Chapter 6
Predictors of Exceptional Longevity: Gender Differences in Effects of Early-Life and Midlife Conditions

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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 individual characteristics have a moderate protective effect on risk of death, people with this trait/condition should be accumulated among long-lived individuals because of cumulative survival advantage. 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; Murabito et al. 2012; Perls and Terry 2003; Sebastiani et al. 2012; Zeng et al. 2010) or psychological (Adkins et al. 1996; Hagberg et al. 2001; Margrett et al. 2010; Martin et al. 2010; Murabito et al. 2012) 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 2001, 2003a, 2006); the theory of technophysio evolution (Fogel 2004; Fogel and Costa 1997); the idea of fetal origin of adult diseases (Barker 1998; Kuh and Ben-Shlomo 1997); and a related idea of early-life programming of aging and longevity (Gavrilov and Gavrilova 2004). These ideas are

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supported by studies suggesting significant effects of early-life conditions on late-life mortality (Barker and Costa 1997; Elo and Preston 1992;Gavrilov and Gavrilova 2003b; Hayward and Gorman 2004; Kuh and Ben-Shlomo 1997; Smith et al. 2009). The role of early-life conditions in shaping late-life mortality is now well recognized and studies of centenarians can contribute to this area of research.

Our search for appropriate data resources for centenarian studies revealed an enormous amount of life span data that could be made readily available for subsequent full-scale studies (Gavrilov et al. 2002; Gavrilova and Gavrilov 1999). Millions of genealogical records are already computerized and, after their strict validation, could be used for the study of familial and other predictors of human longevity. Computerized genealogies provide the most complete information on the life span of centenarians' relatives when compared to other sources such as death certificates or census data.

Studies of centenarians require serious work on age validation (Jeune and Vaupel 1999; Poulain 2010, 2011) and careful design including the choice of an appropriate control group. Taking general population as a control group is one of the most popular approaches in centenarian studies. Preston et al. (1998) suggested an original methodology to study longevity in the United States. The researchers collected individual death certificates for people who died at ages 85+ during Jan. 1–14, 1985. Death certificate data were then linked to the 1900 U.S. census. Individual data from the 1900 U.S. census were used as a control group. Population-based census data are available as a part of the Integrated Public Use Microdata Series (IPUMS) project at the University of Minnesota (Ruggles et al. 2004). We applied method suggested in Preston Hill et al. (1998) in our earlier study of centenarians taken from computerized family histories and compared to U. S. 1900 census data from the IPUMS dataset (Gavrilova and Gavrilov 2007). The results of this earlier study demonstrated that the region of childhood residence and the household property status were the two most significant variables that affect the chances of a household producing a future centenarian (for both sons and daughters). Spending a childhood in the Mountain Pacific and West Pacific regions in the United States were found to increase chances of long life (by a factor of three) compared to the Northeastern part of the country (Gavrilova and Gavrilov 2007). Also a farm (particularly an owned farm) residence in childhood was associated with better survival to advanced ages. These findings were consistent with the hypothesis that lower burden of infectious diseases during childhood, expressed as lower child mortality in families of farm owners and families living in the West (Preston and Haines 1991), might have far-reaching consequences for survival to extreme old ages. Some of these results are consistent with other studies of childhood conditions and survival to age 85+ (Hill et al. 2000; Preston et al. 1998). These studies, also based on linkage to early censuses, demonstrated a significant advantage in survival to age 85 for children living on farms for both African Americans (Preston et al. 1998) and native-born Caucasians (Hill et al. 2000). On the other hand, the Northeast and Midwest were found to be the best regions of childhood residence for subsequent survival to age 85+ (Hill et al. 2000). The main limitation of our earlier study was selection of population-based sample as control group that was compared with centenarians taken from computerized genealogies (Gavrilova and Gavrilov 2007).

In this article, we consider more correct approaches to choosing a control population in centenarian studies: (1) selection of centenarians and controls from the same population universe and (2) use of nonbiological relatives as a control group. These approaches are illustrated using data on American centenarians, their relatives and unrelated shorter-lived controls obtained from the same online genealogies.

Data Collection

In this study, we compare centenarians born in the United States to their peers in the same birth cohort who were also born in the United States but died at age 65. Both cases and controls were randomly sampled from the same population universe (computerized family histories) and had the same birth year window (1890–91). These records were then linked to historical U.S. censuses (1900, 1910, 1930). The main focus of the study is on the 1900 and 1930 censuses that correspond to the childhood and adulthood periods of their individual lives. The age at death for controls is selected assuming that the majority of deaths at age 65 occur due to chronic age-related diseases rather than injuries or infectious diseases (Gavrilov and Gavrilova 2015).

Sample sizes of male centenarians are small in the majority of longevity studies and to resolve this problem and have a sample balanced in regard to gender, males are oversampled in this study. This oversampling does not affect the analyses because male and female data are studied separately, taking into account that men and women may respond differently to the same set of risk factors. To obtain a more homogeneous birth cohort regarding the secular changes in mortality and life course events, a narrow birth-date window was used: 1890–91.

Prevalence of centenarians in modern populations is very low: about 1 per 10,000 population (Hadley et al. 2000), and therefore traditional methods of population sampling are difficult and not feasible for obtaining large samples of centenarians. Case-control design proved to be the most appropriate and cost-effective approach for studies of rare conditions (Breslow and Day 1993; Woodward 2005) and hence is extremely useful for centenarian studies. Breslow and Day (1993) suggested the classic case-control design can be expanded in a variety of ways. One such expansion is a design suggested in (Preston et al. 1998). According to this design, a survival to advanced ages (rather than disease or death) is considered to be a case and relative survival probabilities are used instead of odds ratios. In this study, we draw centenarians and controls randomly from the same universe of online family histories to ensure comparability and avoid possible selection bias when centenarians and controls are drawn from different populations. Also, we used data from historical sources collected when centenarians and controls were children or young adults, thereby avoiding a limitation related to self-report or recall bias.

Only records from genealogies of presumably good quality with available information on exact (day, month, year) birth dates and death dates (for centenarians) as well as information on birth and death dates of both parents are used in the sampling procedure for both cases and controls.

Individuals born in 1890–91 represent an interesting birth cohort to study. These people experienced high exposure to infections during childhood and decreasing infectious disease load later in life. It is important to note that nonagenarians and centenarians living now in the United States have very similar experiences as those born at the end of the 19th century. Therefore, more detailed analysis of past history and life course of this birth cohort may be important for understanding the underlying factors and causes of mortality among the currently living old age cohorts.

Centenarians represent a group with really rare condition of successful survival (only two men and 14 women out of 1000 from the 1900 U.S. birth cohort survived to age 100) but common enough for obtaining samples of sufficient size. In this study, we analyzed early-life and adulthood effects that operate throughout life by comparing centenarians of each gender to the respective control groups.

Data quality control procedure in this study included: (1) preliminary quality control of computerized family histories (data consistency checks), (2) verification of the centenarian's death date, (3) verification of the birth date (for centenarians and controls), and (4) verification of family information (parents, spouses and siblings). These methods of age validation were based on the approaches proposed by the experts in this area (Jeune and Vaupel 1999; Poulain 2010) and our own research experience. All records (for centenarians and controls) were subjected to verification and quality control using several independent data sources. Our primary concern was 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; Hill et al. 2000; Rosenwaike and Stone 2003; Shrestha and Rosenwaike 1996). Therefore, the primary focus in this study was on the age verification for long-lived individuals, which involved death-date verification using the U.S. Social Security Administration Death Master File (DMF) and birth-date verification using early U. S. censuses.

According to our experience, the linkage to DMF selects out the majority of incorrect records for alleged centenarians (Gavrilova and Gavrilov 2007). A definite match was established when information on first and last names (spouse's last name for women); day, month and year of birth matches in DMF; and family history (Sesso et al. 2000) was verified. In the case of disagreement in day, month or year of birth, the validity of the match is verified on the basis of additional agreement between place of the last residence and place of death.

The procedure of death-date verification using DMF is not feasible for validating death dates of controls because data completeness of DMF is not very high for deaths before the 1970s. We found that approximately 30% of deaths in the control group could be confirmed through the U.S. state death indexes, cemetery records and obituaries, which cover longer periods of time. Taking into account that exact ages of death for controls are not particularly important for the study design, it is possible to rely on death-date information recorded in family histories for controls not found in external sources, as it was done in the Utah Population Database for individuals who died before 1932 (Kerber et al. 2001).

Verification of birth dates was accomplished through a linkage to the 1900 U.S. census data recorded when the person was a child (when age exaggeration is less common compared to claims of exceptional longevity made at old age). The preference is given to the 1900 census because it is more complete and detailed in regard to birth-date verification (it contains information on month and year of birth) compared to the 1910 and 1920 censuses. If a person cannot be found in the 1900 census, then he/she was searched in the 1910 census. We obtained a good linkage success rate (92–95%) in our study because of the availability of powerful online indexes provided by the Ancestry.com service and supplemental information in family histories (Gavrilova and Gavrilov 2007). These indexes allowed us to conduct searches on the following variables: first and last names (including Soundex), state, county, township, birthplace, birth year (estimated from census), immigration year and relation to head-of-household. Data on birth dates, birth places and names of siblings produced unambiguous matches in an overwhelming majority of cases.

Ancestry.com has a powerful search engine, which helps researchers find a person in multiple historical sources simultaneously (including all historical U.S. censuses up to 1940) based on all information available in computerized genealogies. Use of this service greatly facilitates the linkage procedure and helps to obtain unambiguous links in practically all studied cases. After the linkage to early censuses, the final database on centenarians and controls combined information on family characteristics (taken from family histories), data on the early-life conditions taken from the 1900–10 U.S. censuses and adult socio-economic status taken from the 1930 census. Early U.S. censuses contain a rich set of variables, which can be used to study the effects of both childhood and adulthood living conditions on human longevity (see Table 6.1).

Below we summarize the core topical domains of the variables analyzed in this study.

Childhood living conditions at household level. This information was obtained from the 1900 and 1910 censuses. Selection of variables was guided by the results obtained in previous studies on child mortality at the turn of the 20th century (Preston and Haines 1991). These studies demonstrated that child mortality is affected by household structure (including presence of a boarder in household), paternal occupation, mother's work, the occupation of household head, maternal and paternal literacy, and family structure (whether the proband lived with both parents, his/her father and stepmother, a stepfather and mother, his/her father only, mother only or on his/her own—for example, in an orphanage) (Preston and Haines 1991). An important factor of survival to advanced age is childhood farm residence —a result found in our earlier study (Gavrilova and 2007) as well as in other studies (Hill et al. 2000; Preston et al. 1998).

Table 6.1 Information available in early U.S. censuses for the search of longevity predictors

Variables	Early U.S. census						
	1860	1870	1880	1900	1910	1920	1930
Age, sex, color/race	+	+	+	+	+	+	+
Month and year of birth				+			
Marital status			+	+	+	+	+
Marriage duration (for married)				+	+		+
Literacy	+	+	+	+	+	+	+
School attendance (for children)	+	+	+	+	+	+	+
Place of birth	+	+	+	+	+	+	+
Places of birth for parents			+	+	+	+	+
Parental nativity		+	+	+	+	+	+
Mother tongue						+	+
Home ownership				+	+	+	+
Farm status				+	+		+
Value of real and personal estate	+	+					+
Number of children born and surviving (for women)				+	+		
Whether deaf and/or dumb					+		
Radio in household							+
Occupation	+	+	+	+	+	+	+
Employment			+	+	+	+	+
Citizenship		+		+	+	+	+
Year of immigration				+	+	+	+
Veteran status					+		+

Infectious burden. The main hypothesis we studied here is that early exposure to infections decreases chances of survival to advanced ages, affecting mortality later in life. Infectious burden is estimated as the within-family infectious burden. Information on all children born and children surviving allowed us to estimate proportion of surviving children for each family where the biological mother is present. Child mortality served as a proxy of infectious disease burden in the family, characterizing the living environment, as suggested by other researchers (Bengtsson and Lindstrom 2000, 2003; Finch and Crimmins 2004; Preston and Haines 1991). We based our estimates of child mortality on information available in the 1910 census whenever possible because by this time the majority of studied mothers had finished their reproductive period.

Seasonal early-life conditions. Effects of seasonal conditions on survival to extreme ages are studied using month of birth as an integral proxy for environmental seasonal conditions (e.g., seasonal infections) before and shortly after the birth. Existing literature on U.S. mortality and our own results based on the within-family approach show that month of birth may be a significant predictor of mortality not only during childhood but also in later life (Costa and Lahey 2005; Doblhammer 2004; Doblhammer and Vaupel 2001; Gavrilov and Gavrilova 1999, 2001).

Adulthood social conditions. Socio-economic achievement at adult ages for men was estimated using occupation status and dwelling ownership status (measured as in the 1900 census). In particular, we tested a hypothesis that farm background is particularly favorable for male survival because sons of farmers also become farmers (Preston et al. 1998). In this case, the farm status in both 1900 and 1930 should bring a significant advantage for survival to 100. In the case of females, estimation of socio-economic achievements through their occupation is not feasible because in 1930 the proportion of women in the labor force was relatively small in the United States. A reasonable proxy variable describing social status of non-working adult women is an occupation of husband (for married women) or occupation of the head of household for single, widowed or divorced women. Urban/rural residence in 1930 is another variable used in the study. Preston and Haines (1991) found that child mortality in 1900 was significantly higher in urban areas than in rural areas. Urban adults in the contemporary United States also have higher mortality despite better infrastructure and access to health services (Hayward et al. 1997).

Familial longevity and other family characteristics. Family histories allow us to obtain information on life span of biological and nonbiological relatives. For this particular study, the most important variables are life spans of mother and father. As yet, no studies have simultaneously examined the net effects of parental longevity and early-life conditions. Studies suggest that effects of parental longevity on longevity of the offspring may be substantial (Gavrilov et al. 2002; Kerber et al. 2001; Pearl and Pearl 1934) and heritability of life span estimates increase dramatically when parents live longer than 80 years (Gavrilova et al. 1998). Therefore, we believe that parental longevity (measured as paternal and maternal life span 80 years and over) may have significant moderating influence on the effects of childhood conditions and can be used as a proxy for genetic influences on life span. Other family variables of interest are paternal and maternal ages at person's birth, sibship size and birth order.

In this ongoing study, we have identified 838 centenarians born in 1890–91 in the United States and 910 controls born in the United States in 1890–91 who died at age 65. Further linkage to the 1900 census resulted in a 98.2% success rate for centenarians and 98.6% success rate for controls. For the 1930 census, 94.9% of centenarian records and 96.4% of control records were successfully linked. Linkage to the 1900 census revealed that 95.6% of centenarians and 96.0% of controls lived with one or both biological parents. According to the 1900 census, 67% of fathers of studied individuals were farmers. Centenarians and controls had approximately equal sibship sizes (7.6 and 7.8 respectively), which are higher compared to the general population in the 1900 census (5.6), suggesting larger sizes of families presented in computerized genealogies. In further analyses, we restricted our sample with records where information was available for both the 1900 and 1930 census. To study effects of marriage history on survival to age 100, only records for individuals married in 1930 were taken into account. Finally, data for 765 centenarians and 783 shorter-lived controls were used in our analyses. Multivariate logistic regression model was used to study survival to age 100. Our main focus was on the following three types of variables:

Early-life conditions drawn from the 1900 census (type of parental household: farm or nonfarm, owned or rented, parental literacy, parental immigration status, paternal occupation, number of children born/survived by mother, size of parental household in 1900, places of birth for household members),
Midlife conditions drawn from the 1930 census (type of person's household, availability of radio in household, person's age at first marriage, person's occupation or husband's occupation in the case of women, industry of occupation, number of children in household, veteran status),
and Family characteristics drawn from computerized genealogies (paternal and maternal life span, paternal and maternal age at person's birth, number of siblings).

Results

In the first step, we studied familial, childhood and adulthood variables separately using univariate analyses. Study of familial characteristics taken from genealogies revealed that paternal and maternal longevity was significantly associated with survival to age 100 for both men and women. Being born in the second half of the year was significantly associated with male longevity. However, loss of parents early in life (before 1910) had no effect on the chances of becoming a centenarian. Childhood conditions recorded in the 1900 census included: paternal and maternal literacy and immigration status, paternal occupation, status of dwelling (owned or rented farm, owned or rented house), household size, grandparent or boarder in household, proportion of surviving children reported by mother and region of birth. Larger household size and having father-farmer were found to be significant predictors of male (but not female) longevity in univariate analyses. Birth in the Northeast region is also predictive for survival to advanced ages in men. This result agrees with findings by (Hill et al. 2000) for people who survived to age 85, but does not agree with the results of our earlier study, which compared centenarians drawn from computerized family histories with population-based controls

(Gavrilova and Gavrilov 2007). This contradictory finding may indicate that the earlier use of population-based control could produce biased results if the studied sample of genealogical records does not represent the general population. Female longevity revealed no significant associations with any of the 1900 census variables. Adulthood conditions in the 1930 census included: dwelling status, occupation of self (husband or head of household for females), radio in household, veteran status of self (or husband), marital status, age at first marriage, availability of children (composite variable based on information taken from the 1930 census and genealogies). Univariate analyses showed that farmer occupation in 1930 was a very strong predictor of longevity for men. In the case of women, having a husband-farmer had no effect on the chances of survival to age 100. For women, availability of a radio in the household was the strongest predictor of longevity among the studied midlife variables. The effect of radio as a proxy for household wealth might potentially explain the latter finding. However, more direct characteristics of household wealth (property ownership) demonstrated no association with exceptional longevity.

In multivariate analyses, when familial, early-life and midlife characteristics are combined, having father-farmer is no longer associated with longevity of men. Parental longevity turned out to be one of the strongest predictors of survival to age 100. Table 6.2 presents the results of multivariate analyses for men. Note that farmer occupation in 1930 is one of the strongest predictors of survival to age 100, which agrees with results of other studies, including our own study of centenarians based on a population-based sample of survivors to age 100 from the 1887 birth cohort (Gavrilov and Gavrilova 2012).

Table 6.3 presents results of multivariate analyses for women. For women, having a husband-farmer has no effect on survival to age 100. Interestingly, having a radio in the household in 1930 has a positive effect on longevity for women but not for men (Table 6.3). This finding can be explained by the fact that women in 1930 spent most of their time at home and were much more exposed to radio (as an educational and entertainment source) compared to men. Listening to radio

Table 6.2 Predictors of male survival to age 100: effects of parental longevity, early-life and midlife conditions, results of multivariate logistic regression

Variable	Odds ratio	95 % CI	p-value
Father lived 80+	1.84	1.35–2.51	<0.001
Mother lived 80+	1.70	1.25–2.32	0.001
Farmer in 1930	1.67	1.21–2.31	0.002
Born in the northeast region	2.08	1.27–3.40	0.004
Born in the second half of year	1.36	1.00–1.84	0.050
Radio in household, 1930	0.87	0.63–1.19	0.374

Note N = 723. Farm childhood in 1900 was found to be nonsignificant predictor for males. Calculated using Stata 13 statistical package (procedure logistic)

Table 6.3 Predictors of female survival to age 100: effects of parental longevity, early-life and midlife conditions, results of multivariate logistic regression

Variable	Odds ratio	95 % CI	p-value
Father lived 80+	2.19	1.61–2.98	<0.001
Mother lived 80+	2.23	1.66–2.99	<0.001
Husband (or head of household) farmer in 1930	1.15	0.84–1.56	0.383
Radio in household, 1930	1.61	1.18–2.20	0.003
Born in the second half of year	1.18	0.89–1.58	0.256
Born in the Northeast region	1.04	0.65–1.67	0.857

Note N = 815. Calculated using Stata 13 statistical package (procedure logistic)

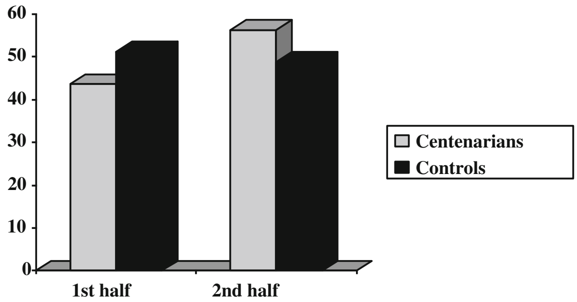

Fig. 6.1 Season of birth and survival to 100: proportion (percent) of people born in the first half and the second half of the calendar year among centenarians and controls (who died at age 65)

improves people's feelings of happiness and energy, and an electro-encephalographic (EEG) study found that listening to radio creates high levels of positive engagement in the brain, according to the findings of the "Media and the Mood of the Nation" research project conducted by Sparkler Research in spring 2011 (Redican and Barber 2012).

Finally, we tested our previous results that season of birth may be predictive for survival to long life and compared season-of-birth among centenarians and shorter-lived controls in this database. Figure 6.1 shows proportion of people born in the first and the second halves of the calendar year for centenarians and controls. Note that more centenarians than controls were born in the second half of the year and this difference is statistically significant (p = 0.008, chi-square test). This result confirms our findings obtained using the within-family analysis (Gavrilov and Gavrilova 2011), which showed that centenarians were born more often in September to November.

These findings are also consistent with our previous results as well as results of other studies, which found positive effects of farming and farm background on late-life survival (Gavrilova and Gavrilov 2007; Preston et al. 1998). Farm childhood background turned out to be particularly favorable for men who usually continue to work on a farm.

Concluding Remarks

This study demonstrated that both midlife and early-life conditions affect survival to age 100 with some gender specificity. At the same time, we found no effects of higher child mortality in the household (a proxy of infectious burden) on longevity as suggested by the inflammatory hypothesis of aging (Finch and Crimmins 2004).

Parental longevity turned out to be one of the strongest predictors of survival to age 100 for both men and women, so this variable cannot be ignored in the population health studies. Overall, parental socio-economic characteristics reported in 1900 census were not predictive for exceptional longevity for both men and women. On the other hand, some early-life characteristics (birth in North East region and birth in the second half of year) turned out to be significant predictors of exceptional longevity for men but not women. The finding of higher male sensitivity to early-life conditions may be explained in terms of reliability theory of aging and longevity (Gavrilov and Gavrilova 2006). Mortality patterns of men and women suggest that female organism is more reliable because it has higher redundancy. However, organisms with higher redundancy are able to accumulate more damage and still stay alive. Hence, women on average are able to survive with more diseases, which is a consequence of higher redundancy of female organism. At the same time men (who have fewer reserves compared to women) experiencing loss of redundancy (damage) early in life would have higher mortality risk throughout their lives due to lack of needed reserves. This may explain higher sensitivity of men to effects of early-life conditions and potential damage to their organisms during this period of life.

This study also found strong positive effect of farmer occupation at middle age on attaining exceptional longevity for men (husband's farmer occupation had no effect on longevity of women). Only limited few factors were related to exceptional longevity of women: parental longevity and availability of radio in household in 1930. This study suggests that men are more sensitive to the effects of early-life conditions on longevity compared to women.

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