular effects) on parental life span were calculated and compared.

TABLE 1

HERITABILITY OF HUMAN LONGEVITY FOR DIFFERENT SEX COMBINATIONS IN OFFSPRING/PARENT PAIRS AND FOR DIFFERENT PARENTAL LONGEVITY RANGES

TYPE OF THE CHILD/PARENT PAIR	REGRESSION SLOPE OF OFFSPRING LIFE SPAN (ADULTS, 30+ YEARS) ON PARENTAL LIFE SPAN $\pm$ STANDARD ERROR		
	(1) Longer-lived parents, 70-100 years (sample size)	(2) Shorter-lived parents, 30-70 years (sample size)	Difference between (1) and (2)
Son—father	0.189 $\pm$ 0.035*** (5,120)	0.037 $\pm$ 0.020 (6,211)	0.152 $\pm$ 0.040***
Son—mother	0.054 $\pm$ 0.031 (5,783)	-0.014 $\pm$ 0.017 (5,218)	0.067 $\pm$ 0.035
Daughter—father	0.265 $\pm$ 0.055*** (2,213)	0.022 $\pm$ 0.031 (2,616)	0.243 $\pm$ 0.063***
Daughter—mother	0.114 $\pm$ 0.048* (2,534)	0.024 $\pm$ 0.028 (2,156)	0.091 $\pm$ 0.056

\*Significant at  $p < 0.05$ ; \*\* $p < 0.01$ ; \*\*\* $p < 0.001$ 

NOTE: The data for analysis are taken from our "European Aristocratic Families" database for extinct birth cohorts (1800-1880). Data for offspring life span were pre-adjusted for secular changes before their use in the linear regression analysis.

In the case of strictly linear dependence for the whole range of parental longevity, the regression slopes for the subsets of longer- and shorter-lived parents should be essentially the same. This is obviously not the case—for all four offspring-parent pairs the heritability of longevity was much higher for longer-lived parents, particularly fathers.

In fact, human life span seems to be not heritable (in the narrow sense of familial resemblance) if parents live shorter lives—all the regression slopes are close to zero and are statistically insignificant (Table 1). This may explain why some of the previous investigators (Philippe, 1978) were frustrated by low heritability estimates for human life span—they simply did not have enough cases of longer-lived parents in their data sets. On the contrary, the regression slopes for the longer-lived parents are quite high, keeping in mind that the theoretical upper

limit for this slope is equal to 0.5, corresponding to 100 percent heritability of the trait (Falconer, 1989; Falconer and Mackay, 1996). For example, the daughters gain 2.65 years of additional life span per each 10 years of additional life span of longer-lived fathers (Table 1), which formally corresponds to 53 percent of the narrow sense heritability (Falconer, 1989).

These results are consistent with the prediction of the evolutionary theory of aging (see section 2.1.) and indicate that there may be an increasing genetic limitation for the further increase of human life expectancy in low-mortality populations.

Another interesting observation using available data is that the paternal longevity effects on offspring life span are more than double those of maternal effects (Table 1). Since the frequency of chromosomal crossing over is much less in fathers compared to mothers (Strickberger, 1976; Vogel and Motulsky, 1997),

the fortunate gene combinations predisposing to longevity are more likely to be transmitted intact (not destroyed by genetic recombination) from fathers rather than from mothers. Other explanations are also possible, so larger biodemographic studies are planned to cast more light on the familial determinants of human longevity.

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