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Analysis of mortality decline along with age and latent congenital defects

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Abstract

Mortality from congenital anomalies is inversely proportional to age after the age of 1 year. The theory of congenital individual risk explains this mortality decline. The overall aim of this study is to test whether the theory describes mortality decline for all diseases within the first year of life and after the age of 1. Mortality decline along with age was analyzed in five countries and for all causes of death. The theory of congenital individual risk describes well the real mortality decline for all diseases except malignant neoplasms after the birth. Decline of mortality is due to the dying out of the more impaired individuals. Mortality decline with the first power of age results from the selection before the birth. It is dominant and the frequency of defects decreases proportionally to the value of individual risk of death. In the case of identically probable defects, the selection does not occur and mortality declines with the square of age. Congenital defects were also identified as a cause of death in the case of infectious diseases occurring before the age of 10. Mortality from malignant neoplasms is age-independent within the age period 1–20 years and, contrary to all other diseases, no small subpopulation with a significant individual risk was identified.

Keywords: Mortality; Age; Congenital anomaly; Infectious diseases; Theory of congenital individual risk

1. Introduction

Mortality represents a decisive criterion in medicine. The fastest and most significant changes in mortality result from decrease of mortality after the birth. In the United States, the mortality from the ''All diseases'' category has decreased 10 540 times within the period from the birth until the age of 10, and 117 000 times in case of ''Other deformities of central nervous system'' category (Basic Tabulation List (BTL) code; B441) from birth until the age of 40. It decreased 58 000 000 times since the birth until the age of 20 for the category of ''Slow fetal growth, fetal malnutrition and immaturity'' (BTL code: B452). The explanation of the mortality decline implies the existence of latent congenital defects which cause death even in case of diseases where no congenital defect was observed (Dolejs, 2001; Vaupel and Yashin, 1985).

1.1. Defect present at the moment of birth

In about 60% of biological deaths under the age of 10 in the United States, a defect present at the moment of birth was identified as a cause of death. The BTL ICD9 (WHO, 1977) calls those deaths: congenital anomalies (BTL code: B44) and certain conditions originating in the perinatal period (BTL code: B45) (WHO, 1977). The mortality caused by a major part of congenital anomalies declines with the first power of age after the first year of life (for $t > 1$; Dolejs, 1998, 2001). The decline can continue till older age in case of certain congenital anomalies. For example, the mortality caused by Spina bifida and hydrocephalus (BTL code: B440) in US was decreasing until the age of 55.

The decline can be possibly explained by the presumption that the organism is developing and adapting

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itself to the congenital anomaly. Nevertheless, the clinical experience excludes the possibility of such a gradual and significant improvement in the resistance against the detrimental effect of congenital anomalies (see the Web sites National Institute of Neurological Disorders and Stroke (the internet address: http://www.ninds.nih.gov/health_and_medical/disorders/spina_bifida.htm) and American Heart Association (the internet address: http://www.americanheart.org). And above that, it is not possible that the process carries over until the age of 55. And as the decline of mortality decreases with the first power of age for a major part of congenital anomalies, the improvement would be same for the main part of congenital anomalies.

1.2. Theory of congenital individual risk

The theory of congenital individual risk offers another explanation. It explains the decline of mortality within a population as the result of the more affected individuals dying off (Dolejs, 2001). The theory starts from two presuppositions:

1) Every impaired individual possesses an individual risk of mortality, defined by the degree of impairment. A congenital defect may be so slight that the baby survives until high age or so severe that it dies during the first hours. Some congenital defects remain undiscovered for the whole lifetime (Shields et al., 1999; Towbin et al., 1999; Castilla et al., 2001). That is the reason why a congenital individual risk of death can assume varied values, being different by several orders. The individual risk of death associated with congenital defect is almost zero in case of a major part of population. Non-zero value of risk is observed in case of more affected individuals and the most impaired ones with an extreme congenital individual risk die during first hours of life.
2) The changes of congenital individual risk value along with age are small when compared with the total range of congenital individual risks within the population. The theory presumes that the congenital individual risk of death is age-independent and depends on the severity of the congenital defect.

The type of the mortality decline along with age is determined by the type of statistical distribution of congenital individual risks within the population at the moment of birth. In the theory, it applies to the dependence of the mortality $R(t)$ upon the age, that (Dolejs, 2001):

$$R(t) = \frac{1}{S(t)} \int_0^{x_{\max}} x \cdot f(x)\, \mathrm{e}^{-xt}\, \mathrm{d}x \quad \text{for } t > 0 \tag{1}$$

where x is the number of deaths per one living per year inside subpopulation with similar impairment, $f(x)$ a frequency function of individual risks x (for $t = 0$), $x_{\max}$ a maximum individual risk of a particular population reflecting the condition of the most impaired individuals in the whole population and $S(t)$ a survival curve (percentage of all living individuals at the age t).

It applies for the log-normal distribution of individual risks $f(x)$, which can be substituted by the formula $f(x) = \text{const.}/x$ in Eq. (1) for large x, that:

$$R^{\mathrm{I}}(t) = \frac{R(1)}{S(t)} \left[\frac{1 - \mathrm{e}^{-x^0_{\max} t}}{t} \right] \quad \text{for } t > 0 \tag{2}$$

where a parameter $R(1)$ corresponds to the mortality rate at the age $t = 1$ year (Dolejs, 2001). If the size of the entire population does not suffer any substantial change, the survival curve of the entire population $S(t)$ is equal to 1. As the most affected individuals die within the first hours of life, the maximum individual mortality risk $x_{\max}$ can be higher than 10 at the moment of birth. The exponential element of Eq. (2) can be ignored for $t > 1$ after the end of the first year (the value of the product $tx_{\max}$ is high for $t > 1$). Consequently, since the end of the first year the mortality decreases with the first power of age:

$$R^{\mathrm{I}}(t) = \frac{R(1)}{t} \quad \text{for } t > 1 \tag{3}$$

The decline corresponds to a linear function with a slope equal to -1 within the log–log scale. The decline was observed for the majority of congenital anomalies in US, Japan and former Czechoslovakia within the interval 1–10 years (Dolejs, 1998, 2001).

It applies for the even distribution or normal distribution with a large variance of congenital individual risks $f(x)$ that (Dolejs, 2001):

$$R^{\mathrm{II}}(t) = \frac{R(1)}{S(t)} \frac{1}{t^2} [1 - \mathrm{e}^{-x^0_{\max} t}(x^0_{\max} t + 1)] \quad \text{for } t > 0 \tag{4}$$

For $t > 1$, the second element in brackets can also be ignored and the mortality declines with the second power of age:

$$R^{\mathrm{II}}(t) = \frac{R(1)}{t^2} \quad \text{for } t > 1 \tag{5}$$

This dependence corresponds to the linear decline with a slope equal to -2 in the log–log scale. The mentioned decline of mortality with $t > 1$ year was observed for other deformities of digestive system (BTL code B444) and for maternal conditions affecting fetus or newborn (BTL code B450) in US (Dolejs, 2001).

So far, all analysis of the mortality decline along with the age under 1 year used only data of one age category and, therefore, the decline was studied only for $t > 1$ year. Now, four age categories within the interval (0; 1)

are used. If the theory of congenital individual risk is correct, the following conclusions should apply.

a) Eq. (2) or Eq. (4) should apply for dependence of mortality upon the age during the first year of life. Then, in case of small values of t, the dependence of mortality logarithm upon the logarithm of age could deviate from the straight line towards lower values. An age limit above which the exponential element can be disregarded should always exist. Past that limit, the mortality logarithm should decrease linearly with the logarithm of age with the slope equal to -1 or -2. This age limit depends upon the value of x_{max}.
b) From the point of view of this theory, the maximum value of individual risk x_{max} within the population is given by the distribution of parameters of the congenital individual risks $f(x)$ and by the number of individuals born (the size of sample). If the parameters of individual risks distribution $f(x)$ do not differ significantly in various countries, the maximum value of x_{max} corresponding to severe defects should grow along with the size of population.

1.3. Other causes of death

The decline of mortality with the first power of age (Eq. (3)) was observed also for three infectious diseases: (1) pneumonia (BTL code B321) in US, former Czechoslovakia, Italy, Portugal and UK within the age interval 1–10 years (Dolejs and Kozak, 2000), (2) meningococcal infections (BTL code B036) in US within the age interval 1–30 years (Dolejs and Djajadisastra, 2000) and (3) AIDS (BTL code B184) in US within the age interval 1–10 years (Dolejs, 2001). A hypothesis was formulated that the deaths in case of those diseases are also caused by a congenital defect (Dolejs, 2001).

For these reasons, the mortality decline since the moment of birth was analyzed for all causes of death that are included into the BTL list (WHO, 1977) for five countries. The categories of diseases with more than 1% of all biological deaths before the age of 10 were selected. For calculation, only publicly accessible data were used.

2. Materials and methods

2.1. Source of data

The mortality calculations are based on the WHO Mortality Database (the internet address: http://www.who.int/whosis/mort/download.htm; files: "infmort", "icd9" and "pop"). The database uses the BTL classification of causes of death (WHO, 1977). For the first year of life, the data from the "infmort" file were used. This file contains the numbers of deaths split according to age into four age categories. These four age categories are hereafter labeled as A, B, C and D (A: $t <$ 1 day, B: 1–7 days, C: 7–28 days, D: 28–365 days). The "icd9" file, which also contains the numbers of deaths split according to age and causes of deaths for each country, was used for the age categories of 1–2, 2–3, 3–4, 4–5, 5–10, 10–15,...,80–85 years. The numbers of living individuals in each age category were obtained from the "pop" file.

2.2. Calculation of mortality

If mortality decreases steeply with the age, the numbers of deaths are low in one age category so that there are no deaths in certain years. On the grounds of that fact, the summary method, used e.g. in paleodemography, was applied. The method was used the first time in 1693 by well-known astronomer and mathematician Edmund Halley (Halley, 1693). It enables calculation of mortality rate of one age category on the basis of the numbers of dead and living individuals for several years. The mortality unit for all age categories sums to per year. For example, in the case of A age category (the first day of life), the mortality per year is equal to:

$$R(A) = \frac{365D(\mathrm{A})}{L(\mathrm{A})} \tag{6}$$

where $D(\mathrm{A})$ is the sum of those who died during the first day of life for the whole period (e.g. 1979–1997 in case of US) and $L(\mathrm{A})$ the sum of the individuals born within that period.

The theory of congenital individual risk describes the dependence of mortality upon age in cohort (i.e. population born within 1 year). The calculation of mortality for the whole period is a compromise between the dependence within cohort and that one within one calendar year. The difference between the mortality dependence upon age in cohort and in the whole period does not show if the life conditions do not change significantly and a population with the same characteristics is born within the given period. That applies well in case of mortality decline under the age of 10.

2.3. Selection of diseases

An accident can be called a non-biological cause of death with an unclear relation to the state of the given organism. (Accidents accounted for 11% of all deaths at the age <10 in US within the period 1979–1997.) As we are interested in the biological causes of death, subtraction of those who died due to an accident (BTL codes: B47–B52) from the total number of dead individuals will be reasonable (Dolejs, 1997). By subtraction, a new

category of all biological death is created under the title of "All diseases", labeled by the symbol "BA".

Certain categories of diseases sampled by the number of deaths for the period 1979–1997 in US were selected from the "All diseases" category. The sampled categories were those with a double-digit BTL code, where the number of dead individuals up the age of 10 exceeded 1% out of all deaths within the "All diseases" category up the age of 10. Apart from the selected categories, another three categories of causes of deaths were created. The three categories are called: "Infectious diseases" labeled as BB (BTL codes: B01–B07), "Malignant neoplasms" represented by the symbol BC (BTL codes: B08–B14, B16–B17) and "Diseases of the cardiovascular system" labeled as BD (BTL codes: B25–B30).

More detailed subcategories marked by three-digit codes were selected according the same criterion from congenital anomalies (BTL code: B44) and certain conditions originating in the perinatal period (BTL code: B45). These categories also include diseases with more than 1% share in all deaths before the age of 10 from "All diseases". Table 1 shows all selected categories and their share in all biological deaths up to 10 years. If we apply the same criterion on the data in other countries, we get practically identical lists of diseases. Table 1 shows the periods for which the ICD9 classification was used and the mortality calculated. Then there are numbers of born individuals for the whole period and numbers of dead individuals under the age of 10 for the "All diseases" category (BA).

2.4. Calculation of survival curve $S(t)$

The survival curve $S(t)$ in Eqs. (2) and (4) is a quantity of the second-order from the perspective of the dependence of mortality on age within the interval of 0–10 years, because the size of population falls by 2% at maximum within the first 10 years. As the total mortality grows exponentially since the age of 15, the decrease in numbers of living individuals over the age of 15 is significant and $S(t)$ is not equal to 1.

The value of $S(1) = 1$ was used for all countries and for the first year of life (the first four age categories). In the case of other age categories, the values corresponding with the mean of age category and the middle calendar year of each period for each country were used. The survival curves of US, Japan, France and Sweden are based on the Berkeley Mortality Database data (the internet address: http://www.demog.berkeley.edu/wilmoth/mortality/index.html). The data for the Czech

Table 1
The list of selected categories of diseases

	Code	Name	Country				
			US	Japan	France	Sweden	Czech Republic
Period			1979–1997	1979–1994	1979–1997	1987–1996	1986–1993
Number of born			72874895	22054500	14112148	1137515	1024200
All biological deaths up to 10 years			824286	166044	129521	7151	12513
Share of deaths up to 10 years from all birth (%)			1.13	0.75	0.92	0.63	1.22
1	BA	All diseases: all codes without B47–B52	100.0	100.0	100.0	100.0	100.0
2	BB	Infection diseases: BTL codes B01–B07	2.5	3.5	2.7	2.5	1.1
3	B03	Other bacterial diseases	1.3	1.3	0.8	1.7	0.4
4	BC	Malignant neoplasms: BTL codes: B08–B14, B16 and B17	3.2	7.2	5.5	5.4	5.5
5	B13	Malignant neoplasm of other and unspecified sites	1.3	1.6	1.5	2.2	1.7
6	B14	Malignant neoplasm of lymphatic and haemop. tissue	1.2	3.4	2.1	1.9	2.5
7	B18	Endocrine and metabolic diseases, immunity disorders	1.8	1.2	2.2	2.4	1.8
8	B22	Diseases of the nervous system	3.4	4.6	4.6	3.8	5.5
9	BD	Diseases of the cardiovascular system: BTL codes: B25–B30	3.6	5.4	2.3	2.3	1.5
10	B28	Diseases of pulmonary circulation, other of heart disease	2.7	4.3	1.6	1.8	1.2
11	B32	Other diseases of respiratory system	4.0	7.0	2.2	2.3	4.5
12	B34	Diseases of other parts of the digestive system	1.5	1.1	1.2	1.1	1.6
13	B44	Congenital anomalies	20.9	29.3	21.4	33.5	27.0
14	B440	Spina bifida and hydrocephalus	1.0	1.1	1.5	1.0	2.5
15	B441	Other deformities of central nervous system	2.3	1.1	1.4	2.2	2.5
16	B442	Congenital anomal. of heart and circulatory systems	8.4	16.6	11.6	13.3	11.0
17	B447	Other congenital anomal. of musculoskeletal system	1.4	1.8	1.5	2.9	2.0
18	B45	Certain conditions originating in the perinatal period	41.1	30.8	22.8	30.4	46.1
19	B451	Obstetric complications affecting foetus or newborn	5.7	0.0	1.1	3.2	1.6
20	B452	Slow fetal growth, fetal malnutrition and immaturity	8.7	2.7	1.8	3.7	20.5
21	B454	Hypoxia, birth asphyxia and other respiratory conditions	16.3	18.1	11.5	13.8	16.1
22	B46	Signs, symptoms and ill-defined conditions	13.9	3.8	31.0	13.5	2.0

Republic are those published by the Czech Statistical Office (1990).

2.5. Determination of the last age category T with decline of mortality

The upper limit of mortality decline T was determined for each group of diseases and each country individually. T marks the upper limit of the last age category with mortality decline (e.g. $T = 10$ years for the category "All diseases" in US). The mortality rate of the next age category has a higher value. The T value is given as the second limit of the interval in Table 2. It is common for both linear and nonlinear regressions.

2.6. Determination of a representative point T_i of an age category

If the mortality rate is strongly age-dependent, then the arithmetic mean of the extreme points of one age category cannot be used as a representative point of the age category. The mortality rate $R(t)$ can be defined in two ways. Either as the ratio of the number of dead individuals for certain period and the number of all living individuals at the beginning of the same period (see Eq. (6)) or as a continuous function. It applies for the latter case that:

$$R(t) = \frac{-\mathrm{d}S(t)/\mathrm{d}t}{S(t)} \tag{7}$$

where $S(t)$ is the percentage of living individuals at the age t.

It is necessary for the analysis of mortality decline to assign one representative point T_i to all dead individuals within one age category $(t_{i-1};\ t_i)$. The number of the living individuals within one age category (the size of whole population) is almost constant. Thus the decrease of deaths $\mathrm{d}(t)$ ($\mathrm{d}(t) \approx -\mathrm{d}S(t)/\mathrm{d}t$) represents the decisive factor for the dependence of the mortality upon the age within one age category. The representative point T_i can be calculated for each age category if the type of function $\mathrm{d}(t)$ is known. As the $\mathrm{d}(t)$ function is also valid within the age category, the number of dead individuals within the age category $(t_{i-1};\ t_i)$ is given by:

$$D_i = D(t_i) - D(t_i - 1) \tag{8}$$

where $D(t)$ is the anti-derivative of the function $\mathrm{d}(t)$. The following equation defines the T_i point:

$$(t_i - t_{i-1})\ \mathrm{d}(T_i) = D(t_i) - D(t_{i-1}) \tag{9}$$

It applies for the function $\mathrm{d}(t) = C/t$, where C is invariable, that:

$$\frac{C}{T_i} = \frac{C(\ln(t_i/t_{i-1}))}{t_i - t_{i-1}} \tag{10}$$

Table 2
The age interval of mortality decline for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	(0; 10)	(0; 15)	(0; 15)	(0; 15)	(0; 15)	(0; 10)	(0; 10)	(0; 10)	(0; 15)	(0; 15)	(0; 55)	(0; 40)	(0; 15)	(0; 15)	(0; 25)	(0; 15)	(0; 20)	(0; 30)	(0; 10)
Japan	(0; 15)	(0; 15)	(1d; 15)	(0; 15)	(0; 15)	(0; 10)	(0; 10)	(0; 15)	(0; 5)	(0; 45)	(0; 45)	(0; 30)	(0; 30)	(0; 25)	(0; 25)	x	x	(0; 15)	(0; 15)
France	(0; 10)	(0; 15)	(0; 15)	(0; 10)	(0; 10)	(0; 10)	(0; 10)	(0; 10)	(0; 15)	(0; 35)	(0; 10)	(0; 30)	(0; 15)	(0; 5)	(0; 25)	x	x	(0; 25)	(0; 15)
Sweden	(0; 10)	(0; 10)	(0; 10)	(0; 15)	(0; 10)	(0; 10)	(0; 10)	(1d; 5)	(1d; 10)	(0; 10)	(0; 10)	(0; 10)	(0; 10)	(0; 10)	(0; 25)	x	x	x	(0; 10)
Czech Republic	(0d; 10y)	(7d; 5y)	(7d; 15y)	(1d; 5y)	(1d; 10y)	(1d; 5y)	(1d; 5y)	(0; 10)	(0; 5)	(0; 50)	(0; 15)	(0; 30)	(0; 15)	(0; 10)	x	x	x	x	(0; 15)

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

and, consequently, T_i is

$$T_i = \frac{t_i - t_{i-1}}{\ln(t_i/t_{i-1})} \tag{11}$$

It applies similarly for $d(t) = C/t^2$, that:

$$T_i = \sqrt{\frac{t_i - t_{i-1}}{1/t_{i-1} - 1/t_i}} \tag{12}$$

In both cases, T_i does not depend on the parameter C. If the number of dead individuals is age-independent, then the arithmetic mean of the extreme point of age categories can be used.

As the function $d(t)$ is not defined for $t_0 = 0$, the value was replaced by the value of 1 min = 0.000001903 years. (As stillbirths are not included in the number of deaths, those born alive must have lived 1 minute, at least.) T_i values for three functions $d(t)$ are listed in Table 5.

First, the arithmetic mean of the outmost values of a particular age category was applied. A visual assessment of the type of mortality decline $d(t)$ was made for this and the next categories and a representative value of T_i from Table 5 was assigned to the age category $(t_{i-1}; t_i)$. The same procedure was applied to all age categories and for each category of diseases and each country separately.

2.7. Types of decline of mortality

The type of decline of mortality along with age (choice between Eqs. (2) and (4)) was determined for each category and each country separately. Two straight lines with the slope −1 and −2 in the log–log scale were drawn through the point of the age category 1–2 years. The smaller sum of squares of the logarithm of mortality rate deviations from those lines within the interval (1; T) represented the criterion for one of the two hypotheses being assigned to slope b. Figs. 1–10 show the dashed line with the slope −1 and the dotted line with the slope −2. (They are not the regression straight lines.) Table 3 shows the type of decline for all data. The "I" symbol marks the hypothesis Ho: $b = -1$ and the "II" symbol marks the hypothesis Ho: $b = -2$.

In case of malignant neoplasms BC (BTL codes: B08–B14, B16–B17), B13 and B14, a hypothesis was proposed that the logarithm of mortality does not depend on age (Ho: $b = 0$) (Dolejs, 1997). The hypothesis was not rejected in case of any of the five countries and for the age interval of (1; 20) (95% CL). The age limit of 20 years was determined on an ad hoc basis.

As it was not proved that the mortality due to malignant neoplasms is age-dependent, the dependence of mortality upon the age was not further studied for these diseases.

3. Results

3.1. Linear regression within the interval (1; T)

Mortality rate for all age categories in the five countries was calculated for the selected categories of causes of death. In the theory of congenital individual risk, the dependence of the logarithm of mortality rate upon the logarithm of age is linear from the first year of age. (The exponential element in Eqs. (2) and (4) can be ignored for $t > 1$.) All previous studies have proved this effect (Dolejs, 1998, 2001). Thus the age category of 1–2 years always was the first point where the linear regression was calculated.

Parameters a and b in Eq. (13) were calculated through the method of the linear regression for all countries within the interval (1; T) and for all categories of diseases listed in Table 1, excluding malignant neoplasms (BC, B13 and B14).

$$\ln(R(t)) + \ln(S(t)) = a + b \ln t \tag{13}$$

Deviations of mortality logarithm from the regression line were proved to be age-independent in all cases (95% CL). Calculation was not made in the case of no death within certain age category and the interval (1; T). In Tables 2–4 and in Tables 6–11, the cases are marked by the symbol "x". The hypothesis for the slope was tested for all data. In case of the decline of the first type (the symbol: "I"), the hypothesis Ho: $b = -1$ (95% CL) was tested. In case of the decline of the second type (the symbol: "II"), the hypothesis Ho: $b = -2$ (95% CL) was tested. Results of the test are written in brackets in Table 3. Tables 6–9 present detailed results of the linear regression.

For the following categories of diseases, the hypothesis Ho: $b = -1$ was not rejected in any of the countries (see Table 3): infectious diseases, symbol BB (BTL codes: B01–B07), other bacterial diseases (BTL code: B03), diseases of the cardiovascular system, symbol BD (BTL codes: B25–B30), diseases of pulmonary circulation, other of hearth diseases (BTL code: B28), congenital anomalies (BTL code: B44) and congenital anomalies of hearth and circulatory system (BTL code: B442). The hypothesis was rejected in those cases where the real mortality values of the last age categories were higher than the theoretical ones. The fact that the real decline of mortality is slower than the theoretical one can be due to an age-independent mortality element (e.g. the category BA; see Table 3 and Fig. 3).

In case of the second and faster decline, the hypothesis was rejected for the category B45 in US and France (see Table 3). The hypothesis Ho: $b = -2$ was not rejected for the age interval (1; T) in Japan (see Table 3). There was no case of death over the age of 1 observed in the Czech Republic in the category B45. The first type of mortality decline was assigned in the category B45 only

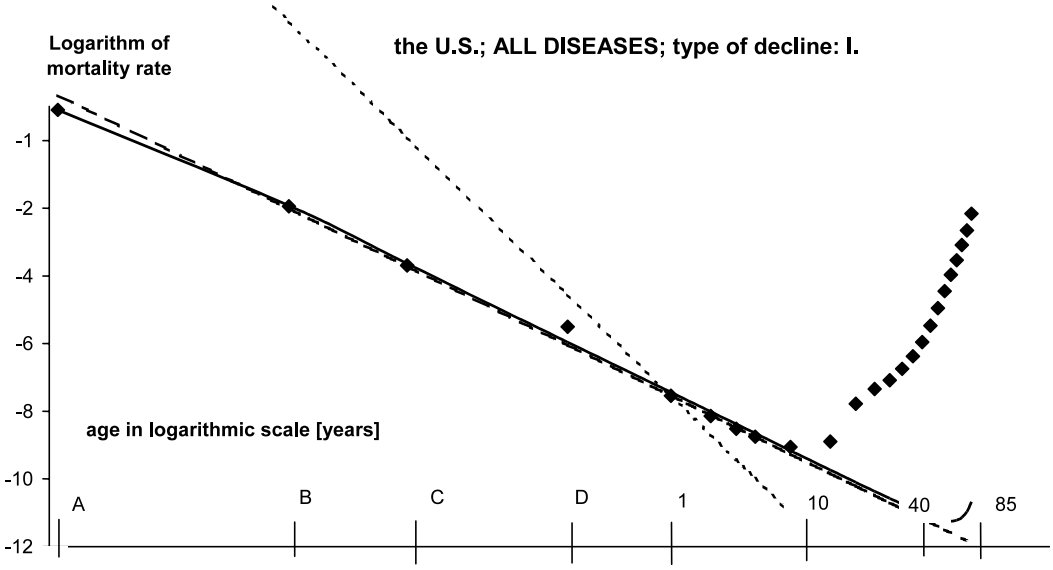

Fig. 1. Plot of logarithm of mortality rates from "All diseases" in the US versus logarithm of age (1979–1997). The dashed line was drawn through the mortality rate of the age category 1–2 years with the slope −1. The dotted line was drawn through the same point with the slope −2. They are not the regression straight lines. The solid line represents the right side of Eq. (2) and the values of parameters x_{max} and $R(1)$ calculated using nonlinear regression. The "A" symbol marks the representative point of the first age category ($t < 1$ day), the "B" symbol marks the representative point of the second age category (1–7 days), the "C" symbol marks the representative point of the third age category (7–28 days) and the "D" symbol marks the representative point of the fourth age category (28–365 days).

in Sweden. There, F-statistics and the coefficient of determination are very low (see Tables 9–11). Fig. 9 shows that in case of a range smaller than the interval (1; T), the model is able to describe well the data in the category B45 in US. The second type of decline was observed also for the subcategories B450, B451, B452 and B454 in US (see Table 3; Dolejs, 2001). The hypothesis Ho: $b = -2$ was not rejected for these diseases in the interval (1; T). Thus the decline of mortality for the B45 category is of the second type (Figs. 9 and 10 and Table 3).

To study the slope frequency, the list of diseases was reduced to prevent some dead individuals from being included twice. For example, in case of BB and B03 categories only the BB was included. This resulted in the following list of diseases: BB, BD, B18, B22, B32, B34, B44, B45 and B46. In case of B45 category, no death was registered in the Czech Republic for $t > 1$ and the slope was not calculated and for that reason $n = 44$. It follows from the histogram that the slope −1 is the dominant one. The arithmetic mean of the slope for the diseases with the first type of decline equals −1.02 with

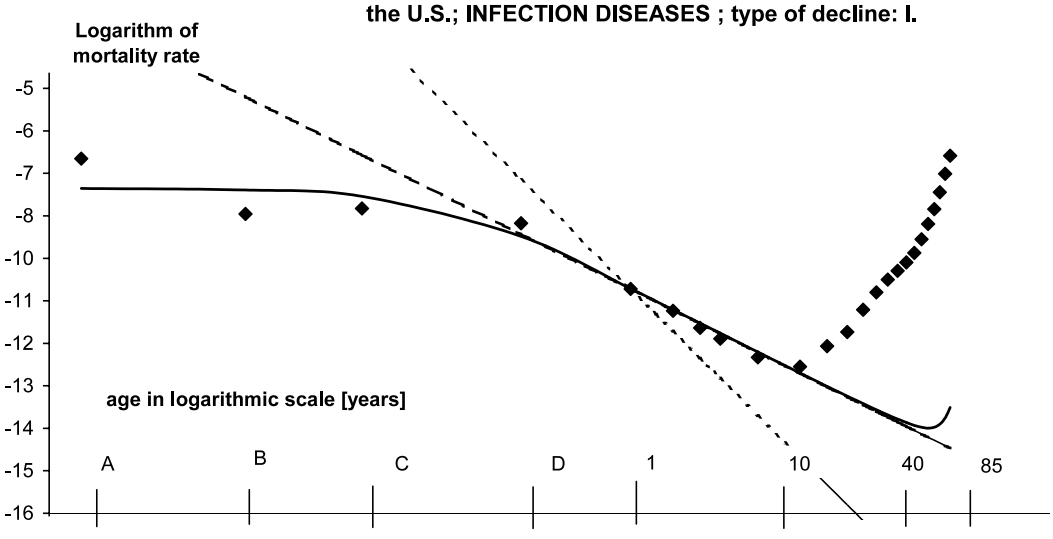

Fig. 2. Plot of logarithm of mortality rates from infection diseases (BTL codes: B01–B07) in US versus logarithm of age (1979–1997).

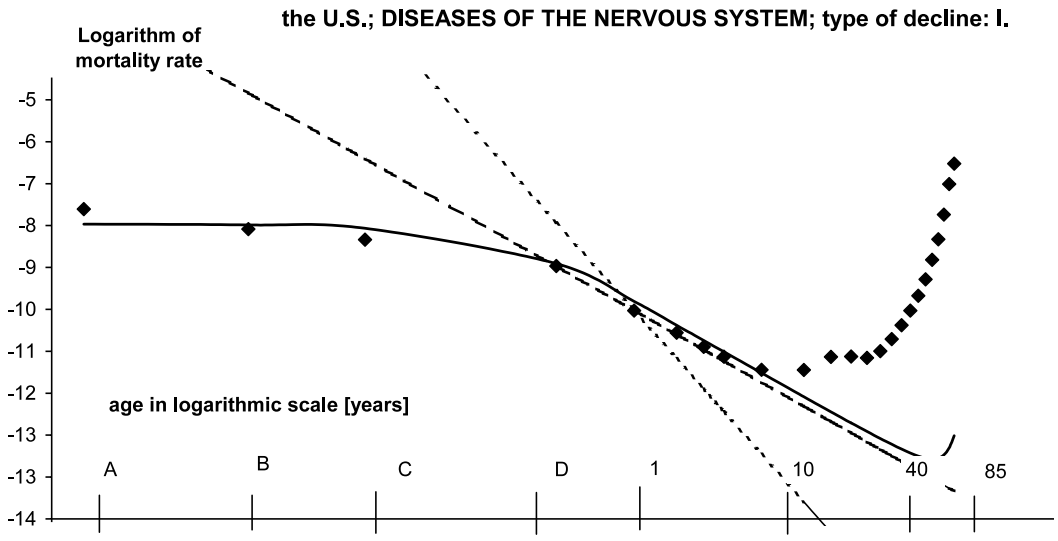

Fig. 3. Plot of logarithm of mortality rates from diseases of the nervous system (BTL code: B22) in US versus logarithm of age (1979–1997).

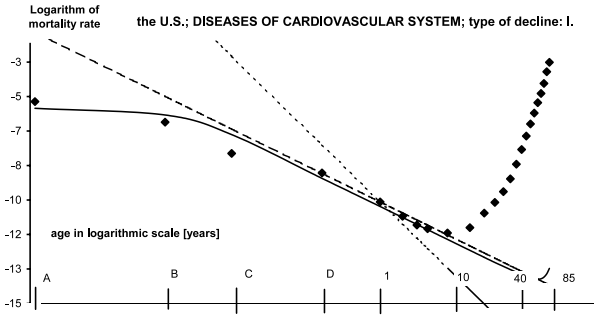

Fig. 4. Plot of logarithm of mortality rates from diseases of the cardiovascular system (BTL codes: B25–B30) in US versus logarithm of age (1979–1997).

the standard deviation equal to 0.40 ($n = 35$). The arithmetic mean of slope for diseases with the second type of mortality decline equals -1.68 with the standard deviation equal to 0.28 ($n = 9$).

3.2. Nonlinear regression within the interval (0; T)

Parameters $x_{\max}$ and $R(1)$ were calculated for all categories of diseases listed in Table 1 for all countries by the means of nonlinear regression. The calculation was made for the quantity $R(t)S(t)$ within the age interval (0; T). Eq. (2) was used in case of the mortality decline of the first type. Eq. (4) was used if the mortality decline falls under the second type. The calculated values of parameter $x_{\max}$ are presented in Table 4. If

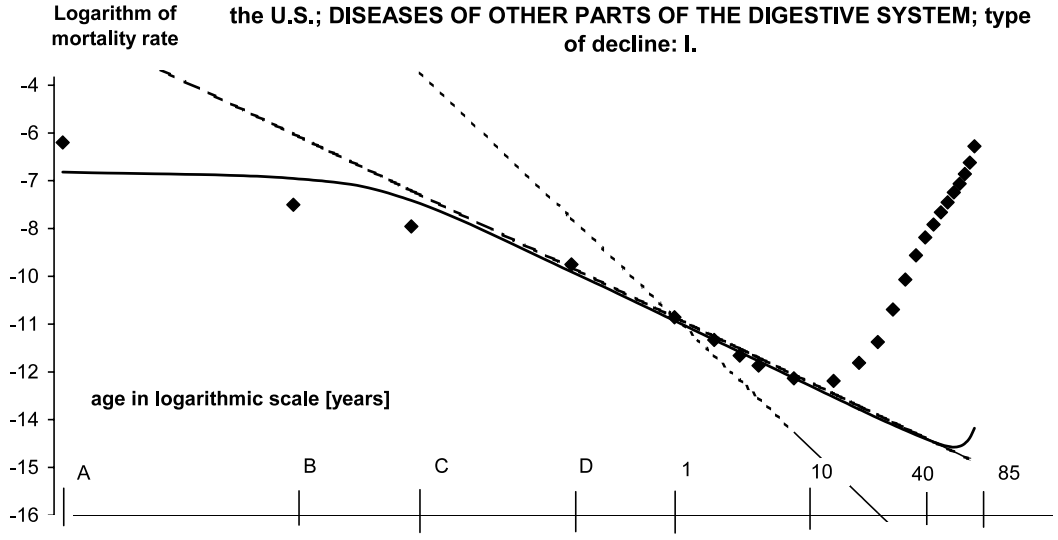

Fig. 5. Plot of logarithm of mortality rates from diseases of other parts of the digestive system (BTL code: B34) in US versus logarithm of age (1979–1997).

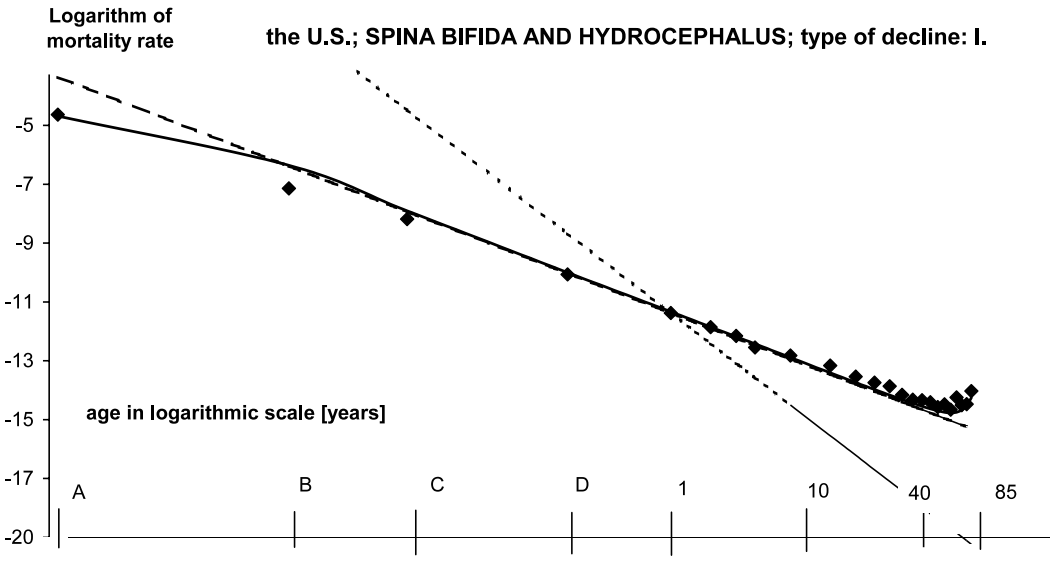

Fig. 6. Plot of logarithm of mortality rates from Spina bifida and hydrocephalus (BTL code: B440) in US versus logarithm of age (1979–1997).

no dead individual existed within the first age category A, the next age category with at least one dead individual was used. (The age limit is provided in Table 2.)

Figs. 1–10 show the dependence of the logarithm of mortality upon the logarithm of age for some categories of diseases in US. The solid line represents the right side of Eq. (2) or Eq. (4) and the calculated values of $x_{\max}$ and $R(1)$ parameters. Tables 10 and 11 contain F-statistics and the coefficient of determination.

In the last age category ($t > 50$ years), general decline of the size of population $S(t)$ took place and thus the theoretical curve rises along with age. In Spina bifida and hydrocephalus category (BTL code: B440), the theoretical dependence (the right side of Eq. (2)) describes the real dependence of mortality upon age until the last age category 80–85 years (see Fig. 6). (The size of the whole population $S(t)$ is not influenced by mortality from Spina bifida and hydrocephalus.)

3.3. Dependence of x_{max} on the size of born population

Table 1 contains the numbers of births. The hypothesis regarding the dependence of the $x_{\max}$ parameter upon the size of the born population was tested for all categories of diseases. The bottom line of Table 4 shows the results of the tests. The hypothesis was not rejected for the following five categories of diseases (95% CL).

"All diseases" (BA), "Endocrine and metabolic diseases, immunity disorders" (B18), "Other diseases of respiratory system" (B32), "Diseases of other parts of the digestive system" (B34) and "Other deformities of

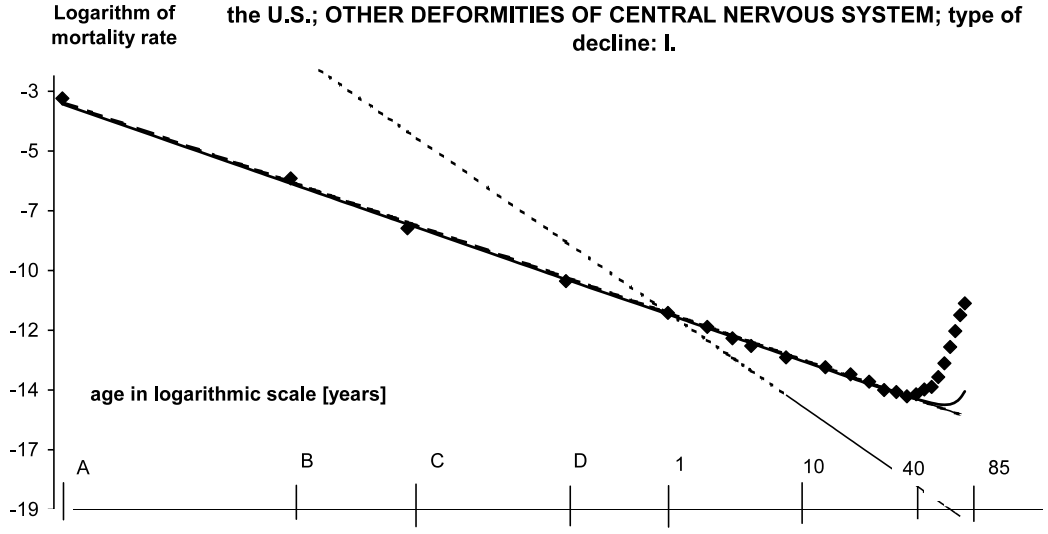

Fig. 7. Plot of logarithm of mortality rates from other deformities of central nervous system (BTL code: B441) in US versus logarithm of age (1979–1997).

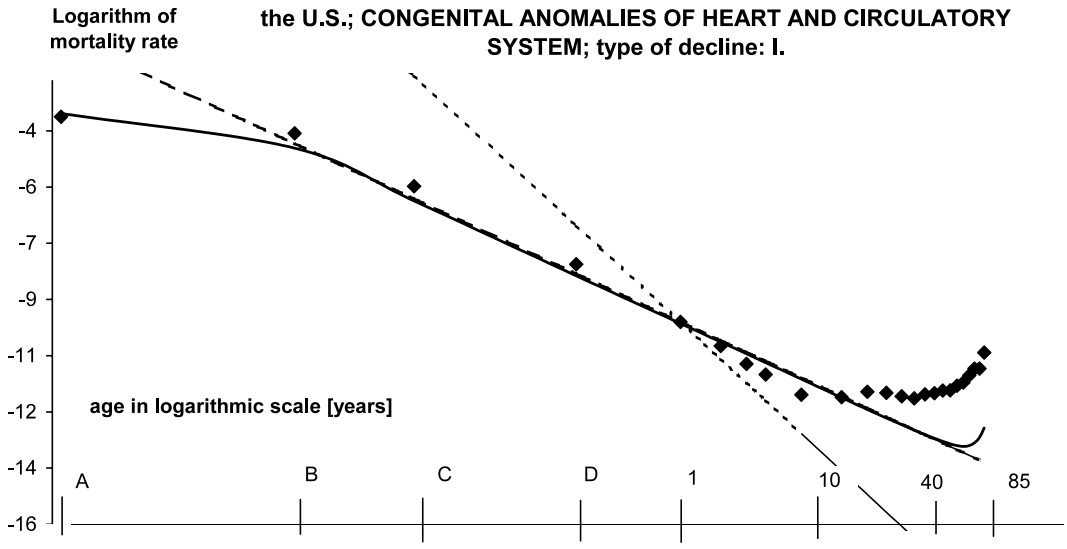

Fig. 8. Plot of logarithm of mortality rates from congenital anomalies of heart and circulatory system (BTL code: B442) in US versus logarithm of age (1979–1997).

central nervous system'' (B441). There, the x_{max} parameter grows along with the size of the born population. The explanation according to the theory is that there were only small differences in the individual risks distribution $f(x)$ among the studied countries and the fact that the maximum value of sample grows along with the sample size becomes apparent. In case of other diseases, the hypothesis assuming the dependence of the parameter upon the size of the born population was rejected (95% CL).

4. Discussion

Mortality enjoys an exclusive position among the other quantities. This quantity is an important criterion guiding the efforts invested by medicine while also being a well-defined quantity. For the age dependence of mortality before the age of 10, an uncertainty in determination of the number of all living individuals is not important, because this number does not change substantially before the age of 10 (the number of living

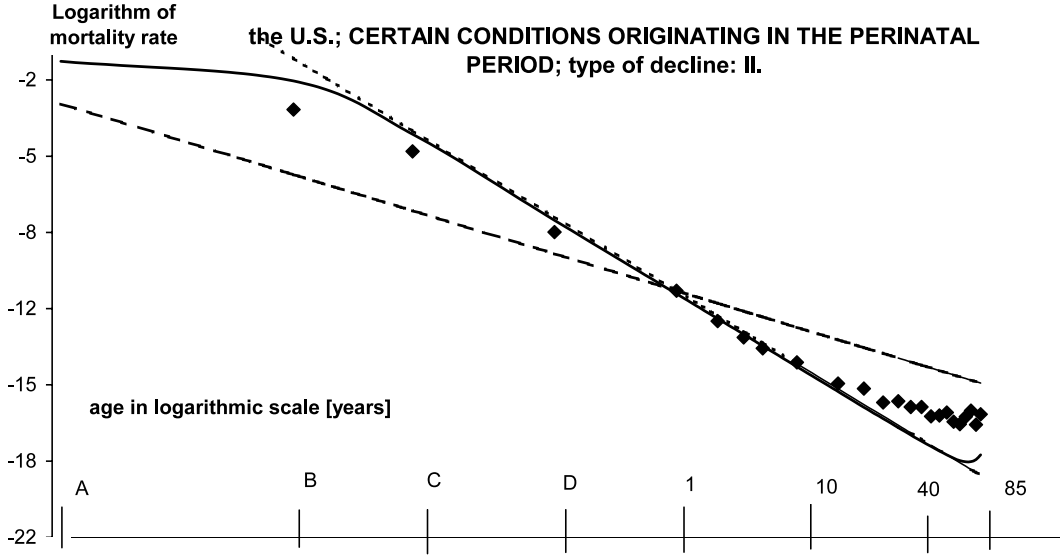

Fig. 9. Plot of logarithm of mortality rates from certain conditions originating in the perinatal period (BTL code: B45) in US versus logarithm of age (1979–1997).

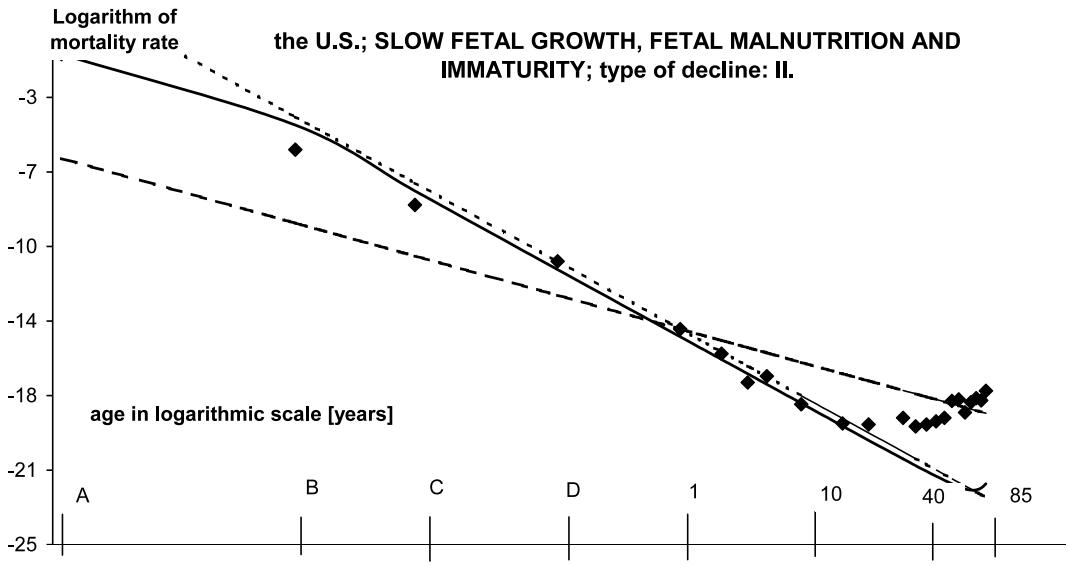

Fig. 10. Plot of logarithm of mortality rates from slow fetal growth, fetal malnutrition and immaturity (BTL code: B452) in US versus logarithm of age (1979–1997).

individuals decreases by less than 2%). The cause of death represents the least reliable data of those available for the calculation of mortality. The age of the dead individual is, on the other hand, the most reliable information in case of developed countries. The "All diseases" category (BA) is the most important and it is not affected by an uncertainty in determination of the cause of death. The theory of congenital individual risks describes very well the age-dependent decline of mortality for the BA category even for the first four age categories ($t < 1$ year) in all the countries (Fig. 1 and Table 3). The x_{max} parameter grows along with the size of the born population for the BA category.

4.1. Additive characteristics of both types of mortality decline

One category of diseases defined by BTL contains more particular diseases (phenotypes) and each phenotype can have a different distribution of congenital individual risk. The same also applies to the B44 category covering all congenital anomalies together. Although there are different phenotypes within one category of diseases, only one type of mortality decline was observed, as a result of additivity of both types of mortality decline. If two different phenotypes P_1 and P_2 have the same type of distribution of individual risk, then the joint phenotype P has the same type of mortality decline too. As the denominator (number of living individuals, see Eq. (6)) is common for all phenotypes, it applies for mortality $R_P(t)$ from two causes P_1 and P_2 as a whole:

$$R_P(t) = R_{P1}(t) + R_{P2}(t) \quad (14)$$

If both dependencies $R_{P1}(t)$ and $R_{P2}(t)$ are of the same type (either of type I or type II), then the decline of mortality $R_P(t)$ is of the same type, too. That applies to both types of mortality decline for $t > 1$ (Eqs. (3) and (5)). The type of decline is not generally the same in all cases. If $t < 1$, then the above applies only for cases with large x_{max}. If, e.g. $R_{P1}(t)$ and $R_{P2}(t)$ are exponential functions, then the above-described rule does not apply.

Even with a significant error in the determination of the cause of death, it is still possible to observe the dependence of mortality on age with a single parameter for $t > 1$. For example, we can create a category containing those who died from Spina bifida (B440) and congenital anomalies of hearth and circulatory system (BTL code: B442), where the mortality declines with the first power of age (for $t > 1$). In the first four age categories ($t < 1$), the resulting type of mortality is the same only if one can disregard the exponential term in Eqs. (2) and (4). If the dependence for $t < 1$ is not linear in the log–log scale for single phenotype, then the sum of more phenotypes can cause deviation from the model. That caused more significant deviation of data in case of other bacterial diseases category (B03) for $t < 1$. Thus, in case of a small x_{max}, the phenotypes can differ within one category of diseases for the first four age categories.

As the mortality from "All diseases" also declines with the first power of age for $t < 1$, the frequency $f(x)$ of total individual risk, which is due to the "complex phenotype", decreases along with the x value. The term of "complex phenotype" includes all inherited characteristics which contribute to the congenital individual risk of death. Usage of the term is supported by the fact that the theory of congenital individual risk is the most suitable for description of mortality decline for the category of "All diseases" (see Tables 9–11 and Fig. 1).

Table 3
The type of decline and the result of the test of hypothesis for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	I (yes)	I (yes)	I (yes)	I (no)	I (no)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (yes)	I (yes)	II (no)	II (yes)	II (yes)	II (yes)	II (no)
Japan	I (yes)	I (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (no)	I (no)	I (yes)	I (no)	II (yes)	x	x	II (yes)	II (no)
France	I (yes)	I (yes)	I (yes)	I (no)	I (no)	I (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (yes)	I (no)	I (yes)	I (no)	II (no)	x	x	II (no)	I (yes)
Sweden	I (no)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	II (yes)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	I (yes)	x	x	x	II (yes)
Czech Republic	I (yes)	I (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (yes)	I (yes)	II (yes)	I (yes)	I (yes)	I (no)	I (yes)	I (yes)	x	x	x	x	II (yes)

The "I" symbol marks the hypothesis Ho: $b = -1$. The "II" symbol marks the hypothesis Ho: $b = -2$. The symbol "yes" marks "hypothesis was not rejected" and the symbol "no" marks "hypothesis was rejected". Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 4
The parameter x_{max} for all categories in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	2560	9	3	57	4	86	75	31	46	2586	762	179924	319	108234	173	943	1050	127	7
Japan	650	2	5	19	2	4	5	10	13	666	848	5162	249	356101	223	x	x	260	3
France	589	14	29	17	10	34	40	9	25	386	504	150	179	153013	129	x	x	136	8248
Sweden	869	16	17	14	8	30	45	2	12	1626	1846	1249	381	1737436078	5870869	x	x	x	8
Czech Republic	747	3	2	12	5	5	12	13	4	1285	549	905	359	126920	x	x	x	x	5
Dependence	Yes	No	No	Yes	No	No	No	Yes	Yes	No	No	Yes	No	No	x	x	x	x	No

The unit of the parameter is per year per person. Dependence marks the hypothesis on the dependence of the x_{max} parameter upon the size of the born population. The symbol "yes" marks "the hypothesis was not rejected" and the symbol "no" marks "the hypothesis was rejected". Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 5
The representative value of age categories T_i for three types of decline up the age of 15 years

		Days	Days	Days	Years	Years	Years	Years	Years	Years
Lower age limit	1 min	1	7	28	1	2	3	4	5	10
Upper age limit	1 day	7	28	365	2	3	4	5	10	15
T_i (in years)										
$d(t) = \text{const.}/t$	0.00038	0.0084	0.042	0.36	1.44	2.47	3.48	4.48	7.21	12.33
$d(t) = \text{const.}/t^2$	0.000072	0.0072	0.038	0.28	1.41	2.45	3.46	4.47	7.07	12.25
$d(t) = \text{const.}$	0.00137	0.0110	0.048	0.538	1.5	2.5	3.5	4.5	7.5	12.5

The dead individuals from a partial category of diseases represent a sample from "complex phenotype", selected according to a specific criterion.

4.2. Malignant neoplasms

The mortality from malignant neoplasms in five studied countries is not age-dependent for the age period of 1–20 years. The same was observed for Japan and the former Czechoslovakia in a previous study (Dolejs, 1997). According to the theory of congenital individual risk, this means that there are not individuals with high individual risk whose dying off would cause mortality decline after the birth, as is the case of congenital defects. In case the maximum individual mortality risk $x_{\max}$ in population is less than 0.005 (less than 0.5% of subpopulation die per year) the exponential element "$\exp(-x_{\max}t)$" in Eqs. (2) and (4) can be substituted by formula "$(1-x_{\max}t)$" up the age of 20 and, consequently, mortality is not dependent of age. It applies for the first type of mortality decline that:

$$e^{-x^0_{\max}t} \cong 1 - x^0_{\max}t \Rightarrow R^{\mathrm{I}}(t) \cong \frac{R(1)}{S(t)}\left[\frac{1-(1-x^0_{\max}t)}{t}\right] = \frac{R(1)}{S(t)}x^0_{\max} \quad (15)$$

and for the second type of mortality decline, we obtain:

$$R^{\mathrm{II}}(t) \cong \frac{R(1)}{S(t)}\frac{1}{t^2}[1-(1-x^0_{\max}t)(x^0_{\max}t+1)] = \frac{R(1)}{S(t)}(x^0_{\max})^2 \quad (16)$$

As there is no dependence of mortality on age until the age of 20, the risk of death from malignant neoplasms cannot only apply to a small subpopulation with high individual risk of death, as was the case with congenital anomalies. In other words, the individual risk of death outside the group of dead individuals should not equal to zero. If there exists a genetically conditioned mortality from malignant neoplasms, it is not revealed in mortality decline under the age of 20.

4.3. Slower decline of mortality

The hypothesis on the slope of the interval (1; 55 years) was rejected for Spina bifida and hydrocephalus (B440) in US (see Table 3 and Fig. 6). The hypothesis was not rejected in case of shorter age interval (1; 10) and a shorter period (1979–1991) (Dolejs, 2001). Fig. 6 shows that the decline of logarithm of mortality corresponds to the slope -1 even for the age categories above 10, but the values of mortality are shifted by a constant. There, a difference revealed between cohorts born 20 and more years apart, and those born at present. The growth of mortality from Spina bifida and hydrocephalus (B440) for the last age categories (for $t > 50$ years) is due to the fall of the $S(t)$ quantity, as the size of the whole population rapidly decreases due to all other diseases (see Fig. 6). The beginning of aging is related to the onset of exponential dependence of mortality rates from all diseases on age. The onset of the Gompertzian area is down to the age of 10 years (Dolejs, 1997; Riggs, 1990). Also the results presented show that the exponential rise could exist earlier and it is "overlap" by the number of deaths caused by congenital frailty and accidents. The evidence that the presupposition about age-independent individual risk is valid until the last age categories for Spina bifida and hydrocephalus (B440) is important evidence from the perspective of aging. It is in contrast with the evidence that individual risk of death from other congenital defects is affected by aging usually after the age of 30 years (see Table 2 and Figs. 1–5).

4.4. Difference between congenital anomalies (B44) and certain conditions originating in the perinatal period (B45)

A defect present at the moment of birth was determined as the cause of death for individuals assigned to the categories of congenital anomalies (B44) or certain conditions originating in the perinatal period (B45) (the perinatal period is from the 28th week of gestation to the 7th day of life). The first type of mortality decline was observed in the B44 category and the second type of mortality decline was observed in the category B45 (see Table 3 and Figs. 6–10).

Table 6
The slopes calculated using the linear regression in log–log scale for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	−0.89	−0.95	−1.16	−0.53	−0.65	−0.96	−1.07	−1.12	−0.86	−1.09	−0.89	−0.98	−1.07	−1.23	−1.68	−1.93	−1.90	−1.99	−1.52
Japan	−0.76	−1.13	−1.23	−0.88	−0.80	−0.97	−1.03	−0.94	−1.20	−1.05	−1.62	−1.65	−1.12	−1.36	−2.17	x	x	−2.48	−1.58
France	−0.84	−1.02	−1.21	−0.58	−0.78	−0.91	−1.08	−1.09	−0.72	−0.81	−1.19	−0.76	−1.24	−2.07	−1.44	x	x	−1.61	−1.03
Sweden	−0.78	−1.25	−1.65	−0.70	−1.00	−0.55	−0.60	−2.18	−1.30	−1.30	−0.47	−1.42	−0.94	−1.51	−1.29	x	x	x	−1.44
Czech Republic	−0.78	−2.81	−1.68	−1.53	−0.30	−1.22	−1.43	−1.28	−1.58	−1.28	−1.50	−1.69	−1.00	−0.97	x	x	x	x	−1.52

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 7
Lower limit of the slope calculated using the linear regression in log–log scale (95% CI) for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	−1.09	−1.16	−1.39	−0.78	−0.92	−1.38	−1.45	−1.42	−1.20	−1.39	−0.93	−1.03	−1.42	−1.61	−1.90	−2.50	−2.37	−2.16	−1.91
Japan	−1.03	−1.34	−1.56	−1.19	−0.98	−1.32	−1.27	−1.33	−1.25	−1.21	−1.77	−1.91	−1.27	−1.66	−2.43	x	x	−3.17	−1.91
France	−1.03	−1.35	−1.50	−0.80	−0.96	−1.37	−1.41	−1.50	−0.98	−1.01	−1.68	−0.89	−1.49	−2.96	−1.77	x	x	−1.96	−1.49
Sweden	−0.91	−2.26	−3.46	−1.05	−1.67	−1.16	−1.64	−3.83	−2.75	−1.63	−2.45	−2.67	−1.54	−2.83	−1.65	x	x	x	−3.93
Czech Republic	−1.13	−7.09	−2.67	−2.42	−0.58	−1.70	−2.23	−1.73	−2.02	−1.59	−2.15	−1.99	−1.49	−1.43	x	x	x	x	−2.56

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 8
Upper limit of the slope calculated using the linear regression in log–log scale (95% CI) for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	−0.68	−0.75	−0.92	−0.28	−0.37	−0.54	−0.70	−0.82	−0.52	−0.78	−0.86	−0.93	−0.71	−0.86	−1.46	−1.36	−1.42	−1.81	−1.13
Japan	−0.49	−0.91	−0.90	−0.57	−0.63	−0.62	−0.79	−0.55	−1.15	−0.89	−1.47	−1.38	−0.97	−1.06	−1.92	x	x	−1.78	−1.26
France	−0.65	−0.70	−0.91	−0.36	−0.60	−0.45	−0.75	−0.68	−0.46	−0.60	−0.69	−0.62	−0.99	−1.17	−1.12	x	x	−1.26	−0.57
Sweden	−0.65	−0.23	0.15	−0.34	−0.33	0.06	0.44	−0.52	0.15	−0.97	1.52	−0.18	−0.34	−0.19	−0.93	x	x	x	1.06
Czech Republic	−0.43	1.48	−0.70	−0.65	−0.01	−0.74	−0.63	−0.84	−1.14	−0.97	−0.84	−1.39	−0.51	−0.52	x	x	x	x	−0.48

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 9
The coefficient of determination of the linear regression r^2 for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	0.985	0.978	0.978	0.896	0.914	0.947	0.965	0.979	0.926	0.961	0.996	0.996	0.946	0.955	0.983	0.957	0.955	0.990	0.981
Japan	0.939	0.982	0.965	0.939	0.976	0.962	0.985	0.919	0.9998	0.956	0.983	0.969	0.978	0.953	0.987	x	x	0.960	0.978
France	0.985	0.950	0.969	0.960	0.984	0.931	0.973	0.960	0.938	0.984	0.950	0.962	0.980	0.980	0.951	x	x	0.955	0.906
Sweden	0.992	0.835	0.738	0.883	0.883	0.730	0.530	0.941	0.730	0.981	0.158	0.815	0.893	0.815	0.928	x	x	x	0.529
Czech Republic	0.944	0.799	0.849	0.965	0.787	0.983	0.967	0.966	0.992	0.884	0.909	0.961	0.890	0.939	x	x	x	x	0.803

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 10
F-statistics of nonlinear regression for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	2474	192	46	112	231	276	179	135	204	932	2272	12058	683	154	777	722	1105	1364	184
Japan	1237	20	10	474	64	150	231	669	95	1641	276	289	1399	207	2474	x	x	901	509
France	1710	985	550	229	159	163	190	161	411	754	236	1237	282	55	1060	x	x	1454	218
Sweden	1818	254	80	153	334	152	157	42	105	375	175	263	241	119	40	x	x	x	126
Czech Republic	636	33	86	72	61	61	56	221	182	297	178	226	259	103	x	x	x	x	241

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

Table 11
The coefficient of determination of the nonlinear regression r^2 for all categories of diseases in five countries

Country	BA	BB	B03	B18	B22	BD	B28	B32	B34	B44	B440	B441	B442	B447	B45	B451	B452	B454	B46
US	0.997	0.960	0.851	0.934	0.967	0.975	0.962	0.951	0.962	0.991	0.993	0.999	0.988	0.950	0.987	0.989	0.992	0.992	0.963
Japan	0.994	0.717	0.597	0.983	0.888	0.956	0.971	0.988	0.940	0.992	0.952	0.963	0.992	0.954	0.996	x	x	0.991	0.985
France	0.996	0.992	0.986	0.970	0.958	0.959	0.965	0.958	0.981	0.984	0.971	0.991	0.972	0.902	0.991	x	x	0.993	0.965
Sweden	0.996	0.973	0.920	0.950	0.979	0.956	0.957	0.894	0.946	0.982	0.961	0.974	0.972	0.944	0.802	x	x	x	0.947
Czech Republic	0.989	0.893	0.935	0.935	0.897	0.897	0.918	0.969	0.968	0.952	0.957	0.954	0.970	0.936	x	x	x	x	0.968

Calculation was not made in the case of no death within certain age category and the interval (1; T) and the cases are marked by the symbol "x".

According to the theory, the individual risks of category B45 have either even distribution or normal distribution with a large variance. The range of congenital individual risks of the category B45 could not be a small one, because the mortality was decreasing until the age of 25. For example, in category of slow fetal growth, fetal malnutrition and immaturity (B452), the mortality has decreased 58 000 000 times. The theory of congenital individual risk explains the decline of mortality with the second power of age as a consequence of the approximate equivalence of the frequency of defects with various severity, even in case of large range of values of congenital individual risk x ($f(x) \approx$ const. for $t = 0$). But in the case of the B44 category, the frequency of defects decreases together with the value of individual risk x ($f(x) \approx$ const./x for $t = 0$). In other words, severe defects are less frequent in the category B44 than in B45. A majority of congenital defects B44 was proved to be genetically conditioned (National Institute of Neurological Disorders and Stroke; American Heart Association; Shields et al., 1999; Towbin et al., 1999; Castilla et al., 2001; Murdoch et al., 2001; Shonberger and Seidman, 2001; Bruneau, 2002). The frequency of genotype decreases along with the value of congenital individual risk x. We can infer that the decrease of frequency of congenital anomalies, along with the risk of death, may be due to the selection. (x could be the coefficient of the selection of phenotype, which survives until the age of reproduction. The constant in the relationship $f(x) \approx$ const./x could be interpret as mutability.) There is no influence that the previous selection would exercise over the frequency of individual risk x in the category B45 so that the defects of various severity can appear with roughly the same frequency (see the list of subcategories of B45 in Table 1).

The difference in mortality decline between the categories B44 and B45 is due to the selection in the B44 category, which does not apply to the category B45.

4.5. Conclusions

Quantification of the severity of a congenital defect, e.g. from a morphological point of view, elicits numerous problems. For example, if the severity of congenital defects is defined on the basis of a morphological viewpoint, comparison of congenital anomaly of heart and Spina bifida is not possible. To quantify a congenital defect, the theory of congenital individual risk uses an individual risk of death x, with a unit of per year quantifying the severity of congenital defect. According to that theory, the decline of mortality with the first power of age is due to the fact that the frequency of congenital individual risk x corresponds to the function $f(x) =$ const./x. The higher the individual risk of death, the less probable is its appearance. The rule results from the selection in previous generations or it results from the selection during pregnancy. If all defects appear with roughly the same frequency as in the category B45, then the frequency of individual risk is not influenced by the previous selection.

Figs. 1–10 and the coefficients of determination and F-statistics (Tables 9–11) show that the theory of congenital individual risk explains the age-dependent decline of mortality after birth for all categories of diseases except malignant neoplasms and accidents. The theory uses only one parameter $R(1)$ for $t > 1$. If the value of the second parameter x_{max} is small, the exponential element makes itself visible during the first year of life, and the model gets two parameters. An alternative theory should have a comparable number of parameters and be able to explain different starting points of a linear decline in the log–log scale for different diseases. And up to that, an alternative theory should explain the age-dependent decline of mortality by 5–7 orders (e.g. in case of categories B441 or B452, see Figs. 7 and 10).

The theory of congenital individual risk describes the age-dependent decline of mortality both for congenital anomalies (BTL code: B44) (the first type of mortality decline) and also for the deaths usually not attributed to a congenital defect (the same type of mortality decline, see Figs. 1–10). The theory achieves best results in description of the "All diseases" category (the first type of mortality decline up the age of 10 years, see Fig. 1). This category has the highest F-statistics and the coefficient of determination (Tables 9–11). In case of "All diseases", the exponential element of Eq. (2) asserts oneself only during the first days of life. There is a linear dependence in log–log scale, in higher age categories (for $t > 1$ day). This rule applies to all studied populations. The theory explains that there is a complex phenotype (congenital frailty) present at the moment of the birth, which causes the deaths. All the results presented support the hypothesis that there was a defect present at the moment of birth, which developed into the cause of death, in all dead individuals except those who died from malignant neoplasms or accidents.

A congenital anomaly is "a development scar and a scar does not tell us about its etiology" (Castilla et al., 2001). The scar is not visible in one-third of biological deaths ("All diseases" except B44; B45 and malignant neoplasms (BC)), or it is not determined to be the cause of death. For example, out of 1806 death from Bronchiolitis under 1 year in US, 179 of dead individuals (9.9%) suffered congenital heart disease (Shay et al., 2001). The theory of congenital individual risk also explains those deaths as a result of congenital frailty. The existence of latent congenital defects could be proved by the direct examination. Eq. (2) applies to those defects as it does to congenital anomalies (B44) so that the latent congenital defects could be also genetically conditioned. The existence of latent defects can be

verified in case any difference is discovered between the genotype of dead individuals under 10 (those not included into the B44 and B45 categories) and of the population that survived until the age of 10. The problem shows resemblance to that associated with the search for genes responsible for longevity (Toupance et al., 1998; Vijg and van Orsouw, 2002; Yashin et al., 1999). According to the theory of congenital individual risk, those who died before the age of 1 year had an extreme phenotype selected due to a high congenital individual risk of death. Therefore, the most significant difference in genotype could be observed between those who died before the age of 1 year, and the population that survived until the age of 10.

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