Theory of the age dependence of mortality from congenital defects

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Abstract

A theory is presented, based on the evidence that the congenital defect of an individual is at one of many different levels. It is supposed that the individual mortality risk from congenital defect is lognormally or normally distributed in the population. The relationship between childhood mortality from seven congenital defects and age is described. It uses data from the US during the period 1979–1991. Mortality from five congenital defects is inversely proportional to age. Mortality from two congenital defects is inversely proportional to the second power of age. The presented theory explains these two observed types of mortality decline with age. Childhood mortality from some infectious diseases is also inversely proportional to age during childhood in different populations. It follows from this theory that the death from these infectious diseases up the age of 10 years may be caused by a hidden congenital frailty. © 2001 Published by Elsevier Science Ireland Ltd.

Keywords: Mortality; Age; Congenital defect; AIDS; Distribution of probability of death

1. Introduction

The main part of a population dies at an age for which an exponential relationship applies (Gompertz, 1825). The Gompertz law was verified to be valid for the majority of partial causes of death (Riggs, 1990, 1991, 1993). Having excluded the deaths resulting from accidents, the Gompertz relation applies for the population over the age of 10 (Dolejs, 1997). The upper age limit is about 95 years (Riggs, 1992; Vaupel et al., 1998). The populations for which the Gompertz law
applies can be considered homogeneous (Vijg, 2000). This means that the probability of death of every individual rises as long as the mortality rate rises within the total population. The answer to the question: ‘At what age does real aging begin?’ is closely related to the onset of exponential dependence of mortality rates on age. The causes of death until the age of 10 years are decidedly different from the dominant causes of death in the period, when the main part of population dies. Congenital defects are dominant cause of death during the age interval 1–10 years. More than 25% of all ‘biological’ deaths were caused by congenital anomaly up to the age of 10 in the US during the period 1979–1991. The term ‘biological’ means that the number of deaths from accidents is excluded from the total number of death.

The total mortality falls in the course of age after the birth and the Weibull distribution is usually used to describe the dependence of total mortality on age up to 10 years. The mortality, \( R \), corresponding to the Weibull distribution is

\[
R(t) = \frac{dF_w}{dt} \cdot \frac{1}{(1 - F_w)} = \frac{m}{a} t^{(m-1)},
\]

where \( t \) is age. The slope of the linear decrease in log–log scale is equal to \((m-1)\), where \( m \) and \( a \) are the Weibull parameters and \( F_w \) is the cumulative distribution function. The mortality rate \( R(1) \) at the age of 1 is equal to \( m/a \). The Weibull distribution is not defined for \( m \leq 0 \) (the Weibull function does not have basic properties of distribution function). It was observed for congenital anomalies, pneumonia and meningococcal infections (Dolejs, 1998b; Dolejs and Kozak, 2000; Dolejs and Djajadasisastra, 2000) that the slope of mortality decline in log–log scale is equal to \(-1 (m = 0)\). Mortality from these diseases is inversely proportional to the age:

\[
R(t) = \frac{R(1)}{t},
\]

where \( R(1) \) is the actual mortality at the age of 1. The cumulative distribution function (the distribution of probability of death), which corresponds to this mortality dependence on-age is

\[
F(t) = 1 - t^{-R(1)} \quad \text{for } t \geq 1.
\]

The actual mortality \( R(1) \) at age 1, is the only parameter of this distribution Eq. (3). The mortality reduction after the birth has two possible explanations (Dolejs, 1998b):

(a) Mortality risk homogeneously declines in all individuals. The cohort risk of death corresponds with a state of every organism and the process, which was applied in every individual, caused the decline of mortality. The development of every organism causes the mortality reduction after the birth (0–10 years).

(b) Mortality is heterogeneous among individuals, and does or does not decline with age of an individual. The cohort includes weaker individuals who are dying out and, consequently, mortality gets lower (Dolejs, 1998a).

The second explanation offers better explanation of the mortality reduction after the birth and it is the subject of this paper.
2. Materials and methods

The mortality rate was calculated using the WHO database (the internet address: www.who.ch/whoisis/mort/mort.htm) for men and women in the US during the period 1979–1991. (The period 1987–1991 was used for AIDS). The database contains the numbers of living people and the numbers of deaths for all causes. The Basic Tabulation List (BTL code) was used in this database for the definition of the causes of death. (During the period 1979–1991, the ICD9 revision coding system was valid (WHO, 1977). The following seven categories were analyzed in this paper:

1. AIDS (BTL code B184);
2. other degenerative and hereditary disorders of the central nervous system (BTL code B222 or ICD9 code 330, 331, 333–336);
3. spina bifida and hydrocephalus (BTL code B440 or ICD9 code 741, 742.3);
4. other deformities of central nervous system (BTL code B441 or ICD9 code 740, 742.0–742.2, 742.4–742.9);
5. other deformities of digestive system (BTL code B444 or ICD9 code 750, 751);
6. maternal conditions affecting fetus or newborn (BTL code B450 or ICD9 code 760); and
7. intestinal obstruction without mention of hernia (BTL code B344 or ICD9 code 560).

These diseases were selected from the database according the condition the birth defect was an important factor for death. The age categories: 0, 1, 2, 3, 4, 5–9, 10–14, ..., 80–84 years were used in the database. The age category ‘0’ was not used in the present study, because it contains three types of deaths: (a) the number of stillborn (dead fetus up 28 weeks or more 1000 g); (b) children, who died due the birth; and (c) children born alive but died before the first birthday.

The expected value of age for one particular age category is not equal to the average of the end points of the age interval (the mortality is extremely dependent on age during childhood). For example, the age category ‘1’ contains the number of deaths of children from the age interval 1; 2) and the expected value is not equal to 1.5. If the dependence of the number of deaths on age is known, the expected value \( \tau \) of age of all children, which died at the age interval \( \langle 1; 2 \rangle \) is

\[
\tau = \frac{\int_{t_1}^{t_2} t \cdot D(t) \, dt}{\int_{t_1}^{t_2} D(t) \, dt}, (4)
\]

where \( D(t) \) is the number of deaths at time \( t \). General formula for the age interval \( \langle A; B \rangle \) is

\[
\tau = \frac{\int_{A}^{B} t \cdot D(t) \, dt}{\int_{A}^{B} D(t) \, dt}, (5)
\]
Table 1
The expected values of age categories

<table>
<thead>
<tr>
<th></th>
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<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low limit A</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>25</td>
<td>30</td>
<td>35</td>
<td>40</td>
<td>45</td>
<td>50</td>
</tr>
<tr>
<td>Upper limit B</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>25</td>
<td>30</td>
<td>35</td>
<td>40</td>
<td>45</td>
<td>50</td>
<td>55</td>
</tr>
<tr>
<td>Function C/T</td>
<td>1.44</td>
<td>2.47</td>
<td>3.48</td>
<td>4.48</td>
<td>7.21</td>
<td>12.33</td>
<td>17.38</td>
<td>22.41</td>
<td>27.42</td>
<td>32.44</td>
<td>37.44</td>
<td>42.45</td>
<td>47.46</td>
<td>52.46</td>
</tr>
<tr>
<td>Function C/T²</td>
<td>1.39</td>
<td>2.43</td>
<td>3.45</td>
<td>4.46</td>
<td>6.93</td>
<td>12.16</td>
<td>17.26</td>
<td>22.31</td>
<td>27.35</td>
<td>32.37</td>
<td>37.39</td>
<td>42.40</td>
<td>47.41</td>
<td>52.42</td>
</tr>
</tbody>
</table>
If the number of deaths declines with age according to Eq. (2), the expected value is given by the formula

$$
\tau = \frac{\int_A^B t \cdot \frac{D(1)}{t} \, dt}{\int_A^B \frac{D(1)}{t^2} \, dt} = \frac{B - A}{\ln B - \ln A},
$$

(6)

where $D(1)$ is the number of deaths at the age of 1. If the number of deaths falls in the course of age with the second power of age, then mortality rate is

$$
R(t) = \frac{R(1)}{t^2},
$$

(7)

and, consequently, the expected value of age is

$$
\tau = \frac{\int_A^B t \cdot \frac{D(1)}{t^2} \, dt}{\int_A^B \frac{D(1)}{t^2} \, dt} = \frac{\ln B - \ln A}{(1/A) - (1/B)},
$$

(8)

The expected values of the age categories up to the age of 55 years are for both types of decline (Eqs. (6) and (8)) in Table 1. These values were used in all calculations and graphs.

The number of deaths is usually small in one age category after the birth. For this reason, the mortality rate was calculated using summary method (Riggs, 1992; Dolejs, 1998a; Dolejs and Kozak, 2000; Dolejs and Djajadasisastra, 2000). The number of deaths was added up in a particular age category for the entire period 1979–1991 (1987–1991 for AIDS). The number of living people was calculated by the same method. The mortality rate was calculated per 1000 living people and it describes the entire period.

### Table 2
The parameters of linear regression for the age interval <1; 5) years in log-log scale

<table>
<thead>
<tr>
<th>Code</th>
<th>Sex</th>
<th>Slope</th>
<th>Lower 95% CL</th>
<th>Upper 95% CL</th>
<th>$r^2$</th>
<th>$R(1)$ per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>B184</td>
<td>Male</td>
<td>−1.1482</td>
<td>−1.5209</td>
<td>−0.7755</td>
<td>0.9887</td>
<td>0.0210</td>
</tr>
<tr>
<td>B222</td>
<td>Male</td>
<td>−0.9091</td>
<td>−1.5887</td>
<td>−0.2295</td>
<td>0.9431</td>
<td>0.0275</td>
</tr>
<tr>
<td>B344</td>
<td>Male</td>
<td>−0.9601</td>
<td>−1.0007</td>
<td>−0.9195</td>
<td>0.9998</td>
<td>0.0039</td>
</tr>
<tr>
<td>B440</td>
<td>Male</td>
<td>−1.0972</td>
<td>−1.3705</td>
<td>−0.8239</td>
<td>0.9933</td>
<td>0.0153</td>
</tr>
<tr>
<td>B441</td>
<td>Male</td>
<td>−1.2259</td>
<td>−2.3718</td>
<td>−0.0800</td>
<td>0.9137</td>
<td>0.0156</td>
</tr>
<tr>
<td>B184</td>
<td>Female</td>
<td>−1.1420</td>
<td>−1.7576</td>
<td>−0.5264</td>
<td>0.9696</td>
<td>0.0226</td>
</tr>
<tr>
<td>B222</td>
<td>Female</td>
<td>−1.0785</td>
<td>−1.2948</td>
<td>−0.8623</td>
<td>0.9957</td>
<td>0.0289</td>
</tr>
<tr>
<td>B344</td>
<td>Female</td>
<td>−1.0888</td>
<td>−1.6521</td>
<td>−0.5255</td>
<td>0.9719</td>
<td>0.0027</td>
</tr>
<tr>
<td>B440</td>
<td>Female</td>
<td>−1.0769</td>
<td>−2.1276</td>
<td>−0.0262</td>
<td>0.9067</td>
<td>0.0143</td>
</tr>
<tr>
<td>B441</td>
<td>Female</td>
<td>−1.2259</td>
<td>−1.8711</td>
<td>−0.5807</td>
<td>0.9709</td>
<td>0.0176</td>
</tr>
</tbody>
</table>
Table 3
The parameters of linear regression for the age interval <1; 10) years in log–log scale

<table>
<thead>
<tr>
<th>Code</th>
<th>Sex</th>
<th>Slope</th>
<th>Lower 95% CL</th>
<th>Upper 95% CL</th>
<th>$r^2$</th>
<th>$R(1)$ per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>b184</td>
<td>1.0195</td>
<td>−1.2989</td>
<td>−0.7402</td>
<td>0.9782</td>
<td>0.0210</td>
</tr>
<tr>
<td>Male</td>
<td>b222</td>
<td>0.8036</td>
<td>−1.1472</td>
<td>−0.4600</td>
<td>0.9486</td>
<td>0.0275</td>
</tr>
<tr>
<td>Male</td>
<td>b344</td>
<td>0.8756</td>
<td>−1.0282</td>
<td>−0.7231</td>
<td>0.9911</td>
<td>0.0039</td>
</tr>
<tr>
<td>Male</td>
<td>b440</td>
<td>1.0325</td>
<td>−1.1962</td>
<td>−0.8689</td>
<td>0.9926</td>
<td>0.0153</td>
</tr>
<tr>
<td>Male</td>
<td>b441</td>
<td>1.2125</td>
<td>−1.6966</td>
<td>−0.7283</td>
<td>0.9549</td>
<td>0.0156</td>
</tr>
<tr>
<td>Male</td>
<td>b184</td>
<td>1.1188</td>
<td>−1.3818</td>
<td>−0.8557</td>
<td>0.9839</td>
<td>0.0226</td>
</tr>
<tr>
<td>Male</td>
<td>b222</td>
<td>0.9114</td>
<td>−1.2249</td>
<td>−0.5980</td>
<td>0.9662</td>
<td>0.0289</td>
</tr>
<tr>
<td>Female</td>
<td>b344</td>
<td>0.8864</td>
<td>−1.3204</td>
<td>−0.4525</td>
<td>0.9337</td>
<td>0.0027</td>
</tr>
<tr>
<td>Female</td>
<td>b440</td>
<td>1.0472</td>
<td>−1.4938</td>
<td>−0.6007</td>
<td>0.9489</td>
<td>0.0143</td>
</tr>
<tr>
<td>Female</td>
<td>b441</td>
<td>1.1260</td>
<td>−1.4520</td>
<td>−0.8001</td>
<td>0.9758</td>
<td>0.0176</td>
</tr>
</tbody>
</table>

3. Results

3.1. Mortality from seven categories of diseases

The dependence of mortality on age in log–log scale is in Figs. 1–14 for men and women for seven categories of diseases. These seven categories were divided according the slope into two sets:

(I) The slope of the decline is equal to −1 in the first set (Eq. (2) and Figs. 1–10). The following five categories ‘AIDS’; ‘Other degenerative and hereditary disorders of the central nervous system’; ‘Spina bifida and hydrocephalus’; ‘Other deformities of central nervous system’ and ‘Intestinal obstruction without mention of hernia’ are in this set. The expected value of age was calculated using Eq. (6) (the next to the last row in Table 1). The parameters of linear regression were calculated for the age intervals <1; 5) years and <1; 10) years in log–log scale. These parameters are shown in Tables 2 and 3. All confidence intervals contain the value −1. The average of the slopes is equal to −1.095 with the standard deviation 0.101 for the first age interval and it is equal to −1.003 with the standard deviation 0.131 for the second one. It follows from these results that the mortality rate is inversely proportional to the age (the model Eq. (2)). The slope of the straight lines is exactly equal to −1 and the straight lines go through the first point in Figs. 1–10 (they are not the regression straight lines).

Table 4
The parameters of linear regression for the age interval <1; 5) years in log–log scale

<table>
<thead>
<tr>
<th>Sex</th>
<th>Code</th>
<th>Slope</th>
<th>Lower 95% CL</th>
<th>Upper 95% CL</th>
<th>$r^2$</th>
<th>$R(1)$ per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>B444</td>
<td>−1.6973</td>
<td>−2.0131</td>
<td>−1.3815</td>
<td>0.9981</td>
<td>0.0102</td>
</tr>
<tr>
<td>Male</td>
<td>B450</td>
<td>−2.1368</td>
<td>−3.8333</td>
<td>−0.4403</td>
<td>0.9676</td>
<td>0.0006</td>
</tr>
<tr>
<td>Female</td>
<td>B444</td>
<td>−1.7025</td>
<td>−2.6444</td>
<td>−0.7607</td>
<td>0.9839</td>
<td>0.0113</td>
</tr>
<tr>
<td>Female</td>
<td>B450</td>
<td>−1.5210</td>
<td>−4.1512</td>
<td>1.1093</td>
<td>0.8694</td>
<td>0.0004</td>
</tr>
</tbody>
</table>
Table 5
The parameters of linear regression for the age interval <1; 10) years in log–log scale

<table>
<thead>
<tr>
<th>Sex</th>
<th>Code</th>
<th>Slope</th>
<th>Lower 95% CL</th>
<th>Upper 95% CL</th>
<th>$r^2$</th>
<th>R(1) per 1000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>b444</td>
<td>−1.8014</td>
<td>−2.0420</td>
<td>−1.5609</td>
<td>0.9947</td>
<td>0.0102</td>
</tr>
<tr>
<td>Male</td>
<td>b450</td>
<td>−1.8203</td>
<td>−2.7705</td>
<td>−0.8702</td>
<td>0.9253</td>
<td>0.0006</td>
</tr>
<tr>
<td>Female</td>
<td>b444</td>
<td>−1.6934</td>
<td>−2.1025</td>
<td>−1.2844</td>
<td>0.9830</td>
<td>0.0113</td>
</tr>
<tr>
<td>Female</td>
<td>b450</td>
<td>−1.4672</td>
<td>−2.6131</td>
<td>−0.3213</td>
<td>0.8470</td>
<td>0.0004</td>
</tr>
</tbody>
</table>

(II) The slope of the decline is less than $-1$ in the second set (Figs. 11–14). The expected value of age was calculated using the formula Eq. (8) (the last row in Table 1). The parameters of linear regression were calculated for the age intervals <1; 5) years and <1; 10) years in log–log scale. These parameters are shown in Tables 4 and 5. All confidence intervals contain the value $-2$. The average of the slopes is equal to $-1.764$ with the standard deviation 0.262 for the first age interval and it is equal to $-1.696$ with the standard deviation 0.162 for the second one. The model Eq. (6) should describe the mortality dependence on age for ‘Other deformities of digestive system’ and ‘Maternal conditions affecting fetus or newborn’. The slope of the straight lines is equal to $-2$ and the straight lines go through the first point in Figs. 11–14. (The dotted lines have the slope equal to $-1$ in Figs. 11–14.)

3.2. Theory of the age dependence of mortality from congenital defects

This theory is based on two pieces of evidence. First, a congenital defect may be so slight that the baby survives until high age, or so severe that it dies during the first hours. Consequently, the birth defect is at one of many different levels. The second assumption is based on the evidence that the continual improvement of the
birth defect with age is not observed. We suppose that the risk of death from congenital defect is not affected by age of an individual and we formulate two following assumptions.

1. The risk of death is independent of age for particular members of the subpopulation (the level of the defect is not affected by the age of an individual).

2. Congenital defect is at one of many different levels.

These two assumptions will be used to calculate mortality rate in whole population. Let the quantity $x$ be the level of congenital defect. If the defect causes death,
the quantity $x$ is risk of death per year. If an individual has the defect, which does not cause death, the quantity $x$ can be interpret as phenotype. The structure of the subpopulation with congenital defect is described by the frequency function $f(x)$. The quantity $f(x)$ is density function and it represents the portion of the subpopulation with the defect $x$ at the interval $(x; x+dx)$. Let $L_0$ be the number of born children. It is supposed that the subpopulation with congenital defect is composed from a lot of different levels of congenital defect. At the beginning, the number of people with defect $x$ is equal to
Fig. 6. Plot of logarithm of mortality rates from Spina bifida and hydrocephalus (ICD9 code 741, 742.3) for male in the US versus logarithm of age (1979–1991).

\[ N(x; t = 0) = f(x) L_0. \]  
\( \text{(9)} \)

It follows from the second assumption, that this number of people declines exponentially with age and it is

\[ N(x; t) = f(x) L_0 \exp(-xt). \]  
\( \text{(10)} \)

Children, who have died after the first birthday, had the defect in reality from some interval \((x_{\text{min}}; x_{\text{max}})\). All levels over \(x_{\text{max}}\) are empty, because the defect is so severe that all of them have died before their first birthday. The categories with \(x\)

Fig. 7. Plot of logarithm of mortality rates from Other deformities of central nervous system (ICD9 code 740, 742.0–742.2, 742.4–742.9) for female in the US versus logarithm of age (1979–1991).
less than the value $x_{\text{min}}$ do not affect the number of deaths also, because such defect does not cause death (the risk of death is so small that nobody dies during the whole period). For example, the lower limit may be stated as: ‘less than one individual dies from the category $x_{\text{min}}$ per 100 years from 100000 people’ and, consequently, the value $x_{\text{min}}$ is about $10^{-7}$. If only less than 5% with the congenital defect $x_{\text{max}}$ survive up the age of 1 year, then the second limit $x_{\text{max}}$ is about:

$$S_x(x_{\text{max}}, t=1) = \exp(-x_{\text{max}} \cdot 1) = 0.05 \Rightarrow x_{\text{max}} = -\ln(0.05) \approx 3,$$

(11)

$$S_x(x_{\text{max}}, t=1) = \exp(-x_{\text{max}} \cdot 1) = 0.05 \Rightarrow x_{\text{max}} = -\ln(0.05) \approx 3,$$
Fig. 10. Plot of logarithm of mortality rates from intestinal obstruction without mention of hernia (ICD9 code 560) for male in the US versus logarithm of age (1979–1991).

where \( S_x(t) \) is the survival function for defect \( x_{\text{max}} \).

The sum of all children in the subpopulation at age \( t \) is

\[
N_x(t) = \int_{x_{\text{min}}}^{x_{\text{max}}} N_x(x; t) dx = \int_{x_{\text{min}}}^{x_{\text{max}}} f(x) \cdot e^{-xt} dx
\]

and the number of deaths \( D_x(t) \) from congenital defect at age \( t \) per year is

\[
D(t) \equiv D_x(t) = -\frac{\partial N_x(t)}{\partial t} = L_0 \int_{x_{\text{min}}}^{x_{\text{max}}} x \cdot f(x) \cdot e^{-xt} dx,
\]

Fig. 11. Plot of logarithm of mortality rates from Other deformities of digestive system (ICD9 code 750, 751) for female in the US versus logarithm of age (1979–1991).
Fig. 12. Plot of logarithm of mortality rates from other deformities of digestive system (ICD9 code 750, 751) for male in the US versus logarithm of age (1979–1991).

where \( D_s(t) \) is the number of deaths from congenital defect per year and \( S_s(t) \) is survival curve of the subpopulation. The mortality rate \( R(t) \) of congenital defect in year \( t \) as calculated against the entire population is defined as \( D_s(t) \) over \( L(t) \)

\[
R(t) = \frac{D_s(t)}{L(t)} = \frac{\int_{x_{\min}}^{x_{\max}} x \cdot f(x) \cdot e^{-x \cdot t} \, dx}{\int_{x_{\min}}^{x_{\max}} f(x) \cdot e^{-x \cdot t} \, dx}
\]

Fig. 13. Plot of logarithm of mortality rates from maternal conditions affecting fetus or newborn (ICD9 code 760) for female in the US versus logarithm of age (1979–1991).
where $L(t)$ is the number of all living people at age $t$ and $S(t)$ survival curve of whole population.

If the size of the entire population does not suffer any substantial change (the change of the number of all people is less than 1% up the age of 15 years in the US), changes within the survival curve of the entire population $S(t)$ can be ignored. Consequently, the value of $S(t) = 1$ everywhere and the final mortality rate is

$$R(t) = \int_{x_{\text{min}}}^{x_{\text{max}}} x \cdot f(x) \cdot e^{-xt} \, dx. \quad (15)$$

It follows from the Eq. (15), that the mortality is determined by function $f(x)$. Further, we will assume that the individual mortality risk is normally or lognormally distributed (two most frequent distributions in nature). The position of the subpopulation with congenital defect in whole population is shown in Fig. 15 and Fig. 16 in case the quantity $x$ is normally or lognormally distributed.

If the quantity $x$ is lognormally distributed, then the mortality as calculated against the entire population is inversely proportional to the age (Eq. (2)). This evidence was particularly induced in the Appendix A (relationships Eqs. (A.1), (A.2), (A.3), (A.4), (A.5), (A.6), (A.7), (A.8), (A.9), (A.10), (A.11), (A.12), (A.13), (A.14), (A.15) and (A.16)). The parameter $R(1)$ depends on the values $\mu$, $\sigma$ (from the lognormal distribution), and $x_{\text{min}}$. It follows from the Eq. (A.16)

$$R(1) = \frac{1}{\sigma \sqrt{2\pi}} e^{\left(-\ln(x_{\text{min}}) - \mu\right)^2/2\sigma^2}. \quad (16)$$

If $x$ is normally distributed (for more details see also the Appendix A; relationships Eqs. (A.17), (A.18), (A.19), (A.20), (A.21), (A.22), (A.23), (A.24), (A.25), (A.26), (A.27) and (A.28)), then the mortality is inversely proportional to the second power of age (Eq. (7)). The parameter $R(1)$ depends on the values $\mu$, $\sigma$ (from the normal distribution) and $x_{\text{min}}$. It follows from the Eq. (15) and Eq. (A.28)
Fig. 15. The position of subpopulation with congenital defect if the quantity $x$ is normally distributed ($\mu = -3.5; \sigma = 1$).

$$R(1) = \frac{e^{-(\mu^2 + \gamma_{\min})/2\sigma^2}}{\sigma \sqrt{2\pi}}.$$ \hspace{1cm} (17)

4. Discussion

The mortality rate from congenital defects decreases linear in log–log scale. The same decline was observed in Japan and former Czechoslovakia (Dolejs, 1998b). The alternative model supposes that the mortality risk from congenital defect homogeneously declines in all individuals and it supposes a continual improvement of every individual. This mechanism has to work up the age of 50 years for Spina Bifida (BTL code 440) and other deformities of central nervous system (BTL code B441). The continual improvement has to cause that the mortality rate falls 50 times in the course of age. This explanation was rejected.

Fig. 16. The position of subpopulation with congenital defect if the quantity $x$ is lognormally distributed ($\mu = -100; \sigma = 100$).
We suppose that mortality risk is heterogeneous among individuals, and does not
affected by age. The level of congenital defect is classified using the individual
mortality risk. The presented theory explains the evidence that this decline of
mortality rate is linear in log–log scale in different countries and the evidence that
the slope of this decline in log–log scale is equal to $-1$. It follows only from the
assumption that the individual mortality risk is lognormally distributed. This result
does not depend of the parameters of the distribution. The depletion of different
categories of the congenital defect offers better explanation than the alternative
model does. The level of the developmental disability decreases throughout the
pregnancy, too (Boue et al., 1975). Spontaneous abortions exercise large elimination
of developmental disabilities in the course of pregnancy. Only 50% of conceptions
are estimated to develop into a birth of a living child (Roberts and Lowe, 1975).
The decline of mortality from congenital defect after the birth seems to be a
continuation of that process. The populations differ in the parameter $R(1)$ (Eq.
(16)) and it is a function of both the genotype and the environment. The mortality
rate in particular age category is the quantity, which is directly investigated. It
follows from the presented theory that the slope of mortality decline (the values
$-1$ or $-2$) demonstrates the type of statistic distribution of the individual
mortality risk from the congenital defect. Unfortunately, it is not direct information
about the phenotype. The relation between the individual mortality risk from the
congenital defect and the phenotype is not known. If we suppose, the multifactorial etiology for disease for which the mortality rate is
inversely proportional to the age, then the individual mortality risk rises exponen-
tially with the phenotype.

If the individual mortality risk is normally distributed it follows form the
presented theory, that the mortality is inversely proportional to the second power
of age. The results show that it is possible for two diseases: ‘Other deformities of
digestive system’ and ‘Maternal conditions affecting fetus or newborn’.

The mortality is inversely proportional to the age also for the infection diseases:
AIDS (in the US), Meningococcal infections (in the US) (Dolejs and Djajadasis-
stra, 2000) and for Pneumonia (in the US, Japan, former Czechoslovakia, Italy,
Portugal and United Kingdom) (Dolejs and Kozak, 2000). The presented theory
may explain this reduction of mortality rate if it is assumed that these infection
diseases have the multifactorial etiology and a hidden congenital frailty causes the
individual mortality risk. This idea is based on the evidence that the slope of the
mortality decline in log–log scale is equal to $-1$ in different populations.

At what age does real aging begin? The answer to the question is closely related
to the onset of exponential dependence of mortality rates on age. The Gompertz
relation applies on the population over the age of 10 years (Dolejs, 1997). The onset
of the Gompertzian area is moved down to the age of 10 years for some diseases
(Riggs, 1990, 1991). The presented theory shows the eventuality, that the total
mortality decline after the birth is caused by the depletion of different categories of
congenital frailty. Consequently, the exponential rise could exist earlier, but it is ‘overlap’ by the number of deaths caused by congenital frailty and accidents. We can not reject the hypothesis that the moment of the birth or even the moment of the conception is the real beginning of aging.

Appendix A

We will approximate following integral from the relationship Eq. (15).

\[ R(t) = \int_{x_{\text{min}}}^{x_{\text{max}}} x f(x) e^{-xt} \, dx = \int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx, \quad (A.1) \]

where \( f(x) \) is the frequency function of the distribution of congenital defect. We will integrate the product of two functions \( h(x) \) and \( g(x) \). We will assume that both of them are continuous and positive over the interval \((x_{\text{min}}, x_{\text{max}})\) (Figs. 15 and 16). In addition, the function \( h(x) \) is falling at this interval. The approximation is valid in case the function \( h(x) \) is almost constant at the interval \((x_{\text{min}}, x_{\text{max}})\) (the changes of \( h(x) \) are very small).

\[ h(x_{\text{min}}) - h(x_{\text{max}}) \approx 0. \quad (A.2) \]

The function \( h(x) \) will be chosen according this assumption. The inequality Eq. (A.3) follows from these assumptions:

\[ h(x_{\text{max}}) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx \leq \int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx \leq h(x_{\text{min}}) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx \equiv R_a(t). \quad (A.3) \]

The integral (Eq. (A.1)) will be approximated by the value \( R_a(t) \). The relative error \( \varepsilon \) of the approximation is

\[ \varepsilon \equiv \frac{\Delta R}{R}, \quad (A.4) \]

where \( \Delta R = R_a(t) - R(t) \) and \( R(t) \) is the actual value of the integral. It follows from the Eq. (A.3)

\[ \Delta R \equiv h(x_{\text{min}}) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx - \int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx \leq (h(x_{\text{min}}) - h(x_{\text{max}})) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx \quad (A.5) \]

and, consequently, the relative error \( \varepsilon \) is

\[ \varepsilon = \frac{h(x_{\text{min}}) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx - \int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx}{\int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx} \leq \frac{(h(x_{\text{min}}) - h(x_{\text{max}})) \int_{x_{\text{min}}}^{x_{\text{max}}} g(x)\, dx}{\int_{x_{\text{min}}}^{x_{\text{max}}} h(x)g(x)\, dx}. \quad (A.6) \]

We will use the Eq. (A.3) once more and the upper estimation of \( \varepsilon \) is
\[ \varepsilon \leq \frac{\int_{x_{\text{min}}}^{x_{\text{max}}} h(x) g(x) \, dx}{\int_{x_{\text{min}}}^{x_{\text{max}}} h(x) g(x) \, dx} \leq \frac{\int_{x_{\text{min}}}^{x_{\text{max}}} (h(x) - h(x_{\text{min}})) g(x) \, dx}{\int_{x_{\text{min}}}^{x_{\text{max}}} h(x) g(x) \, dx} \]  

(A.7)

and, consequently,

\[ \varepsilon \leq \frac{h(x_{\text{min}})}{h(x_{\text{max}})} - 1 = \varepsilon_{\text{max}} \Rightarrow \ln \left[ \frac{h(x_{\text{min}})}{h(x_{\text{max}})} \right] = \ln(1 + \varepsilon_{\text{max}}), \quad \text{(A.8)} \]

where \( \varepsilon_{\text{max}} \) is the maximal error of the approximation.

For small \( \varepsilon_{\text{max}} \) we may approximate:

\[ \ln(1 + \varepsilon_{\text{max}}) \approx \varepsilon_{\text{max}} \]  

and the maximal error \( \varepsilon_{\text{max}} \) of the approximation is

\[ \varepsilon_{\text{max}} = \ln \left[ \frac{h(x_{\text{min}})}{h(x_{\text{max}})} \right] = \ln(h(x_{\text{min}})) - \ln(h(x_{\text{max}})). \]  

(A.9)

Lognormal distribution of individual mortality risk \( x \)

The frequency function of the lognormal distribution is

\[ f(x) = \frac{1}{\sigma \sqrt{2\pi x}} e^{-\frac{-(\ln(x) - \mu)^2}{2\sigma^2}}, \]  

(A.11)

where \( \mu \) and \( \sigma \) are the parameters of this distribution. If this function is used in the Eq. (A.1), then the mortality rate is

\[ R(t) = \int_{x_{\text{min}}}^{x_{\text{max}}} e^{-xt} \frac{1}{\sigma \sqrt{2\pi x}} \frac{1}{\sigma \sqrt{2\pi x}} e^{-\frac{-(\ln(x) - \mu)^2}{2\sigma^2}} \, dx. \]  

(A.12)

We chose \( h(x) \) and \( g(x) \):

\[ h(x) = \frac{1}{\sigma \sqrt{2\pi x}} e^{-\frac{-(\ln(x) - \mu)^2}{2\sigma^2}} g(x) = e^{-xt} h(x_{\text{min}}) = \frac{1}{\sigma \sqrt{2\pi x}} e^{-\frac{-(\ln(x_{\text{min}}) - \mu)^2}{2\sigma^2}}. \]  

(A.13)

The maximal error \( \varepsilon_{\text{max}} \) of this approximation (Eqs. (A.10) and (A.13)) is

\[ \varepsilon_{\text{max}} = \ln \left[ \frac{h(x_{\text{min}})}{h(x_{\text{max}})} \right] = \ln \left[ \frac{e^{-\frac{-(\ln(x_{\text{min}}) - \mu)^2}{2\sigma^2}}}{e^{-\frac{-(\ln(x_{\text{max}}) - \mu)^2}{2\sigma^2}}} \right] = \frac{(\ln(x_{\text{max}}) - \mu)^2 - (\ln(x_{\text{min}}) - \mu)^2}{2\sigma^2}. \]  

(A.14)

In other words, if the error \( \varepsilon_{\text{max}} \) is small, then the lognormal distribution can be substituted in the integral Eq. (A.1) by the formula \( C/x \).

Consequently, mortality as calculated against whole population is

\[ R(t) = h(x_{\text{min}}) \int_{x_{\text{min}}}^{x_{\text{max}}} \frac{1}{x} e^{-xt} \, dx = h(x_{\text{min}}) \frac{e^{-x_{\text{min}}t} - e^{-x_{\text{max}}t}}{t}. \]  

(A.15)

We approximate the numerator in Eq. (A.15) using values \( x_{\text{min}} = 10^{-7} \) and \( x_{\text{max}} = 3 \): at the age of 1 \( \exp(-x_{\text{max}}) = 0.05 \), at the age of 2 \( \exp(-2x_{\text{max}}) = 0.0025 \).
and, consequently, \( \exp(-t x_{\text{max}}) \) is about 0; \( \exp(-t x_{\text{min}}) = 1 \) at the interval (1; 100) years and the numerator is about 1.

It follows from Eqs. (A.13) and (A.15) that the mortality rate is

\[
R(t) = h(x_{\text{min}}) \left[ \frac{e^{-x_{\text{min}}t} - e^{-x_{\text{max}}t}}{t} \right] \approx \frac{1}{\sigma \sqrt{2\pi}} e^{\left(-\frac{(\ln(x_{\text{min}}) - \mu)^2}{2\sigma^2}\right)} \frac{1}{t}.
\]

(A.16)

**Normal distribution of individual mortality risk** \( x \)**

The frequency function of the normal distribution is

\[
f(x) = \frac{1}{\sigma \sqrt{2\pi}} e^{\left(-\frac{(x - \mu)^2}{2\sigma^2}\right)},
\]

(A.17)

where \( \mu \) and \( \sigma \) are the parameters of this distribution. If this function is used in the Eq. (A.1), then the integral is

\[
R(t) = \frac{1}{\sigma \sqrt{2\pi}} \int_{x_{\text{min}}}^{x_{\text{max}}} e^{-x'x} e^{\left(-\frac{(x' - \mu)^2}{2\sigma^2}\right)} dx
\]

\[
= \frac{e^{-\frac{\mu^2}{2\sigma^2}}}{\sigma \sqrt{2\pi}} \int_{x_{\text{min}}}^{x_{\text{max}}} x e^{-\frac{x^2}{2\sigma^2}} \exp(-x(t-(\mu/\sigma^2))) dx.
\]

(A.18)

Let \( h(x) \) and \( g(x) \) be

\[
h(x) = \frac{e^{-\frac{(x^2 + x_{\text{max}}^2)/2\sigma^2}}}{\sigma \sqrt{2\pi}}, \quad g(x) = xe^{-x(t-(\mu/\sigma^2))} \quad h(x_{\text{min}}) = \frac{e^{-\frac{(x_{\text{min}}^2 + x_{\text{max}}^2)/2\sigma^2}}}{\sigma \sqrt{2\pi}}.
\]

(A.19)

For small \( x_{\text{min}} \) (10\(^{-7}\)) and big \( x_{\text{max}} \) (3) the following relationship is valid

\[
x_{\text{max}}^2 - x_{\text{min}}^2 \approx x_{\text{max}}^2.
\]

(A.20)

It follows from the Eq. (A.10)

\[
\varphi_{\text{max}} = \ln\left[ \frac{h(x_{\text{min}})}{h(x_{\text{max}})} \right] = \ln\left[ \frac{e^{-x_{\text{min}}^2/2\sigma^2}}{e^{-x_{\text{max}}^2/2\sigma^2}} \right] = \frac{x_{\text{max}}^2 - x_{\text{min}}^2}{2\sigma^2} \approx \frac{x_{\text{max}}^2}{2\sigma^2}.
\]

(A.21)

If this value is small the normal distribution can be substituted by the formula

\[
f(x) \approx \frac{e^{-\frac{(x^2 + x_{\text{min}}^2)/2\sigma^2}}}{\sigma \sqrt{2\pi}} e^{-x(t-(\mu/\sigma^2))}.
\]

(A.22)

Consequently, mortality as calculated against whole population is

\[
R(t) = \frac{e^{-\frac{(x^2 + x_{\text{min}}^2)/2\sigma^2}}}{\sigma \sqrt{2\pi}} \int_{x_{\text{min}}}^{x_{\text{max}}} xe^{-x(t-(\mu/\sigma^2))} dx.
\]

(A.23)

The following formula will be used to calculate this integral

\[
\int xe^{Ax} dx = \frac{e^{Ax}}{A}(Ax - 1),
\]

(A.24)

where \( A = -(t-(\mu/\sigma^2)) \). Using the Eq. (A.24), we obtain relationship
\[ R(t) = h(x_{\text{min}}) \left[ \frac{e^{-x_{\text{max}}(t - (\mu/\sigma^2))}}{(t - (\mu/\sigma^2))^2} - x_{\text{max}}(t - (\mu/\sigma^2)) - 1 \right] - e^{-x_{\text{min}}(t - (\mu/\sigma^2))} \left[ (t - (\mu/\sigma^2))^2 - x_{\text{min}}(t - (\mu/\sigma^2)) - 1 \right]. \] (A.25)

This relationship is more simple if we use the evidence that \( x_{\text{min}} \) is very small and \( x_{\text{max}} \) is about 1 (estimated values from the Eq. (11) \( x_{\text{min}} = 10^{-7} \) and \( x_{\text{max}} = 3 \)):

\[ R(t) \approx \frac{1}{\sigma/\sqrt{2\pi}} e^{-(\mu^2 + x_{\text{max}}^2)/2\sigma^2} \left( t - \frac{\mu}{\sigma^2} \right)^2. \] (A.26)

If the square of \( \sigma \) is much more than \( \mu \), then the denominator is

\[ \left( t - \frac{\mu}{\sigma^2} \right) \rightarrow t \] (A.27)

and, consequently, the result mortality rate is

\[ R(t) \approx \frac{\exp\left(-\left(\mu^2 + x_{\text{min}}^2\right)/2\sigma^2\right)}{\sigma/\sqrt{2\pi}} \frac{1}{t^2}. \] (A.28)

References


