ACHIEVING EXCEPTIONAL SURVIVAL
Are socioeconomic conditions in childhood still important?

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Introduction

The proportion of people aged more than 65 years in the European Union as well as in Canada and the United States is currently more than 15% in average and is likely to rise to a third within half a century. Similarly, centenarians are the fastest growing segment of the population in many developped countries. However, not everyone will reach the old age, thus making important the identification of determinants involved in longevity.

It is well know that longevity has a strong familial component and that siblings and parents of persons with exceptional longevity have significantly lower mortality compared to population-based controls (Gudmundsson et al., 2000; Kerber et al., 2001; Perls et al., 1998, 2002; Willcox et al., 2006; Mazan and Gagnon, 2007; Jarry et al., 2012). The correlation of ages at death among siblings can be attributed in part to genetic background shared by 50 % of its members, but it can also be the result of the shared environment and same resources early in life. In the last decades a lot of attention has been paid to the influence of socioeconomic features during childhood on adult health and mortality, supporting the lifecourse theories of social health disparities. Most studies have shown that an adverse environment in childhood leads to levels of morbidity (Blackwell et al., 2001; Hass, 2008; Moody-Ayers et al., 2004) and mortality (Elo and Preston, 1996; Galobardes et al., 2004; Osler et al., 2005) higher than the average. In this perspective, lifecourse studies examine a range of potential processes through which biologic, social or physical exposures acting at different stages of life can have long-term effects on disease risks in later life and lead to inequalities in mortality. Further evidence suggesting that childhood conditions may influence mortality in older ages comes from the critical period model which claims that early-life insults during a specific window have irreversible health effects later in life (Barker, 1998). There is thus, without a doubt, multiple mechanisms through which conditions in early life may affect one's health and mortality as an adult (Hertzman, 1999; Ben-Shlomo and Kuh, 2002).

Despite the ample evidence on the influence of socioeconomic childhood conditions on longevity outcomes later in life, less established in the literature is whether childhood conditions have the same effect within long lived families. Because genetic influence may be greater as one gets old, we believe that environment in childhood could be less predictive among siblings of centenarians than among individuals from the general population. Furthermore, most of the existing studies do not address the question of a possible change of this influence over time and it is unclear whether the influence is stable across the lifecourse or whether it decreases in old age.

In the first part of this study, we examine whether and how the effect of early-life socioeconomic conditions, such as father's occupation and place of residence, influence longevity in the general population as well as in families of centenarians. In particular, we verifiy if early-life factors that influence a normal person's survival also have an effect on the longevity of long-lived persons, in this case, siblings of centenarians. Then, in the second part, we examine whether and how the effect of early-life socioeconomic conditions change over the lifespan of individuals : Does the influence of socioeconomic conditions in childhood diminish or disappear completely in older age groups ?

Data and methods

This study relies on 806 centenarians and their families. Table 1 reports the year of birth of centenarians by sex. We used individual and familial variables gathered from the 1901 and 1911 canadian census records and linked them to their subsequent age at death. Centenarians' information was obtained from a list of registered deaths provided by the Institut de la Statistique du Québec, which contains records on centenarians who died between 1985-2005 in the Province. Families were reconstituted by linking these centenarians to their family members through the 1901 and 1911 Canadian censuses, which are available on the Internet through Ancestry and Automated Genealogy. A total of 5,338 siblings of centenarians have been identified. Once the database was completed, we searched for the date of death of each of these individuals through the Quebec Consolidated Deaths Index from the Société de généalogie du Québec. This database allows users to find dates of death and of birth, maiden names, etc. of persons who died in Québec between 1926 and 1996. For deaths occurring beyond 1996, we used a list of registered deaths over 85 years old for the years 1997-2004 provided by l'Institut de la Statistique du Québec. Linkage was made on the basis of information contained in both the censuses and death registers, particularly through the name(s) of the subject, his date and place of birth and the name(s) of his parents. We identified 3,100 siblings of centenarians for whom we had information on their date of death. Of these, 2,954 (1,541 women and 1,413 men) lived at least to age 40, and their average year of birth was 1895. To compare the siblings of centenarians to that of their birth cohorts, we used a control sample extracted from the Canadian Families Project five-percent 1901 Canadian Census sample (Sager, 2001; Perls and Terry, 2007). Then were selected from this random sample, families with at least one child born between 1885 and 1901. Only French Canadian Catholics who went on to live at least to age forty were selected, i.e., 8,204 individuals, for whom we found 3,784 deaths (1,906 women and 1,878 men).

We conducted three separate analysis to identify factors associated with longevity. We first compared households that raised a centenarian with the general population households and applied a method of conditional logistic regression to verify the influence of early life conditions on the relative odds of a household to produce

a future centenarian.

The logistic regression model is written as follow

$$ln[P/(1-P)] = \beta_0 + \beta_i X_i + e \tag{1}$$

where $\mathbf{X} = \beta_0 + \beta_1 X_1$ are the coefficients for the linear predictor and X_i represents the values of the explanatory variables.

We then performed gender-specific proportional hazard models with a Gompertz specification of the risk of mortality after age 40, controlling for a number of factors such as the year of birth and family size. Because siblings' survival experiences are likely to be clustered, we added a family-specific random effect that represents unobserved influences common to all members of a family and accounts for random unmeasured family-level traits shared by siblings. After testing a series of interactions between father's occupation and place of residence, we decided to combine those two variables, generating a new one. This new variable distinguishes five main groups of occupation: (1) "Farmer"; (2) "Urban white collar"; (3) "Rural white collar"; (4) "Urban worker" and (5) "Rural worker".

Table 1: Birth year of the centenarians

Birth year	Women	Men	Total
1890	40	16	56
1891	50	7	57
1892	64	10	74
1893	61	10	71
1894	61	12	73
1895	67	16	83
1896	73	11	84
1897	66	13	79
1898	70	15	85
1899	74	11	85
1900	49	10	59
Total	675	131	806

We modeled the risk of mortality after age 40 in which our estimated hazard μ_t is

$$\mu(t, Z_{ij}, X_{ij}) = Z_{ij}, \mu_0(t) e^{\beta X_{ij}} \tag{2}$$

where X_{ij} is the vector of control variables and $\mu_0(t)$ is the baseline hazard which we assume is of the Gompertz form, $\mu_t = exp(t)$

The frailties, which are assumed to depend on genetic or environmental unobserved characteristics at the family scale, are now assumed to be independent and identically distributed.

Finally, we ran a logit model that measured the effect of these variables on the odds of surviving, first from age 40 to age 75 and then, from age 75 to age 90. The choice of this categorization was motivated by a previous article in which is emphasized a crossover in the trajectories of mortality at this age (Jarry et al., 2012). Analysis were done separately by sex and by sample.

Results: Childhood determinants of exceptional longevity

In comparing households that raised a child-future centenarian to those of the control sample extracted from the Canadian Families Project, we found that both the father's education and place of residence as well as the father's literacy were significant variables that affected the chances of a household producing a future centenarian. Thus, rural and farm residence appeared to provide better survival to advanced ages unless the father was a worker. Having a father illiterate increased the chances of living a longer life than average by a factor of 1.5 whereas having spent a childhood on a farm also increased chances of belonging to a centenarian family which confirms Gavrilova and Gavrilov (2005) observations that suggest that farm background may be predictive for survival to age 100, as well as those of Preston et al. (1998). We were intrigued by the finding that individuals born to illiterate fathers had better chances of growing up in a centenarian family and thus to be associated with excess longevity. However, considering that the centenarians and their siblings grew up mostly in the countryside, it is not surprising to find that their father was more often than not illiterate.

Table 2: Odds for family to be in centenarian group for selected characteristics

	Odds ratio	*P-value*	95% Confidence interval	
Father's literacy				
Father illiterate	1.486	0.000	1.193	1.852
Father literate	reference	reference	reference	reference
Father's occupation				
Urban worker	0.283	0.000	0.221	0.364
Rural worker	0.588	0.000	0.474	0.729
Urban white collar	0.467	0.001	0.296	0.735
Rural white collar	1.899	0.021	1.102	3.272
Farmer	reference	reference	reference	reference

To examine the effect of childhood conditions on the risk of mortality after age 40, we estimated a gender-specific proportional hazard models (Table 3). We found that childhood conditions affecting later-life mortality vary by gender, the effect being stronger for men than for women, and by population sample, the influence being stronger for individuals of the general population than for siblings of centenarians. In the

general population, early-life conditions had an effect on late survival and sons raised in a rural setting and by a father that was a farmer experienced a lower mortality. As for male siblings of centenarians, those whose father was an urban worker experienced 54% higher risk of mortality than those whose father was a farmer.

Table 3: Gompertz proportionnal hazard models of mortality risks after age 40 accounting for unobserved heterogeneity

	Centenarian family		**General Population**	
	Hazard ratio		**Hazard ratio**	
Gompertz model	Female	Male	Female	Male
Year of birth	0.996	1.005	0.985*	1.003
Family size	0.994	0.991	0.991	0.993
Father's literacy				
Father illiterate	1.055	1.068	1.144$^{\&}$	0.925
Unknown	1.000	1.000	1.451$^{\&}$	0.953
Father literate				
Father's occupation				
Urban worker	1.029	1.422***	1.180**	1.398***
Rural worker	0.969	1.081	0.991	1.307***
Urban white collar	0.951	1.215	1.097	1.529***
Rural white collar	1.156	1.284	1.517$^{\&}$	1.381
Unknown	1.207$^{\&}$	0.926	1.080	1.203
Farmer				
Gamma	0.088***	0.094***	0.079***	0.093***
Theta	5.91e-08	0.056$^{\&}$	2.89e-07	0.128***
N	1413	1541	1906	1878

p<0.001 ***, p<0.005 **, p<0.01 *, p<0.05 $^{\&}$

For women, there are few childhood conditions that generate substantial shifts in their adult mortality risk. Being raised by a father who was an urban worker is the only aspect of early life context that seems to have a highly statistically significant negative effect on women survival in the general population. However, the father's literacy appears to be more important for women than for men. The protective effect of living in a rural setting or of being raised by a father who was a farmer is less evident for women. Several hypotheses related to the historical context of the period could explain these results. First, it is not surprising to find that children raised in an rural setting rural and by a father that was a farmer experienced a lower mortality. At the turning of the 20th century, living on a farm provided a healthy environment whereas the urban populations were those facing the greatest health risks as a result of the overcrowding dwellings, difficult working conditions and poor sanitation. Second, the stronger protective effect of rural setting and farming

experienced by men compared to women could also be attributed to a cumulative advantage of men becoming themselves farmers in adulthood. This could be associated to the Pathway model in which the parents socioeconomic status has an indirect influence on the health status, particularly through a transmission of socioeconomic status across different generations and, in this case, by preserving the protective effects of rural area. On the other hand, while males who grew up in the country side seem to have benefitted more of this favorable environment than females, males who grew up in the city might have been more affected by this adverse environment because they were probably more exposed to difficult and unsafe conditions of industrial and factory work than their sisters (Gossage, 1999; Bohnert and Gagnon, 2008). In contrast, females raised by farmers, who did not inherit farmland, where more likely to move to the city or to migrate on their spouse's familial land. These findings strongly agree with results observed by Preston et al. (1998), Bohnert and Gagnon (2008) as well as Gavrilova and Gavrilov (2005) who all found a stronger beneficial effect of farm childhood on longevity for males than for females.

Another way to see if socioeconomic factors become more or less important accross the course of life, is to compare the effect of childhood conditions on the odds of surviving, first from age 40 to age 75 and then, from age 75 to age 90. We found that, for men, father's occupation and urban/rural status had an influence in achieving 75 in both samples even though the effect was more powefull in the general population (Table 4). However, when looking at the odds of achieving age 90 (for those who survived to age 75), the influence of early-life conditions vanishes in the centenarian sample, while it remains present, although less important, in the control group. As for women, it seems that having a father who was an urban worker or an urban white collar reduces the chance to achieve age 75 in the general population (Table 5). This variable no longer has influence beyond that age nor for sisters of centenarians.

Table 4: Random Effects Logit Model of mortality risks for Men

	Survival to age 40 to 75		**Survival to age 75 to 90**	
	General Population	Siblings of Centenarians	General Population	Siblings of Centenarians
Year of birth	0.974[&]	1.000	1.046	0.975[&]
Family size	1.022	1.009	0.895	1.020
Father's literacy				
Father illiterate	1.268	0.929	0.870	0.889
Father literate				
Father's occupation and urban-rural status				
Urban worker	0.531***	0.510***	0.532[&]	1.017
Rural worker	0.652**	0.766[&]	0.505[&]	1.012
Urban white collar	0.414***	0.647	0.721	0.863
Rural white collar	0.578	0.625	1.934	1.157
Unknown	0.708	0.871	1.279	1.269
Farmer				
rho	0.096**	0.058[&]	0.233[&]	0.144[&]
N	1878	1541	825	877

p<0.001 ***, p<0.005 **, p<0.01 *, p<0.05 [&]

Table 5: Random Effects Logit Model of mortality risks for Women

	Survival to age 40 to 75		**Survival to age 75 to 90**	
	General Population	Siblings of Centenarians	General Population	Siblings of Centenarians
Year of birth	1.045***	1.012	1.003	1.012
Family size	1.022	1.021	0.995	0.978
Father's literacy				
Father illiterate	0.730[&]	1.073	0.688	0.748
Father literate				
Father's occupation and urban-rural status				
Urban worker	0.652***	0.956	0.870	0.786
Rural worker	1.005	1.166	0.781	0.920
Urban white collar	0.664[&]	0.719	1.057	1.760
Rural white collar	0.821	1.495	0.176	0.554
Unknown	1.105	1.055	1.279	0.616
Farmer				
rho	0.042	0.045	0.051	0.058[&]
N	1906	1413	1122	974

p<0.001 ***, p<0.005 **, p<0.01 *, p<0.05 [&]

Discussion

There is growing evidence of the long term benefits of investing in children knowing that detrimental environment during critical periods of development can have long run consequences (Almond and Currie, 2010). Early life constitute one such critical period who is particularly sensitive to the familial environment. One of the most important insight from our analyses is that early-life estimates for late life traits vary significantly across our two samples. Our estimates show that the effet of socioeconomic factors in early-life on mortality later in life is much smaller for a sibling of centenarian compared to an "average individual". Thus, mortality determinants among older individuals may be different from those among younger persons (Mitchell et al., 2001).

Many studies suggest that people that achieve exceptional old age do so because of genetic variations that affect their basic mechanisms of aging. In this regard, centenarians are believe to be a model of healthy aging: "What makes these people live a very long life is not a lack of genetic predisposition to diseases, but rather enrichment of longevity-associated variants that may be protective and may even cancel the genetic effects of disease-associated variants" (Perls et al., 2002). Christensen and Vaupel (1996) suggest that individuals surviving to extreme ages are particularly robust and either are not very susceptible to the health hazards

of certain environmental risk factors or they have compensating characteristics. We can hypothesis that this could also be true for all members of long-lived families and thus long-lived siblings of centenarians may be less vulnerable to adverse environmental conditions, including early life environment, because of a favorable genetic background or biological robustness. Researchers often wonder how much of longevity is due to genetic factors and how much is due to environment and the potentially increased role of genetics with age is a notion that has empirical support. An interesting strain of explanation thus refers to the changing importance for mortality of social and biological factors: at advanced ages, it is argued, biological factors gain relevance and social factors play only a minor role (Roland and Muszynska, 2009). In an article published in 2006, Hjelmborg and colleagues, using Danish and Finnish twin cohorts, confirmed that genetic influences on human life span are minimal before age 60 but increase thereafter (Hjelmborg et al., 2006). Perls also believes that the older a person gets, the more likely it is that his or her genes are contributing to those extended years:"Perhaps sociodemographic advantages play key roles at younger ages, while genetic advantages distinguish the ability to go from old age to extreme old age"(Perls, 2007). In other words, the longer you live, the more your death could be determine by your genetics rather than by other environment factors, which closely agree with our results.

In a previous paper, we demonstrated a strong familial component to longevity in our sample (Jarry et al., 2011). It seemed undeniable that having or not having a centenarian sibling is a powerful determinant of survival after age 40 for both men and women. Survival curves from age 40 for siblings of centenarians, men and women, compared with their respective birth cohorts, are shown in Figure 1.

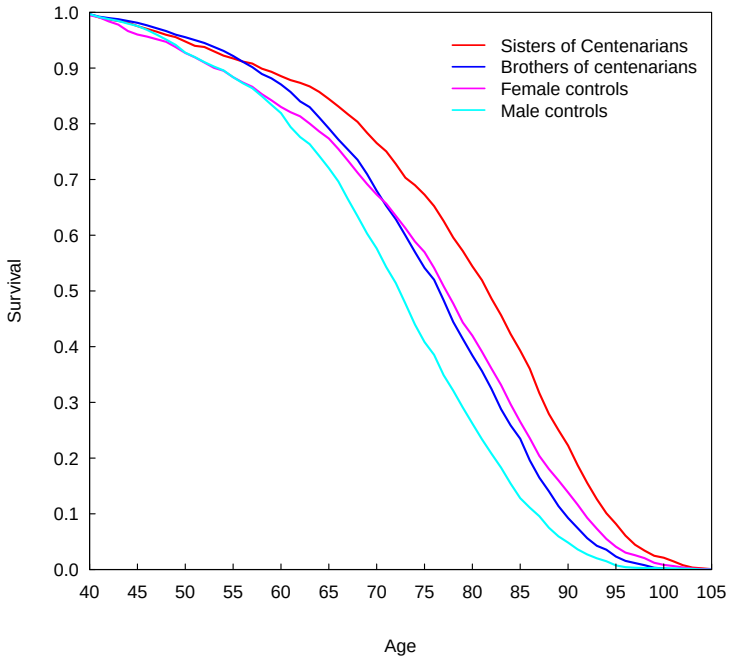
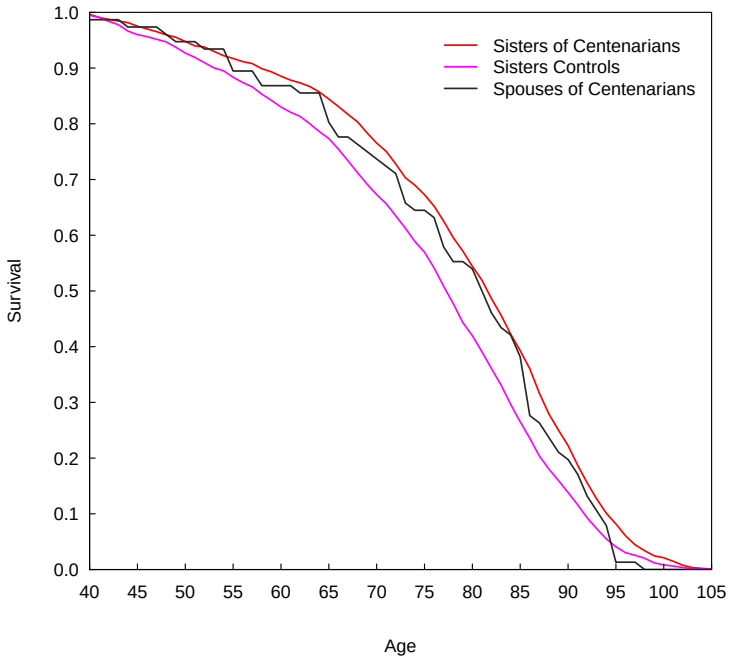


Figure 1: Comparison of Survival Curves of Siblings of Centenarians from Age 40 to Higher Ages with their Respective Birth Cohort

The survival probabilities demonstrate that siblings of centenarians experienced a longer life than the general population and kept this advantage through very old ages (p=0.001). For sisters of centenarians, the median life expectancy was about 4 years higher (82 years) when compared with women from their birth cohort (78 years). As for brothers of centenarians, the survival advantage was also considerable, their median age at death being of 77 years compared to 73 years for men in the general population. Moreover, sisters of centenarians were 1.6 times more likely to survive from age 40 to age 90 and 2.5 times more likely to survive from age 40 to age 100. As for brothers of centenarians, they were found to be approximately 1.5 times more likely to survive from age 40 to age 80 and nearly twice more likely to reach 90 when compared with men from their birth cohort. Furthermore, we have shown that environment in adulthood plays a major role in survival, as there is a significant survival benefit for husbands of centenarians compared to the general population (Figure 2). Nevertheless, although the environmental component shared by spouses seems primarily responsible for the shared survival advantage up to the mean age at death, it does not seem to play much in achieving the oldest ages. After age 75, the survival correlation between spouses lessens and men seem to benefit more from being a sibling than a spouse of centenarian. In other words, what appears to allow living until the average age for men is predominantly the result of a shared environment in adulthood, while shared living conditions in childhood and genetics could explain the advantage of brothers of centenarians compared with spouses of centenarians in achieving old ages. These results support the hypothesis that socioeconomic conditions during childhood exert a quite smaller influence on the ability to achieve exceptional old age

probably at the expense of genetic heritage.

In summary, our analyses suggest an important role of early life socioeconomic conditions in mortality outcomes in later life. However, the effect of these factors on longevity is not equal for all individuals and changes across ages. The effect of early life conditions is greater for men compared to women, for "normal individuals" compared to long-lived siblings of centenarians and for younger group ages compared to the oldest ages. Our analyses, however, suggests that genetics might be an important clue to achieving exceptional old age.



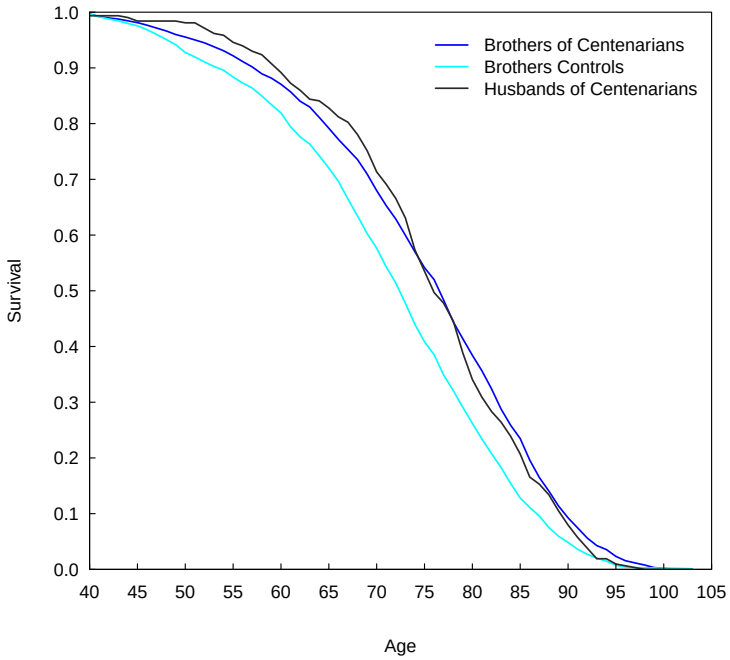


Figure 2: Comparison of Survival Curves of Wives and Husbands of Centenarians from age 40 with their respective birth cohort and Siblings of Centenarians

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