Early-life Predictors of Exceptional Longevity in the United States: Why Centenarians are Different From Their Shorter-lived Siblings

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Abstract

Knowledge of strong predictors of mortality and longevity is very important for actuarial practice. This study presents the first results of a large project on exceptional longevity in the United States, which investigates the biological and social correlates of why some people survive to extreme old age (older than 100 years). These are important issues not only for human-mortality and population-aging demographic forecasts and the policy implications on health care and pension expenditures, but also for improving our understanding of the fundamental mechanisms of human aging and longevity. This study explores the effects of parental age at a person's birth and the month of birth on chances of survival to age 100. We have developed and analyzed a computerized database of 1,711 validated centenarians born in the United States between 1880 and 1895, as well as their shorter-lived siblings. Comparison was conducted using within-family analysis via conditional logistic regression, which allows researchers to control for unobserved shared childhood or adulthood environments and common genetic background. We found significant beneficial effects of a young maternal age at a person's birth on survival to age 100 with particularly strong positive influence at a maternal age of 20 of 24. The effect of a young mother is particularly prominent in smaller families, pertinent today because of the smaller average family size in contemporary population. We also found the season of birth has significant long-lasting effect on survival to age 100, and individuals born in September to November have the highest chance of becoming centenarians. These results support the idea of early-life programming of human aging and longevity. The study was supported by National Institute on Aging Grant AG028620.

Keywords: Human Longevity, Maternal Age, Family Histories.

Introduction

Studies of centenarians (people living to 100 and older) could be useful in identifying factors leading to long life and avoidance of fatal diseases. Even if some middle-life factors have a moderate protective effect on risk of death, people with this trait/condition should be accumulated among long-lived individuals. Thus, study of centenarians may be a sensitive way to find genetic, familial, environmental, and life-course factors associated with lower mortality and better survival.

Most studies of centenarians in the United States are focused on either genetic (Hadley et al. 2000; Perls et al. 2000; Perls 2001; Puca et al. 2001; Perls et al. 2002; Perls and Terry 2003; Christensen et al. 2006; Pawlikowska et al. 2009; Testa et al. 2009) or psychological (Adkins et al. 1996; Hagberg et al. 2001; Jang et al. 2004; Martin et al. 2008) aspects of survival to advanced ages. On the other hand, several theoretical concepts suggest that early-life events and conditions may have significant long-lasting effect on survival to advanced ages. These concepts include (but are not limited to) the reliability theory of aging and the High Initial Damage Load (HIDL) hypothesis in particular (Gavrilov and Gavrilova 2004b; Gavrilov and Gavrilova 2004a; Gavrilov and Gavrilova 2006); the theory of technophysio evolution (Fogel and Costa 1997; Fogel 2004); the idea of fetal origin of adult diseases (Kuh and Ben-Shlomo 1997; Barker 1998); and a related idea of early-life programming of aging and longevity. These ideas are supported by studies suggesting significant effects of early-life conditions on late-life mortality (Elo and Preston 1992; Fogel and Costa 1997; Kuh and Ben-Shlomo 1997; Barker 1998; Preston et al. 1998; Gavrilov and Gavrilova 2003; Hayward and Gorman 2004; Costa and Lahey 2005). The existence of correlations between early growth patterns and subsequent fitness is now well established not only for human beings but for some other mammalian species as well (Lummaa and Clutton-Brock 2002).

In this study, we analyze effects of early-life characteristics (parental age at birth and month of birth) on survival to age 100 using a large set of centenarians and their shorter-lived siblings.

Data and Methods

Data

This study compares centenarians to their shorter-lived siblings who share the same childhood conditions and genetic background using a large set of computerized family histories.

1.1. Collecting Data on Centenarians

Family histories (genealogies) proved to be a useful source of information for studies in historical demography (Adams and Kasakoff 1984; Anderton et al. 1984; Anderton et al. 1987; Adams and Kasakoff 1991; Bean et al. 1992; Kasakoff and Adams 2000) and biodemography (Gavrilov and Gavrilova 2001; Kerber et al. 2001; Gavrilov et al. 2002). In this study, we conducted a large-scale search in many hundreds of online family histories using an innovative technique known as web automation (Sklar and Trachtenberg 2002). This technique allowed us to search online databases on a large-scale basis for people with exceptional longevity (or other traits). In particular, a technique was developed to scan more than 300,000 online databases in the Rootsweb WorldConnect project (http://wc.rootsweb.ancestry.com), a publicly available data source. Application of web-automation techniques to this online source identified more than 40,000 records of centenarians born between 1880 and 1895 with known information about their parents (see Table 1).

1.2. Collecting Data on Centenarian Relatives

After collecting data on centenarians, the next step was to collect detailed data on their parents from computerized genealogies using the web-automation technique. After this procedure, we selected the most detailed genealogies where information on birth and death dates of both parents was available. As a result of this procedure, the total number of centenarian records slightly decreased from 24,451 to 23,127 (see Table 1).

In the next step, we collected data with the web-automation technique on centenarian siblings for those centenarians who had detailed data on parental birth and death dates. We collected 172,091 records for centenarian siblings. However, a significant proportion of these records did not contain information about the death dates of siblings, which created some difficulties for within-family study of human longevity. So, the next step was to identify the most detailed data on families with complete information on birth and death dates for siblings. As a result of this identification procedure, we found 1,711 families where information on birth and death dates was known for more than 80 percent of siblings. Table 1 shows the number of records obtained in each stage of data collection.

TABLE 1
Number of Centenarians at Different Stages of Data Collection and Cleaning

Type of Records	Centenarians			Number of Siblings
	Males	Females	Total	
All initial records for centenarians born from 1880-1895	7,174	18,277	25,451	
Centenarians having detailed information on birth and death dates of their parents	6,370	16,757	23,127	172,091
Centenarians having detailed information on birth and death dates of their siblings	707	2,127	2,834	21,893
Centenarians after data cleaning with confirmed death dates	398	1,313	1,711	13,654
Centenarians used in data analyses (including additional centenarian siblings)	450	1,495	1,945	13,392

Because of data overlapping, some centenarians were found in more than one genealogy, so we removed duplicate records, leaving the most informative ones in the database. Also note that the proportion of males (23 percent) found in genealogies (see Table 1) is close to the official estimates (20 to 25 percent) of male/female ratio of centenarians in the United States based on the census data (Krach and Velkoff 1999), which somewhat mollifies concerns about quality of genealogies and male overrepresentation in them.

1.3 Validation of Centenarians' Age

Data quality control is an important part of all centenarian studies and, in our case, it included, (1) preliminary quality control of computerized family histories (data consistency checks), (2) verification of the centenarian's death date, and (3) verification of the birth dates for centenarians and their siblings for a sample of centenarian families. All records (for centenarians and controls) were subjected to verification and quality control using several independent data sources. The study's primary concern was about the possibility of incorrect dates reported in family histories. Previous studies demonstrated that age misreporting and age exaggeration in particular are more common among long-lived individuals (Elo et al. 1996; Rosenwaike and Hill 1996; Shrestha and Rosenwaike 1996; Rosenwaike et al. 1998; Hill et al. 2000; Rosenwaike and Stone 2003). Therefore, the primary focus in our study was on the age verification for long-lived individuals. We followed the approach of age verification and data linkage developed by a team of demographers at the University of Pennsylvania (Elo et al. 1996; Preston et al. 1996; Rosenwaike and Hill 1996; Rosenwaike et al. 1998; Hill et al. 2000; Rosenwaike and Stone 2003). This approach involves death-date verification using Social Security Administration Death Master File (DMF) and birth-date verification using early U.S. censuses. To validate the age of the centenarians, these records were linked to the Social Security Administration DMF records for death-date validation. More details about this procedure were published elsewhere (Gavrilova and Gavrilov 2007).

Data consistency checks used information about paternal, maternal and centenarian/sibling birth dates. This procedure helped us to remove about 100 records with incorrect information about parents or their children. Also, whether parents died before the person's birth was checked, which removed several more erroneous records.

TABLE 2
Distribution of Centenarians by Age at Death

Age at Death	Centenarians Born From 1880-1895	Centenarians Born From 1880-1889 Used in the Analyses		
	Both Sexes	Males	Females	Total
99	339	58	145	203
100	536	82	287	287
101	365	59	200	200
102	273	33	137	137
103	186	24	110	110
104	89	12	50	50
105	77	11	48	48
106	47	8	26	26
107	18	2	11	11
108	5	0	3	3
109	5	2	4	4
110	3	0	1	1
111		0	0	0
112	2	0	1	1
Total	1,945	291	790	1,081

Verification of death dates was accomplished through a linkage of family history data to the Social Security Administration DMF. This is a publicly available data source (available at the Rootsweb site) that allows a search for individuals using various criteria: birth date, death date, first and last names, Social Security number and place of last residence. This resource covers deaths that occurred between 1937 and 2010 (Faig 2001) and captures about 95 percent of deaths recorded by the National Death Index (Sesso et al. 2000). Many researchers suggest that the quality of SSA/Medicare data for older people is superior to vital statistics records because of strict evidentiary requirements in application for Medicare, whereas age reporting in death certificates is made by proxy informant (Kestenbaum 1992; Faig 2001; Kestenbaum and Ferguson 2001; Rosenwaike and Stone 2003). Definite matches were established when information on first and last names (spouse's last name for women), and day, month and year of birth matched in the DMF and family history (Sesso et al. 2000). In the case of disagreement in day, month or year of birth, the validity of the match was verified on the basis of additional agreement between the place of the last residence and place of death. DMF covers about 90 percent of all deaths for which death certificates are issued (Faig 2001) and 92 to 96 percent of deaths for people older than 65 (Hill, Rosenwaike, 2001).

In this study, we left only those records of centenarians that were found in the DMF with the same birth and death years with a few cases when death year was different (however, in these cases the individual still had a centenarian status). Our previous work with centenarian data cleaning found that incorrect death dates was the main source of errors in this data. At the same time, birth dates were correctly reported in almost 100 percent of all cases with correct death dates. For this reason, in this study we made sample checks of birth dates for approximately 15 percent of cases and in all cases birth years of centenarians agreed with information reported in 1880, 1900 or 1910 censuses (as well as information about siblings). In addition to that, verification of centenarian birth dates was accomplished through the DMF.

As a result of data quality checks, we found 1,711 records of centenarians born between 1880 and 1895 with verified birth and death dates. Given the fact that longevity is often clustered in families, we found other centenarians in studied families so that the total number of centenarians became 1,945. Distribution of centenarians by their lifespan is presented in Table 2. Note that some centenarians did not live exactly 100 years. This is because we used a broader definition of centenarians assuming that these are individuals whose birth and death years differ by 100. This definition does not take into account months and days of birth and death. For the study of seasonal effects on exceptional longevity, such definition may lead to biased results with more centenarians being born in the second half of the year. Thus, only records for centenarians who lived 100 complete years or more (and their relatives) were used in the season-of-birth study, which reduced the final number of centenarians to 1,574.

1.4 Data Collection and Validation for Siblings of Centenarians

Further study was done for the records of 1,711 previously validated centenarians born between 1880 and 1895 with confirmed birth and death dates. All birth dates of centenarian siblings were reconstructed using information available in computerized genealogies and early censuses. The procedure of death-date verification using DMF is not feasible for validating death dates of shorter-lived siblings (used as controls), because DMF data completeness is not very high for deaths before the 1970s. Fortunately, state death indexes, cemetery records and obituaries cover longer periods of time. Taking into account that exact ages of death for controls (siblings) are not particularly important for comparison, we relied on death date information recorded in family histories for siblings not found in external sources. This approach was used in the Utah Population Database study for individuals who died before 1932 (Kerber et al. 2001). Death dates were reconstructed for 99.99 percent of siblings using the Social Security Death Master File, state death indexes and online genealogies (only 124 out of 13,392 cases were left unresolved). As a result, each case (centenarian) had seven control siblings on average. Overall, this procedure allowed us to reconstruct information for 13,654 siblings of centenarians.

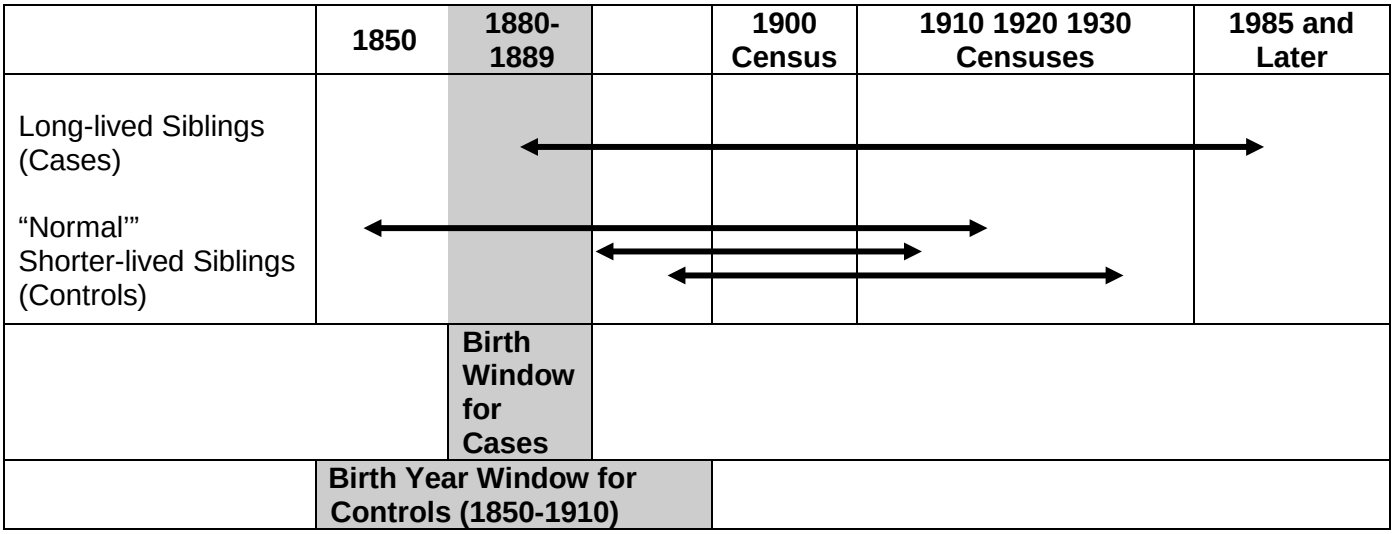
Research Design and Statistical Methods

This study explored the effects of early-life factors (birth order, paternal age, maternal age, month of birth) on the likelihood of survival to advanced ages. Centenarians (cases) were compared to their “normal” shorter-lived siblings (controls) using a within-family approach. During the process of data inspection, we found that some siblings were born after 1910 and their death dates were not indicated (hence, they potentially could become centenarians). To decrease this kind of data truncation, we used data for our index centenarians who were born between 1880 and 1889 rather than 1880 and 1895. For this subgroup, there were no siblings born after 1910 with unknown death dates.

The study applied a case-sibling design (see Figure 1), a variant of a matched case-control design in which siblings of cases (long-lived individuals) are used as controls (Woodward 2005). This approach allows investigators to study within-family differences, not being confounded by between-family variation and unobserved between-family differences. Long-lived people born mostly between 1880 and 1889 were used as cases. Siblings were born between 1850 and 1910.

The main approach used in this study is based on comparison of children within rather than across families. Within a family, children are born to parents at different ages and this variation may be used to estimate the net effect of parental age more conclusively (Kalmijn and Kraaykamp 2005). Similarly, we can estimate the net effects of birth months.

Figure 1
Description of Case-Sibling Design in This Study



Circles indicate birth, diamonds indicate death.

The statistical analyses of within-family effects were performed using a conditional multiple logistic regression model (fixed-effect model) to investigate the relationship between an outcome of being a case (long-lived person) and a set of prognostic factors (Breslow and Day 1993; Hosmer and Lemeshow 2001). Only within-family variation is taken to influence the uncertainty of results (as reflected in the confidence interval) of a within-family study using a fixed-effect model. Variation between the estimates of effect from each family (heterogeneity) does not affect the confidence interval in a fixed-effect model. The fixed-effects logit model can be written as (StataCorp 2009):

$\Pr(y_{it} = 1|x_{it}) = F(\alpha_I + \mathbf{x_{it}}\beta)$, where $F(z) = \exp(z)/[1 + \exp(z)]$ is a cumulative logistic function; $i = 1,2, \ldots n$ denotes the families (independent units) and $t=1,2,\ldots T_i$ denotes the children for the ith family; x_{it} denotes vector of within-family covariates including maternal age and birth order. The likelihood to survive to advanced ages (to be in the long-lived group) is used as a dependent variable. Analyses were conducted using Stata Statistical Software, Release 11 (StataCorp 2009). The following variables were included in the model: birth order, paternal age, maternal age, month of birth and sex (male or female).

Results

Parental Age at Birth

First, we studied the effects of such variables as parental ages at birth and birth order. We found no statistically significant effects of birth order on the chances to survive to advanced ages on this particular data sample (data not shown).

We explored the role of the father's age as a potential predictor for survival to age 100. When the first child is born, the father is younger and can provide resources for a longer period than for his later-born children. We found siblings born to fathers younger than 40 had higher chances to survive to 100 than siblings born to older fathers (50 and older, see Table 3, Model 1). However, control for maternal age decreased this dependence and made it statistically insignificant (Table 3, Model 2). Thus, it is possible that the effects of a young father's age in exceptional longevity may be driven by the correlated effects of a young mother. Comparing male centenarians with their shorter-

lived brothers increased effects of a young father on longevity although this effect remained statistically not significant due to reduction in the sample size (Table 3, Model 4). For daughters, effects of paternal age are nonsignificant (Table 3, Model 3).

TABLE 3
Effects of Paternal Age on Human Longevity; Odds Ratios (With p-Values) to Become a Centenarian as Predicted by Conditional Logistic Regression (Fixed Effects)

Variable	Model 1	Model 2	Model 3 Daughters Only	Model 4 Sons Only
Paternal Age				
<30	1.80 (0.008)	1.76 (0.058)	1.54 (0.100)	2.57 (0.071)
30-39	1.61 (0.026)	1.63 (0.061)	1.45 (0.135)	1.96 (0.186)
40-49	1.21 (0.367)	1.22 (0.380)	1.11 (0.670)	1.42 (0.484)
50+	Reference	Reference	Reference	Reference
Maternal Age				
<25		1.06 (0.612)		
40+		1.05 (0.774)		
Female Sex	3.20 (<0.001)	3.20 (<0.001)		
Pseudo R^2	0.0680	0.0681	0.0041	0.0112
Number of Observations	6,413	6,413	2,633	1,109

Data presented in Table 3 demonstrate effects of paternal ages for siblings who survived to age 20. The next question is whether paternal age effects are observed for longevity benefits at older ages. For this reason, we studied data for siblings who survived to age 50 and age 70. Table 4 shows that survival to age 100 is affected by paternal age after age 50 and age 70 when data are not controlled for maternal age.

Another question studied was related to the family size. Families in our dataset were rather large with median size of nine children and with some families having up to 18 children. So we divided families of centenarians into ones with less than nine children ever born and families with nine children and more. It should be noted that in many large families, some siblings died in infancy or early childhood. The results of our study are presented in Table 4. Note that the effect of a young father is higher in smaller families compared to larger families, although it has borderline statistical significance.

In the next step, we included into analysis maternal age at birth, and it turned out that a young maternal age at childbirth was the most important predictor of exceptional survival, while the effects of paternal age at birth have become statistically insignificant (Table 3, Model 2 and Table 5, Model 2). We found that the odds to become a centenarian are 1.5 to 1.6 times higher for children born to younger mothers compared to siblings (brothers and sisters) born to mothers older than age 30 in the same families and even after controlling for paternal age (see Table 5). For daughters, maximum chances of survival to 100 shifted from younger ages to age group 25 to 29 (Table 5, Model 3). For sons, effects of maternal age became stronger, particularly at maternal age 20 to 24 (Table 5, Model 4).

TABLE 4
Effects of Paternal Age on Human Longevity; Odds Ratios (With p-Values) to Become a Centenarian as Predicted by Conditional Logistic Regression (Fixed Effects) for Different Subgroups

Variable	Siblings Survived to Age 50	Siblings Survived to Age 70	Small and Medium Family Size (<9); Siblings Survived to Age 20	Large Family Size (9+); Siblings Survived to Age 20
Paternal Age				
<30	1.81 (0.009)	1.91 (0.005)	2.25 (0.055)	1.55 (0.099)
30-39	1.59 (0.031)	1.66 (0.022)	1.70 (0.197)	1.61 (0.058)
40-49	1.21 (0.363)	1.24 (0.319)	1.19 (0.656)	1.22 (0.417)
50+	Reference	Reference	Reference	Reference
Female Sex	3.24 (<0.001)	2.93 (<0.001)	3.32 (<0.001)	3.11 (<0.001)
Pseudo R^2	0.0717	0.0632	0.0804	0.0615
Number of Observations	5,778	4,813	2,352	4,061

It was found that for people older than 50, the odds to live to 100 are 1.5 times higher for those born to mothers younger than 25 compared to siblings born to 40-year-old mothers (Table 6). Moreover, even at age 75, it still helps to be born to a young mother—the odds to celebrate the 100th birthday are 1.6 times higher for siblings born to mothers younger than 20 compared to those born to 40-year-old mothers (Table 6).

TABLE 6
Effects of Maternal Age on Human Longevity; Odds Ratios (With p-Values) to Become a Centenarian as Predicted by Conditional Logistic Regression (Fixed Effects)

Variable	Model 1	Model 2	Model 3 Daughters Only	Model 4 Sons 0nly
Maternal Age				
<20	1.60 (0.022)	1.66 (0.029)	1.43 (0.121)	1.72 (0.162)
20-24	1.49 (0.007)	1.51 (0.013)	1.37 (0.067)	1.77 (0.042)
25-29	1.46 (0.008)	1.44 (0.018)	1.57 (0.006)	1.24 (0.435)
30-34	1.13 (0.404)	1.12 (0.492)	1.07 (0.708)	1.29 (0.360)
35-39	1.05 (0.747)	1.04 (0.814)	1.10 (0.552)	0.92 (0.769)
40+	Reference	Reference	Reference	Reference
Paternal age				
<25		0.90 (0.501)		
50+		0.94 (0.798)		
Female sex	3.21 (<0.001)	3.21 (<0.001)		
Pseudo R^2	0.0691	0.0693	0.0062	0.0109
Number of observations	6,413	6,413	4,732	1,681

Study of survival to 100 in medium and large families showed that the effect of maternal age on survival significantly increases in medium families compared to large families. In medium families, siblings born to mothers younger than 20 had more than twice the chances to survive to age 100 compared to their brothers and sisters born to 40-year-old mothers (Figure 1 and Table 6,).

Figure 1
Maternal Age at Person's Birth and Odds to Become a Centenarian; Within-Family Study of 2,153 Centenarians and Their Siblings Who Survived to Age 50; Data on Families With Less Than Nine Children

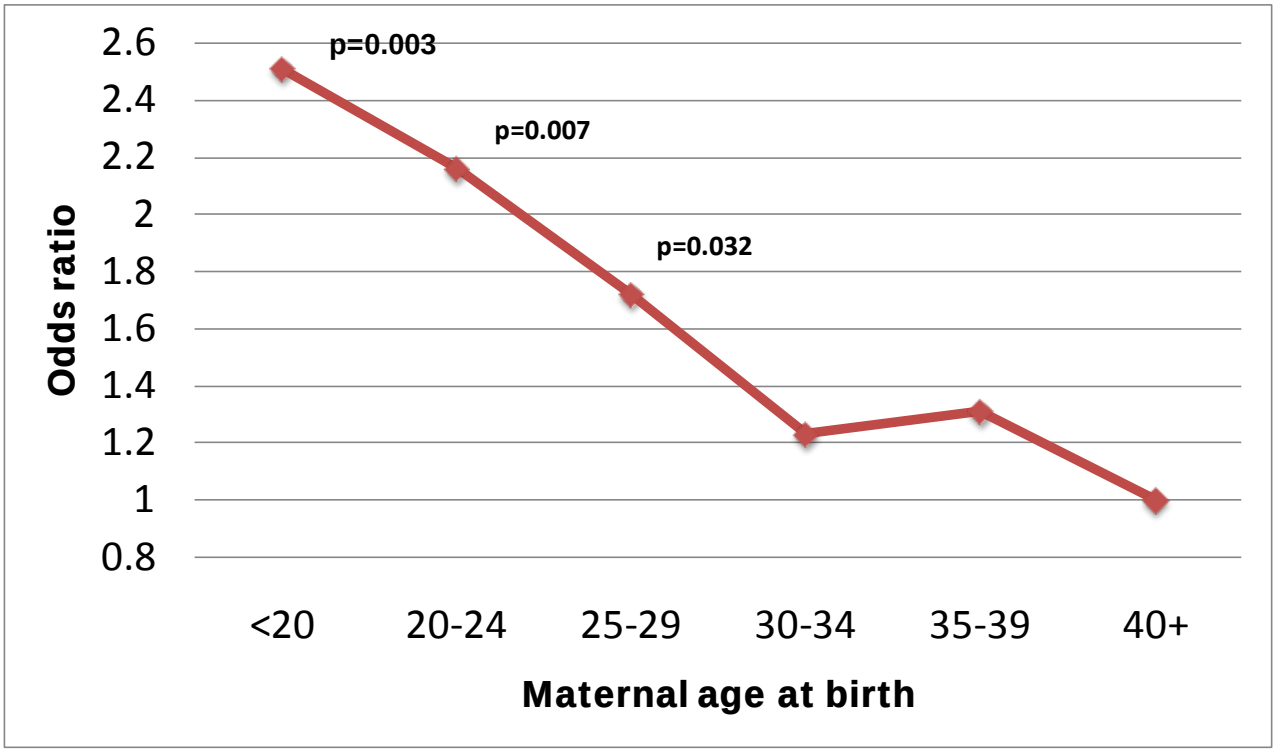


TABLE 6
Effects of Maternal Age on Human Longevity; Odds Ratios (p-Values) to Become a Centenarian as Predicted by Conditional Logistic Regression (Fixed Effects) for Different Subgroups

Variable	Siblings Survived to Age 50	Siblings Survived to Age 70	Siblings Survived to Age 20; Small and Medium Family Size (<9)	Siblings Survived to Age 20; Large Family Size (9+)
Maternal Age				
<20	1.57 (0.029)	1.61 (0.026)	2.33 (0.012)	1.29 (0.337)
20-24	1.52 (0.006)	1.53 (0.006)	1.94 (0.010)	1.29 (0.164)
25-29	1.46 (0.008)	1.48 (0.009)	1.63 (0.049)	1.41 (0.049)
30-34	1.15 (0.368)	1.13 (0.446)	1.13 (0.631)	1.17 (0.380)
35-39	1.05 (0.757)	1.05 (0.769)	1.26 (0.369)	0.94 (0.766)
40+	Reference	Reference	Reference	Reference
Female Sex	3.25 (<0.001)	2.95 (<0.001)	3.34 (<0.001)	3.11 (<0.001)
Pseudo R^2	0.0731	0.0645	0.0832	0.0625
Number of Observations	5,778	4,813	2,352	4,061

Thus, within-family analysis of the paternal- and maternal-age effects on human longevity demonstrated that a young age of the mother increases the chances of siblings to reach longevity. Within-family approach has great advantages over other methods because it is free of confounding caused by between-family differences.

Month of Birth

To analyze net effects of birth month on exceptional longevity, not confounded by possible changes in birth and infant death seasonality, childhood conditions and genetic background, we conducted a matched study using a multivariate conditional logistic regression method. In this study, we used the whole sample of centenarians born between 1880 and 1895. To discriminate between effects due to differential survival early in life from effects of birth month acting later in life, we analyzed survival to age 100 among siblings conditional on their survival to different adult ages. Table 7 presents the odds ratios to become a centenarian for siblings born in different months who survived to 30, 50 and 70 years of age. These results demonstrate that people born in September to November have significantly higher chances of exceptional longevity than people born in March. This month-of-birth effect is observed even for siblings who survived to age 70, suggesting a very long-lasting influence of season of birth on longevity.

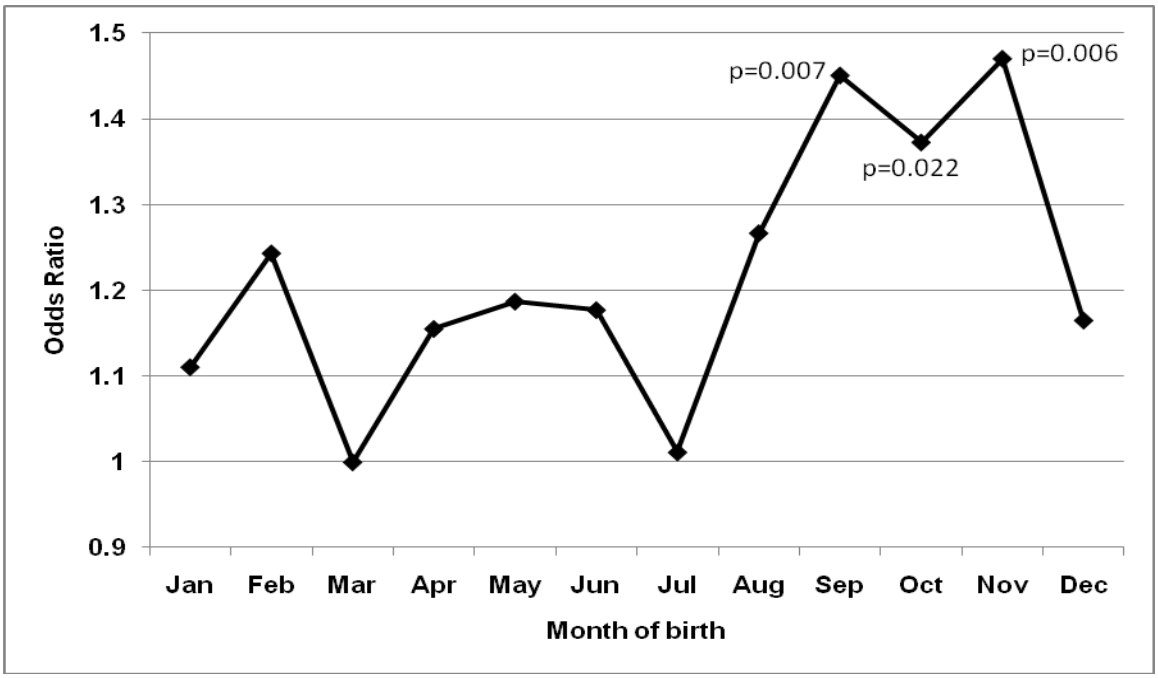
TABLE 7
Effects of Month of Birth on Human Longevity[†]; Odds Ratios (p-Values) to Become a Centenarian as Predicted by Conditional Logistic Regression (Fixed Effects) for Different Age Cut-off Subgroups

Variable	All Siblings	Siblings Survived to Age 30	Siblings Survived to Age 50	Siblings Survived to Age 70
Month of Birth				
January	1.13 (0.387)	1.11 (0.472)	1.11 (0.463)	1.09 (0.537)
February	1.25 (0.101)	1.25 (0.109)	1.24 (0.124)	1.16 (0.303)
March	Reference	Reference	Reference	Reference
April	1.15 (0.320)	1.15 (0.337)	1.16 (0.320)	1.09 (0.567)
May	1.20 (0.218)	1.17 (0.288)	1.19 (0.251)	1.15 (0.373)
June	1.20 (0.229)	1.00 (0.254)	1.18 (0.284)	1.11 (0.486)
July	1.03 (0.855)	1.19 (0.991)	1.01 (0.941)	1.00 (0.990)
August	1.25 (0.110)	1.24 (0.125)	1.27 (0.100)	1.21 (0.198)
September	**1.44 (0.006)**	**1.43 (0.009)**	**1.45 (0.007)**	**1.39 (0.022)**
October	**1.43 (0.008)**	**1.37 (0.021)**	**1.37 (0.022)**	1.27 (0.099)
November	**1.51 (0.003)**	**1.48 (0.005)**	**1.47 (0.006)**	**1.41 (0.017)**
December	1.17 (0.266)	1.13 (0.380)	1.17 (0.283)	1.11 (0.486)
Female Sex	3.77 (<0.001)	3.82 (<0.001)	3.80 (<0.001)	3.41 (<0.001)
Pseudo R^2	0.0811	0.0861	0.0871	0.0766
Number of Observations	12,132	10,393	9,724	8,123

[†] Statistically significant seasonal effects are highlighted in bold.

Figure 2 shows the odds ratios for becoming a centenarian by month of birth for siblings who already survived to age 50. It should be noted that this approach enables us to estimate net effects of birth months independent on any between-families variation.

Figure 2
Month of Birth and Odds Ratios for Becoming a Centenarian, Within-family Study of Centenarians and Their Siblings Who Survived to Age 50 (9,724 Studied People)



Discussion

In this study, we used large sample of centenarians and their siblings to study early-life effects on human longevity. This study shows good agreement with our previous results obtained using significantly smaller sample size (Gavrilova and Gavrilov 2007; Gavrilova and Gavrilov 2010). We found significant positive effects of a young maternal age on survival to age 100 with maximum effect observed predominantly at age 20 to 24. Paternal age effects were also observed, but they were mainly driven by correlated young maternal age. Effect of a young mother is particularly prominent in small and medium families, which is important taking into account smaller family sizes in contemporary population.

The finding of a beneficial effect of young maternal age on offspring survival to age 100 in humans may have biological explanation. There is empirical evidence that the quality of female eggs in human beings rapidly declines with age (Bickel 2005; Pellestor et al. 2005) and this deterioration starts rather early—before age 30 (Heffner 2004). Maternal age influences the biology of the mother-fetus relationship, with a negative effect on fetal development and predisposition to severe diseases such as type I diabetes (Gloria-Bottini et al. 2005).

Experiments on laboratory mice found the offspring born to younger mothers live longer (Tarin et al. 2005). This study also demonstrated that the largest effect is observed at later life. Animal studies have also found that hormonal profiles in pregnant mice are different depending on maternal age (Wang and vom Saal 2000). This may explain why adult offspring of adolescent and middle-aged mothers have lower body weight and delayed puberty and male offspring have smaller reproductive organs than those born to young adult mothers (Wang and vom Saal 2000). Female offspring produce progeny whose birth weight depended on the age at pregnancy of their grandmothers, demonstrating a transgenerational effect of maternal age (Wang and vom Saal 2000). Delayed motherhood in mice has also been demonstrated to have negative effects on

behavioral traits of young adult offspring (Tarin et al. 2003). Data on the long-term effects of maternal age in human beings are scarce. One study showed that the lifespan of children decreased with increasing maternal age (Kemkes-Grottenthaler 2004). Our earlier studies have not detected an association of maternal age with offspring mortality in historical populations of European aristocracy (Gavrilov and Gavrilova 1997; Gavrilov and Gavrilova 2000), but we believe this might be due to limitations in the data or the tools to analyze them.

The fact that lifespan of offspring depends on the mother's age at their birth even in laboratory animals indicates that some fundamental biological mechanisms may be involved. Such possible epigenetic mechanisms as changes in genomic imprinting in oocytes of aging females may be a plausible hypothesis (Comings and MacMurray 2001; Comings and MacMurray 2006). Another plausible biological hypothesis is the telomere theory of reproductive senescence in females (Keefe et al. 2005), which posits that eggs ovulating from older females have shorter telomeres because of late exit from the oogonial “production line” (Polani and Crolla 1991) during fetal life, with incomplete restoration by telomerase (Keefe et al. 2005). Telomeres are DNA repeats that cap and protect chromosome ends, so that longer telomeres in eggs of younger females may be beneficial for offspring lifespan. However, in human beings, some additional sociobehavioral mechanisms may be also involved, on top of more general biological mechanisms.

We also found a survival advantage for individuals born in September through November compared to individuals born in March. These results are in agreement with previous publications on the effects of birth month on lifespan in the Northern hemisphere (Gavrilov and Gavrilova 1999; Doblhammer and Vaupel 2001; Vaiserman et al. 2002; Lerchl 2004; Abel and Kruger 2010) and in the United States in particular (Doblhammer 2004; Gavrilov and Gavrilova 2008). These studies show better survival for people born in September through December compared to people born in the middle of the year. At the same time, our study does not demonstrate significant differences in survival for siblings born during other seasons. This does not agree with some other studies, which showed decline in mean age at death for people born in the summer months and relatively high mean age at death for people born in winter months (Vaiserman et al. 2002; Doblhammer 2004; Lerchl 2004). These differences in the month-of-birth pattern between our study and other publications can be partially explained by changes in seasonality of births and seasonality of infant mortality over time. Studies based on the analysis of cross-sectional death certificates do not have information about population at risk (Doblhammer 2004) and hence may be affected by secular changes in seasonality of births and infant deaths. Although these secular effects probably do not modify the entire month-of-birth pattern in life expectancy, they can modulate amplitudes observed for specific months. It would be reasonable to suggest that a decreasing trend of summer infant deaths resulted in increased representation of summer-born individuals in later-born age groups, leading to an apparent drop in the mean age at death for these months. Our study is based on survival of adults in real birth groups, so it is not affected by changes in seasonality of births and infant deaths.

It should be noted that our previous study of U.S. mortality in extinct birth groups also found substantial seasonality in life expectancy at age 80 (Gavrilov and Gavrilova 2008). In this study, 80-year-olds born in May or June showed significantly lower life expectancy compared to individuals born in the end of the year. Higher life expectancy was observed also for winter-born individuals. This month-of-birth pattern of life expectancy is similar to the pattern reported earlier for mean age at death obtained from the U.S. death certificates (Doblhammer 2004). However, in the study of centenarians and their siblings presented in this article, we do not find a specific survival advantage for people born in the winter months. It is possible that certain unobserved socioeconomic or other characteristics of parents (such as possible preferential winter births for wealthier social groups), which are controlled for in the case-sibling design study, may result in apparently better survival of winter-born individuals in a general population. Further research is needed for a better explanation of this phenomenon.

The results obtained in this study demonstrate that factors acting early in life may have significant long-lasting effects on survival to advanced ages. These results are consistent with the reliability theory of aging and the High Initial Damage Load (HIDL) hypothesis in particular (Gavrilov and Gavrilova 1991; Gavrilov and Gavrilova 2004a), which emphasizes the importance of the initial level of damage in determining future human longevity. More specific explanation of the observed effects of early-life conditions on longevity can be provided by the inflammation hypothesis suggested by Finch and Crimmins (2004). According to this hypothesis, a strong acute-phase inflammatory response required for survival early in life initiates chronic inflammation, which promotes chronic diseases of aging. The results obtained in our study suggest that optimizing the process of early-development can potentially result in avoiding many diseases in later life and significantly extending healthy life span.

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