



# Compensation Effect of Mortality as a Challenge to Life Extension





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# Compensation Effect of Mortality as a Challenge to Life Extension

# ABSTRACT

The compensation effect of mortality (CEM) refers to mortality convergence at advanced ages, when higher values for the Gompertz slope parameter are compensated by lower values of the intercept parameter (initial mortality) in different populations of humans. The age of this convergence point is called the "species-specific life span." Because of CEM, factors associated with life span extension are usually accompanied by a paradoxical increase in the actuarial aging rate (a slope parameter of the Gompertz law). The main objective of this study is to evaluate the stability of CEM and to analyze the relationship between the slope and the intercept parameters of the Gompertz-Makeham equation in contemporary human populations. We used United Nations abridged life tables for 241 countries and regions (covering 13 time periods per country, from 1950 to 2015, total 6,266 life tables). Parameters of the Gompertz-Makeham model (intercept parameter R, slope parameter  $\alpha$  and Makeham term A) were estimated for each population (life table) using the method of nonlinear regression in the age interval 30–80 years. Then parameters of linear regression for lnR as a dependent variable and  $\alpha$  as a predictor variable have been estimated. Applying the Gompertz-Makeham model to mortality data from the OECD countries with better demographic statistics (1,118 life tables) produced the following estimate of the species-specific lifespan: 94.69± 0.46. This new estimate of the species-specific lifespan (the age of mortality convergence) is virtually the same as an estimate obtained more than 30 years ago for much older UN data, 95±2 years. Thus, the convergence point of CEM is stable despite significant mortality decline over the past 50 years and is not affected by factors decreasing mortality at younger ages.

Populations with a slow aging process can be found among those with both a slow actuarial aging rate and low initial mortality (intercept parameter of the Gompertz law) and are identified in this study.

# INTRODUCTION

The compensation effect of mortality (CEM) refers to mortality convergence at advanced ages, when higher values for the slope parameter of the Gompertz model are compensated by lower values of the intercept parameter (initial mortality) in different human populations (Gavrilov and Gavrilova 1991). The age of this convergence point is called the "species-specific life span." Because of CEM, factors associated with life span extension are usually accompanied by a paradoxical increase in the actuarial aging rate (a slope parameter of the Gompertz law).

In 1960 Bernard L. Strehler and Albert S. Mildvan found an inverse relationship between the parameters of the Gompertz law: in those countries where the values of the pre-exponential multiplier (designated as  $R_0$ ) were high, the values of the exponential index ( $\alpha$ ) were reduced (Strehler and Mildvan 1960). Subsequently, this observation became known as the Strehler-Mildvan correlation, and it acquired the status of a fundamental law describing the survivorship of organisms.

Later Gavrilov and Gavrilova questioned the Strehler-Mildvan approach and demonstrated that varying the Makeham parameter from 0 to 0.01 per year is sufficient to produce spurious Strehler-Mildvan correlation (Gavrilov and Gavrilova 1991).Comparison of this spurious correlation with correlation published by Strehler and Mildvan (1960) showed very good agreement between these two correlations. This example shows that a discussion of what appear to be purely methodological questions can lead to important conclusions. Indeed, the correlation claimed by

Strehler and Mildvan is widely cited without any serious critical analysis, and attempts to use the Strehler and Mildvan correlation in constructing mathematical models of aging lead to absurd results. From the data presented in the article by Strehler and Mildvan, it follows that the slope coefficient of the linear regression of  $\ln R_0$  with  $\alpha$  is only 68.5 years. However, in the framework of the "General theory of mortality and aging" by Strehler and Mildvan, this quantity ought to correspond to the age at which so-called vitality, "the capacity of an individual organism to stay alive" (p.15), becomes zero. The inconsistency of these consequences of the Strehler-Mildvan correlation was pointed out by the French demographer Hervé Le Bras (1976). Indeed, the value of the species-specific limit to the human life span turns out to be significantly less than the average life span for many countries.

Later, Gavrilov and Gavrilova attempted to improve the approach applied by Strehler and Mildvan and take into account the Makeham parameter. In the course of this study they found the so-called compensation law of mortality (Gavrilov and Gavrilova 1991). It turns out that, within the limits of a single species, the values of the age-dependent component of mortality (Gompertz term) are correlated in such a way that, when extrapolated, they meet at a single point. It can be seen that this intersection at a single point is related to the fact that the reduction in the level of the age-dependent component of mortality in the transition to more fortunate populations is compensated by an increase in the relative rates at which it grows with age (or actuarial aging rate), hence the name "compensation effect of mortality" (Gavrilov and Gavrilova 1991). It is clear that the coordinates of the point of intersection, because of the very principle used to calculate them, are invariant relative to the living conditions and genetic characteristics of the populations under comparison. In other words, they reflect the most general (species-specific) characteristics of the life span distribution for populations of the same biological species. On these grounds, the coordinate corresponding to the age at which all the dependencies intersect has been called the "species-specific life span" (Gavrilov and Gavrilova 1991). It was found that for humans its value is 95±2 years (Gavrilov and Gavrilova 1991).

It should be noted that the CEM is observed regardless of the parameter estimation when the logarithm of mortality for several populations is plotted against the age. In this case one can see an inevitable mortality convergence at older ages (around age 95 years). Parameter estimation of the Gompertz model serves merely as quantification of this effect.

Summarizing this earlier research on the topic, we need to note that these studies were conducted many years ago, and practically no new empirical studies of CEM or the Strehler-Mildvan correlation have been conducted since that time. Most studies on the topic are focused on theoretical developments of the Strehler-Mildvan theory of aging (Yashin et al. 2002a; Li and Anderson 2015; Burger and Missov 2016). A few empirical studies on the topic did not take into account the Makeham parameter producing spurious correlation between the Gompertz parameters (Yashin et al. 2002b; Hawkes et al. 2012). This approach has been criticized by some researchers (Golubev 2004).

The main objective of this study is to conduct large-scale empirical analyses of correlation between the Gompertz parameters taking into account the Makeham term (also known as background mortality) and to test the CEM using contemporary data. Special emphasis has been placed on the effect of the historical decline of the Makeham parameter. Possible factors that may produce a spurious dependence between the Gompertz parameters are also considered.

## DATA USED

In this study we used abridged life tables calculated for five-year age intervals from the United Nations database (United Nations 2015). The database contains mortality data for 1,687 populations of each sex and covers 13 five-year time periods. Five-year values of death rates were used as estimates of hazard rates. This database is useful for providing initial screening of populations with unusual parameter values of the Gompertz function and CEM.

## STATISTICAL ANALYSES

In the first step of the analysis we have calculated parameters  $R_0$  and  $\alpha$  of the Gompertz-Makeham equation:

$$\mu_x = A + R_0 \exp(\alpha x)$$

where  $\mu_x$  is the hazard rate, x is age and A,  $R_0$  and  $\alpha$  are parameters.

Parameters of the Gompertz-Makeham model were estimated using the nonlinear regression method in the age interval 30–80 years (*nlin* procedure in Stata package (StataCorp, version 14)). The threshold of 30 years was selected to avoid a hump of external deaths at younger ages. The upper threshold of 80 years was chosen to avoid mortality deceleration.

We have estimated parameters for the following four models:

- 1. Traditional Gompertz-Makeham model
- 2. Gompertz-Makeham model with constraint (Makeham parameter,  $A \ge 0$ )
- 3. Gompertz-Makeham model with age centered in the middle of age interval (x- 60)
- 4. Gompertz model used by Strehler and Mildvan.

Model no. 2 eliminates the possibility of a negative Makeham parameter, which contradicts the meaning of this parameter as nonnegative background mortality. Therefore, this model constrains parameter  $A \ge 0$ , so it remains nonnegative.

Model no. 3 eliminates an additional source of spurious correlation between the Gompertz parameters. It was shown that a least-squares fit often leads to an ill-defined nonlinear optimization problem, which is extremely sensitive to sampling errors and the smallest systematic demographic variations (Tarkhov et al. 2017). The best fit for the Gompertz parameters in this case turns out to be related by a form of Strehler-Mildvan correlation (Tarkhov et al. 2017). To alleviate the problem of collinearity, we estimate parameters of the Gompertz-Makeham equation using the age mean centered at 60 years.

Finally, model no. 4 is the Gompertz model used by Strehler and Mildvan (1960). This model is used to demonstrate the magnitude of bias caused by neglecting the Makeham parameter.

For each model, we run linear regressions between the Gompertz parameters (ln R and  $\alpha$ ) of the form

 $\ln R_0 = \ln M - B\alpha$ 

Thus, the species-specific lifespan (slope parameter, B) and the intercept parameter have been estimated.

### RESULTS

Table 1 shows parameters of linear regression between logarithm of parameter  $R_0$  and  $\alpha$  (equation 3) based on the standard Gompertz-Makeham model for three groups of countries in the UN database. Organisation for Economic Co-operation and Development (OECD) countries have the best quality of demographic statistics, and these countries also demonstrate the highest value of species-specific lifespan (94.7 ± 0.5 years). Note that the same value of the species-specific lifespan has been reported by Gavrilov and Gavrilova (1991) in their earlier study (95 ± 3 years). Correlation between  $lnR_0$  and  $\alpha$  for OECD countries is shown in Figure 1.

Note that Greece (females) has the highest value of the actuarial aging rate ( $\alpha$ ), whereas Latvia (males) has the lowest value (Figure 1).

Taking more recent data (after 1980) does not change results significantly (Table 1). For countries with slightly lower data quality, both species-specific lifespan and species-specific force of mortality are lower compared to OECD countries. Analyzing data for all countries provides even lower values of species-specific lifespan and species-specific force of mortality (Table 1). Thus, both estimates for species-specific lifespan and species-specific force of mortality are declining as long as the quality of data is getting worse.

### Table 1

CHARACTERISTICS OF CEM BASED ON THE STANDARD GOMPERTZ-MAKEHAM MODEL. UNITED NAT	rions
DATABASE.	

	Regression Coefficients			
Population	ln <i>M</i> ±σ	B ±σ (Years)	Correlation Coefficient	Number of
			Between $\ln R_0$ and $\alpha$	Life Tables
OECD countries	0.05 0.07			550
Men	$-0.85 \pm 0.07$	93.55± 0.79	-0.9806	559
Women	-0.82 ±0.11	94.24 ±0.93	-0.9740	559
Total	-0.76 ±0.05	94.69± 0.46	-0.9871	1,118
OECD countries				
Period after 1980				
Men	-1.11±0.09	91.87 ±0.94	-0.9846	301
Women	-1.62± 0.13	88.63± 1.13	-0.9767	301
Total	-0.97±0.06	93.81 ±0.57	-0.9893	602
GQ* countries				
Men	-1.11± 0.05	90.52±0.60	-0.9787	988
Women	-1.07± 0.07	91.77 ± 0.64	-0.9765	988
Total	-0.94± 0.04	92.71 ±0.35	-0.9862	1,976
GQ* countries				
Period after 1980				
Men	-1.16± 0.07	90.95± 0.73	-0.9834	532
Women	-1.45± 0.10	89.43 ±0.86	-0.9762	532
Total	-1.03±0.05	92.81± 0.45	-0.9880	1,064
All countries				
Men	-1.49 ±0.04	84.87 ±0.41	-0.9646	3,133
Women	-1.14 ±0.04	89.73 ±0.42	-0.9679	3,133
Total	-1.13 ±0.03	89.42 ± 0.27	-0.9727	6,266
All countries				
Period after 1980				
Men	$-1.71 \pm 0.05$	83.57 ± 0.52	-0.9692	1,687
Women	-1.45 ±0.06	87.80 ±0.56	-0.9678	1,687
Total	-1.33 ±0.04	88.40± 0.35	-0.9745	3,374

\*GQ =countries with a sufficiently good quality of vital statistics (including the Eastern European countries and countries of the former Soviet Union).

INVERSE RELATIONSHIP BETWEEN MORTALITY INTERCEPT PARAMETER ( $LN(R_0)$ , *Y*-AXIS) AND MORTALITY SLOPE PARAMETER (ALPHA, *X*-AXIS) FOR OECD COUNTRIES. GOMPERTZ-MAKEHAM MODEL. CALCULATED FOR MORTALITY RATES IN 2010–2015, AGE INTERVAL 30–80 YEARS.



For the Gompertz-Makeham model with constraint (Makeham parameter,  $A \ge 0$ ) we obtain similar results as in the case of the standard Gompertz-Makeham model (Table 2). The species-specific lifespan in this case is equal to 95.0 ± 0.5 years for OECD countries. As in the previous case, both estimates for species-specific lifespan and species-specific force of mortality are declining when the quality of data is getting worse. Correlation between  $\ln R_0$  and  $\alpha$  for OECD countries for the model with constraint is shown in Figure 2. Note that Figure 2 is similar to Figure 1, so that this model does not significantly change parameter estimates for  $R_0$  and  $\alpha$  in the Gompertz-Makeham equation.

### Table 2

# CHARACTERISTICS OF CEM BASED ON THE GOMPERTZ-MAKEHAM MODEL WITH MAKEHAM PARAMETER CONSTRAINED TO BE NON-NEGATIVE. UNITED NATIONS DATABASE.

	Regression Coefficients			
Population	lnM ±σ	B ±σ (Years)	Correlation Coefficient Between $In R_0$ and $\alpha$	Number of Life Tables
OECD countries				
Men	-0.81 ±0.08	93.94 ±0.84	-0.9785	559
Women	-0.81± 0.11	94.34± 0.93	-0.9737	559
Total	-0.72 ±0.05	95.02 ±0.48	-0.9863	1,118

-1.10± 0.09	91.86 ±0.97	-0.9836	301
-1.62± 0.13	88.66± 1.13	-0.9765	301
-0.95 ±0.06	93.91 ±0.58	-0.9889	602
-1.09 ±0.06	90.76± 0.63	-0.9770	988
-1.05 ±0.07	91.92 ±0.66	-0.9759	988
-0.91± 0.04	92.97 ± 0.36	-0.9855	1,976
-1.14 ±0.07	91.15 0.75	-0.9827	532
-1.44± 0.19	89.52 0.87	-0.9757	532
-1.01± 0.05	92.99 0.45	-0.9876	1,064
-1.45± 0.04	85.29 ±0.44	-0.9614	3,133
-1.10± 0.04	90.09 ± 0.42	-0.9675	3,133
-1.08± 0.03	89.88 ± 0.28	-0.9716	6,266
-1.70 ±0.05	83.71 ±0.54	-0.9663	1,687
-1.41 ±0.06	88.14 ±0.57	-0.9668	1,687
-1.29 ±0.04	88.76 ± 0.36	-0.9733	3,374
	$\begin{array}{c} -1.10 \pm 0.09 \\ -1.62 \pm 0.13 \\ -0.95 \pm 0.06 \\ \end{array}$ $\begin{array}{c} -1.09 \pm 0.06 \\ -1.05 \pm 0.07 \\ -0.91 \pm 0.04 \\ \end{array}$ $\begin{array}{c} -1.14 \pm 0.07 \\ -1.44 \pm 0.19 \\ -1.01 \pm 0.05 \\ \end{array}$ $\begin{array}{c} -1.45 \pm 0.04 \\ -1.10 \pm 0.04 \\ -1.08 \pm 0.03 \\ \end{array}$ $\begin{array}{c} -1.70 \pm 0.05 \\ -1.41 \pm 0.06 \\ -1.29 \pm 0.04 \\ \end{array}$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$	$\begin{array}{ c c c c c c c c c c c c c c c c c c c$

\*GQ = countries with a sufficiently good quality of vital statistics (including the Eastern European countries and countries of the former Soviet Union).

For the model with age centered at 60 years, we obtain virtually the same estimates of the species-specific lifespan (94.7 ± 0.5 years) for OECD countries (Table 3). In this case we need to add 60 years to the estimated regression coefficient (*B*) to obtain the species-specific lifespan. For this model, we obtain similar results as in the case of the previous two models. The only difference with the previous models is the magnitude of the correlation coefficient between  $\ln R_0$  and  $\alpha$ : 0.99 in the case of model no. 1 and 0.91 in the case of model no. 3 (age centered at 60 years). This difference in the values of correlation coefficients reflects the contribution of the spurious correlation between estimates of  $\ln R_0$  and  $\alpha$  caused by statistical noise (Tarkhov et al. 2017). As one can see, this contribution is relatively small ( $0.99^2 - 0.91^2 = 0.152$ , or 15% of variance explained) and does not affect the final estimates of linear regression parameters (Table 3). Thus, the inverse correlation between the Gompertz parameters remains valid even after controlling for possibility of spurious correlation between estimates of  $\ln R_0$  and  $\alpha$  caused by statistical noise. The inverse relationship between  $\ln R_{60}$  and  $\alpha$  when the age is centered at 60 years is shown in Figure 3.

### Table 3

# CHARACTERISTICS OF CEM BASED ON THE GOMPERTZ-MAKEHAM MODEL WITH AGE CENTERED AT 60 YEARS. UNITED NATIONS DATABASE.

	Regression Coefficients			
Population	ln <i>M</i> ±σ	B ±σ (Years)	Correlation Coefficient between $lnR_{60}$ and $\alpha$	Number of Life Tables
OECD countries				
Men	-0.85± 0.07	33.55 ±0.79	-0.8737	559
Women	-0.82± 0.11	34.24± 0.93	-0.8421	559
Total	-0.76 ±0.05	34.69± 0.46	-0.9142	1,118
OECD countries				
Period after 1980				
Men	-1.11 ±0.09	31.87 ±0.94	-0.8904	301
Women	-1.62 ±0.13	28.63 ±1.13	-0.8266	301
Total	-0.97± 0.06	33.81 ±0.57	-0.9252	602
GQ* countries				

Men	-1.11 ±0.05	30.52±0.60	-0.8493	988
Women	-1.07 ±0.07	31.77± 0.64	-0.8433	988
Total	-0.94 ± 0.04	32.71 ± 0.35	-0.9027	1,976
GQ* countries				
Period after1980				
Men	-1.16 ±0.07	30.95 ±0.73	-0.8793	532
Women	-1.45 ±0.10	29.43 ±0.86	-0.8286	532
Total	$-1.03 \pm 0.05$	32.81 ±0.45	-0.9144	1,064
All countries				
Men	-1.49 ±0.04	24.87 ±0.41	-0.7312	3,133
Women	-1.14 ±0.04	29.73 ± 0.42	-0.7873	3,133
Total	-1.13± 0.03	29.42 ± 0.27	-0.8096	6,266
All countries				
Period after1980				
Men	-1.71 ±0.05	23.57 ± 0.52	-0.7431	1,687
Women	-1.45 ±0.06	27.80 ±0.56	-0.7728	1,687
Total	$-1.33 \pm 0.04$	28.40 ±0.35	-0.8130	3,374

\*GQ =countries with sufficiently good quality of vital statistics (including the Eastern European countries and countries of the former Soviet Union).

Correlation between  $\ln R_{60}$  and  $\alpha$  for this model is slightly weaker compared to the previous two models (compare Tables 1–3). Note the unusually low value of actuarial aging rate (parameter  $\alpha$ ) for Japan (females) compared to its  $R_{60}$  value (Figure 3). Also note an unusually high value of actuarial aging rate (parameter  $\alpha$ ) for Turkey (males) compared to its  $R_{60}$  value. Thus, using the model with age centered at age 60 allows us to detect human populations that have unusual values of the actuarial aging rate. These differences are masked when data are analyzed in a traditional way without age centering (see Figures 1 and 2).

INVERSE RELATIONSHIP BETWEEN MORTALITY INTERCEPT PARAMETER (LN(R0), Y-AXIS) AND MORTALITY SLOPE PARAMETER (ALPHA, X-AXIS) FOR OECD COUNTRIES. GOMPERTZ-MAKEHAM MODEL WITH CONSTRAINT (MAKEHAM PARAMETER NOT NEGATIVE). CALCULATED FOR MORTALITY RATES IN 2010–2015, AGE INTERVAL 30– 80 YEARS.



INVERSE RELATIONSHIP BETWEEN MORTALITY INTERCEPT PARAMETER AT AGE 60 (LN( $R_{60}$ ), Y-AXIS) AND MORTALITY SLOPE PARAMETER (X-AXIS) FOR OECD COUNTRIES. AGE VARIABLE IS CENTERED AROUND 60 YEARS (X- 60). GOMPERTZ-MAKEHAM MODEL. CALCULATED FOR MORTALITY RATES IN 2010–2015, AGE INTERVAL 30–80 YEARS.



Figure 4 illustrates mortality convergence for five populations based on Human Mortality Database (<u>www.mortality.org</u>) data. Note that mortality dependence for Japanese females does not follow the general convergence pattern because of the low slope corresponding to a slower than expected aging rate.

Finally, we tested the effect of not controlling for the Makeham term on the parameters of the inverse correlation between  $\ln R_0$  and  $\alpha$ . The results of using model no. 4 (the Gompertz model) are presented in Table 4. Note that the value of the species-specific lifespan is 95.5 ± 0.6 years, which is similar to estimate obtained in the case of the Gompertz-Makeham model. However, this estimate is significantly higher than the estimate obtained by Strehler and Mildvan in their 1960 article (68.5 years). The reason for this difference lies in the fact that the UN database in our current analysis covers a relatively recent time period (after 1950) when the Makeham term became close to zero whereas Strehler and Mildvan analyzed older data when the Makeham term was much larger (Gavrilov and Gavrilova 1991). Thus, we may conclude that for contemporary data accounting for the Makeham term does not significantly change parameters of the inverse dependence between  $\ln R_0$  and  $\alpha$ . The inverse relationship between  $\ln R_0$  and  $\alpha$  for OECD countries is shown in Figure 5.

### Table 4

# CHARACTERISTICS OF CEM BASED ON THE GOMPERTZ MODEL (STANDARD STREHLER-MILDVAN CORRELATION). UNITED NATIONS DATABASE.

	Regression Coefficients			
			Correlation Coefficient	Number of
Population	ln <i>M</i> ±σ	B ±σ (Years)	between $InR_0$ and $\alpha$	Life Tables
OECD countries				
Men	-0.84 ±0.09	93.85 ±0.96	-0.9720	559
Women	-0.93± 0.12	93.69± 1.12	-0.9627	559
Total	-0.71 ±0.06	95.54 ± 0.56	-0.9814	1,118
OECD countries				
Period after1980				
Men	-1.14 ±0.11	91.74 ±1.12	-0.9783	301
Women	-1.72 ±0.16	88.05 ±1.38	-0.9652	301
Total	-0.90 ±0.07	94.91± 0.69	-0.9845	602
GQ* countries				
Men	-1.15 ±0.06	90.28 ±0.68	-0.9730	988
Women	-1.10 ±0.08	91.74± 0.74	-0.9691	988
Total	-0.92 ±0.04	93.22 ±0.40	-0.9820	1,976
GQ* countries				
Period after 1980				
Men	-1.19± 0.07	90.76 ±0.81	-0.9795	532
Women	-1.50± 0.11	89.27 ±1.04	-0.9656	532
Total	-0.99 ±0.05	93.54 ±0.52	-0.9841	1,064
All countries				
Men	-1.22± 0.04	88.21 ±0.47	-0.9585	3,133
Women	-0.99 ±0.04	91.80 ±0.41	-0.9702	3,133
Total	-0.94 ±0.03	91.91 ±0.28	-0.9719	6,266
All countries				
Period after 1980				
Men	-1.54 ±0.05	85.72 ±0.59	-0.9623	1,687
Women	-1.24 ±0.06	90.36± 0.57	-0.9681	1,687
Total	-1.15 ±0.04	90.75± 0.37	-0.9725	3,374

\*GQ = countries with sufficiently good quality of vital statistics (including the Eastern European countries and countries of the former Soviet Union).

Figure 4

MORTALITY CONVERGENCE FOR FIVE POPULATIONS WITH EXCEPTION OF THE JAPANESE FEMALES. AGE-SPECIFIC DEATH RATE IN A LOG SCALE AS A FUNCTION OF AGE. SOURCE: HUMAN MORTALITY DATABASE, YEAR 2010.



INVERSE RELATIONSHIP BETWEEN MORTALITY INTERCEPT PARAMETER ( $LN(R_0)$ , *Y*-AXIS) AND MORTALITY SLOPE PARAMETER (*X*-AXIS) FOR OECD COUNTRIES. GOMPERTZ MODEL (MAKEHAM PARAMETER NEGLECTED). CALCULATED FOR MORTALITY RATES IN 2010–2015, AGE INTERVAL 30–80 YEARS.



# DISCUSSION AND SUMMARY

In this study we analyzed the relationship between the slope and intercept parameters of the Gompertz-Makeham equation in human populations, which we designate as  $\alpha$  (alpha) and  $R_0$  parameters following notations used in the seminal paper by Strehler and Mildvan (1960). We tested correlation between the Gompertz parameters using world-wide data while adjusting for the Makeham term. We used the UN abridged life tables for 241 countries and regions (covering 13 time periods per country, from 1950 to 2015.)

Parameters of the Gompertz-Makeham model were estimated for each population (life table) using the method of nonlinear regression in the age interval 30–80 years (*nlin* procedure in the Stata package, version 14). Then parameters of liner regression for  $\ln R_0$  as a dependent variable and  $\alpha$  have been estimated. We call the slope parameter of this linear regression the species-specific life span, given its properties and dimension (time). This value corresponds to the age at which all the mortality dependencies in semi-log-scale intersect (Gavrilov and Gavrilova 1991).

We have estimated parameters for the following four models:

- 1. Traditional Gompertz-Makeham model
- 2. Gompertz-Makeham model with constraint (Makeham term,  $A \ge 0$ )
- 3. Gompertz-Makeham model with age centered in the middle of age interval (x-60)

### 4. Gompertz model used by Strehler and Mildvan (no adjustment for the Makeham term)

In the case of models no. 1 and no. 2,  $\ln R_0$  and  $\alpha$  were highly correlated (correlation coefficient, *r*=0.99). OECD countries have the best quality of demographic statistics, and these countries also demonstrate the highest value of a species-specific lifespan (94.7 ± 0.5 years), which is similar to earlier estimates (Gavrilov and Gavrilova 1991).

For the model with age centered at 60 years (model no. 3), we obtain virtually the same estimates of the speciesspecific lifespan (94.7 ± 0.5 years) for OECD countries as for the first two models. At the same time, the correlation coefficient between  $\ln R_0$  and  $\alpha$  for model no. 3 is lower: 0.91 compared to 0.99 found for model no. 1. This difference in the values of correlation coefficients reflects the contribution of the spurious correlation between estimates of  $\ln R_0$  and  $\alpha$  caused by statistical noise (Tarkhovet al. 2017). We found that this contribution is relatively small (0.99<sup>2</sup>-- 0.91<sup>2</sup> = 0.152, or 15% of variance explained) and does not affect the final estimates of the speciesspecific lifespan. Thus, the inverse correlation between the Gompertz parameters remains valid even after controlling for the possibility of spurious correlation between the Gompertz parameters caused by statistical noise. Use of an age-centered model also helps to identify populations with an unusually slow or high actuarial aging rate. We found that Japanese females represent a population with unusually low values of an actuarial aging rate (parameter  $\alpha$ ) compared to their  $R_{60}$  value.

One of the possible explanations for the CEM, based on the principles of the reliability theory of aging, is that the rate of the primary processes that destroy the organism in aging is a species-specific invariant (Gavrilov and Gavrilova 1991; Gavrilov and Gavrilova 2006). This explanation should not be confused with the programmed death hypothesis, which presupposes the existence of a kind of time bomb. Simply, the existence of a powerful homeostasis has the consequence that the majority of the organism's vital parameters, on which the rate of its destruction also depends, are indeed invariant with respect to many external influences and genetic characteristics. For example, the human body temperature is approximately 36.7°C and practically independent of sex, ethnic characteristics and climate. It is therefore natural that many destructive processes that are dependent on temperature and other similar factors are so invariant that some of them (for example, the racemization of L-amino acids) even can be used to estimate the age of the organism (Man et al. 1983).

The species-specific lifespan found in this study is equal to  $94.5 \pm 0.5$  years, which is the same as reported for the period before the 1960s:  $95 \pm 2$  years (Gavrilov and Gavrilova, 1991). It turns out that the convergence point of CEM is stable despite significant mortality decline over the past 50 years and is not affected by factors that decrease mortality at younger ages. Further research showed that CEM is observed for human populations with different levels of familial longevity including siblings of centenarians and siblings of short-lived individuals (Gavrilova and Gavrilov 2022). As a result, familial longevity (and probably longevity genes associated with it) has little or no effect on survival after age 100 years (past the age of the species-specific lifespan).

Because of CEM, factors associated with life span extension are usually accompanied by a paradoxical increase in the actuarial aging rate (a slope parameter of the Gompertz law), and this is a challenge to the significant life extension. To find populations with a slow aging process we need to look for populations with both a slow actuarial aging rate and low initial mortality (the intercept parameter of the Gompertz law). Such populations were identified in this study. The population of Japanese females is an example of such a population. Analyzing life style and genetic backgrounds of populations with slow aging may be a promising approach toward finding the ways to life extension.

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