Biodemography of mortality at extreme old ages: A study of rodents and humans

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The growing number of persons living beyond age 80 underscores the need for accurate measurement of mortality at advanced ages. Earlier studies suggested that the exponential growth of mortality with age (Gompertz law) is followed by a period of deceleration, with slower rates of mortality increase.

Mortality deceleration was challenged in this study by using large samples of survival records for laboratory mice and rats suggesting that mortality deceleration at advanced ages cannot be considered as a general biological phenomenon. This study also challenges earlier conclusions using several sets of human data. Three independent sources of data for the U.S. mortality at advanced ages were analyzed: (1) the U.S. Social Security Administration's Death Master File (DMF), which allowed us to analyze mortality for the extinct birth cohorts (1890-1899); (2) Age-specific death rates for the 1890-1899 U.S. birth cohorts obtained from the Human Mortality Database; (3) Data on 1,711 siblings of validated centenarians drawn from verified and accurate U.S. family histories. The United States turns out to be the largest country with a reasonably good mortality statistics and substantial numbers of survivors to age 100 in every single-year birth cohort. Mortality at advanced ages (85-106 years) was fitted by the Gompertz and the logistic (Kannisto) models and the goodness-of-fit for these models was compared using Akaike and Bayesian information criteria. All analyses were conducted separately for men and women. It was found that for all three data sources the Gompertz model showed better mortality fit than the logistic model in the studied age interval. It was also found that mortality estimates obtained from the DMF data showed good correspondence with the same year Human Mortality Database cohort data.

Simulations showed that some estimates of mortality as well as kernel smoothing of hazard rates may produce spurious mortality deceleration at extreme ages, while the Sacher estimate turns out to be the most accurate estimate of hazard rate. Possible reasons of finding apparent mortality deceleration in earlier studies are also discussed.

Mortality trajectories at very advanced ages

It is now considered as an established fact that mortality at advanced ages has a tendency to deviate from the Gompertz law, so that the logistic model often is used to fit human mortality (Horiuchi and Wilmoth 1998). The estimates of hazard rate at extreme ages are difficult to obtain because of small numbers of survivors to these ages in most countries. Data for extremely long-lived individuals are scarce and subjected to age exaggeration. Traditional demographic estimates of mortality based on period data encounter well known denominator problem. More accurate estimates are obtained using the method of extinct generations (Vincent 1951). In order to obtain good quality estimates of mortality at advanced ages researches are forced to pool data for several calendar periods. Single-year life tables for many countries have very small numbers of survivors to age 100 that makes estimates of mortality at advanced ages unreliable. The aggregation of deaths for several calendar periods however creates a heterogeneous mixture of cases from different birth cohorts. Mortality deceleration observed in these data might be an artifact of data heterogeneity. In addition to that, many

assumptions about distribution of deaths in the age/time interval used for mortality estimation are not valid at extreme old ages when mortality is particularly high.

Mortality deceleration and subsequent mortality plateau (logistic formula) is often presented as universal mortality law. Indeed, the existence of mortality plateaus is well established for a number of lower organisms, mostly insects, including fruit flies , medflies and house flies (Carey et al. 1992; Curtsinger et al. 1992; Curtsinger, Gavrilova and Gavrilov 2006; Gavrilov and Gavrilova 2006; Vaupel et al. 1998). In the case of mammals, however, data are much more controversial. Although Lindop and Sacher reported short-term periods of mortality deceleration in mice at advanced ages (Lindop 1961; Sacher 1966) Austad later argued that rodents do not demonstrate mortality deceleration even in the case of large samples (Austad 2001). Study of baboons found no mortality deceleration at advanced ages (Bronikowski et al. 2002). Recent study of mortality in primates also failed to find mortality deceleration at older ages (Bronikowski et al. 2011). In the case of humans, this problem is not yet resolved, because of scarceness of data and/or their low reliability. Thus, more studies on larger human birth cohorts are required to establish with certainty the true mortality trajectory at advanced ages.

We carried out a study based on the analysis of mortality data for large samples of mice, rats and humans. Data on the laboratory mice and rats have an advantage of more accurate age reporting at advanced ages compared to human data.

Mice data. For mice we used data from the NIH Interventions Testing Program, courtesy of Richard Miller (U of Michigan) and the Argonne National Laboratory data, courtesy of Bruce Carnes (U of Oklahoma). many samples had 1000 or more animals of each sex. The results of mortality estimates for mice data are shown in figures 1-2.
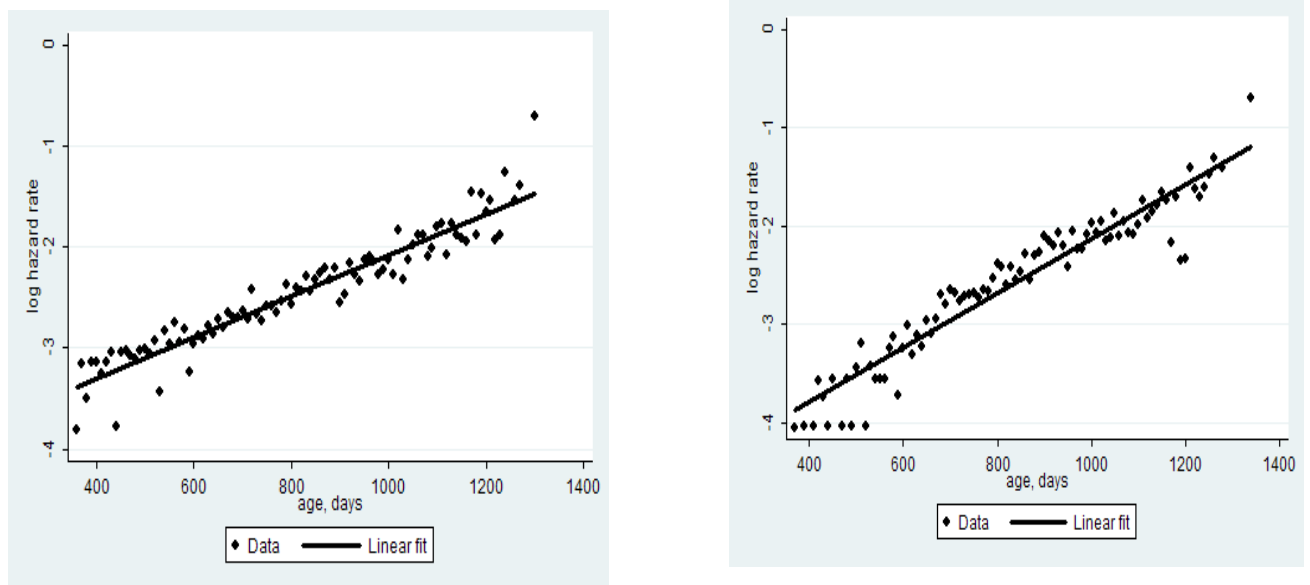

Figure 1. Actuarial estimates of hazard rates (10-day interval) for male (a) and female (b) mice. Miller data.

We compared the Gompertz and the Kannisto models for mice mortality using the Bayesian information criterion. The values of BIC for several mice populations are presented in Table 1. Note that in all cases Gompertz model demonstrates better fit than logistic model for mortality of adult mice aged one year or more.

Rats data.

Data for rat mortality were taken from the published life tables: Dunning, Curtis (1946); Weisner, Sheard (1935), Schlettwein-Gsell (1970). In all cases the initial samples of rats were 1000 animals or larger.
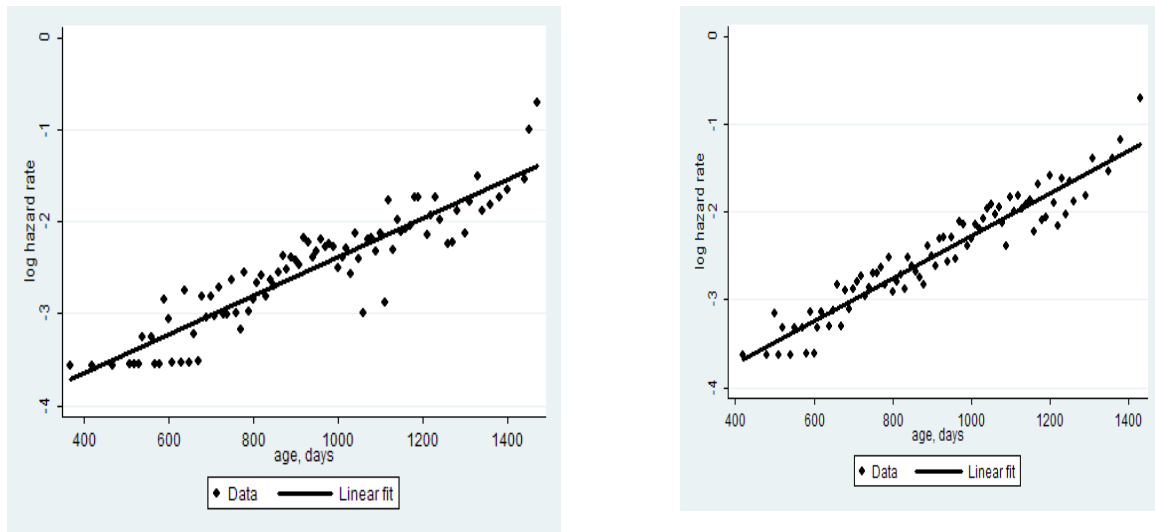
Figure 2. Actuarial estimates of hazard rates (10-day interval) for male (a) and female (b) mice. Argonne National Laboratory data.

Table 1. Values of BIC for mouse data.

Dataset	Sex	Cohort size	AIC criterion	
			Gompertz	Kannisto
Miller data, controls	M	1281	-597.5	-565.6
	F	1104	-496.4	-495.4
Miller data, experiments with no life extension	M	2181	-660.4	-571.3
	F	1911	-580.6	-577.2
ANL data, early controls	M	364	-585.0	-556.3
	F	431	-566.3	-558.4
ANL data, late controls	M	487	-639.5	-638.7
	F	510	-549.6	-548.0

We may conclude that in all cases the Gompertz model described rodent mortality better than the Kannisto model. These results are in line with earlier reports by Austad and recent data obtained for primates (Bronikowski et al., 2011).

We also carried out a study based on the analyses of data taken from the U.S. Social Security Administration Death Master File (SSA DMF). Social Security Administration Death Master File (DMF) is a publicly available data source that allows a search for deceased individuals in the United States using various search criteria: birth date, death date, first and last names, social security number, place of last residence, etc. This resource covers deaths that occurred in the period 1937-2010 and captures about 95% of deaths recorded by the National Death Index (Sesso, Paffenbarger and Lee 2000). According to other estimates, DMF covers about 92-96 percent of deaths for persons older than 65 years (Hill, Rosenwaike, 2001).

Social Security Administration Death Master File (DMF) was used in our study of age-related mortality dynamics after ages 85 years. The advantage of this data source is that some

already extinct birth cohorts covered by DMF could be studied by the method of extinct generations (Kannisto 1988, 1994; Vincent 1951). Information available in DMF includes: names of the deceased, his/her social security number, date, month, year of birth, month and year of death, state of SSN issuance, place of the last residence. In this study information from the DMF was collected for individuals who lived 88 years and over and died before 2011. DMF database is unique because it represents mortality experience for very large birth cohorts of the oldest-old persons. In this study mortality measurements were made for cohorts, which are more homogeneous in respect to the year of birth and historical life course experiences. Availability of month of birth and month of death information provides a unique opportunity to obtain hazard rate estimates for every month of age, which is important given extremely high mortality after age 100 years.
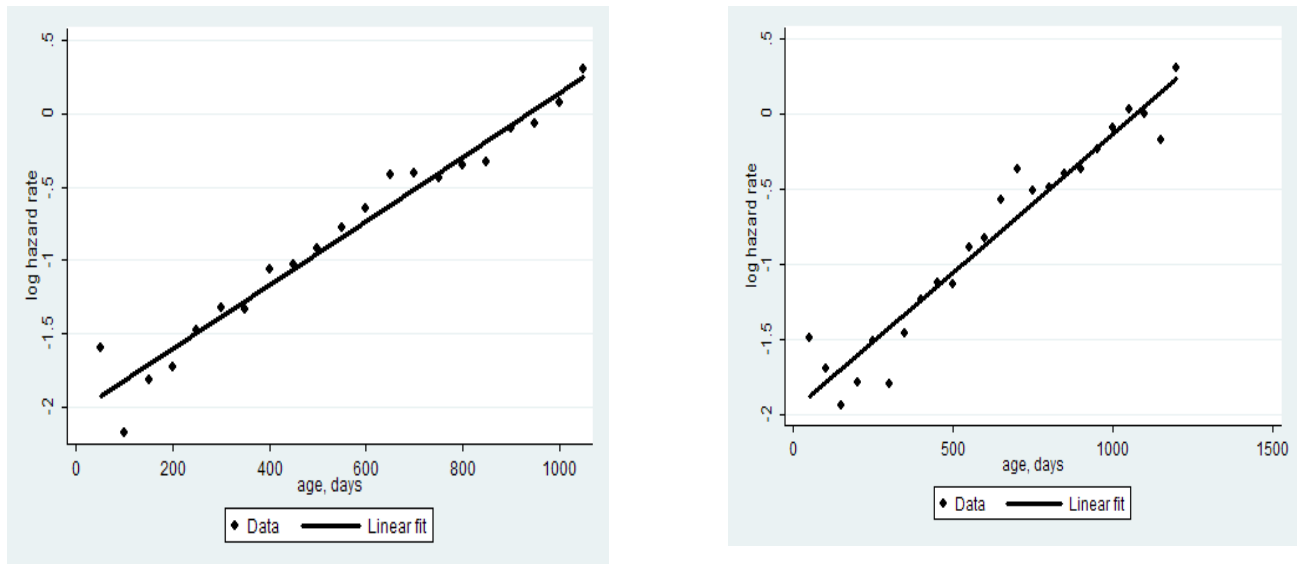

Figure 3. Actuarial estimates of hazard rates (50-day interval) for male (a) and female (b) laboratory Wistar rats. Data source: Weisner, Sheard (1935).

Table 2. Values of BIC for rats data.

Line	Wistar (1935)		Wistar (1970)		Copenhagen		Fisher		Backcrosses	
Sex	M	F	M	F	M	F	M	F	M	F
Cohort size	1372	1407	1372	2035	1328	1474	1076	2030	585	672
Gompertz	-34.3	-10.9	-34.3	-53.7	-11.8	-46.3	-17.0	-13.5	-18.4	-38.6
Kannisto	7.5	5.6	7.5	1.6	2.3	-3.7	6.9	9.4	2.48	-2.75

We obtained data for persons who died before 2011 and were born in 1890-1899 from the National Technical Information Service (NTIS) – an official distributor of DMF data. The last deaths in the obtained dataset occurred in September 2011. Assuming that the number of living persons belonging to these birth cohorts in 2010 is close to zero, it is possible to construct a cohort life table using the method of extinct generations, which is considered to be the most accurate method to study old-age mortality (Kannisto 1994). In the first stage of our analyses we calculated an individual life span in completed months:

Lifespan in months = (death year – birth year) x 12 + death month – birth month

Having this information it is possible to estimate hazard rates at each month of age by standard methods of survival analysis. All calculations were done using the Stata statistical software, release 11 (StataCorp 2009). This software calculates nonparametric estimates of major survival functions including the Nelson-Aalen estimator of hazard rate (force of mortality). In this study, survival times were measured in months, so the estimates of hazard rates initially had a dimension of month^{-1}. For the purpose of comparability with other published studies, which typically use the year^{-1} time scale, we transformed the monthly hazard rates to the more conventional units of year^{-1}, by multiplying these estimates by a factor of 12 (one month in the denominator of hazard rate formula is equal to 1/12 year). It should be noted that hazard rate, in contrast to probability of death, can be greater than 1, and therefore its logarithm can be greater than 0 (and we indeed observed these values at extreme old ages in some cases). In this study we focus our analyses on 1890-1899 birth cohorts for persons applied for SSN in non-Southern states, because we found that data quality for earlier cohorts and 'Southern' states are not particularly good (Gavrilov, Gavrilova, 2011).

Results of the hazard rate estimates for 1898 female birth cohort are presented in Figure 3. Note that mortality trajectory in semi-log scale is linear up to the age 106-107 years. After age 106 years data points show high variation suggesting declining data quality (possible age misreporting). One approach to evaluate data quality at advanced ages is to calculate female to male ratio at advanced ages. Taking into account that female mortality is always lower than male mortality it is reasonable to expect that the female-to-male ratio should continuously increase with age. On the other hand, old men have a tendency for age exaggeration and in populations with poor age registration there is a relative excess of men at very advanced ages (Caselli et al. 2006; Willcox et al. 2008). In our previous study we calculated female-to-male ratio after age 95 years for 1890-1894 U.S. birth cohorts from the SSA DMF (Gavrilov, Gavrilova, 2011). It was shown that the female to male ratio was growing steadily with age up to ages 106-107 years. After this age the female-to-male ratio starts to decrease indicating declining quality of age reporting. Thus, the estimates of hazard rates obtained from the SSA DMF are of acceptable quality up to the age of 106 years. For this reason we used age interval 88-106 years for mortality modeling.
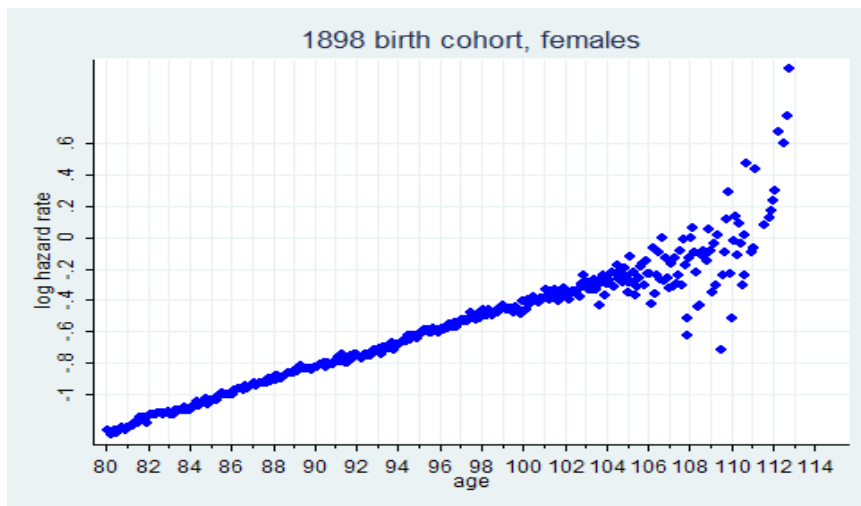

Figure 3. Nelson-Aalen monthly estimates of hazard rates using Stata 11

Next step of our study was to compare two competing models of mortality at advanced ages - the Gompertz and the logistic models - using data of reasonably good quality. Study of data quality of at advanced ages described above suggests that age reporting among the oldest-old in the United States is good until the age of 106 years. It means that comparing mortality models beyond this age is not feasible because of poor quality of mortality data. It was

shown that age reporting for persons applied to Social Security Numbers in the Southern states of the U.S. is significantly less accurate compared to persons applied in the Northern states regardless of race. (Rosenwaike and Stone 2003). For this reason, we used a subsample of deaths for persons applied to SSNs in the 'Northern' states and born in 1886-1895, because these data have reasonably good quality. We applied the Gompertz and logistic (Kannisto) models (Thatcher, Kannisto and Vaupel 1998) to mortality modeling in the age interval 88-106 years using nonlinear regression method for parameter estimation. Calculations were performed using Stata statistical software, release 11 (StataCorp 2009). Akaike information criterion (AIC) was used as a goodness-of-fit measure. Table 1 shows values of BIC for both Gompertz and logistic model for ten studied birth cohorts. Note that in 8 out of 10 cases (studied birth cohorts), the Gompertz model demonstrates better fit (lower AIC) than the logistic model for age interval 85-106 years.
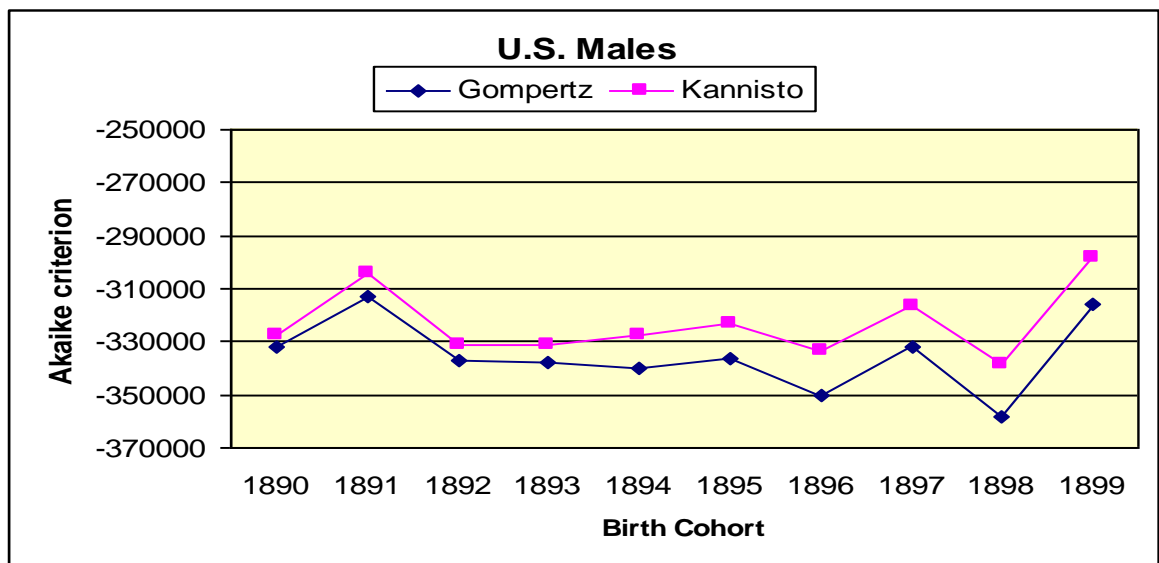

Figure 4. Akaike information criterion (AIC) to compare Kannisto and Gompertz models, birth cohort (men, non-Southern states)
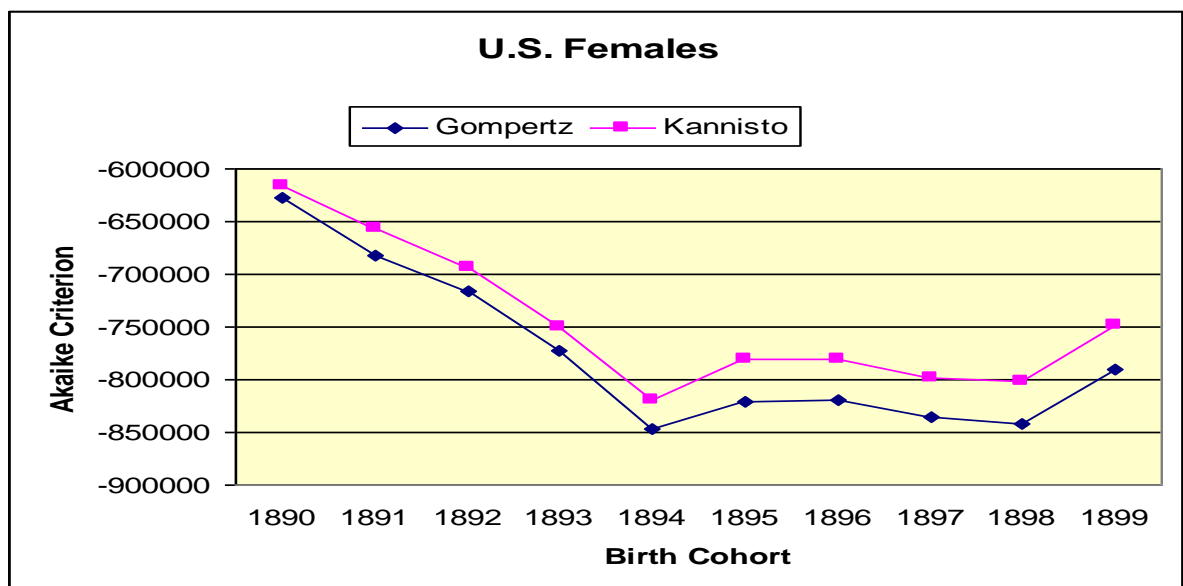

Figure 5. Akaike information criterion (AIC) to compare Kannisto and Gompertz models, birth cohort (women, non-Southern states)

Note that in all cases Gompertz model demonstrates better fit than logistic model for describing mortality of U.S. men and women in age interval 85-106 years

Human Mortality Database data

Another study of mortality trajectories in humans was carried out for the U.S. cohort death rates taken from the Human Mortality Database. In this case the U.S. cohort central death rates were compared using the Gompertz and the Kannisto models in the 80-106 years age interval. This was done with nonlinear weighted regression model for parameter estimates (Stata 11) where age-specific exposure values were used as weights (Muller at al., Biometrika, 1997). Model goodness-of-fit was estimated using AIC and BIC. Figures 6 and 7 shows AIC values for studied populations of men and women.
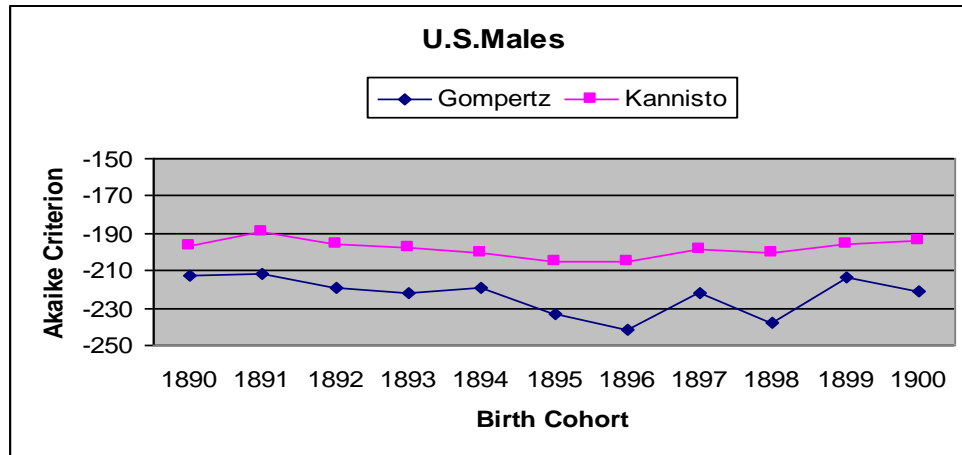

Figure 6. Akaike information criterion (AIC) to compare Kannisto and Gompertz models, by birth cohort (men, HMD U.S. data)
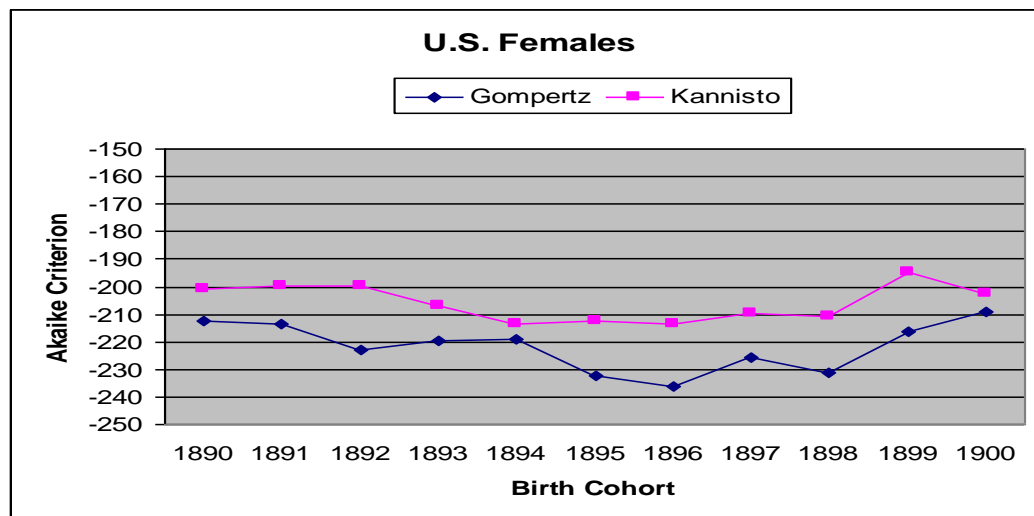

Figure 7. Akaike information criterion (AIC) to compare Kannisto and Gompertz models, by birth cohort (men, HMD U.S. data)

Note that in all studied cases the Gompertz model showed better fit of the data compared to the Kannisto model.

At this moment, we cannot make a conclusion that Gompertz model fits mortality data better than the logistic model beyond the age of 106 years, because of low quality of age reporting at very old ages. At the same time, the data indicate that the Gompertz model fits mortality data well until the age 106 years. Taking into account that survival beyond age 106 years is rather rare event, it would be reasonable to suggest the use of Gompertz model rather than logistic model for closing cohort life tables in demographic practice. In this case, mortality modeling could be done first for hazard rate (mortality force) function and then all life table functions (including probability of death, q_x) could be derived on the basis of modeled values of hazard rate. Thus the Gompertz model fits mortality reasonably well up to the age of 106 years.

Comparison of DMF data with mortality from the Human Mortality Database (for the same birth cohort) showed that DMF mortality estimates are similar to mortality estimates obtained from the Human mortality database (see Figure 8). Note that the slope of mortality in semi-log scale does not change at advanced ages refuting the hypothesis of two-stage Gompertz.
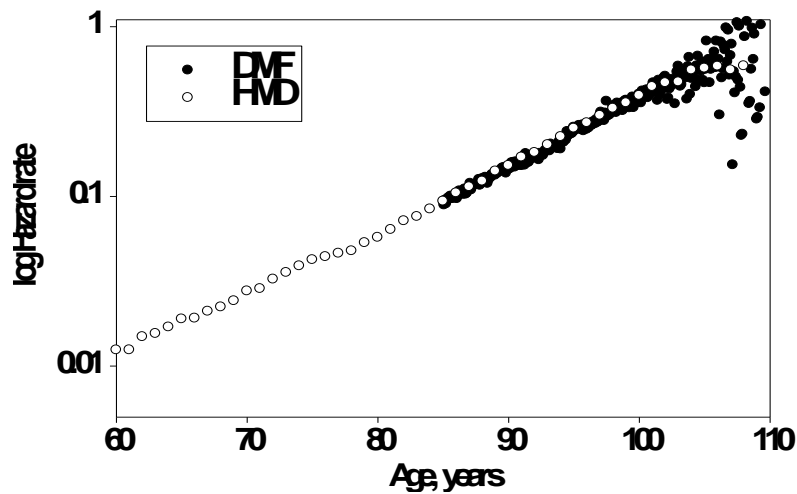

Figure 8. Mortality of U.S. females born in 1898 according to DMF data and HMD data.

Our study of late-life mortality based on the U.S. SSA Death Master File and HMD suggests that for rather homogeneous single-year birth cohorts mortality at advance ages does not decelerate up to very advanced ages. In order to make an independent check of our findings we used another dataset. We have developed and analyzed a new computerized database on 1,711 validated centenarians born in the United States in 1880-1895, as well as their 13,392 shorter-lived siblings. These data were collected from the Rootsweb publicly available database using web-automation technique for centenarians having information on lifespan of their parents and the majority of their siblings. Additional validation of centenarian age through the SSA DMF and early censuses ensured high quality of life histories and information on siblings in particular. For the purpose of mortality study, we used only those siblings who were born before 1880, i.e. not in the same time window as the selected centenarians. As a result, 1,895 siblings born in 1856-1879 were identified and 1681 siblings survived to age 60 were used for mortality analysis. Figure 9 shows the hazard rate trajectory (in semi-log scale) for this group of siblings using 6-month age intervals for hazard rate estimation by actuarial method (Kimball 1960). Note that mortality trajectory after age 60 years does not show a tendency for deceleration despite rather heterogeneous nature of the sample (mixture of different birth cohorts, men and women).
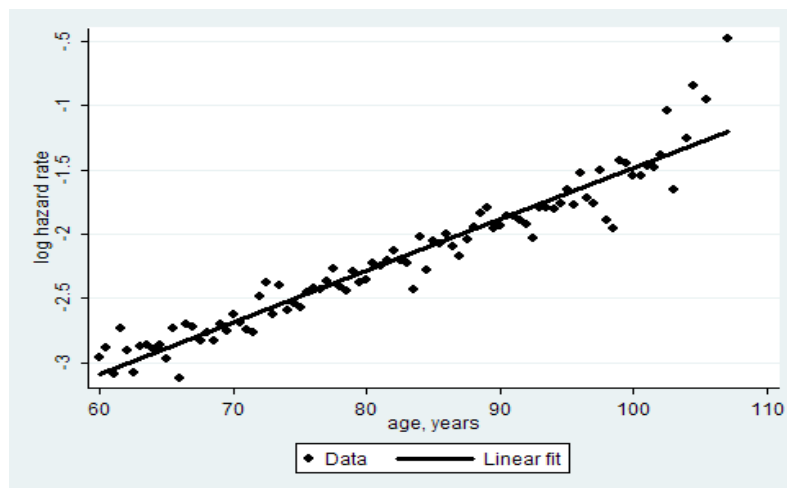

Figure 9. Age-specific hazard rate for 1681 siblings of centenarians born before 1880 and lived 60 years and more. Hazard rate was estimated for 6-month age intervals.

Few people survive to advanced ages and, in standard mortality tables, it is frequently necessary to compile data over an entire decade to obtain a sufficiently large sample. Our work shows that the observed deceleration in measured mortality rates could result in part from the heterogeneity of the data. There consequently remains a great deal of research to carry out if we are to improve our understanding of mortality at advanced ages. The second problem we examined is frequently overlooked by demographers and actuaries: the problem of correct estimation of the instantaneous mortality rate (hazard rate). At the most advanced ages, the rates of death are so high that it is impossible to assume that the number of dying is distributed uniformly within the studied one-year intervals. As a result, the estimates of mortality rates (or central death rates) are biased downwards at advanced ages. And finally, the third problem is related to the fact that elderly people tend to round their ages up, thereby exaggerating their true age. In the United States, this may have made impaired the accuracy of mortality rate estimates in the past.

Study of rodent data help to reinforce our previous findings that mortality in homogeneous cohorts is not subjected to deceleration at old ages (Gavrilova, Gavrilov, 2011). Data for laboratory animals do not suffer from age misreporting and animal environmental conditions can be strictly controlled over time.

The results of our study suggest that mortality deceleration is not a universal phenomenon at advanced ages, but rather a result of age misreporting, data heterogeneity and problems with proper estimation of hazard rates.