



The size of the subpopulation susceptible to malignant neoplasm of the brain

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Abstract

A decline of mortality dependence on age from the exponential relation is observed for some diseases. This decline could be explained by the existence of an inherently susceptible population subset which is depleted faster than the general population. A model is presented which describes this situation using malignant neoplasm of the brain. The model assumes that only those who are members of the subset can die of malignant neoplasm of the brain. This model was used to fit the actual mortality curve of malignant neoplasm of the brain for women and men in the USA in 1979. The size of this subset equalled one of two parameters used to fit the actual data. The decline of mortality dependence upon age can be explained by this model. The size of the subpopulation is 0.390% for men and 0.417% for women. The theoretical curves resulting from that model capture the actual mortality due to malignant neoplasm of the brain. © 1998 Elsevier Science Ireland Ltd. All rights reserved.

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1. Introduction

Human death rate increases exponentially within the age interval of 30–85 years. This relationship was recognized by Benjamin Gompertz (1825). The Gompertz relationship may be expressed as:

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$$R(t) = R_0(10)^{\alpha \cdot t} \quad (1)$$

where $R(t)$ is a death rate at age t , R_0 is a theoretical value at birth (approximation for $t = 0$) and α is a slope of exponential term. The Gompertz equation becomes a linear function when expressed logarithmically:

$$\log R(t) = \alpha \cdot t + \log R_0 \quad (2)$$

Excluding accidents, the Gompertzian area for total mortality starts before age 20. The mortality of many individual diseases is also exponentially dependent on age (Harman, 1991; Strehler and Mildvan, 1960). The onset of the Gompertzian area begins at age 10 for many individual causes of death (Riggs, 1990a, 1991a).

The mortality curves of some diseases do not conform to the exponential relation after a certain age (age 55 for malignant neoplasm of the brain) (Riggs, 1990b, 1991b, 1992, 1993; Neilson et al., 1992). The existence of inherently susceptible population subset which is depleted faster than the general population (Riggs, 1991b; Neilson et al., 1992) can explain that decline of mortality dependence upon age. A size of such a subpopulation susceptible to amyotrophic lateral sclerosis (ALS) has been estimated (Neilson et al., 1992). A model that can simulate the whole mortality curve for malignant neoplasm of the brain is proposed. The size of the subpopulation is one of two finding parameters in this model. The size of the subpopulation is clearly determined by the declining shape of the curve.

2. Methods

This model is applicable to a population from birth to age 90. In the model, the basic unit of time equals 1 year. The number of living people in year t is calculated from the number of living people at the beginning of the previous year and the number of people that died within year t . The basic assumption in this model is that only a member of the susceptible subpopulation can die from a specific cause (for example, malignant neoplasm of the brain). All members of the population can die from all other causes. The number of deaths was computed from the, 'theoretical' mortality rates which were calculated using the Gompertz equation (exponential dependence on age). Assumptions of this model can be expressed by the following items:

(1) The first finding parameter p was the proportional size of the subpopulation. Only a member of the subpopulation could die from a specific cause (for example, malignant neoplasm of the brain). $p = L_a(1)/L(1)$; where $L(1)$ is the number of living people at the beginning of the first year and $L_a(1)$ is size of the subpopulation at the same time.

(2) The number of deaths, $D(t)$, in year t from all causes was calculated from the number of living people at the beginning of year t and the mortality rate $R(t)$:

$$D(t) = L(t) \cdot R(t) \quad (3)$$

For $R(t)$, validity of Eq. (1) was assumed. The Gompertz parameters α and $\log R_0$ were calculated using linear regression within the interval of 40–84 years.

(3) The number of deaths, $D_a(t)$, from one specific cause (for example, malignant neoplasm of the brain) in year t was calculated in the same way, from the size of the subpopulation, $L_a(t)$, at the beginning of year t and from the mortality rate, $R_a^{ins}(t)$, inside the subpopulation (as calculated using the number of living people in the subpopulation at age t).

$$D_a(t) = R_a^{ins}(t) \cdot L_a(t) \tag{4}$$

(4) The model assumed Gompertzian dependence on age for the mortality rate, $R_a^{ins}(t)$, inside the subpopulation (Fig. 1):

$$R_a^{ins}(t) = R_{a0}^{ins} \cdot \exp(\alpha_a \cdot t) \tag{5}$$

(5) The number of deaths, $D_r(t)$, from all causes, except for the specific cause, inside the subpopulation was calculated such that:

$$D_r(t) = \frac{D(t) - D_a(t)}{L(t) - L_a(t)} \cdot L_a(t) \tag{6a}$$

or

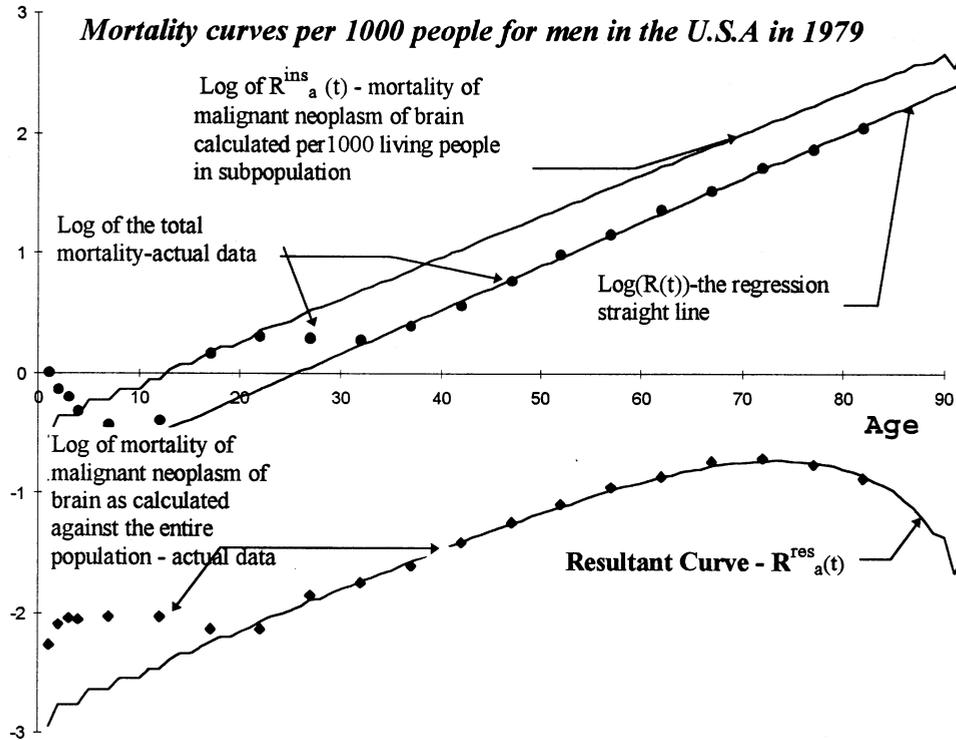


Fig. 1. The scheme of mortality curves.

$$D_r(t) = R(t) \cdot L_a(t) \quad (6b)$$

(6) The number of all living people in the next year was calculated using the relation:

$$L(t+1) = L(t) - D(t) \quad (7)$$

(The actual number of births in 1979 was used as the value for $L(1)$.)

(7) The number of living people inside the subpopulation for the next year was calculated such that:

$$L_a(t+1) = L_a(t) - D_a(t) - D_r(t) \quad (8)$$

(Note that $L_a(1) = p \cdot L(1)$ was used for the first year.)

Numbers of deaths, $D(t+1)$, $D_a(t+1)$ and $D_r(t+1)$, for the year $t+1$ were calculated using Eq. (3), Eq. (4) and Eqs. (6a) and (6b). These equations are valid for mortality rate R_a (as calculated against the entire population at age t), since being so small that the impact of malignant neoplasm of the brain upon total mortality can be neglected when compared to all other causes combined. This assumption was satisfied for the actual data ($R_a(t)/R(t) < 0.13$ for all age groups, Fig. 1).

The resultant mortality rate, R_a^{res} (per 1000 living people), of cause a as calculated against the entire population at age t ($R_a^{\text{res}} = 1000 \cdot D_a(t)/L(t)$) was fit on a logarithmic scale to the actual data (logarithm of the mortality rate of malignant neoplasm of the brain per 1000 living people versus age). This calculation was done for two populations—men and women in the USA in 1979. Next, initial parameters were used in the model: $L(1)$, p , α , $\log R_o$, α_a , $\log R_{oa}$.

The number of deaths from all causes, the number of deaths from malignant neoplasm of the brain (ICD9 code 191, WHO, 1977), and the number of living people were taken from the WHO Mortality Database. These values were used to calculate general mortality rates and mortality rates from malignant neoplasm of the brain. Linear regression within the interval of 42–84 years was used to calculate the parameters α and $\log R_o$. The number of men and women in the USA in 1979 in the age category 0–1 year was employed as the value $L(1)$. The parameters α_a and $\log R_{oa}$ were calculated using linear regression within the interval 22–57 years for the actual mortality rates of malignant neoplasm of the brain. The value of the slope α_a (for mortality rate as calculated against the entire population at age t) is lowered by depletion of the subpopulation if compared with the value α_a^i (the slope of mortality rates calculated in the subpopulation). The value α_a was used as the initial parameter of the fitting process only. The depletion of the subpopulation did not influence the parameter $\log R_{oa}$ and, consequently, its value was constant during the fitting process. The initial parameters of the fitting process, including the regression coefficients, are shown in the Table 1.

Only two parameters α_a^i and p were changed to minimize the sum of squares of deviations. The time unit used in the model was 1 year. The sum of the squares was calculated for points which corresponded to the mean value of the 5-year age categories (5-year age groups were the time units of the actual data; deviations were

Table 1
Initial values to fitting process

α_a	Log R_{0a}	Regression coefficient (22–57 years) for mortality of B130	α	Log R_0	Regression coefficient (42–82 years) for total mortality	$L(1)$	
Women	0.0340	-3.06	0.9934	0.0376	-1.274	0.9989	1 673 000
Men	0.0329	-2.80	0.9928	0.0365	-0.937	0.9994	1 753 000

Table 2
Results of fitting process

	p	α_a^i	Sum of squares
Women	0.00417	0.0353	0.0187
Men	0.00390	0.0341	0.0083

calculated for the values $t = 22, 27, 32 \dots 82$ years). All calculations were made using the spread sheet Excel.

3. Results

The final values of the fitting process are shown in Table 2. The curves which correspond to these parameters are illustrated in Fig. 2, for both women and men. The curves simulate the actual data exceedingly well. The resulting values, which are presented in Table 2, depend on the mortality $R_a^{\text{ins}}(t)$ of both the specific cause a and on general mortality, $R(t)$.

Eqs. (5), (6) and (6b) are valid if mortality $R(t)$ is not significantly effected by the mortality $R_a(t)$ (the number of deaths, $D_a(t)$, is much less than the total number of deaths, $D(t)$). Since the subpopulation is less than 1%, this assumption can be made.



Fig. 2. The actual mortality data and the resultant curves calculated using the model for men and women in the USA in 1979 (as calculated against entire population—1000 living people).

4. Discussion

The size of a susceptible subpopulation was estimated for amyotrophic lateral sclerosis (ALS) (Neilson et al., 1992). That estimate did not use the value for general mortality, $R(t)$, but only the values of mortality from ALS. The difference between the value $R_a(t)$ (actual data) and $R_a^{\text{theor}}(t)$ (calculated using the Gompertz relation) was calculated. Depletion of a susceptible subpopulation has to depend on the ratio $R(t)/R_a(t)$.

The conclusion that the slope α_a has to be higher than the slope α is a necessary condition for depletion of a susceptible subpopulation (Riggs, 1991b). The phenomenon of the subpopulation being depleted faster than the general population is caused by the fact that specific cause mortality in the subpopulation ($R_a^{\text{ins}}(t)$ in Fig. 2) is higher than that of the general mortality. The mortality from any single specific cause in the general population at age t must be lower than general mortality, as a matter of fact. A deviation from the Gompertzian mortality curve can even occur in the case where slope α_a equals zero. For this to occur, the initial value of the mortality $R_a^{\text{ins}}(0)$ (inside the subpopulation) has to be high compared to general mortality. If the subpopulation is small compared to the total population (less than 5%), then mortality within the subpopulation can be many times higher than general mortality. Consequently, depletion of the subpopulation should be considered (and is not unimportant) in the case where α_a is less than α .

This model can quantitatively describe the decline of mortality rates from the Gompertz relation for some specific diseases. On the condition that death from malignant neoplasm of the brain can only occur within a susceptible subpopulation, for example, the size of that subpopulation is 0.390% for men and 0.417% for women in the USA in 1979.

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