

HUMAN DEMOGRAPHY

The plateau of human mortality: Demography of longevity pioneers

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Theories about biological limits to life span and evolutionary shaping of human longevity depend on facts about mortality at extreme ages, but these facts have remained a matter of debate. Do hazard curves typically level out into high plateaus eventually, as seen in other species, or do exponential increases persist? In this study, we estimated hazard rates from data on all inhabitants of Italy aged 105 and older between 2009 and 2015 (born 1896–1910), a total of 3836 documented cases. We observed level hazard curves, which were essentially constant beyond age 105. Our estimates are free from artifacts of aggregation that limited earlier studies and provide the best evidence to date for the existence of extreme-age mortality plateaus in humans.

Survival to extreme ages tests the limits of evolutionary demographic potential. Here we report a curve of death rates by age for recent cohorts of Italians, a curve that is essentially level from age 105 and beyond. In so doing, we address what is both nearly the oldest question and also the most current question in the formal study of human senescence: Are there limits to the rise in risks of death by age?

In his 1825 proposal of the first model for accelerating, exponential increases in human mortality by age, Benjamin Gompertz (1) cautiously included an upper bound on ages of applicability. For a long time, the question of whether to attribute apparent deviations at extreme ages to age misreporting or to structural processes seemed impossible to settle. After 1990, as data improved, studies (2–7) began to build a case for genuine deceleration of mortality rates from about age 80 onward, in contrast to the clearly exponential curves observed for younger adults. When a mor-

tality curve levels out, it is said to reach a plateau. The findings for humans are consistent with discoveries of plateauing mortality at extreme ages in other species (8) and have stimulated a wave of biodemographic and evolutionary theorizing. Other studies, however, have reached an opposing conclusion: The better the data, the lesser the appearance of leveling (9, 10). A recent work (11) based on the analysis of sparse but high-quality data from a collection of countries reported exponential increases persisting even beyond age 110.

If claims of extreme-age plateaus in human mortality turned out to be generally illusory, much of the demographic modeling of the past two decades would have to be rethought. Here, to the contrary, we show a clean case where the plateau is real.

Accurate mortality data for people at advanced ages are difficult to obtain. In vital statistics, the very old are often aggregated in one age-group. Even in countries with reliable vital registration,

age exaggeration is common among the oldest old. These difficulties prompted the establishment of an international research team to collect, analyze, and meticulously check data on people who reach ages ≥ 110 years—“supercentenarians”—in 15 countries, including Italy. The Max Planck Institute for Demographic Research’s International Database on Longevity (IDL) (www.supercentenarians.org), updated through 2010, is the result of this decade-long effort.

This database made it possible to estimate mortality rates after age 110 (12). The hazard function, the usual continuous-age version of mortality rates as a function of age, turned out to appear constant at least up to age 114, after which data became too sparse for reliable statements. For this result, data on supercentenarians had to be pooled from 11 countries to arrive at adequate sample sizes. Country-specific estimates were not feasible because individual countries do not provide enough observations to limit sampling variation. Within the limits of precision, supercentenarian hazards showed no improvement over time. These findings have been challenged (11) with analysis of the same IDL data by different methods. In the wake of limitations on precision and continuing controversy, the IDL project is now being extended to cover people who survive to age 105 and beyond.

In conjunction with the IDL extension, the Italian National Institute of Statistics (ISTAT)

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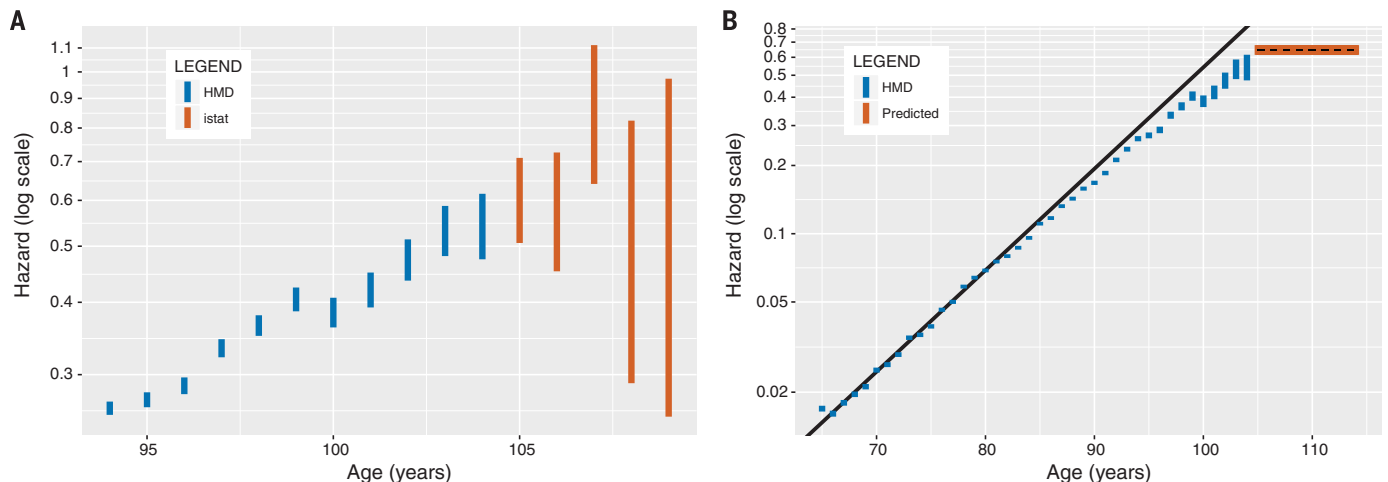


Fig. 1. Yearly hazards on a logarithmic scale for the cohort of Italian women born in 1904. Confidence intervals were derived from Human Mortality Database (HMD) data for ages up to 105 and from ISTAT data beyond age 105. (A) Closeup with 95% confidence intervals based solely on single-cohort data. (B) Broad view with estimated plateau beyond age 105 (black dashed line) and 95% confidence bands (orange) predicted from the model parameters based on the full ISTAT database, along with a straight-line prediction (black) from fitting a Gompertz model to ages 65 to 80.

Table 1. Distribution of the observed cases. Age at entry into study is given in computed years.

Cohort	Age at entry into study	Males		Females		No. reaching 105
		Censored	Observed deaths	Censored	Observed deaths	
1896	112	0	0	0	4	≥4
1897	111	0	0	0	1	≥1
1898	110	0	0	0	5	≥5
1899	109	0	0	1	12	≥13
1900	108	0	0	0	23	≥23
1901	107	0	7	0	46	≥53
1902	106	0	17	2	134	≥153
1903	105	0	23	2	195	≥220
1904	105	0	35	5	302	342
1905	105	2	40	10	331	383
1906	105	2	48	19	348	417
1907	105	11	55	40	354	460
1908	105	19	57	106	345	527
1909	105	28	33	219	296	576
1910	105	64	22	423	150	659
Total		126	337	827	2546	≥3836

has recently collected and validated the individual survival trajectories of all inhabitants of Italy aged 105 and older in the period from 1 January 2009 to 31 December 2015; these data were used for the present study. For several reasons, these data allow estimation of mortality at extreme ages with accuracy and precision that were not possible before. First, individual trajectories provide information on survival in continuous time, therefore avoiding possibly misleading patterns of death rates that are computed on prespecified age intervals and are often obtained by aggregating heterogeneous birth cohorts. Second, the validation procedure has been developed specifically for this population segment and meets the highest validation criteria provided by the IDL protocol. It is based on the resident population of the Italian municipalities that is recorded yearly on 1 January. Each municipality where individuals aged ≥105 have been reported was contacted by ISTAT. A death certificate was required for each deceased subject. This certificate includes, among other information, the date of birth of the deceased individual, as certified by the civil status officer. A certificate of survival was required for all individuals who were expected to still be alive at the end of the study period. For supercentenarians, those most problematic in terms of age reporting, birth certificates were also collected. Hence, age misreporting is believed to be minimal in these data. The project includes all individuals 105 and older in the period from 1 January 2009 to 31 December 2015, so the data are also free of age ascertainment bias.

The present study based on ISTAT data includes 3836 cases, 463 of whom are males, across 15 birth cohorts (one for each year from 1896 to 1910). Fewer than 4% of these individuals were born abroad. Of those, many have clear Italian heritage (13). Altogether, 472 individuals born be-

fore 31 December 1903 (birth cohorts 1896–1903) entered the study at ages older than exactly 105 and, as such, provided left-truncated survival trajectories. Death during the follow-up was observed in 2883 cases; as a result, 953 individuals were right-censored (i.e., still alive at the end of the study). Table 1 displays the distribution of observed deaths and censored trajectories across gender and cohort. Increases in samples from row to row bear testimony to improvements in survival from cohort to cohort at ages before 105 and lead us to expect the downward cohort trend in hazards beyond age 105 in our data to be described below.

For context, Fig. 1A shows confidence intervals for logarithms of yearly hazards for the single-year cohort of Italian women born in 1904. For ages before 105, intervals were derived from vital statistics in the Human Mortality Database (www.mortality.org). These widening intervals, also likely distorted by age misreporting, only hint at decreasing slopes. Beyond age 105, intervals were derived from ISTAT data restricted to this single cohort, with separate intervals for each year of age. Even with these high-quality data, separating out cohorts and ages leaves too much uncertainty to tell whether hazards continue upward, level out, or decrease beyond 105. Hence, we fit a model that combines cohorts and ages to circumvent this challenge. Our best-estimated trajectory for the 1904 cohort from our modeling is the flat curve (the plateau) shown in Fig. 1B. On a log scale, exponential curves become straight lines. A straight-line fit based on ages 65 to 80, where the Gompertz model does appear to hold, fails at older ages and far overshoots our estimated plateau beyond age 105.

To determine from the full ISTAT data whether log-hazard slopes are level, upward, or downward after age 105, our modeling approach compares a null hypothesis of constant hazards

to alternatives with a nonzero Gompertz slope parameter. We include a (modest) exponential cohort trend and a proportional gender effect, setting the hazard at age x years beyond 105 equal to

$$ae^{bx}e^{\beta_1 C + \beta_2 M}$$

with b constrained to zero for the null model. Here, C is cohort birth year minus 1904, and $M = 1$ for males but is otherwise set to 0. Parameters include initial hazard a at 105, Gompertz slope b , cohort effect β_1 , and gender effect β_2 .

Parameters estimated by standard maximum likelihood methods for truncated and censored survival data (14) are shown in Table 2. A likelihood ratio test fails to reject the constant-hazard null model at a level as generous as 0.44. Under the alternative hypothesis, the Gompertz slope parameter estimate $b = 0.013$ [standard error (SE) = 0.017] is not statistically significant at the 5% level and is practically indistinguishable from 0. This near-negligible slope stands in contrast to the slope as large as 0.103 at younger ages (65 to 80) in Fig. 1B, which is paired with a log hazard at 65 of $\log(0.015)$. For variant models and power calculations, see tables S1 and S2.

The estimated cohort effect $\beta_1 = -0.020$ (SE = 0.008), though small, is in line with expectations, statistically significant, and noteworthy (13). The 463 male survivors older than 105 are too few for the gender effect to come out statistically significant, though the estimate $\beta_2 = 0.033$ is plausible.

For the baseline cohort born in 1904, the estimated level of the plateau is $a = 0.645$. It corresponds to an annual probability of dying of $1 - e^{-0.645} = 0.475$ and an expectation of further life of $1/0.645 = 1.55$ years. This outcome is consistent with the probability estimated elsewhere for supercentenarians (12). With 90% of person-years at risk (a measurement of total time at risk) coming before age 108, the ISTAT data do

Table 2. Parameter estimates for preferred model. Difference in log-likelihoods: 0.292. AIC, Akaike information criterion; a, baseline hazard; b, Gompertz slope; β_1 , cohort effect; β_2 , gender effect.

Parameter	Estimate (SE)	Log-likelihood	AIC
<i>Constant hazard model</i>			
a	0.645 (0.016)	-4250.662	8507.325
β_1	-0.020 (0.008)		
β_2	0.033 (0.058)		
<i>Gompertz hazard model</i>			
a	0.629 (0.026)	-4250.370	8508.740
b	0.013 (0.017)		
β_1	-0.016 (0.009)		
β_2	0.034 (0.058)		

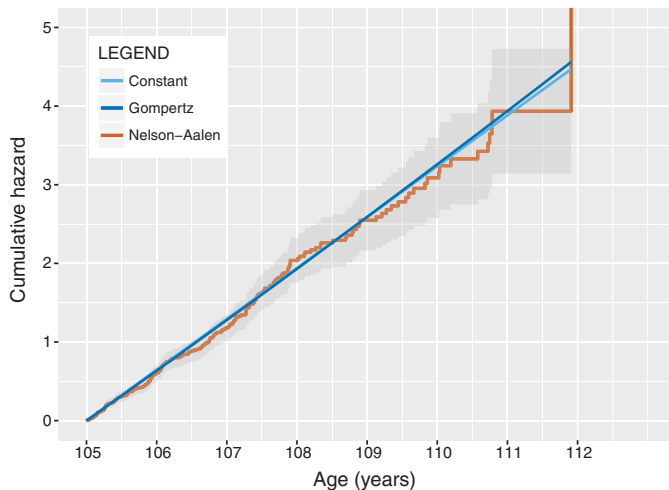


Fig. 2. Cumulative hazard beyond age 105 for the cohort of Italian women born in 1904, as determined by the Nelson-Aalen estimator. Straight lines represent cumulative hazards of the estimated plateau predicted from ISTAT data, under a constant hazard (light blue) and a Gompertz hazard model (darker blue). The shaded area indicates the 95% confidence bands of the Nelson-Aalen estimate.

not enable us to rule out alternatives, such as a plateau followed somewhat later by a decline, but supercentenarian estimates provide indications against such alternatives.

Our estimates based on all ISTAT cohorts together produce excellent fits for single cohorts. We examine the cumulative hazard, the integral under the hazard curve, for which nonparametric confidence bounds are available (14). Hazards that are constant imply cumulative hazards that are linearly increasing; poor fit would stand out as curvature. The plot in Fig. 2 shows absence of curvature in the data for Italian women born in 1904.

The increasing number of exceptionally long-lived people (Table 1) and the fact that their mortality beyond 105 is seen to be declining across cohorts—lowering the mortality plateau or postponing the age when it appears—strongly suggest that longevity is continuing to increase over time and that a limit, if any, has not been reached. Our results contribute to a recently rekindled debate (15–17) about the existence of a

fixed maximum life span for humans, underwriting doubt that any limit is as yet in view.

Our findings further provide fundamental knowledge about the biodemography of human longevity. By using clean data from a single nation and straightforward estimation methods, we have shown that death rates, which increase exponentially up to about age 80, do decelerate thereafter and reach or closely approach a plateau after age 105. Thus, these well-estimated hazard curves share the qualitative pattern observed for extreme ages in widely differing species (8, 18), regularities calling for common structural and evolutionary explanations.

An important structural contributor to mortality rate deceleration must be the impact of selective survival in heterogeneous populations. The fixed-frailty proportional hazard model of Vaupel *et al.* (19) [with precursor (20)] implies approach to plateaus (5, 8, 18), and Gamma-Gompertz distributions for deaths arise naturally in the framework (21–24). Enhanced care for the extremely old may help to mitigate in-

creases in mortality. Evolutionary theories of senescence, including the mutation accumulation theory and age-dependent effects of genetic load (25), also offer promising ingredients toward a joint explanation of both the phases of exponential increase and extreme-age plateaus. Ongoing theoretical progress depends on empirical clarity, and we hope to promote such clarity with the data and estimates reported here.

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SUPPLEMENTARY MATERIALS

www.sciencemag.org/content/360/6396/1459/suppl/DC1
Materials and Methods
Fig. S1
Tables S1 to S3
References (26, 27)

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Mortality rates level off at extreme age

The demography of human longevity is a contentious topic. On the basis of high-quality data from Italians aged 105 and older, Barbi *et al.* show that mortality is constant at extreme ages but at levels that decline somewhat across cohorts. Human death rates increase exponentially up to about age 80, then decelerate, and plateau after age 105.

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