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Survival analysis on mortality data at oldest ages: First results on longevity pioneers in France.

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Abstract. Studying mortality at extreme old ages has been very challenging, mostly because data of good quality are sparse. Decades of hard work of many research teams offered a new type of data on deaths at oldest ages where validated information at individual level are at disposal, which allows us to make use of methods that could not be of use otherwise. Following Barbi et al. (2018), we adopt herein the same analysis, using proportional hazard model on up-to-date French data on deaths at age 105 onwards, to study the evidence for the existence of a plateau of human mortality in France, as it was stated to be proven in Italy. As results, we find a statistically significant and positive Gompertz slope parameter, suggesting that mortality keeps increasing after age 105 instead of being constant. We also find significant effect of sex but no cohort effect on mortality of French semi-supercentenarians.

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Introduction

The shape of mortality at very old ages has been subject of long-time debate, with opinions mainly being divided between a continuation of exponential increase of mortality with ages and a mortality deceleration (i.e., a slowing of mortality increase) as ages advance. The latter, if true, leads to another subcategory of scenarios where the increase of mortality not only decelerates but also becomes constant after a certain age, which is called “the plateau of human mortality”. Hence, if this plateau exists, there would be no limit to human longevity. As a matter of fact, the debate is held on two stages separately: the existence of a deceleration of mortality increase and the existence of plateau of mortality, knowing that the non-existence of the former refutes automatically the latter, and the existence of the former does not necessarily lead to the latter, while the other way around holds true. It is equally noteworthy that the use of methods varies, or rather, is constrained by data that were made available. Different combinations of data and methods fuel current debate with increasing controversies and make it difficult for all to come to a conclusion.

The deceleration of mortality has been well documented since the last decades using aggregated data by authors such as Horiuchi and Wilmoth (1998), Thatcher et al. (1998), Thatcher (1999), and more recently using aggregated validated cohort data (Ouellette and Bourbeau, 2014; Ouellette, 2016). Meanwhile, using single-year extinct birth cohorts from Social Security Administration Death Master File in United-States (US), Gavrilov and Gavrilova (2011) show that in 8 of 10 studied birth cohorts, Bayesian Information Criteria indicates a better fit of Gompertz model compared to logistic model for age interval 88-106 years, suggesting that the mortality trajectory at advanced ages follows an exponential growth up to at least age 105 without noticeable deceleration. Gavrilova and Gavrilov (2015) continue the same approach by extending the number of extinct birth cohorts and age ranges, find the same better performance of Gompertz model over Kannisto model, which suggests the lack of deceleration of mortality

increase for cohorts in US for age interval 80-106. In 2017, Gavrilova, Gavrilov and Krut'ko use individual data from International Database of Longevity¹ (IDL, updated in 2008) to find that mortality keeps increasing after age 110 for all birth cohorts, even though with slower rate for older cohorts. This finding suggests that mortality deceleration at older ages is not a universal phenomenon.

Upon the subject of the limit of human lifespan, many approaches were suggested: either by estimating the level of the plateau of mortality, which would allow eventually to conclude on the absence of limit of human longevity, or by estimating directly the maximum age and its plausible ranges. Using nonparametric approach on individual data of IDL (updated in 2008), Gampe (2010) estimates a constant force of mortality after age of 110 at 0.7 and concludes that there is no limit of human life span. Using gamma-Gompertz model on data of several countries from Human Mortality Database (HMD), Rau et al. (2017) confirm this idea, even though they give higher estimation of force of mortality after age 110 of 0.8 for women and 1.2 for men. On the other hand, Dong et al. (2016) draw attention on the existence of said limit, based on the lack of shifting of improvement in survival to older groups over time and the stagnation of maximum lifespan despite increasing number of oldest old people. The fact of having controversial results simply by different combinations of data and statistical methods is best illustrated by the case of using extreme value theory (EVT). Applying this method on mortality data in the Netherlands, Aarssen and de Haan (1994) show that there exists a finite age limit with 95% confidence interval of 113-124 years. Adopting the same tool on individual data from INSEE for women in France, Barbi et al. (2003) find no evidence to refute the hypothesis that there is no clear limit to human lifespan. Rootzén and Zholud (2017) also come to the same conclusion, this time using IDL data (updated in 2016). Meanwhile, Gbari et al. (2017) make use of individual data of Belgium and find no evidence of a leveling-off and support the existence of an upper limit to human lifetime.

Most recently, Barbi et al. (2018) published in *Science* a study using newly available Italian data on survivors and deaths above age 105, stating having provided evidence for existence of the plateau of human mortality. Their interesting paper using survival analysis on individual-level data gives us idea of testing the same method on our dataset of French population, to see what this method can unfold on mortality at oldest ages and notably whether it could lend us evidence of a plateau of human mortality for French population.

¹ The International Database on Longevity (IDL) is the result of remarkable effort from research teams of many countries to bring together information on individuals who attain extreme ages that were verified thoroughly and thus validated. The IDL constitutes as consequence good materials for the demographic analysis of mortality at the highest ages. In its first version, IDL data contain information on individuals who attained an age of 110 years or more. In its upcoming updated version, IDL data will include also information of individuals who attained 105 years old or more (semi-supercenarians).

Data

Being one of the very few countries in the world in possession of long-history and well-developed civil registrations, data on deaths at age 105 onwards in France come from nominative transcripts from *Répertoire national d'identification des personnes physiques* (RNIPP). Having the same data host as vital statistics (INSEE²) but holding a different approach, RNIPP is a list of individual records where each person is linked to an identification number. By doing so, the system of RNIPP is capable to identify a person without error. Since 2014, under a convention signed between INSEE and French institute of demographic studies (INED), an extract of the RNIPP with limited records where the difference between the date of death and the date of birth is equal or superior to 104 years, is provided to INED. This extract is updated on yearly basis by INSEE for INED according to mutual conditions, and thus makes continuous studies on mortality at extreme old ages in France empirically possible. For the sake of accuracy, we include in our dataset only individuals born and died in France metropolitan, excluding all cases born and/or died in foreigner countries and in DOM-TOM (French overseas departments and territories).

Given that the quality of data at oldest ages depends heavily on the accuracy of reported age at death, the validation of these data follow a pre-determined protocol where the coherence of information found between death certificate and birth certificate must be verified thoroughly for each individual. For deaths occurred at registered ages 110 onwards, the validation process was performed exhaustively for all the supposed supercentenarians. For deaths occurred at registered ages between 105 and 109, which are quite numerous, in a first step the validation process was applied to a first set extracted from RNIPP data, covering deaths occurred between 1988 and 2002. On this set, the exhaustive check was done for the oldest individuals (alleged ages 107, 108, 109). For the rest, a random sample (half of cases alleged age 106 and a third of cases at alleged age 105) were checked. These checks resulted in a very high degree of accuracy of registered ages: 99.7% of cases whose necessary documents were gathered are correct. Consequently, in a second step, we considered that the more recent data given by the subsequent RNIPP extracts do not require any further validation process at ages 105-109. More details on this process can be found in Ouellette et al. (forthcoming). Globally, according to the IDL protocol, French data validation process hence meets the highest validation criteria.

For this study, we collect data on extinct cohorts whose members were followed from age 105 until extinction. As a consequence, there is no occurrence of left-truncated nor right-censored situation, which might be source of biases estimations without proper handling, in our analysis framework. The distribution of observed deaths across birth cohorts and sex can be described in table 1.

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Altogether, we have 19 extinct birth cohorts, covering 3789 observed deaths above age 105 from 1988 to 2016, of which 3485 are females and 304 are males, all free from age misreporting and without data truncating nor censoring. It is clear that females outnumber males considerably at oldest ages, and the number of female survivors increases steadily across birth cohorts.

Table 1. Distribution of deaths by birth cohorts and sex of French population.

Birth cohorts	Females	Males
1883	71	10
1884	73	5
1885	79	11
1886	95	10
1887	124	8
1888	123	11
1889	148	13
1890	142	15
1891	164	13
1892	150	14
1893	204	22
1894	207	21
1895	223	12
1896	240	21
1897	264	19
1898	279	20
1899	236	20
1900	308	27
1901	355	32

Statistical method

Individual trajectories provide us information in continuous time, hence allow us to avoid making assumption about the evolution of mortality within a particular age interval or to avoid aggregating different birth cohorts. Taking advantage of such data, we model survival time after having attained age 105 using Cox proportional hazard model with fixed covariates, where the baseline hazard function follows the Gompertz law and the fixed covariates chosen are birth cohorts and sex:

$$h(t) = h_o(t)\{\exp(\beta_1 C + \beta_2 M)\} = a \exp(bt) \exp(\beta_1 C + \beta_2 M)$$

Herein, C is cohort birth year minus 1891 and $M = 1$ for males and 0 for females, thus β_1 captures cohort effect, β_2 captures gender effect, a is the initial hazard at age 105 and b is the Gompertz slope. As such, the baseline hazard function $h_o(t)$ can be interpreted as the hazard function for subject who was born in 1891 and is female. The key attractions of Cox proportional

hazard with fixed covariates lie on the fact that it allows us to conduct straightforward test for the significance of each parameter, and even if the baseline hazard in the model remains unspecified, it is still possible to evaluate the effect of explanatory variables. In fact, the ratio between the hazard of subject i and that of subject j is computed by the following formula:

$$\frac{h_i(t)}{h_j(t)} = \exp[\beta_1(C_i - C_j) + \beta_2(M_i - M_j)]$$

Since $h_o(t)$ is canceled out, the ratio of the hazards between subjects i and j is constant over time. Graphically, when plotted, the log hazards of subject i and j will be strictly parallel to each other. Hence, the choice of baseline cohort does not have effect on interpretations of our models.

In this paper, we will first study the age pattern of mortality curve, and more precisely by verifying the hypothesis of having a constant mortality above age 105 against the hypothesis that mortality will keep increasing after this age. Statistically, we test the null hypothesis of Gompertz slope parameter being equal to zero against its alternative of nonzero Gompertz slope parameter. This comparison will be done using likelihood-ratio test. For this objective, the likelihood-ratio chi-square statistics is computed as the difference between $-2 \log$ -likelihood of the full model and the null model. By rule of thumbs, we reject the null hypothesis if the p-value is sufficiently small. To check on the sensitivity of our parameter estimates, we also run the same test on other model specifications.

Once this test is done, we will investigate the effect of cohort and sex on mortality after age 105. To do so, we need to choose the model with the best capacity of fitting our observed data. For this matter, we rely on the Akaike Information Criteria (AIC) whose value is determined by the formula: $AIC = -2L + 2k$, where L is the value of maximized likelihood given estimated parameters and k is the number of parameters being estimated. The absolute values of AIC are not interpretable but the difference between AICs can indicate the order of fitting capacity of their respective models. The smaller AIC is, the better the model fits data. When the best model specification is chosen, we will then test the statistical significance of parameters capturing the effect of cohort and sex, its interpretation will base on the hazard ratio given by significant parameters.

Results

1. Constant mortality vs. Gompertz mortality after age 105

We estimate parameters for model of null hypothesis ($b = 0$) and that of alternative hypothesis ($b \neq 0$) by method of maximum likelihood and show results in table 2. A likelihood-ratio test rejects the null hypothesis of constant hazard after age 105 (p-value = 8.181711e-08). Comparison based on AIC also shows that model with nonzero Gompertz slope depicts data better (10878 vs. 10904.77). Based on reported estimations, Gompertz slope b is effectively significant and adopts higher value than what is estimated for Italian population in Barbi et al.

(2018) (0.062 vs. 0.013). Despite the small number of male survivors, gender effect comes out as significant while cohort shows no effect. A positive estimate of gender parameter seems plausible for us and is in agreement with findings from Barbi et al. (2018).

Table 2. Parameter estimates for constant hazard model and Gompertz slope model.

Parameter	Estimate(SE)	Log-likelihood	AIC
<i>Model 1 - Constant hazard, both effects</i>			
a	0.638 (0.013)	-5449.384	10904.77
β_1	0.000 (0.003)		
β_2	0.144 (0.060) *		
<i>Model 2 - Gompertz hazard, both effects</i>			
a	0.580 (0.016)	-5435.002	10878.00
b	0.062 (0.011)		
β_1	0.000 (0.003)		
β_2	0.156 (0.060) **		

We also investigate the cumulative hazard, which is the integral under the hazard curve. We can estimate this indicator using either non-parametric approach or parametric function. For the former, we use Kaplan-Meier estimator. For the latter, we compute the cumulative hazard under both constant and Gompertz hazard by the relation: $H(t) = -\ln[S(t)]$, using parameter estimates reported in table 2. From figure 1, even though both cumulative hazard curves from parametric models lie within confidence band, it seems that Gompertz hazard model (blue curve) fits better to non-parametric estimates than the strictly linear curve under constant hazard assumption (green line).

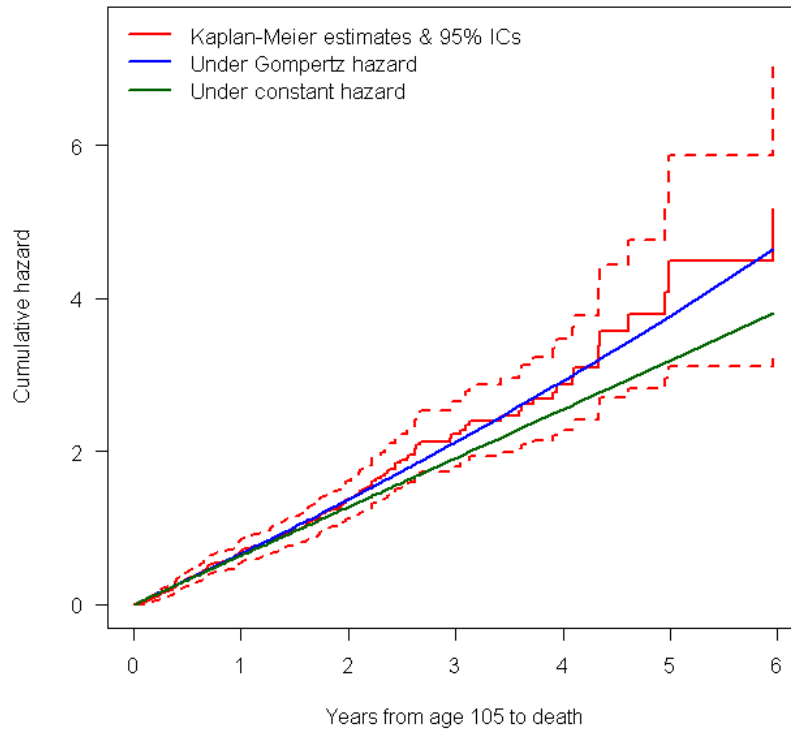


Figure 1. Cumulative hazard beyond age 105 for cohort of French women born in 1891.

2. Cohort and gender effect on mortality after age 105

We continue to investigate other model specifications, aiming firstly to test the sensitivity of parameter estimates, and secondly to choose the model with best performance that could help us drawing reliable remarks about cohort and gender effect on mortality after age 105. Results are presented in table 3.

Across all model specifications, we find that Gompertz slope parameter b is positive and statistically different from 0. Likelihood-ratio tests performed for model 3 vs. model 4 (p-value = $1.314011e-07$), model 5 vs. model 6 (p-value = $8.20229e-08$), model 7 vs. model 8 (p-value = $1.322053e-07$) consistently lead to rejection of null hypothesis where Gompertz slope parameter is equal to 0. Using goodness-of-fit indicator AIC whose ranking is reported in appendix 1, we find that models that take into account Gompertz slope performs systematically better than those assuming constant hazard. Among them, model 6 that includes Gompertz baseline hazard and gender effect shows the best performance. According to this, gender has significant effect on mortality after age 105. Assuming all being equal, the hazard of subject being male is 1.168 times higher than the hazard of female subject (hazard ratio = $\exp(0.155) = 1.168$). As for cohort effect, no effect is detected across model specifications.

Table 3. Parameter estimates in different model specifications.

Parameter	Estimate (SE)	Log-likelihood	AIC
<i>Model 3 – Constant hazard, no effect</i>			
<i>a</i>	0.645 (0.01)	-5452.158	10906.32
<i>Model 4 – Gompertz hazard, no effect</i>			
<i>a</i>	0.589 (0.014)	-5438.235	10880.47
<i>b</i>	0.061 (0.011)		
<i>Model 5 – Constant hazard, gender effect</i>			
<i>a</i>	0.638 (0.011)	-5449.385	10902.77
β_2	0.144 (0.060) *		
<i>Model 6 – Gompertz hazard, gender effect</i>			
<i>a</i>	0.581 (0.014)	-5435.006	10876.01
<i>b</i>	0.062 (0.011)		
β_2	0.155 (0.060) **		
<i>Model 7 – Constant hazard, cohort effect</i>			
<i>a</i>	0.645 (0.012)	-5452.152	10908.3
β_1	0.000 (0.003)		
<i>Model 8 – Gompertz hazard, cohort effect</i>			
<i>a</i>	0.588 (0.015)	-5438.235	10882.47
<i>b</i>	0.061 (0.011)		
β_1	0.000 (0.003)		

Discussion

While considering only data purged from left truncation and right censoring phenomenon, our sample size is 1.3 times bigger than that of Italy (3789 vs. 2883). We made this choice of limiting our data environment exclusively to cohorts whose members could be followed from age 105 until extinction in order to run our analyses without including left truncated and right censored data, in contrary to the case of Italian data reported in Barbi et al. (2018). From another study that we initiate on this topic, preliminary results show that running estimations on complete or incomplete mortality data actually does not render significant difference in terms of value of parameter estimates but rather provides narrower interval confidences for the case of complete mortality data. In other words, data without truncation and censoring allow us to have more precise parameter estimates but have no effect on estimated values. However, an increase in number of observations could very likely change both the level of parameters estimates and their precision. Thus, our next step is to extend our data sample to all deaths occurred above age 105. As such, not only we can increase considerably the number of observations for better estimations, but also the number of birth cohorts integrated to better account for cohort effect. In particular, the lack of cohort effect observed in this paper might effectively be due to the limited number of extinct cohorts. On the scale of 28 years of observation (1988-2016) at our disposal, by including all concerned cohorts, it seems more likely to us to catch the changes of mortality across birth cohorts as well as across observed years. Alternatively, if the cohort effect varies

with ages and thus could not be captured under assumption of proportional hazard, extending the number of birth cohorts will definitely give us more information for more accurate tests. Besides, we also hold doubt that the choices of starting age, which seem arbitrary to us in Barbi et al. (2018) and hence in our paper so that our results could be comparable to theirs, might have effect on modeling age pattern of mortality at oldest ages.

Conclusion

Using standard survival analysis on data of deaths occurred above age 105 in France, we found no evidence for the plateau of human mortality after age 105. Our estimate of Gompertz slope b is not only statistically different from 0 across all model specifications but also has higher value than that estimated from Italian dataset. We also found a significant gender effect and no cohort effect on mortality after age 105 in France. Given many controversies induced by different combinations of data and methods, every new study constitutes to us an additional shedding light to the ongoing debate rather than a final universal answer. Nevertheless, if generalizable remarks were of request, research done on the base of data combining different countries, notably as in the case of IDL, would constitute a reasonable direction. This paper is no exception by all means, with many rooms for improvement.

Appendix 1. Model specifications ordered by AIC.

Rank	Model description	AIC
1	Gender effect, with slope b	10876.01
2	Both effects, with slope b	10878
3	Gompertz hazard	10880.47
4	Cohort effect, with slope b	10882.47
5	Gender effect, without slope b	10902.77
6	Both effects, without slope b	10904.77
7	Constant hazard	10906.32
8	Cohort effect, without slope b	10908.3

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