# Estimation and sensitivity of Gompertz parameters with mortality deceleration rate

**Article** *in* Journal of Applied Mathematics and Computing · March 2005

DOI: 10.1007/BF02936574



**1 author:**

Pitchaimani M
University of Madras
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*J. Appl. Math. & Computing Vol.* **18***(2005), No. 1 - 2, pp. 311 - 320*

# ESTIMATION AND SENSITIVITY OF GOMPERTZ PARAMETERS WITH MORTALITY DECELERATION RATE

M. PITCHAIMANI

Abstract. Studies in the evolutionary biology of aging require good estimates of the *age-dependent* mortality rate coefficient (one of the Gompertz parameters). In this paper we introduce an alternative algorithm for estimating this parameter. And we discuss the sensitivity of the estimates to changes in the other model parameters.

AMS Mathematics Subject Classification: 92D10, 62F10, 62L10, 62N05, 62P10.
*Key words and pharses*: Deceleration rate, Gompertz survival model, logistic frailty model, maximum lifespan, mortality rate, sensitivity, survival function, unique.

## 1. Introduction

Human mortality rates show a profound relation with chronological age in the mortality increase exponentially with chronological age from 25 to 30 years of age onward [1]. Benjamin Gompertz (1825) was the first to recognize this dependency of mortality rate on chronological age and expressed it mathematically by the equation

$$m(t) = Ae^{\alpha t}, \tag{1}$$

where $m(t)$ is the mortality rate at time $t$, $A$ is the mortality rate at reproductive maturity (or $A > 0$ is called the *age-independent* mortality rate coefficient or the initial mortality rate ($IMR$)) and $\alpha(\geq 0)$ is the Gompertz exponent, which describes the rate of acceleration of age - specific mortality with chronological age. The exact shape of the function describing mortality rates in humans has implications for predictions of demography trends [2].

Received February 5, 2004. Revised September 20, 2004.

The corresponding survival function can be obtained by integrating the mortality rate function equation (1);

$$S(t) = e^{\frac{A}{\alpha}(1-e^{\alpha t})}. \tag{2}$$

The two parameters $A$ and $\alpha$ are of interest to many investigators in biogerontology and the evolutionary biology of aging [3-5]. Species comparisons in mortality rate accelerations are aided by calculations of $MRD$ (mortality rate decrement) which changes in the same direction as lifespan and is given by

$$MRD = \frac{\ln 2}{\alpha}.$$

Usually, an experimentalist knows the individuals lifespans and can make use of standard techniques such as $MLE$ or linear regression [6, 7] to estimate the model parameters.

A problem arises when, for some reason, the lifespans are not known exactly or not known at all. Under these conditions, it becomes much more difficult to estimate the two model parameters. In such cases Lakshminarayanan and Pitchaimani obtained the unique solution and the asymptotic formulae of $A$ and $\alpha$ in [5, 8].

## 2. Estimation of parameters

Until recently, it was impossible to determine whether this exponential rise continued to advanced ages. For humans, the scattered data available suggested mortality decelerated at the highest ages, but questions about data reliability precluded strong conclusions. It is well known that among most mammals, mortality rates are generally lowest at puberty and then accelerate at a constant rate during the major phase of adult life. When examined from puberty onwards, the mortality rate accelerations during adult aging fit the Gompertz model, at least up through the average lifespan [3]. However extensive deviations from the Gompertz model were recently documented, in which mortality rate accelerations slow markedly by the average lifespan e.g., in laboratory populations of fruit flies [9]. In human populations, according to published studies [10], the acceleration of mortality rate slows after 85 years. After 105 years, the mortality rate appears to cease increasing and may even decrease at these extremely advanced ages. Current evidence indicates that human mortality rates at ages above 85 are less than that predicted by the Gompertz law. In extreme old age, mortality rate may level off or even decline [11].

The CLOV report also suggest that at higher age beyond 80 days, the function $m(t)$ tends to fluctuate; it rises first $\frac{dm(t)}{dt} \geq 0$, then declines $\frac{dm(t)}{dt} \leq 0$. There is an additional evidence for the exponential decay at higher ages. Quite

recently Wang and co-workers disclosed an elegant experiment for the senescence accelerated mouse (SAM), showing that the mouse mortality function also approaches a constant value at higher age (Wang et al., 1998 [12]).

All the evidences accumulated so far suggest strongly that the exponential decay of populations at higher age is a general theorem [13]. Note that not all populations show mortality decelerate at higher ages (*see*, Finch *et al.*, 1996 [14]).

In the above cases, the Gompertz equation (1) is a poor description of mortality dynamics. To correct for departures from Gompertz, the logistic frailty model was also examined :

$$m(t) = \frac{Ae^{\alpha t}}{1 + s\frac{A}{\alpha}(e^{\alpha t} - 1)} \tag{3}$$

(Vaupel, 1990[15], Taira 2002[16]). Early in life ($t$ near zero), mortality increases exponentially at a rate determined by $A$ and $\alpha$. The parameter $s$ determines the extent to which mortality rates decelerate late in life. Higher values of $s$ indicate greater deceleration. Note that when $s = 0$, equation (3) reduces to equation(1).

The corresponding survival function can be obtained by integrating the mortality rate function equation (3);

$$S(t) = \left[1 + s\frac{A}{\alpha}(e^{\alpha t} - 1)\right]^{-\frac{1}{s}}. \tag{4}$$

Usually, an experimentalist knows the individual lifespans and can make use of standard techniques such as $MLE$ or linear regression to estimate the model parameters [17]. A problem arises when, for some reason, the lifespans are not known exactly or not known at all. Under these conditions, it becomes much more difficult to estimate these parameters.

Evolutionary biologist of aging are often stuck with a survival curve and no associated lifespan data. In this field, it is vital to have reasonable estimates for $\alpha$. If we assume that we know $A$ and $s$ (a not unreasonable assumption, biologically), and if we further assume that we also know $S(t)$, then equation (4) is a transcendental equation in the unknown $\alpha$ and may be solved using standard numerical methods [18].

It is difficult, in general, to decide upon a particular value of $t$, to use in equation (4). However if we are examining the issue of evolution of longevity, then choosing $t = t_{\max}$, the known maximum lifespan, is a reasonable starting value. Finally for ease of analysis we may setting $S(t_m) = \frac{1}{N}$ (the population contains only one number left from an original population size N)[19]. We obtain

the following equation for $t_m$ (the time at which the population has only one number and which approximates the maximum lifespan $t_m^*$)

$$t_m^* \simeq t_m = \frac{1}{\alpha}\ln\left[1+\frac{N^s-1}{s}\frac{\alpha}{A}\right],$$

$$\text{or } \alpha = \frac{1}{t_m}\ln\left[1+\frac{N^s-1}{s}\frac{\alpha}{A}\right]. \tag{5}$$

Equation (5) gives

$$\frac{A}{\alpha} = \frac{1}{s}\frac{N^s-1}{e^{\alpha t_m}-1},$$

$$\text{or} \quad \alpha = As\frac{e^{\alpha t_m}-1}{N^s-1}. \tag{6}$$

Equation (6) allows us to study the effects of $A$ and $s$ on the estimated value of $\alpha$.

The basic equation (6) is transcendental, involving exponential function, and hence, its solution may not be unique. Hence it is necessary to investigate the uniqueness of solution of (6).

## A Necessary Condition for Uniqueness

**Theorem 1.** *To have a unique solution of equation (6), it is necessary that* $\dfrac{Ast_m}{N^s-1} < 1$.

*Proof.* Suppose $\alpha_1$ and $\alpha_2$ are two solutions of equation (6), that is,

$$\alpha_1 = As\frac{e^{\alpha_1 t_m}-1}{N^s-1}, \quad \alpha_2 = As\frac{e^{\alpha_2 t_m}-1}{N^s-1}.$$

Consider

$$\begin{aligned}\alpha_1-\alpha_2 &= As\frac{e^{\alpha_1 t_m}-1}{N^s-1} - As\frac{e^{\alpha_2 t_m}-1}{N^s-1}\\ &= \frac{As}{N^s-1}\left[\left(e^{\alpha_1 t_m}-1\right)-\left(e^{\alpha_2 t_m}-1\right)\right].\end{aligned}$$

Hence,

$$\begin{aligned}|\alpha_1-\alpha_2| &\le \frac{As}{N^s-1}\left|(e^{\alpha_1 t_m}-1)-(e^{\alpha_2 t_m}-1)\right|\\ &= \frac{As}{N^s-1}\left|\alpha_1 t_m\frac{e^{\alpha_1 t_m}-1}{\alpha_1 t_m} - \alpha_2 t_m\frac{e^{\alpha_2 t_m}-1}{\alpha_2 t_m}\right|\\ &= \frac{As}{N^s-1}\left|\frac{\alpha_1 t_m}{\alpha_1 t_m/(e^{\alpha_1 t_m}-1)} - \frac{\alpha_2 t_m}{\alpha_2 t_m/(e^{\alpha_2 t_m}-1)}\right|\end{aligned}$$

Thus,

$$|\alpha_1 - \alpha_2| \leq \frac{Ast_m|\alpha_1 - \alpha_2|}{(N^s - 1)\min\left(\frac{\alpha_1 t_m}{e^{\alpha_1 t_m} - 1}, \frac{\alpha_2 t_m}{e^{\alpha_2 t_m} - 1}\right)}. \tag{7}$$

Suppose we have a unique solution of (6). It follows from (7) that

$$\frac{Ast_m}{(N^s - 1)\min\left(\frac{\alpha_1 t_m}{e^{\alpha_1 t_m} - 1}, \frac{\alpha_2 t_m}{e^{\alpha_2 t_m} - 1}\right)} \quad < \quad 1. \tag{8}$$

Since $0 < \frac{x}{e^x - 1} \leq 1$, $\forall x \geq 0$, from (8), we get

$$\begin{aligned} \frac{Ast_m}{(N^s - 1)} &< \min\left(\frac{\alpha_1 t_m}{e^{\alpha_1 t_m} - 1}, \frac{\alpha_2 t_m}{e^{\alpha_2 t_m} - 1}\right) \\ &< \max\left(\frac{\alpha_1 t_m}{e^{\alpha_1 t_m} - 1}, \frac{\alpha_2 t_m}{e^{\alpha_2 t_m} - 1}\right) \\ &\leq 1. \end{aligned}$$

Note that $\max\left(\frac{\alpha t_m}{e^{\alpha t_m} - 1}\right)$ attains only if $\alpha t_m = 0$. Hence, the above inequality implies that $\frac{Ast_m}{N^s - 1} < 1$. □

Sources of data, for each species may be found in [5]. In the following discussion, we will examine parameter sensitivity in the above model formulations.

## 3. Sensitivity to parameter changes

We may consider how equation (6) behaves when $N$, $A$, $t_m$ and $s$ are large. To do this, we consider the partial derivatives of $\alpha$ with respect to $N$, $A$, $t_m$ and $s$. These are given by

$$\frac{\partial \alpha}{\partial N} = As^2 N^{s-1} \frac{e^{\alpha t_m} - 1}{N^s - 1} \frac{1}{[Ast_m e^{\alpha t_m} - (N^s - 1)]}, \tag{9}$$

$$\frac{\partial \alpha}{\partial A} = \frac{\alpha}{A} \frac{(N^s - 1)}{(N^s - 1) - Ast_m e^{\alpha t_m}}, \tag{10}$$

$$\frac{\partial \alpha}{\partial t_m} = \frac{As\alpha e^{\alpha t_m}}{(N^s - 1) - Ast_m e^{\alpha t_m}}, \tag{11}$$

$$\frac{\partial \alpha}{\partial s} = \frac{(N^s - 1)(Ae^{\alpha t_m} - 1) - AsN^s \ln N(e^{\alpha t_m} - 1)}{[(N^s - 1) - Ast_m e^{\alpha t_m}](N^s - 1)} \tag{12}$$

respectively. Considering the R.H.S. in (9),

$$As^2N^{s-1}\frac{e^{\alpha t_m}-1}{N^s-1}\frac{1}{[Ast_me^{\alpha t_m}-(N^s-1)]}$$

and using (6), we get

$$\begin{aligned}&As^2N^{s-1}\frac{(e^{\alpha t_m}-1)}{\frac{A}{\alpha}s(e^{\alpha t_m}-1)}\frac{1}{\left[Ast_me^{\alpha t_m}-\frac{As}{\alpha}(e^{\alpha t_m}-1)\right]}\\&=\alpha sN^{s-1}\frac{1}{\left[Ast_me^{\alpha t_m}-\frac{Ast_m}{\alpha t_m}(e^{\alpha t_m}-1)\right]}.\end{aligned}$$

Thus we obtained

$$\frac{\partial\alpha}{\partial N}=\frac{\alpha sN^{s-1}}{\left[Ast_me^{\alpha t_m}-\frac{Ast_m}{\alpha t_m}(e^{\alpha t_m}-1)\right]}. \tag{13}$$

Since $e^x\geq\dfrac{e^x-1}{x}$, $\forall x\geq 0$, we obtain

$$\frac{\partial\alpha}{\partial N}\geq 0,\quad \forall N. \tag{14}$$

As a consequence of the inequality $e^x\geq\dfrac{e^x-1}{x}$, $\forall x\geq 0$,
we obtain $\dfrac{e^x-1}{x}\leq e^x$, $\forall x\geq 0$. In view of this, equations (10) and (11) satisfy

$$\frac{\partial\alpha}{\partial A}=\frac{\alpha}{A}\frac{(N^s-1)}{(N^s-1)-Ast_me^{\alpha t_m}}\leq 0 \tag{15}$$

and

$$\frac{\partial\alpha}{\partial t_m}=\frac{As\alpha e^{\alpha t_m}}{(N^s-1)-Ast_me^{\alpha t_m}}\leq 0 \tag{16}$$

Finally, rewrite equation (12) to get

$$\begin{aligned}\frac{\partial\alpha}{\partial s}&=\frac{\alpha(N^s-1)-\alpha\ln N}{s[(N^s-1)-Ast_me^{\alpha t_m}]}\\&=\frac{\frac{\alpha}{s}\left[Ast_m\frac{(e^{\alpha t_m}-1)}{\alpha t_m}-\ln N\right]}{Ast_m\frac{(e^{\alpha t_m}-1)}{\alpha t_m}-Ast_me^{\alpha t_m}}.\end{aligned} \tag{17}$$

From (6), we get

$$\ln N=\frac{1}{s}\ln\left(1+t_mAs\frac{(e^{\alpha t_m}-1)}{\alpha t_m}\right).$$

Next we substitute the value of $\ln N$ into the above equation (18). Then we get

$$\frac{\partial \alpha}{\partial s} = \frac{\frac{\alpha}{s}\left[Ast_m\frac{(e^{\alpha t_m}-1)}{\alpha t_m} - \frac{1}{s}\ln\left(1+t_m As\frac{(e^{\alpha t_m}-1)}{\alpha t_m}\right)\right]}{Ast_m\frac{(e^{\alpha t_m}-1)}{\alpha t_m} - Ast_m e^{\alpha t_m}}. \tag{18}$$

Since $\ln(1+x) \leq x$ and $\dfrac{e^x-1}{x} \leq e^x$, $\forall x \geq 0$, we obtain

$$\frac{\partial \alpha}{\partial s} \leq 0. \tag{19}$$

If we send $N$ to $\infty$ in (9), we get

$$\lim_{N\to\infty}\frac{\partial \alpha}{\partial N} = 0.$$

On the other hand, if we send $N$ to 1 in equation (9), we get

$$\lim_{N\to 1}\frac{\partial \alpha}{\partial N} = \infty.$$

Similarly, if we send $N$ to $\infty$ in (10), (11) and (12), we get

$$\lim_{N\to\infty}\frac{\partial \alpha}{\partial A} = 0, \quad \lim_{N\to\infty}\frac{\partial \alpha}{\partial t_m} = 0,$$

and

$$\lim_{N\to\infty}\frac{\partial \alpha}{\partial s} = 0.$$

Thus, we see that $\alpha$ is relatively insensitive to changes in $N$. That is, $\alpha$ does not change rapidly as the sample size becomes larger. Finally, if we send N to 1 in (10),(11) and (12), we get

$$\frac{\partial \alpha}{\partial A}, \frac{\partial \alpha}{\partial t_m} \text{ and } \frac{\partial \alpha}{\partial s} \longrightarrow -\infty \text{ as } N \to 1.$$

Thus, as the population size decreases, we see a greater change in the sensitivity of $\alpha$.

## 4. Sensitivity of the Newton-Raphson scheme

From standard arguments, we have that the $n^{th}$ approximation to the solution of equation (6) for $\alpha$ is given by

$$\alpha^{(n+1)} = \alpha^{(n)} - \frac{f_N(\alpha^{(n)})}{f'_N(\alpha^{(n)})}. \tag{20}$$

Note that $'$ indicates derivative with respect to $\alpha$ and the specified functions are given by

$$\begin{aligned} f_N(\alpha^{(n)}) &= As\frac{e^{\alpha^{(n)}t_m}-1}{N^s-1}-\alpha^{(n)}, \\ f'_N(\alpha^{(n)}) &= Ast_m\frac{e^{\alpha^{(n)}t_m}}{N^s-1}-1. \end{aligned} \tag{21}$$

We are particularly interested in the sensitivity of equation (20) with respect to the initial sample size $N$.

We begin by observing that

$$\frac{\partial\alpha^{(n+1)}}{\partial N} = \frac{\partial\alpha^{(n)}}{\partial N}-\frac{f'_N(\alpha^{(n)})\dot{f}_N(\alpha^{(n)})-f_N(\alpha^{(n)})\dot{f}'_N(\alpha^{(n)})}{[f'_N(\alpha^{(n)})]^2} \tag{22}$$

where the $\bullet$ indicates the derivative with respect to $N$ and $'$ indicates a derivative with respect to $\alpha$. We observe, however, that

$$\dot{f} = \frac{\partial f}{\partial\alpha}\,\frac{\partial\alpha}{\partial N}.$$

This allows us to reduce equation (22) to the following

$$\frac{\partial\alpha^{(n+1)}}{\partial N} = \frac{f_N(\alpha^{(n)})\frac{\partial}{\partial N}\left(\frac{\partial f_N(\alpha^{(n)})}{\partial\alpha^{(n)}}\right)}{\left(\frac{\partial f_N(\alpha^{(n)})}{\partial\alpha^{(n)}}\right)^2}. \tag{23}$$

Substitution of equation (21) into equation (23) yields the following equation

$$\frac{\partial\alpha^{(n+1)}}{\partial N} = \frac{\left[As\frac{1-e^{\alpha^{(n)}t_m}}{N^s-1}+\alpha^{(n)}\right]\left[As^2t_m\frac{e^{\alpha^{(n)}t_m}N^{s-1}}{(N^s-1)^2}\right]}{\left[Ast_m\frac{e^{\alpha^{(n)}t_m}}{N^s-1}-1\right]^2}. \tag{24}$$

Letting $\xi = \dfrac{1}{(N^s-1)}$, we can simplify equation (24) to

$$\begin{aligned} \frac{\partial\alpha^{(n+1)}}{\partial N} &= \frac{\left[As(1-e^{\alpha^{(n)}t_m})\xi+\alpha^{(n)}\right]\left[As^2t_me^{\alpha^{(n)}t_m}\xi^2\frac{\xi+1}{\xi}\left(\frac{\xi}{\xi+1}\right)^{\frac{1}{s}}\right]}{[Ast_me^{\alpha^{(n)}t_m}\xi-1]^2} \\ &= \frac{\left[As(1-e^{\alpha^{(n)}t_m})\xi+\alpha^{(n)}\right]\left[As^2t_me^{\alpha^{(n)}t_m}\xi(\xi+1)\left(\frac{1}{1+\frac{1}{\xi}}\right)^{\frac{1}{s}}\right]}{[Ast_me^{\alpha^{(n)}t_m}\xi-1]^2}. \end{aligned} \tag{25}$$

We now examining the following two limits, $N\to 1$ ($\xi\to\infty$) and $N\to\infty$ ($\xi\to 0$). Clearly, as $\xi\to 0$, the right hand side of equation (26) tends to zero.

After a little algebra equation (26), becomes

$$\frac{\partial \alpha^{(n+1)}}{\partial N} = \frac{\left[As(1-e^{\alpha^{(n)}t_m})\xi + \alpha^{(n)}\right]\left[As^2 t_m e^{\alpha^{(n)}t_m}(1+\frac{1}{\xi})\left[\frac{1}{1+\frac{1}{\xi}}\right]^{\frac{1}{s}}\right]}{[Ast_m e^{\alpha^{(n)}t_m} - \frac{1}{\xi}]^2} \quad (26)$$

Now it is clearly, as $\xi \to \infty$, equation (26) tends to $\infty$. i.e.,

$$\lim_{\xi \to 0} \frac{\partial \alpha^{(n+1)}}{\partial N} = 0 \quad \text{and} \quad \lim_{\xi \to \infty} \frac{\partial \alpha^{(n+1)}}{\partial N} = \infty,$$

i.e., increases as $\xi$ increases (sample size becomes small). Thus, as the sample size decreases, we see a greater change in the sensitivity of $\alpha^{(n+1)}$ with respect to the initial sample size $N$.

**Remark 1.** There were no recorded samples with mortality deceleration rate ($s$) to compare with the unique condition $\frac{Ast_m}{N^s - 1} < 1$.

**Remark 2.** In [5], the authors have presented a model without mortality deceleration rate ($s$) and have numerically and analytically examined that the population size decreases, and realized a greater change in the sensitivity of $\alpha$.

**Remark 3.** There were no recorded samples with mortality deceleration rate ($s$) to compare with the sensitivity of $\alpha$.

## 5. Closing comments

The purpose of this discussion has been to address the issue of parameter sensitivity of a new method for estimating the *age-dependent* mortality rate coefficient $\alpha$ of the Gompertz mortality rate model with deceleration rate (or logistic frailty model). Such a method is necessary when attempting to estimate Gompertz mortality rate coefficients in the absence of mortality data by age.

## Acknowledgement

The author deeply thank the referee(s) for their valuable comments.

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**M. Pitchaimani** received his M. Sc degree from C. P. A. College, Bodinayakanur, in 1996 and M.Phil. and Ph. D. degrees in Mathematics from Madurai Kamaraj University, Madurai, India. His research interests are in Asymptotic Techniques, Discrete Dynamical Systems and Survival Models.

School of Mathematics, Madurai Kamaraj University, Madurai - 625 021, India
e-mail: mpitchaimani@yahoo.com