

Searching for longevity determinants: following survival of newborns in a in-land village in Sardinia (1866-2006)

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Abstract

The scientific debate on longevity and its determinants is lively and involves researchers from different disciplines. Finding a clear cut explanation for why some people live longer than others is not an easy task. Variables that are shown to be significant for longer survival in certain populations are not always relevant to individuals of other populations.

Recently, researchers have identified in Sardinia the *Blue Zone* (BZ), thus denominated due to the significant number of cases of centenarians recorded as well as a low sex ratio value. A village located in this area was selected for the carrying out of a more detailed analysis at individual level and socio-demographic determinants of longevity were examined.

Based on careful review of the existing literature, the empirical model considered factors such as sex differential, the contribution of familial transmission, and the role played by environment operationalised considering early-life conditions. The analysis of the data enabled to the estimation of mortality trajectories, which in turn confirmed the exceptional longevity of the population understudy and in particular of males.

The investigation of differential survival among members of the same community brought to light the relevance of certain familial variables on survival, which are not exclusively genetic.

Keywords: *Longevity, differential mortality, survival analysis, historical demography.*

Introduction

Findings from different researches have shown that there is not one single explanation for longer survival; rather, several variables must be taken into account. Moreover, not only processes taking place inside the body determine the destiny of an individual, but also the environment and particular conditions experienced across the life course eventually affect lifespan.

The major aim of the present contribution is to participate to the ongoing debate on longevity determinants, in particular with respect to the case of Sardinia (Deiana et al. 1999; Caselli and Lipsi 2006). Research has been centred on finding possible socio-demographic determinants of longevity, focusing in particular on differential survival after 50-year old.

With this purpose in mind, the research was focused on the study of one specific setting: the population of Villagrande Strisaili. The reason behind this choice was related to the fact that this municipality - according to the work of Poulain et al. (2004) – belongs to the *Blue Zone* longevity area and recorded the highest value of ELI (Extreme Longevity Index), which measures the proportion of newborns in the period 1880-1900 who became centenarians.

The creation of an appropriate database was the first important step towards subsequent survival analysis. It was decided to build a family reconstructed database. Newborns in the village during a period of 50 years – from 1866 to 1915 – constituted the core of the individual database, where information on related family members was also included. Each individual is followed from birth to death, as he/she goes through marriage and family formation.

Based on the information collected, the following step was to assess whether the particularity of the municipality of Villagrande Strisaili that had emerged in prior research was confirmed when analyzing individual data. Could ELI estimates be considered a reliable measure of longevity? By both prolonging the period of analysis and enlarging the dimension of the population under study, the following became the research question: *Is the population of Villagrande Strisaili in actual fact a long-living community?* To answer this question, the study involved examining complete survival of all newborns in Villagrande Strisaili between 1866 and 1915 until the present.

Beyond the preliminary results concerning the longevity of Villagrande Strisaili at population level, an important aim of the present study was also to investigate differential survival among members of the same community.

The basic presumption was related to the fact that given that Villagrande Strisaili newborns might be assumed to have shared the same geographical location and environmental conditions, why do some people live longer than others? What is the contribution of the familial component on human survival? Do contextual variables influence longer lifespan? The related research question can be summarized as follows: *Which individual and/or familial and/or contextual variables lead to longer survival?*

This work is developed in the attempt to answer to all these questions, trying to bring the light on relevant variables toward survival that could also open the way to further studies.

The possible determinants of longevity

The identification of the possible determinants of human longer survival is not an easy task as longevity proves to be connected to more than one factor.

In quest of the answer, many researchers have chosen to study centenarians, who are considered to be a reliable example of a successful ageing process (De Benedictis et al. 1999; Blanche et al. 2001; Perls et al. 2007). Most studies are carried out within specific research fields such as genetics, medicine, biology, demography, anthropology, nutrition and so on. The major consequence of this discipline-specific approach is that often only a selected number of variables are considered, and this renders the search for significant variables difficult.

Nevertheless, a critical review of the existing literature may provide useful indications on the possible candidate determinants for longevity.

Among them, sex certainly represents the first factor to take into consideration when investigating differential longevity. Several studies have in fact established the existence of sex-specific-diseases that eventually lead to differentials in survival between the two sexes, with females in general recording longer survival than males (Franceschi et al. 2000; Guralnik et al. 2000; Austad 2006).

It was also noted that familial mechanisms may play a role, both in terms of inherited genetic traits and in particular common familial environment (Herskind

et al. 1996; Boquet-Appel and Jacobi 1990; Perls et al. 2002). The contribution of one or the other familial component – genetic or environmental - is not always easy to measure, as limitations exist in data availability and operationalisation of variables.

Often researchers combine demographic data with other familial environmental variables. Variables such as marital status, family size, parity and so on, have often been used for investigation and results in different studies and settings did not always coincide (Modin 2002; Van Poppel and Liefbroer 2005; Gavrilov and Gavrilova 2006; Ikeda et al. 2007). The study of environmental effect has also included the role played by early-life conditions on later survival (Ben-Shlomo and Kuh 2002; Bengtsson and Lindstrom 2003).

In addition to the variables mentioned above, it is worth pointing out that several studies have also considered other factors and their effect on longevity. These are: individual personality traits, religion, nutrition and lifestyle, anthropometrical measures, and physical environment.

There are therefore many variables that proved to contribute on lifespan. However, variables that are shown to be significant for longer survival in certain populations are not always relevant to individuals of other populations. Individually each variable cannot explain the phenomenon of extreme life but, like small pieces of a puzzle, each contributes to the larger picture.

The municipality of Villagrande Strisaili

The area of investigation of the present study is the municipality of Villagrande Strisaili, located in the in-land of Sardinia at an altitude of 700 meters.

At the first general population census for the unified Italy in 1861 – which introduced the modern system of population data collection - Villagrande Strisaili recorded 1,251 inhabitants and 1,111 at the next census 10 years later.

From 1861 up to the 1971 census, the population grew continuously, at which time, for the first time, it registered a decrease in the population stock. The pace of growth (r) was estimated to be 14.7 per thousand inhabitants per year until the 1971 census, when the village reached its maximum size: 4,029 inhabitants.

Between 1971 and 2001, the decline of the population was estimated to be on average 4 per thousand inhabitants per year (r) until more recent years when a

more intense decline is recorded with a growth rate of -7 per thousand. This declining trend was partially determined by the greater weight of death of the elderly component of its population, but more significantly it has to be attributed to the new increase of out-migration flows of the young component, which seeks job opportunities outside the local territory. This phenomenon of depopulation is not registered only in Villagrande Strisaili, but is prevalent in most of the municipalities in the inland and rural areas of Sardinia (Gatti and Puggioni, 1998). According to latest available ISTAT data on resident population at January 1st, 2009 Villagrande Strisaili counts 3,466 inhabitants.

In the past, the main economic activity was sheep farming and it still remains one of the major sources of sustenance (Olla 1969). However, the development of small companies specialized in cheese and cured meat production as well as in other local products is a substantial asset to the local economy. The community of Villagrande Strisaili proves to be still attached to its traditions of the past. This link with the past is confirmed by the current diet of its inhabitants, prevalently the Mediterranean diet (Tessier and Gerber 2005) and the central role of the family (Salzman 1998).

Data and Methods

Data

The present research was based on individual data. Data collection was developed in various steps over a period of 6 years and involved several researchers.

The civil status registers were the basic data sources used and facilitated the identification of the core body of the newborn in the village during the period from 1866 to 1915 (2,552 newborns). Data was initially systematically collected. Since the major aim was not the reconstruction of the population as such but rather the compilation of survival histories, the objective of subsequent data collection was to reach the highest possible level of known survival and this implied the use of different data sources, namely population registers, parish registers, military lists and, in exceptional cases, interviews of still living relatives of the newborn and key informants.

Overall, the level of completeness and coverage was high and data was carefully validated. Exact date of death was found for 92.7 percent of newborns (2,365 cases). This percentage increases when the number of individuals still alive at the time (43 cases) of last data collection in September 5, 2006 is taken into account, reaching a final coverage of 94.3 percent. Residual 116 individuals (4.5 percent) were right censored according to last information available on their survival, while only 28 newborns had no other known event either than their birth. Individual information was organized into a family reconstructed database denominated *VI-llagrande L-ongevity D-atabase* (VILD) and survival at more advanced ages focused on 50-year-old and over survivors (1,162 newborns). The information available from VILD both at individual and at family level were operationalized as reported in table 1.

Table 1 – Operationalisation of theoretical issues concerning longevity into variables of the empirical model

Theoretical background	Operationalisation	Variable in empirical model
Gender		Sex
Familial transmission Genetic component	<i>Survival of other family members</i>	Age at death of Father
		Age at death of Mother
		At least 1 sib lived 90 and over
Familial transmission Biological effect	<i>Parental age at birth of Ego</i>	Age of Father at birth of Ego
		Age of Mother at birth of Ego
Familial trasmission Shared environment	<i>Familial environment</i>	Type of family
	<i>Family size</i>	Ever born children
		Birth order
		No. of living children at Ego birth
	<i>Familial support</i>	Age of Ego at loss of Father
		Age of Ego at loss of Mother
Contextual early-life conditions	<i>Infant mortality rate</i>	Local infant mortality rate
	<i>Cohort Effect</i>	Cohort of birth
		Season of birth

Methods

The methods used for data analysis are those of survival analysis. A preliminary exploration and description of the data was performed using nonparametric

methods such as Kaplan-Meier estimation (KM) and life tables, testing for significance (Blossfeld and Rohwer 2002). Both methods have generally proved to be effective for earlier investigation. However, the identification of possible longevity determinants implies the use of a parametric model, since it allows measurement of the effect of variables on survival. Among the different possibilities, the Cox proportional hazard model in its robust version proved to be the most suitable considering the available data in the VILD (Cox 1972; 1975). More precisely, the model applied to the VILD consisted of time-constant variables, whose proportionality was checked (Schoenfeld 1982). With regard to tied events, they were handled applying the Efron method (Hertz-Picciotto and Rockhill 1997).

Mortality trajectories among the VILD newborns

From the analysis of survival data, it firstly emerged that infant mortality was particularly low in Villagrande Strisaili. It was estimated at 117.5 per thousand, while for Sardinia estimates were 162.8 per thousand (Coletti 1908), which generally recorded low level of early deaths compared to the mainland Italy (Gatti 2002). With respect to child mortality from birth to 5 years, Villagrande Strisaili recorded general favourable conditions for early survival.

The circumstances change when considering survival after 5 years up to adulthood. VILD estimates were significantly higher than in Sardinia and at national level. The survival advantage recorded among VILD newborns in the first 5 years of life is not maintained at subsequent ages, but rather created a postponement of deaths particularly from age 6 to age 10 when children were considered to be independent and able to contribute to family upkeep.

Adult mortality was more difficult to analyse as complete information on the causes of death was not reported in the death act. However, in general VILD newborn males faced a critical period of high mortality due to their participation in WWI when 40 VILD newborns died. As for females, the main cause of death until age 50 was the risk of maternal mortality, which was estimated at 11.1 per thousand. This latter figure turns out to be a bit lower than estimate observed in other populations (Gatti 1999), and confirms that, in general, favourable conditions for infant delivery existed in Villagrande Strisaili.

From age 50 the risk of death increased exponentially for both males and females as mortality is related to the ageing process. Among the VILD newborns, 45.5 percent of males and 52.3 percent of females reached 50 years and their proportion is similar to Italian birth cohorts (HMD) for the same period (i.e. on average 52 percent). However, this similarity is not confirmed at subsequent ages. The proportion of VILD newborns that reached more advanced ages was in fact greater than in Italy. Among the VILD newborns, the number of males and females that reach 90 years and over are, firstly, exceptionally equal in number and, secondly, one individual out of 5 that reached 50 years went on to celebrate his/her 90th birthday, while in Italy this proportion was one female out of 6 and only one male out of 10. This result confirmed the indications derived from the work done for the identification of the *Blue Zone* (Poulain et al., 2004), which indicated a particularly favourable survival of males.

Searching for longevity determinants

Kaplan-Meier estimation (KM) was initially executed for each of the variables considered in the empirical model (see Table 1). This preliminary analysis enabled to detect – at this early stage - the relevance of familial component both in terms of genetic and of shared environment among the available variables.

However, the use of KM estimation presents some limitations as it enables to consider only one variable at a time and moreover does not allow measurement of the effect of each variable on individual survival. Therefore the Cox PH model was preferred to conduct further analysis.

Table 2 presents the results of Cox PH model, where all variables met the proportionality assumption (GOF chi-square = 31.60, p-value = 0.168).

At first glance, from the estimates of the model two interesting results emerge. The first is that sex plays an insignificant role in survival, while we would expect women to record a significant advantage over men. The second result concerns the significant differences detected among birth cohorts, with more recent cohorts recording higher survival estimates. This result is somehow obvious, as the latter had experienced improved economic and living conditions compared to earlier ones.

However, the estimates reported point out additional important elements. With

Table 2 – Cox PH estimates of survival of 50-year-old VILD newborns considering the effect of all variables included in the empirical model

Variable	coef	exp(coef)	se(coef)	z	p
Sex					
Females (ref.)	0	1			
Males	0,0165	1,02	0,031	0,541	0,590
Genetic component					
Paternal age at death (continous)	0,0046	1,01	0,002	1,889	0,059
Maternal age at death (continous)	-0,0066	0,99	0,002	-2,932	0,003
Having at least 1 sib 90yrs					
no (ref.)	0	1			
yes	-0,1258	0,88	0,033	-3,843	0,000
Biological effect					
Paternal age at birth					
less than 35 years (ref.)	0	1			
35 ┤ 45 years	-0,0794	0,92	0,042	-1,883	0,060
older than 45 years	-0,0600	0,94	0,030	-1,997	0,046
Maternal age at birth					
less than 25 years (ref.)	0	1			
25 ┤ 35 years	0,0256	1,03	0,044	0,577	0,560
older than 35 years	0,0369	1,04	0,031	1,177	0,240
Shared environment					
Type of family					
Simple (ref.)	0	1			
Remarriage	-0,1242	0,88	0,038	-3,310	0,001
Ever born children					
1 to 3 (ref.)	0	1			
4 to 6	0,0722	1,08	0,074	0,982	0,330
> 6	0,0556	1,06	0,031	1,776	0,076
Birth order					
Being first born (ref.)	0	1			
Being later born	0,0110	1,01	0,049	0,224	0,820
Living sibs at Ego's birth					
0 to 2 (ref.)	0	1			
3 to 5	0,0066	1,01	0,046	0,143	0,890
> 5	0,0750	1,08	0,042	1,771	0,077
Age of Ego at loss of Father					
before 5 yrs (ref.)	0	1			
5 yrs and over	-0,1951	0,82	0,068	-2,885	0,004
Age of Ego at loss of Mother					
before 5 yrs (ref.)	0	1			
5 yrs and over	-0,1505	0,86	0,160	-0,939	0,350
Contextual early-life conditions					
Infant Mortality Rate					
less than 0.10 (ref.)	0	1			
0.10 ┤ 0.15	-0,0106	0,99	0,039	-0,271	0,790
greater than 0.15	0,0170	1,02	0,026	0,664	0,510
Season of birth					
Winter (ref.)	0	1			
Spring	0,0018	1,00	0,040	0,046	0,960
Summer	0,0404	1,04	0,026	1,558	0,120
Autumn	-0,0165	0,98	0,020	-0,841	0,400
Cohort of birth					
1866-1875 (ref.)	0	1			
1876-1885	-0,2936	0,75	0,060	-4,906	0,000
1886-1895	-0,1205	0,89	0,031	-3,905	0,000
1896-1905	-0,0570	0,95	0,019	-2,927	0,003
1906-1915	-0,0771	0,93	0,016	-4,930	0,000

respect to genetic component variables, it emerges in fact that having at least one sibling that reached 90 years proves to be significant ($p = 0.000$), while only maternal age at death proves to have statistically relevant influence. It is worth noting that age of father at death acts appositely to maternal age reducing the probability of survival. However, since estimates are not significant, it is difficult to speculate on possible reasons for the pattern observed.

The importance of familial dimension proves to be significant also when considering the familial environment. Being born in a family where remarriage occurs proves to be highly significant ($p = 0.000$) and particularly the role of the presence of the father emerges. The loss of the father at an early age in fact implies reduced survival, indicating that economic support occupies a central role in family dynamics and in the level of general welfare.

According to the presented estimates the so-called biological effect variables show to have a limited discriminatory power on longer survival and similarly the other familial shared environment variables considered in the model as well as the contextual early-life conditions, with the exception of birth cohort.

Discussion

The analysis of mortality data at population level revealed that the community of Villagrande Strisaili is a long-living community and that the indications deriving from prior research on the identification of the *Blue Zone* were correct.

The estimation of accurate mortality trajectories of Villagrande Strisaili newborns was greatly favoured by the creation of *Villagrande Longevity Database* (VILD), which present various strong points. On the one hand, it provide high quality data thanks to the data collection strategy adopted and on the other hand, it included information not only on single individuals but also on all family links, including all people alive or dead at the time of the study, thus avoiding consensus concerns. From the results presented, it emerges that both sex and the role of familial variables deserve further investigation. Sex is not a determinant for longer survival among VILD newborns. Males and females record similar survival risk at all advanced ages, which is unexpected result. In addition the relevance of family indicates that the latter is to be considered not only as gene-transmitter but it also influences survival as social environment.

The results achieved in the present research open the way to further studies of this type. The possibilities are vast since a database such as the VILD enables different combinations for comparison with other settings or another possibility lies in the improvement and optimisation of the data contained in VILD itself as well as in the methodology applied.

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