

# Mortality as an Indicator of Aging: Possibilities and Limitations

V. N. Krut'ko<sup>a</sup> and V. I. Dontsov<sup>a, \*</sup>

<sup>a</sup>Federal Research Center “Computer Science and Control” of Russian Academy of Sciences,  
Moscow, 117312 Russia

\*e-mail: dontsovvi@mail.ru

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**Abstract**—Using data gathered from 40 countries throughout a historical period covering two and a half centuries, we studied the peculiarities of age-related changes in the aging rate for the countries in the world and elucidated the possibilities and limitations of the method for quantitatively measuring the aging effect according to parameters related to the analysis of population mortality. Mortality rate and its derivatives are variables of the Gompertz formula:  $m(t) = R_0 \exp(kt)$ , where  $m$  is the mortality rate at time  $t$  (age),  $R_0$  is the initial mortality level, and  $k$  is the rate of mortality increase; both components are believed to be associated with aging, and of the Gompertz–Makeham formula (with an additional coefficient  $A$  as the constant mortality rate, which depends on external conditions). The  $A$  and  $R_0$  components are not necessarily uniform for different ages and affect each other, changing controversially, as well as the  $R_0$  and  $k$  components. To characterize the external effects on mortality, it is better to use the  $R_0$  of the Gompertz formula; when the values of external effects on mortality are high, the  $k$  component of the Gompertz formula can be used to evaluate aging. At the same time, when the  $A$  coefficient is low, it is better to use the  $k$  component of the Gompertz–Makeham formula. In this case, absolute comparison of the components of the Gompertz and Gompertz–Makeham formulas is not reasonable because these components may differ considerably. The mortality increment  $d(m)$  is the best indicator to reflect the biological nature of aging and the changes of the latter for an exact age. However, it may reflect certain particular changes in total mortality for certain ages. Using this indicator, it can be observed that the main patterns of the aging process have persisted throughout all historical periods and for all countries. The mortality curves for early periods of history are discontinuous and distorted due to the faults of the methods for collecting primary data and not because of actual events. Hence, it is necessary to remember that the components of the formulas may have biological meaning only when mathematical proof is supported by biological methods and data.

**Keywords:** aging, mortality, Gompertz–Makeham formula, aging rate, mortality change in history, aging rate change

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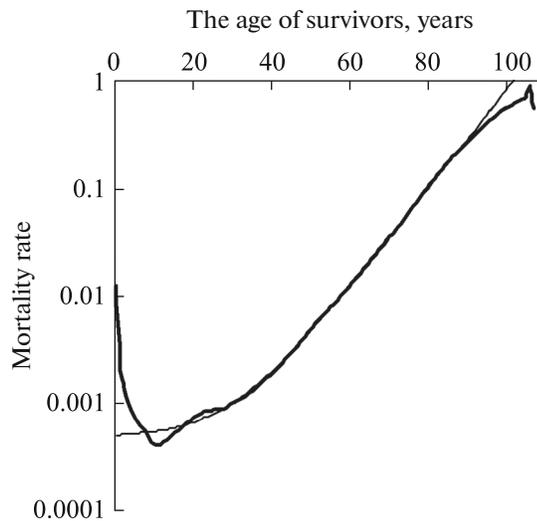
The sharp and continuing aging of the population in the 20th century accompanied with declining birth rates has created pronounced socio-economic difficulties, which determines the growing interest in aging problems around the world and the possibilities of influencing it [1]. At the same time, the value of methods for quantifying the aging process is growing, especially at the level of populations and countries. Analysis of age-related mortality has been such a universally accepted method for assessing aging at the population level [2] since the time when B. Gompertz conducted his research [3] (an exponential increase in the intensity of mortality with age as the basic law of aging). However, the use of this method has not yet allowed us to answer a number of questions, that is, about the nature of aging, interpretation of the method itself, about the biological limit of the life span [4, 5], changes in the rate of aging throughout life, changes in the history and speed of aging for different countries, about the existence of a decrease in the aging rate of

long-lived individuals, about an increase in the maximum life span over history [6, 7], whether an exponential and uniform increase in mortality is preserved throughout life or in the age of long-lived individuals decreases to a plateau [7], and a number of other questions.

The aim of the study was to analyze the peculiarities of the age-related changes in the aging rate for countries through history and to define the abilities and limitations of the method of aging evaluation with the parameters associated with the estimation of the mortality of the population.

## MATERIALS AND METHODS

Changes in age-specific mortality for 40 countries over the 1750–2014 period were studied using Human Mortality Database [8]. Survival tables were used for a



**Fig. 1.** Changes in the mortality rate with age (the Netherlands, 1950–1959). The Y-axis is the mortality rate (logarithmic scale), the X-axis is the age of survivors. The real mortality rate curve is given by the bold line, the calculated mortality rate curve via processing data with the Gompertz–Makeham formula is shown with the thin line.

cohort of 100 000 people with the survival for each year from 1 to 110 years for historical periods of 10 years.

The indicators of the Gompertz and Gompertz–Makeham formulas were calculated according to survival tables (in the latter case, the Gompertz formula was enhanced by the Makeham coefficient  $A$ ) using well-known methods [2, 9]:  $m = A + R_0 \exp(kt)$ , where  $A$  is a constant, which indicates the external factors that affect mortality and  $R_0$  and  $k$  are coefficients, which are believed to reflect the biological nature of mortality, i.e., the rate of aging. Graphs were built for changes in the total age-specific intensity of mortality  $m$  and its increment  $d(m)$ , as well as graphs of the difference in total mortality and external influences on it ( $m - A$ ).

The true mortality rate was compared with the predicted one calculated by the parameters of the Gompertz–Makeham formula, and the correlation coefficient  $r$  was estimated. Linear smoothing over three to five points was used to smooth the effect of random outliers in the increment curve of the mortality rate.

## RESULTS

Although the Gompertz formula (B. Gompertz, 1825) was originally obtained purely empirically based on mortality statistics [3] it can be deduced theoretically. From the generally accepted definition, “aging is a decrease in overall viability with age” and the idea that this is a spontaneous probabilistic process we can consider the decrease in the viability of  $X$  with age as a process similar to the process of radioactive decay,

where the number of elements decreases over time and depends only from their presence at the moment:  $dX/dt = -kX$ , where  $k$  is a proportionality coefficient. Accordingly, at time  $t$ , the number of remaining viable elements will be  $X(t) = X_0 \exp(-kt)$ .

At the same time, the general vulnerability and ultimately the total mortality rate for a population are inversely proportional to viability:  $m = 1/X$ , which leads us to the well-known Gompertz–Makeham formula with its generally accepted coefficients and a correction (the Makeham coefficient):  $m(t) = R_0 \exp(kt) + A$ .

To assess the aging rate, we used the indicator  $m - A$  (the mortality rate without the background external component  $A$ ), the age-specific mortality coefficient  $k$ , which determines the rate of increase in mortality, as dependent on aging, and the coefficient  $R_0$ , which determines the initial mortality rate and characterizes the “initial level of aging.” One can also use the increase rate of the mortality  $d(m)$ , which is offset by the constant  $A$ . The indicator  $d(m)$  reflects the aging rate itself better than  $m - A$ , since in the latter case the average value of the coefficient  $A$  is used, which in reality can vary significantly for different age periods.

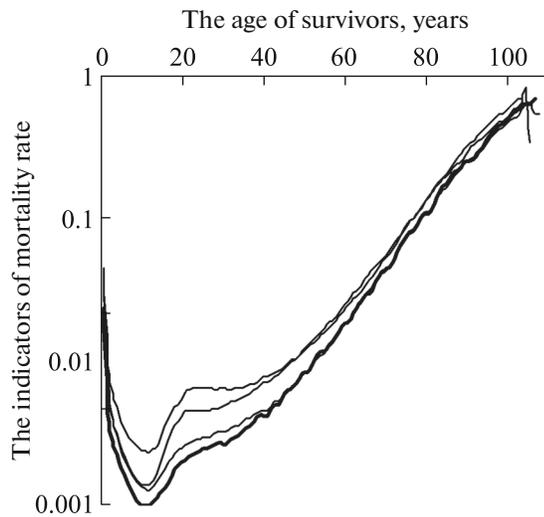
Finally, a decrease in the aging rate allows one to survive to an older age, which allows the age of complete extinction for a standard cohort (100 000 people), the maximum life span, to be used for the assessment of aging.

The graph for the Netherlands for 1950 can be considered as an ideal example of the Gompertz–Makeham graph (Fig. 1); it is a close to linear graph that coincides with the real mortality rate curve  $m$  for 20–90 years and with a downward deviation from the Gompertz–Makeham curve for the real mortality curve for centenarians.

However, in most cases there are graphs of the intensity of mortality of various forms for different countries and different age periods (Fig. 2). It is generally accepted that the differences are due to differences in external influences on mortality, which are reflected by the coefficient  $A$  of the Gompertz–Makeham formula.

The use of mortality indicators without an external coefficient ( $m - A$ ) and the use of the mortality increment  $d(m)$ , which also removes external influences on mortality, shows that if a linear section is observed for 55–75 years for the graph of total mortality  $m$ , then it is also observed for 20–90 years for the  $m - A$  and  $d(m)$  graphs (Fig. 3).

Several other features can be noted. The contribution of the external coefficient  $A$  to the total mortality  $m$  decreases sharply with age, since it can no longer “compete” with the exponential increase in mortality due to aging itself; in addition, a “step” at 20–40 years for general mortality is also determined in many respects by the constant  $A$ .



**Fig. 2.** Changes in the mortality rate with age for different countries in 1930–1939. The Y-axis gives the intensity of mortality (logarithmic scale), the X-axis gives the age of survivors. From bottom to top: Australia (bold line), Canada, France, Finland.

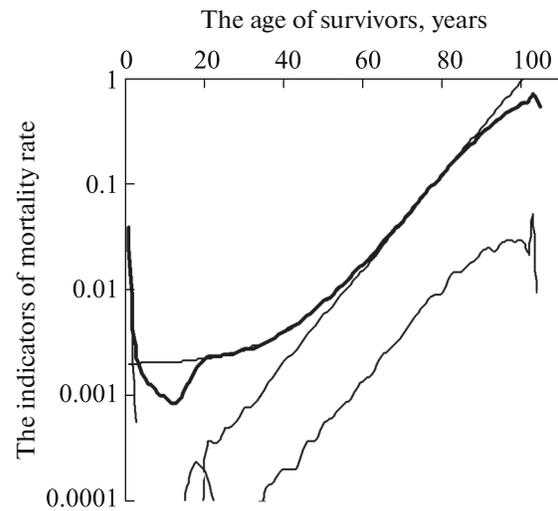
The  $m - A$  and  $d(m)$  graphs are parallel, since they reflect the same process, which is the aging rate itself, and are linear for a much larger age period than the graph of the actual mortality rate  $m$ . However, parallelism and the linear form of the graph are not always observed (Fig. 4) and the “step” may not be offset by the constant  $A$ .

Fluctuations in the  $d(m)$  graph may also not be related to changes in aging itself (Fig. 4), but apparently reflect specific features of changes in the overall mortality rate for a few age periods.

For Russia in 2014, the  $m - A$  graph shows an inversion (increase) in the overall mortality of long-lived individuals, which is typical for the late 20th and early 21st centuries. However, the  $d(m)$  graph shows a decrease, which indicates the persistence of the phenomenon of aging retardation for ages of long-lived individuals, as is always noted in history in all countries [10].

As well, based on the nature of the indicators, the same aging rate for  $m - A$  is expressed by a horizontal line, as well as for the graph of total mortality  $m$ , while for the  $d(m)$  graph it is 0 and the decrease in the aging rate is recorded as negative values.

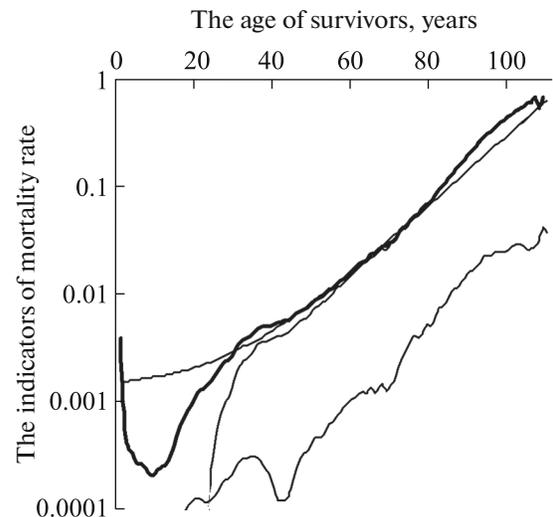
The estimation of aging by the components of the Gompertz–Makeham formula ( $A$ ,  $R_0$ , and  $k$ ) also has its limitations. As an example, for the World War I period, the graph for Italy (1910–1919) shows a “hump” of mortality for young and middle ages (Fig. 5a), which makes it impossible to calculate the Gompertz–Makeham formula by conventional methods (Fig. 5b).



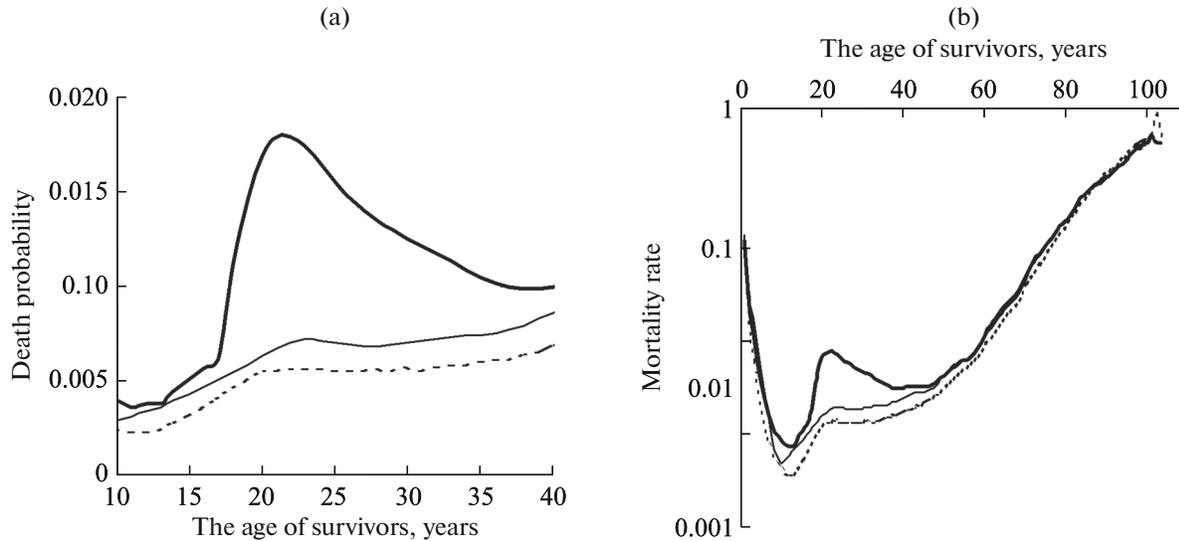
**Fig. 3.** Changes in various indicators of the mortality rate with age (Denmark, 1930–1939). The Y-axis gives the indicators (logarithmic scale), the X-axis gives the age of survivors. From top to bottom: the calculated and real mortality rate curves (thin and bold lines); the difference in the overall intensity of mortality and the external component:  $m - A$  (middle line); increase in the mortality rate  $d(m)$  (bottom line).

Thus, the  $A$  parameter can vary dramatically for different ages; in addition, it is likely that similar effects are not the same for people of different ages due to the aging process.

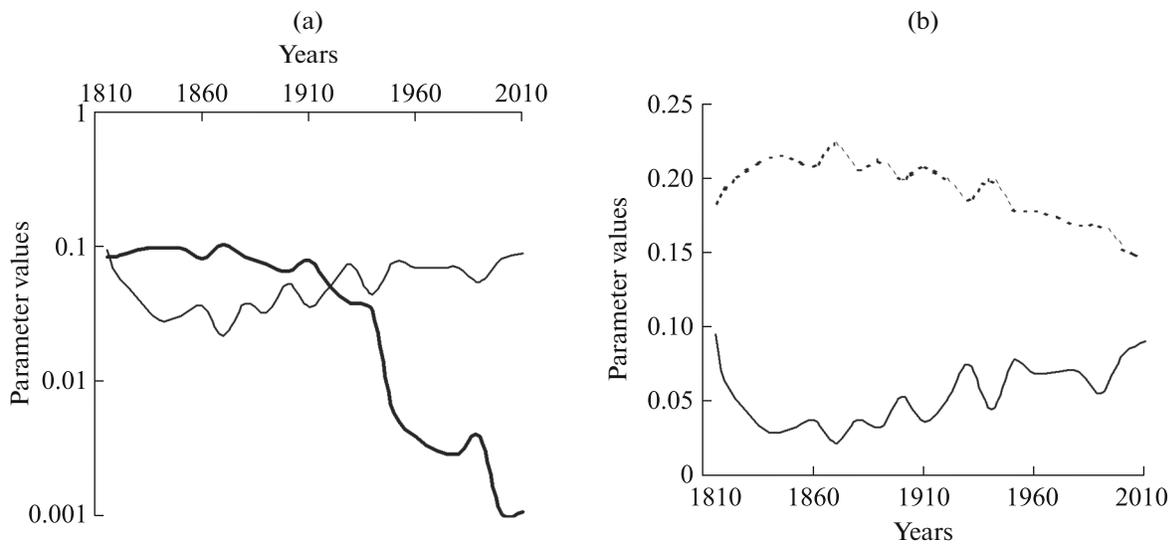
All three indicators of the formula are closely related. Based on the example of France in 1850–2000



**Fig. 4.** Changes in various indicators of mortality with age (Russia, 2014). The Y-axis gives the indicators (logarithmic scale), the X-axis gives the age of survivors. From top to bottom: calculated and real mortality curves (thin and bold lines); the difference in the overall mortality rate and the external component,  $m - A$  (middle line); increase in the mortality rate  $d(m)$  (bottom line).



**Fig. 5.** The selective influence of external conditions on mortality in a narrow range of ages (Italy, 1910–1919). The X-axis gives the age of survivors; the Y-axis gives (a) probability of death (per year), from top to the bottom: 1910–1919 (bold line), 1900–1909 (thin line), and 1920–1929 (dotted line); (b) mortality rate, logarithmic scale, the same notation for curves.



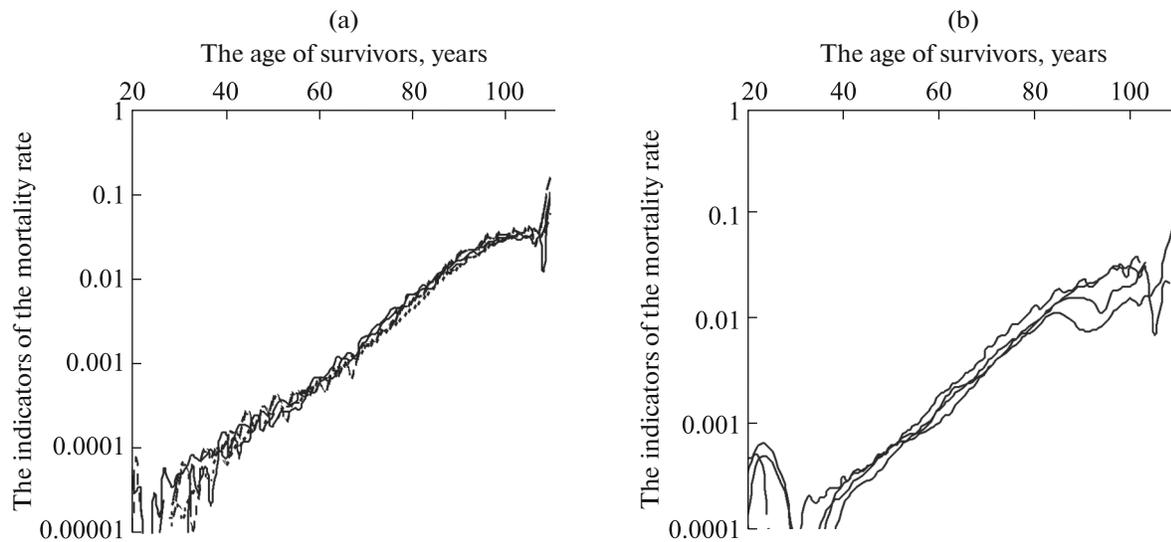
**Fig. 6.** Change in the components of the Gompertz–Makeham formula in history (France, 1850–2000). The Y-axis is parameter values, the X-axis is years; (a), components  $A \times 10$  and  $R_0 \times 1000$ , logarithmic scale; (b), components  $R_0 \times 1000$  and  $k \times 2$ , normal scale.

it is seen (Fig. 6) that the components  $A$  and  $R_0$  actually complement each other, reacting in antiphase to changes. The changes in the similar values of  $R_0$ , which are significant at times, hardly suggest changes in the initial level of aging in the coming years: this is a purely mathematical phenomenon. Similarly, the  $R_0$  and  $k$  coefficients change in antiphase.

In some cases, the Gompertz graph is preferable to the Gompertz–Makeham graph, since its component  $k$  does not react significantly to external influences.

However, for low values of  $A$  (and  $R_0$ ), which are typical in modern times for all developed and most developing countries, there is an increase in  $k$  for the Gompertz graph, but not for the Gompertz–Makeham graph. Apparently, this also reflects the mathematical features of calculating the components of the formula, rather than the actual acceleration of aging in modernity.

Thus, it is better to use the  $R_0$  component of the Gompertz formula to characterize the external effects on mortality and the  $k$  component for high values of



**Fig. 7.** The increase in the mortality rate for different countries (a) and in the history of one country (b). The Y-axis gives the increase in the mortality rate,  $d(m)$ , logarithmic scale; the X-axis gives the age of survivors. (a), Ireland, Canada, Portugal, Finland, 2000–2010; (b) France, 1816, 1850, 1900, and 1950.

the external effects on mortality to assess aging. At the same time, it is better to use the component  $k$  of the Gompertz–Makeham formula for low values of external influences on mortality. It should also be noted that direct absolute comparison of the components of the Gompertz and Gompertz–Makeham formulas is senseless, since they can vary significantly.

If all components of the formulas reflect the average values for the entire age period (1–110 years), then the increment rate of the mortality rate responds to changes in aging itself and for the present moment and therefore is preferable for assessing the aging rate itself. Figure 7 shows that the graphs of this parameter almost coincide for different countries (Fig. 6a) and different historical periods of the same country (Fig. 6b).

The use of this indicator also allows one to see the preservation of the effect of reducing the aging rate for the ages of centenarians in all historical periods.

Another feature of the graphs of mortality rate for the early historical periods (until the 1850s) is the cyclical nature of all indicators. The 10-year period of cycles that coincide with the period of data presentation indicates that this is a phenomenon of recording deaths, which makes it difficult to analyze the patterns of changes in mortality and aging for these periods. Similarly, another complication of the study is the angular form of the graph for a number of countries, replaced by a direct linear graph by the end of the 20th century, which is also the result of insufficient accuracy of recording data.

The sharp increase in mean life span during last 200 years (from 1750–1950 it increased from 35–40 to 70–75 years) has not been accompanied by an increase in the maximum life span (it ranges from 102

to 105 years for different countries, without a tendency to an increase over 200 years). However, from the middle of the 20th century, the mean life span entered the area of long-lived individuals (ages over 80 years). This sharply increases the number of survivors with long lives (for 1850 and 2010 in France; up to 80 years, from 7.8 to 65.6%; up to 100 years, from 0.5 to 14.3%; up to 105 years, from 0 to 0.9%) and, apparently, increases the maximum life span purely statistically (from 105 to 114 years for France, 1850 and 2010, respectively).

## DISCUSSION

Demographic methods, such as age-specific assessment of mortality rate based on survival tables, are considered optimal for quantitative assessment of the human aging rate. The Gompertz–Makeham graph is the most important; its coefficients are given a certain biological value:  $A$  is the Makeham constant, which reflects external influences on mortality;  $R_0$  and  $k$ , respectively, reflect the initial level of aging and the value of its exponential increase with age [2, 3, 9].

However, the estimation of aging by the coefficients of the Gompertz–Makeham formula has its limitations. The example of the World War I period, when the probability of death for a narrow range of ages was sharply increased, reflects the possible unevenness of external influences on mortality of different ages. The component  $A$ , which is a constant, does not take such cases into account. In addition, it is likely that similar effects are not the same for people of different ages due to the aging process itself.

Moreover, all three indicators of the formula turn out to be closely associated and actually complement each other, influencing each other and changing in

antiphase:  $A$  and  $R_0$ ,  $R_0$  and  $k$ . At the same time, sharp and frequent fluctuations of components for the closest ages suggest that this is apparently a purely mathematical phenomenon and not real changes in biological aging. For two and a half centuries and these 40 countries one can easily see that all components of the formula respond to external influences, such as hunger, war, and epidemics, which are clearly external causes of changes in mortality.

In addition, the components of the Gompertz and Gompertz–Makeham formulas are not identical and react differently to external influences on mortality. The Gompertz formula allows one to use  $R_0$  to characterize the external effects on mortality and to evaluate aging,  $k$  for high values of the external effects on mortality. However, for the low values it is better to use the  $k$  component of the Gompertz–Makeham formula. Moreover, an absolute comparison of the components of the Gompertz and Gompertz–Makeham formulas is not valid, since they can vary significantly.

It is important that all components of the formulas reflect the values for the entire 1–110 year age period. At the same time, the increment rate of mortality rate responds to a change in aging itself for the present moment; in addition, this indicator does not require special complex calculations, being simply the difference between adjacent values of the mortality rate  $m$ .

Thus, the increment rate of the mortality rate  $d(m)$  is preferable for assessing the actual rate of aging, which has long been noted in the literature [9]. It is interesting that the graphs of this indicator practically coincide for different countries and different historical periods for the same country until the middle of the 20th century. This indicator also allows one to see the persistence of the phenomenon of aging retardation, which is always noted in history and for all countries for the ages of long-lived individuals: the phenomenon of inversion of mortality for these ages for the present is the result of external influences on mortality [10].

The accuracy of data logging for survival tables is also important for all indicators. The cyclical nature of all indicators and the 10-year cycle period, which is noted for the early historical periods (until the 1850s) and coincides with the period of data presentation, indicates that this is a phenomenon of recording deaths, as well as an angular graph of mortality observed for a number of countries. All this dramatically complicates the analysis of patterns of changes in mortality and aging for early historical periods.

On the whole, however, we can conclude that throughout all historical periods and all countries the typical laws of aging are preserved: a linear increase in the aging rate (on a logarithmic scale, reflecting the exponential law of the increase in the aging rate with age) from the period of growth and development to the age of long-lived individuals, and a decrease in the rate of aging at the ages of long-lived individuals.

The decrease in the aging rate for long-lived individuals reflects the heterogeneity of the population, since heredity can apparently account for up to 25% of the changes in life span that form the phenomenon of long-lived individuals [9, 11].

The influence of external conditions on the aging rate is also quite likely and is noted in the literature using various methods for assessing aging [12–15].

In addition, we looked at aging by bringing together pathological changes in natural aging and changes in age-related diseases [16]. Changes in overall viability are equivalent to the effect on biological aging, regardless of the reasons; therefore, it can be expected that the prevention of age-related diseases and a high level of medical and social assistance will have a significant effect on the apparent rate of aging [16]. At the same time, at older ages of long-lived individuals, pronounced changes in physiological indices during natural aging under this effect for ordinary people who have survived to these ages lead to an inversion of reduced mortality at elderly ages.

A sharp increase in the mean life span over 200 years (1750–1950) was not accompanied by an increase in the maximum life span; however, from the middle of the 20th century, the mean life span had entered the region of long-lived individuals (over 80 years of age). This sharply increased the number of survivors to the oldest ages and statistically increased the maximum life span, which, therefore, was no longer an indicator of only biological aging. The maximum life span is recognized as the most important indicator of aging both for humans and animals in experiments on the effect of geroprotectors on the life span, however, as can be seen, this indicator should also be used carefully.

In general, the gerontological analysis of population changes in the historical dynamics of life span and causes of death in various countries is currently one of the most pressing scientific and practical issues [17], as well as the modeling of quantitative analysis of the life span [18]. However, often this method is carried out inaccurately, while not considering the limitations of aging in the analysis of population mortality.

## CONCLUSIONS

The study of changes in age-related mortality uses a long-standing generally accepted method to study the rate of aging, both in animal experiments when studying the effects of substances that extend life and for humans. Processing data from survival tables and calculating the coefficients of the Gompertz–Makeham formula is the most important method for assessing aging, since the coefficients of the formula are given biological meaning associated with aging of the body.

However, a comparison of the coefficients of the Gompertz–Makeham formula for different countries

over large historical periods shows that all components of the formula can be mathematically related and reflect the influence of external conditions on mortality, which requires caution in interpreting their indicators. In addition, the possibility of inaccuracy in recording the primary data for survival tables should be considered.

The best indicator of the rate of aging is apparently the indicator of the increase in the mortality rate, which reflects its changes for a given age. Its use allows us to see that the basic laws of the aging process persist throughout all historical periods and for all countries: the aging rate varies linearly (on a logarithmic scale) within 20–90 years, with a subsequent decrease in the aging rate of long-lived individuals, which is apparently of a hereditary nature.

#### COMPLIANCE WITH ETHICAL STANDARDS

The authors declare that they have no conflict of interest. This work does not describe any studies using humans and animals as objects.

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